

## UPDATED 06.01.2019 CLINICAL GUIDELINES

Medical Oncology



## **Overview Statement**

The purpose of these clinical guidelines is to assist healthcare professionals in selecting the medical service that may be appropriate and supported by evidence to improve patient outcomes. These clinical guidelines neither preempt clinical judgment of trained professionals nor advise anyone on how to practice medicine. The healthcare professionals are responsible for all clinical decisions based on their assessment. These clinical guidelines do not provide authorization, certification, explanation of benefits, or guarantee of payment, nor do they substitute for, or constitute, medical advice.

Federal and State law, as well as member benefit contract language, including definitions and specific contract provisions/exclusions, take precedence over clinical guidelines and must be considered first when determining eligibility for coverage. All final determinations on coverage and payment are the responsibility of the health plan. Nothing contained within this document can be interpreted to mean otherwise.

Medical information is constantly evolving, and HealthHelp reserves the right to review and update these clinical guidelines periodically.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from HealthHelp. All trademarks, product names, logos, and brand names are the property of their respective owners and are used for purposes of information/illustration only



# Table of Contents

	1
Overview Statement	2
Table of Contents	3
Acute Myeloid Leukemia	5
Anal Cancer	
Antiemetic	21
Bladder Cancer	
Bone Cancer	
Brain Cancer	
Breast Cancer	63
Cervical Cancer	
Chronic Myeloid Leukemia	114
Colon Cancer	121
Endometrial Cancer	136
Esophageal Cancer	143
Gastric Cancer	161
Growth Factor Support	172
Head and Neck Cancers	
Hepatobiliary Cancer	196
Hodgkin Lymphoma	
Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com   © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000	Page 3 of 387



Kidney Cancer	211
Myelodysplastic Syndrome	
Melanoma	
Mesothelioma	
Multiple Myeloma	
Non-Hodgkin: Adult T-Cell Leukemia/Lymphoma	241
Non-Hodgkin: Diffuse Large B-Cell Lymphoma	
Non-Hodgkin: Follicular Lymphoma	
Non-Small Cell Lung Cancer	
Occult Primary Tumors	
Ovarian Cancer	
Penile Cancer	
Pancreatic Cancer	
Prostate Cancer	
Rectal Cancer	
Small Cell Lung Cancer	
Testicular Cancer	
Thymoma	
Thyroid Cancer	
Uterine Cancer	
Vulvar Cancer	



HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult,

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

## Acute Myeloid Leukemia

- Ind. 5498 Induction therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Age less than 60 years;
  - Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Azacitidine

Cytarabine

Cytarabine + Daunorubicin

Cytarabine + Clofarabine

Cytarabine + Daunorubicin + Cladribine

Cytarabine + Mitoxantrone

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 5 of 387



Decitabine

High-dose Cytarabine

High-dose Cytarabine + Daunorubicin

High-dose Cytarabine + Fludarabine

High-dose Cytarabine + Fludarabine + Idarubicin

High-dose Cytarabine + Idarubicin

Hydroxyurea

Ind. 5498 Induction therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following.

- Age between 60 and 74 years;
- Better-risk cytogenetics;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Azacitidine

Cytarabine

Cytarabine + Daunorubicin

Cytarabine + Idarubicin

Cytarabine + Mitoxantrone

Decitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 6 of 387



Ind. 5498 Induction therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- 75 years of age or older;
- Normal cardiac function.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

### Hydroxyurea

Ind. 5498 Induction therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age between 60 and 74 years;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Clofarabine

Ind. 5498 Induction therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Age less than or equal to 60 years;

ASSOCIATED CHEMOTHERAPY REGIMENS



## High-dose Cytarabine + Topotecan

Ind. 5498 Induction therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Not a candidate for intensive Anthracyclin and Cytarabine induction therapy;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cytarabine + Clofarabine

Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 60 years;
- Post-induction therapy;
- Better-risk cytogenetics.

ASSOCIATED CHEMOTHERAPY REGIMENS

High-dose Cytarabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 8 of 387



Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 60 years;
- Post-induction therapy;
- Normal cardiac function.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Cytarabine + Idarubicin

Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 60 years;
- Post-induction therapy;
- Intermediate-risk cytogenetics.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cytarabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 9 of 387



Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age 60 years or older;
- Post-induction therapy.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Azacitidine

Decitabine

Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age less than 60 years;
- Post-induction therapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Azacitidine

Decitabine

Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 10 of 387



- Age 60 years or older;
- Post-induction therapy;
- Normal cardiac function.

Cytarabine + Daunorubicin

Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age less than 60 years;
- Post induction therapy
- Better risk cytogenics

ASSOCIATED CHEMOTHERAPY REGIMENS

## High-dose Cytarabine

Ind. 5499 Post-Remission Therapy for Acute Myeloid Leukemia per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age 60 years or older;
- Patient has complete response.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Azacitidine

## Decitabine



Ind. 5500 Salvage Therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 60 years;
- Normal cardiac function;
- Induction failure;
- Late relapse (greater than 12 months).

#### ASSOCIATED CHEMOTHERAPY REGIMENS

#### Azacitidine

Azacitidine + Sorafenib

Cladribine + High-dose Cytarabine

Cladribine + High-dose Cytarabine + Idarubicin

Cladribine + High-dose Cytarabine + Mitoxantrone

Clofarabine + Cytarabine + Idarubicin

Clofarabine + High-dose Cytarabine

Clofarabine + Idarubicin

Cytarabine

Decitabine

Decitabine + Sorafenib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 12 of 387



Etoposide + High-dose Cytarabine

Fludarabine + High-dose Cytarabine

Fludarabine + High-dose Cytarabine + Idarubicin

High-dose Cytarabine + Daunorubicin

High-dose Cytarabine + Idarubicin

Mitoxantrone + Etoposide + High-dose Cytarabine (MEC)

Ind. 5500 Salvage Therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 60 years;
- Normal cardiac function;
- Induction failure;
- Early relapse (less than 12 months).

ASSOCIATED CHEMOTHERAPY REGIMENS

Cladribine + High-dose Cytarabine

Cladribine + High-dose Cytarabine + Idarubicin

Cladribine + High-dose Cytarabine + Mitoxantrone

Clofarabine + Cytarabine + Idarubicin

Clofarabine + High-dose Cytarabine



Clofarabine + Idarubicin

Cytarabine

Fludarabine + High-dose Cytarabine

Fludarabine + High-dose Cytarabine + Idarubicin

High-dose Cytarabine + Daunorubicin

High-dose Cytarabine + Idarubicin

Mitoxantrone + Etoposide + High-dose Cytarabine (MEC)

Ind. 5500 Salvage Therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age between 60 and 74 years;
- Normal cardiac function;
- Induction failure.

ASSOCIATED CHEMOTHERAPY REGIMENS

Azacitidine

Azacitidine + Sorafenib

Cladribine + High-dose Cytarabine

Cladribine + High-dose Cytarabine + Mitoxantrone

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 14 of 387



Clofarabine + Cytarabine + Idarubicin

Clofarabine + High-dose Cytarabine

Clofarabine + Idarubicin

Cytarabine

Decitabine

Decitabine + Sorafenib

Mitoxantrone + Etoposide + High-dose Cytarabine (MEC)

Ind. 5500 Salvage Therapy for Acute Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Central Nervous System (CNS) disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cytarabine

Liposomal Cytarabine

Methotrexate



#### REFERENCES

- Fernandez HF, Sun Z, Yao X, et al. Anthracycline dose intensification in acute myeloid leukemia. N Engl J Med. 2009;361:1249–1259.
- Kern W, Estey EH. High-dose cytarabine arabinoside in the treatment of acute myeloid leukemia review of three randomized trials. Cancer. 2006;107:116–124.
- Weick JK, Kopecky KJ, Appelbaum FR, et al. A randomized investigation of high-dose versus standard-dose cytosine arabinoside with daunorubicin in patients with previously untreated acute myeloid leukemia: a Southwest Oncology Group study. Blood. 1996:88:2841–2851.
- Bishop JF, Matthews JP, Young GA, et al. A randomized study of high-dose cytarabine in induction in acute myeloid leukemia. Blood. 1996;87:1710–1717.
- Krug U, Röllig C, Koschmieder A, et al. Complete remission and early death after intensive chemotherapy in patients aged 60 years or older with acute myeloid leukaemia: a web-based application for prediction of outcomes. Lancet. 2010;376: 2000–2008.
- Löwenberg B, Ossenkoppele GJ, van Putten W, et al. High-dose daunorubicin in older patients with acute myeloid leukemia. N Engl J Med. 2009;361:1235–1248.
- Burnett AK, Milligan D, Prentice AG, et al. A comparison of low-dose cytarabine and hydroxyurea with or without all-trans retinoic acid for acute myeloid leukemia and high-risk myelodysplastic syndrome in patients not considered fit for intensive treatment. Cancer. 2007;109:1114–1124.
- Fenaux P, Mufti GJ, Hellstrom-Lindberg E, et al. Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: a randomised, open-label, phase III study. Lancet Oncol. 2009;10:223–232.
- Cashen AF, Schiller GJ, O'Donnell MR, DiPersio JF. Multicenter, phase II study of decitabine for the first-line treatment of older patients with acute myeloid leukemia. J Clin Oncol. 2010;28:556–561.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Acute Myeloid Leukemia. Version 1.2017. 24 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/aml.pdf.
- Kantarjian HM, Erba HP, Claxton D, et al. Phase II study of clofarabine monotherapy in previously untreated older adults with acute myeloid leukemia and unfavorable prognostic factors. J Clin Oncol. 2010;28:549–555.
- Mayer RJ, Davis RB, Schiffer CA, et al. Intensive postremission chemotherapy in adults with acute myeloid leukemia. N Engl J Med. 1994;331:896–903.
- Löwenberg B, Pabst T, Vellenga E, et al. Cytarabine dose for acute myeloid leukemia. N Engl J Med. 2011;364: 1027–1036.
- Martin MG, Welch JS, Augustin K, et al. Cladribine in the treatment of acute myeloid leukemia: a single-institution experience. Clin Lymphoma Myeloma. 2009;9:298–301.
- Montillo M, Mirto S, Petti MC, et al. Fludarabine, cytarabine, and G-CSF (FLAG) for the treatment of poor risk acute myeloid leukemia. Am J Hematol. 1998;58:105–109.
- Parker JE, Pagliuca A, Mijovic A, et al. Fludarabine, cytarabine, G-CSF and idarubicin (FLAG-IDA) for the treatment of poorrisk myelodysplastic syndromes and acute myeloid leukaemia. Br J Haematol. 1997;99:939–944.



- Amadori S, Arcese W, Isacchi G, et al. Mitoxantrone, etoposide, and intermediate-dose cytarabine: an effective and tolerable regimen for the treatment of refractory acute myeloid leukemia. J Clin Oncol. 1991;9:1210–1214.
   Becker PS, Kantarjian HM, Appelbaum FR, et al. Clofarabine with high dose cytarabine and granulocyte colony-stimulat-
- ing factor (G-CSF) priming for relapse and refractory acute myeloid leukaemia. Br J Haematol. 2011;155:182–189.
- Ravandi F, Alattar ML, Grunwald, MR, et al. Phase 2 study of azacytidine plus sorafenib in patients with acute myeloid leukemia and FLT-3 internal tandem duplication mutation. Blood. 2013:121:4655–4662.



## Anal Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5379 Metastatic Anal Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Metastatic disease

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Cisplatin

- Ind. 5378 Non-Metastatic Anal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:
  - Nodal involvement;
  - Stage T1 or T2;



• Stage T3 or T4.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Mitomycin

Capecitabine + Mitomycin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 19 of 387



#### REFERENCES

- Ajani JA, Winter KA, Gunderson LL, et al. Fluorouracil, mitomycin, and radiotherapy vs fluorouracil, cisplatin, and radiotherapy for carcinoma of the anal canal: a randomized controlled trial. JAMA. 2008;299(16):1914–1921.
- Goodman KA, Rothenstein D, Cambridge L, et al. Capecitabine plus mitomycin in patients undergoing definitive chemoradiation for anal squamous cell carcinoma. Int J Radiat Oncol Biol Phys. 2014;90(1):532-533.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer. Version 1.2017. 23 Nov 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/anal.pdf
- Thind G, Johal B, Follwell M, Kennecke HF. Chemoradiation with capecitabine and mitomycin-C for stage I-III anal squamous cell carcinoma. Radiation Oncology. 2014;9:124.
- Faivre C, Rougier P, Ducreux M, et al. 5-fluorouracil and cisplatin combination chemotherapy for metastatic squamouscell anal cancer. Bull Cancer. 1999;86(10):861-865.



## Antiemetic

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Antiemetic treatments used in conjunction with Medical Oncology may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens.

- Ind. 5541 Utilization of antiemetic's may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Emetic risk level for prescribed chemotherapy regimen matches the level of utilization for the prescribed antiemetic requested.
  - Emetic risk level for prescribed chemotherapy regimen does not match the level of utilization for the prescribed antiemetic requested; and ANY of the following:
    - § Patient is 65 years of age or older;
    - Prior exposure to the same chemotherapy regimen resulted in nausea and vomiting
    - **§** Patient has comorbidities.





#### REFERENCES

- National Comprehensive Cancer Network (NCCN). NCCN Guidelines for supportive care. NCCN Guidelines for Myeloid Growth Factors. Available at: https://www.nccn.org/professionals/physician\_gls/pdf/myeloid\_growth.pdf.
- American Society of Clinical Oncology (ASCO) Choosing Wisely. October 29, 2013. Available at: http://www.choosingwisely.org/societies/american-society-of-clinical-oncology/.
- American Society of Clinical Oncology (ASCO) 2015 Recommendations for the Use of WBC Growth Factors Update. Published online ahead of print July 13, 2015, doi 10.1200/JCO.2015.62.3488. Available at: https://www.asco.org/practice-guidelines/quality-guidelines/guidelines/supportive-care-and-treatment-relatedissues#/9806



## Bladder Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5383 First-line Radiosensitizing Chemotherapy for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Stage T3 or T4;
  - Complete removal of visible tumor;
  - Creatinine level normal;
  - Adjuvant therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Cisplatin

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Paclitaxel



Ind. 5383 First-line Radiosensitizing Chemotherapy for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Complete removal of visible tumor;
- Ts/Muscle invasion;
- Creatinine level normal;
- Definitive therapy;
- Not a surgical candidate.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Cisplatin

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Paclitaxel

Ind. 5383 First-line Radiosensitizing Chemotherapy for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Complete removal of visible tumor;
- Ts/Muscle invasion;
- Definitive therapy;
- Not a surgical candidate.

ASSOCIATED CHEMOTHERAPY REGIMENS

Mitomycin + 5-Fluorouracil (5-FU)



## Gemcitabine

Ind. 5383 First-line Radiosensitizing Chemotherapy for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Complete removal of visible tumor;
- Adjuvant therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Mitomycin + 5-Fluorouracil (5-FU)

Gemcitabine

Ind. 5384 First-line Radiosensitizing Chemotherapy with Conventionally Fractioned Radiation for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Stage T3 or T4;
- Complete removal of visible tumor;
- Ts/Muscle invasion;
- Creatinine level normal;
- Definitive therapy
- Not a surgical candidate.

ASSOCIATED CHEMOTHERAPY REGIMENS

## 5-Fluorouracil (5-FU)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 26 of 387



5-Fluorouracil (5-FU) + Mitomycin

Capecitabine

Cisplatin

Docetaxel

Gemcitabine

Paclitaxel

Ind. 5381 First-Line Therapy for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Normal creatinine level.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dose-dense Methotrexate + Vinblastine + Doxorubicin + Cisplatin (DDMVAC)

Gemcitabine + Cisplatin

Ifosfamide + Mensa + Doxorubicin + Gemcitabine

Ind. 5381 First-Line Therapy for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical records demonstrates that the therapy is first line:

ASSOCIATED CHEMOTHERAPY REGIMENS

Bacillus Calmette-Guerin (BCG)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 27 of 387



Gemcitabine + Carboplatin

Gemcitabine + Paclitaxel

Gemcitabine

Ind. 5381 First-Line Therapy for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Patient is not eligible for cisplatin-based chemotherapy
- Disease progression with platinum-containing chemotherapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Pembrolizumab Atezolizumab

Ind. 5382 Second-Line Therapy (Palliative) for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Metastatic disease

ASSOCIATED CHEMOTHERAPY REGIMENS

Albumin-bound Paclitaxel

Atezolizumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 28 of 387



### Docetaxel

Dose-dense Methotrexate + Vinblastine + Doxorubicin + Cisplatin (DDMVAC)

Gemcitabine

Gemcitabine + Cisplatin

Gemcitabine + Paclitaxel

Ifosfamide + Mesna

Ifosfamide + Doxorubicin + Gemcitabine

Methotrexate

Nivolumab

Paclitaxel

Pemetrexed

Ind. 5382 Second-Line Therapy (Palliative) for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Second-line treatment; and EITHER of the following:
  - S Disease progression during or after platinum-based chemotherapy;
  - S Disease progression 12 months after platinum-based neoadjuvant or adjuvant chemotherapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 29 of 387



Atezolizumab

Nivolumab

Durvalumab

Avelumab

Pembrolizumab

Ind. 5382 Second-Line Therapy (Palliative) for Locally Advanced or Metastatic Bladder Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Intravesicular treatment of BCG refractory bladder carcinoma in situ.

ASSOCIATED CHEMOTHERAPY REGIMENS

Valrubicin

Ind. 5382 Second-Line Therapy (Palliative) for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Recurrent disease

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 30 of 387



Albumin-bound Paclitaxel

Docetaxel

Gemcitabine

Gemcitabine + Cisplatin

lfosfamide + Mesna

Methotrexate

Mitomycin

Paclitaxel

Pemetrexed

Valrubicin

Ind. 5382 Second-Line Therapy (Palliative) for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Persistent disease

ASSOCIATED CHEMOTHERAPY REGIMENS

Mitomycin

## Valrubicin



- Ind. 5382 Second-Line Therapy (Palliative) for Locally Advanced or Metastatic Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Patient is not eligible for cisplatin-based therapy

Avelumab

Pembrolizumab

Ind. 5380 Perioperative Chemotherapy (Neoadjuvant/Adjuvant) for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following.

- Creatinine level normal;
- Adjuvant/neoadjuvant therapy; and EITHER of the following:
  - Stage Tis (any grade);
  - **§** Stage T2 with a Transurethral resection surgery having been performed.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bacillus Calmette-Guerin (BCG)

Mitomycin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 32 of 387



- Ind. 5380 Perioperative Chemotherapy (Neoadjuvant/Adjuvant) for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following.
  - Creatinine level normal;
  - Adjuvant/neoadjuvant therapy; and EITHER of the following:
    - Stage T3 or T4;
    - S Node positive.

Cisplatin + Methotrexate + Vinblastine (CMV) + Leucovorin

Dose-dense Methotrexate + Vinblastine + Doxorubicin + Cisplatin (DDMVAC)

Ind. 5380 Perioperative Chemotherapy (Neoadjuvant/Adjuvant) for Bladder Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following.

- Ts/Muscle invasion;
- Creatinine level normal;
- Adjuvant/neoadjuvant therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Methotrexate + Vinblastine (CMV) + Leucovorin

Dose-dense Methotrexate + Vinblastine + Doxorubicin + Cisplatin (DDMVAC)

Gemcitabine + Cisplatin



#### REFERENCES

- Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med. 2003;349(9):859–866.
- Sternberg CN, de Mulder PH, Schornagel JH, et al. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. J Clin Oncol. 2001;19(10):2638–2646.
- Dash A, Pettus JA, Herr HW, et al. A role for neoadjuvant gemcitabine plus cisplatin in muscle-invasive urothelial carcinoma of the bladder: a retrospective experience. Cancer. 2008; 113(9):2471–2477.
- Von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol. 2000;18(17):3068–3077.
- Von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. J Clin Oncol. 2005;23(21):4602–4608.
- Griffiths G, Hall R, Sylvester R, et al. International phase III trial assessing neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle-invasive bladder cancer: long-term results of the BA06 30894 trial. J Clin Oncol. 2011;29(16): 2171–2177.
- Neoadjuvant chemotherapy in invasive bladder cancer: update of a systematic review and meta-analysis of individual patient data advanced bladder cancer (ABC) meta-analysis collaboration. Eur Urol. 2005;48(2):202–205.
- Adjuvant chemotherapy in invasive bladder cancer: a systematic review and meta-analysis of individual patient data Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. Eur Urol. 2005;48(2):189–199.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. Version 2.2017. 15 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/bladder.pdf
- Sternberg CN, de Mulder P, Schornagel JH, et al. Seven year update of an EORTC phase III trial of high-dose intensity M-VAC chemotherapy and G-CSF versus classic M-VAC in advanced urothelial tract tumours. Eur J Cancer. 2006; 42(1):50–54.
- Soto Parra H, Cavina R, Latteri F, et al. Three-week versus four-week schedule of cisplatin and gemcitabine: results of a randomized phase II study. Ann Oncol. 2002;13(7): 1080–1086.
- Bellmunt J, von der Maase H, Mead GM, et al. Randomized phase III study comparing paclitaxel/cisplatin/gemcitabine and gemcitabine/cisplatin in patients with locally advanced or metastatic urothelial cancer without prior systemic therapy: EORTC Intergroup Study 30987. J Clin Oncol. 2012;30(10):1107–1113.
- Coppin CM, Gospodarowicz MK, James K, et al. Improved local control of invasive bladder cancer by concurrent cisplatin and preoperative or definitive radiation. J Clin Oncol. 1996;14(11):2901–2907.



- Kaufman DS, Winter KA, Shipley WU, et al. The initial results in muscle-invading bladder cancer of RTOG 95-06: phase I/II trial of transurethral surgery plus radiation therapy with concurrent cisplatin and 5-fluorouracil followed by selective bladder preservation or cystectomy depending on the initial response. The Oncologist. 2000;5(6):471–476.
- James ND, Hussain SA, Hall E, et al; BC200I Investigators. Radiotherapy with or without chemotherapy in muscle-invasive bladder cancer. N Engl J Med. 2012;366(16):1477–1488.
- Hussain SA, Stocken DD, Peake DR, et al. Long-term results of a phase II study of synchronous chemoradiotherapy in advanced muscle invasive bladder cancer. Br J Cancer. 2004;90(11):2106–2111.
- Mitin T, Hunt D, Shipley W, et al. Transurethral surgery and twice-daily radiation plus paclitaxel-cisplatin or fluorouracilcisplatin with selective bladder preservation and adjuvant chemotherapy for patients with muscle invasive bladder cancer (RTOG 0233): a randomized multicentre phase 2 trial. Lancet Oncol. 2013;14(9):863–872.
- Atasoy BM, Dane F, Alsan Cetin I, et al. Concurrent chemoradiotherapy with low dose weekly gemcitabine in medically inoperable muscle-invasive bladder cancer patients. Clin Trans Oncol. 2014;16 (1):91–95.



## Bone Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5385 Chemotherapy for Chordoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Age less than 70 years;
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 36 of 387



Erlotinib

Imatinib

Imatinib + Cisplatin

Imatinib + Sirolimus

Sorafenib

Sunitinib

Ind. 5385 Chemotherapy for Chordoma per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the ALL of the following:

- Advanced or metastatic disease;
- Age less than 70 years;
- First-line treatment;
- Positive Epidermal Growth Factor Receptor (EGFR).

ASSOCIATED CHEMOTHERAPY REGIMENS

Lapatinib

Ind. 5386 First-Line Therapy for Ewing's Sarcoma and Mesenchymal Chondrosarmoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

• Normal cardiac function;



- Age less than 70 years;
- First-line treatment (Primary/Neoadjuvant/Adjuvant); and EITHER of the following:
  - Sewing's sarcoma;
  - Mesenchymal chondrosarcoma.

VAC + IE

VAIA

VIDE

- Ind 5387 Primary Therapy for Metastatic Disease at Initial Presentation for Ewing's Sarcoma and Mesenchymal Chondrosarcoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Normal cardiac function;
  - Age less than 70 years;
  - Advanced or metastatic disease;
  - First-line treatment; and EITHER of the following:
    - § Ewing's sarcoma;
    - **§** Mesenchymal Chondrosarcoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

VAC + IE

## VAIA



VIDE

Vincristine + Cyclophosphamide + Dactinomycin (CVD)

Vincristine + Cyclophosphamide + Doxorubicin (CVD)

Ind. 5388 Second-Line Therapy for Ewing's Sarcoma and Mesenchymal Chondrosarcoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Age less than 70 years;
- Second-line treatment; and EITHER of the following:
  - Sewing's sarcoma;
  - Mesenchymal chondrosarcoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Ifosfamide + Mesna + Etoposide

Cyclophosphamide + Topotecan

Docetaxel + Gemcitabine

Ifosfamide + Mesna + Etoposide

Irinotecan + Temozolomide

Cycolophosphamide + Sirolimus



Ind. 5389 Chemotherapy for Giant Cell Tumor of the Bone per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age less than 70 years;
- Locally advanced and/or unresectable tumor.

ASSOCIATED CHEMOTHERAPY REGIMENS

Denosumab

## Interferon alfa

Ind. 5390 First-Line Chemotherapy for Osteosarcoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Advanced or metastatic disease in a member who is less than 70 years of age with high grade, clear cell or extra-compartmental disease; and EITHER of the following:
  - **§** First-line treatment; and EITHER of the following:
    - Neoadjuvant chemotherapy;
    - Adjuvant therapy;
  - Dedifferentiated tumor.

ASSOCIATED CHEMOTHERAPY REGIMENS

Doxorubicin + Cisplatin

Epirubicin + Cisplatin + Ifosfamide + Mesna

MAP

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 40 of 387



Methotrexate + Cisplatin + Doxorubicin + Ifosfamide + Mesna

Ind. 5391 Second-Line Therapy Chemotherapy for Osteosarcoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 70 years;
- Relapsed disease;
- Relapse, refractory, advanced, or metastatic disease;
- Second-line treatment; and EITHER of the following:
  - § High grade, clear cell, or extra-compartmental tumor;
  - **§** Dedifferentiated tumor.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Ifosfamide + Mesna + Etoposide

Cyclophosphamide + Etoposide

Cyclophosphamide + Topotecan

Gemcitabine

Gemcitabine + Docetaxel

Ifosfamide + Mesna + Etoposide

Methotrexate + Etoposide + Ifosfamide + Mesna

## Sorafenib

## Sorafenib + Everolimus

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 41 of 387



Ind. 5391 Second-Line Therapy Chemotherapy for Osteosarcoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Relapse, refractory, advanced, or metastatic disease;
- Second-line treatment;
- Indicator lesion on 99mTc-MDP

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Radium-223

#### REFERENCES

- Casali PG, Messina A, Stacchiotti S, et al. Imatinib mesylate in chordoma. Cancer. 2004;101:2086–2097.
- Stacchiotti S, Longhi A, Ferraresi V, et al. Phase II study of imatinib in advanced chordoma. J Clin Oncol. 2012;30:914–920.
- Casali PG, Stacchiotti S, Sangalli C, et al. Chordoma. Current Opin Oncol. 2007;19:367–370.
- Stacchiotti S, Marrari A, Tamborini E, et al. Response to imatinib plus sirolimus in advanced chordoma. Ann Oncol. 2009;20:1886–1894.
- Singhal N, Kotasek D, Parnis FX. Response to erlotinib in a patient with treatment refractory chordoma. Anti Cancer Drugs. 2009;20:953–955.
- George S, Merriam P, Maki RG, et al. Multicenter phase II trial of sunitinib in the treatment of nongastrointestinal stromal tumor sarcomas. J Clin Oncol. 2009;27:3154–3160.
- Stacchiotti S, Tamborini E, LoVullo S, et al. A phase II study on lapatinib in advanced EGFR-positive chordoma. Ann Oncol. 2013;24(7):1931–1936.
- Grier HE, Krailo MD, Tarbell NJ, et al. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. N Engl J Med. 2003;348:694–701.
- Paulussen M, Craft AW, Lewis I, et al: European Intergroup Cooperative Ewing's Sarcoma Study-92. Results of the EICESS-92 Study: two randomized trials of Ewing's sarcoma treatment—cyclophosphamide compared with ifosfamide in standard-risk patients and assessment of benefit of etoposide added to standard treatment in high-risk patients. J Clin Oncol. 2008;26:4385–4393.



- Juergens C, Weston C, Lewis I, et al. Safety assessment of intensive induction with vincristine, ifosfamide, doxorubicin, and etoposide (VIDE) in the treatment of Ewing tumors in the EURO-E.W.I.N.G. 99 clinical trial. Pediatr Blood Cancer. 2006 Jul;47(1):22–29.
- Miser JS, Krailo MD, Tarbell NJ, et al. Treatment of metastatic Ewing's sarcoma or primitive neuroectodermal tumor of bone: evaluation of combination ifosfamide and etoposide—a Children's Cancer Group and Pediatric Oncology Group study. J Clin Oncol. 2004;22:2873–2876.
- Bernstein ML, Devidas M, Lafreniere D, et al. Intensive therapy with growth factor support for patients with Ewing tumor
  metastatic at diagnosis: Pediatric Oncology Group/Children's Cancer Group Phase II Study 9457—a report from the
  Children's Oncology Group. J Clin Oncol. 2006;24(1):152–159.
- Hunold A, Weddeling N, Paulussen M, Ranft A, Liebscher C, Jürgens H. Topotecan and cyclophosphamide in patients with refractory or relapsed Ewing tumors. Pediatr Blood Cancer. 2006;47:795–800.
- Kushner BH, Kramer K, Meyers PA, et al. Pilot study of topotecan and high-dose cyclophosphamide for resistant pediatric solid tumors. Med Pediatr Oncol. 2000;35(5):468–474.
- Saylors RL 3rd, Stine KC, Sullivan J, et al; Pediatric Oncology Group. Cyclophosphamide plus topotecan in children with recurrent or refractory solid tumors: a Pediatric Oncology Group phase II study. J Clin Oncol. 2001;19:3463–3469.
- Casey DA, Wexler LH, Merchant MS, et al. Irinotecan and temozolomide for Ewing sarcoma: the Memorial Sloan-Kettering Experience. Pediatr Blood Cancer. 2009 Dec;53(6): 1029–1034.
- Wagner LM, McAllister N, Goldsby RE, Rausen AR, McNall- Knapp RY, McCarville MB, Albritton K. Temozolomide and intravenous irinotecan for treatment of advanced Ewing sarcoma. Pediatr Blood Cancer. 2007;48:132–139.
- Wagner LM, Crews KR, Iacono LC, et al. Phase I trial of temozolomide and protracted irinotecan in pediatric patients with refractory solid tumors. Clin Cancer Res. 2004;10(3): 840–848.
- McNall-Knapp RY, Williams CN, Reeves EN, et al. Extended phase I evaluation of vincristine, irinotecan, temozolomide, and antibiotic in children with refractory solid tumors. Pediatr Blood Cancer. 2010 Jul 1;54(7):909–915.
- Blaney S, Berg SL, Pratt C, et al. A phase I study of irinotecan in pediatric patients: a pediatric oncology group study. Clin Cancer Res. 2001 Jan;7(1):32–37.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Bone Cancer. Version
  2.2017. 7 Nov 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/
  professionals/physician\_gls/pdf/bone.pdf.
- Furman WL, Stewart CF, Poquette CA, et al. Direct translation of a protracted irinotecan schedule from a xenograft model to a phase I trial in children. J Clin Oncol. 1999 Jun;17(6): 1815–1824.
- McGregor LM, Stewart CF, Crews KR, et al. Dose escalation of intravenous irinotecan using oral cefpodoxime: a phase I study in pediatric patients with refractory solid tumors. Pediatr Blood Cancer. 2012;58:372–379.
- Miser JS, Kinsella TJ, Triche TJ, et al. Ifosfamide with mesna uroprotection and etoposide: an effective regimen in the treatment of recurrent sarcomas and other tumors of children and young adults. J Clin Oncol. 1987;5:1191–1198.
- Van Winkle P, Angiolillo A, Krailo M, et al. Ifosfamide, carboplatin, and etoposide (ICE) reinduction chemotherapy in a large cohort of children and adolescents with recurrent/refractory sarcoma: the Children's Cancer Group (CCG) experience. Pediatr Blood Cancer. 2005;44:338–347.
- Navid F, Willert JR, McCarville MB, Furman W, Watkins A, Roberts W, Daw NC. Combination of gemcitabine and docetaxel in the treatment of children and young adults with refractory bone sarcoma. Cancer. 2008;113:419–425.



- Bernstein-Molho R, Kollender Y, Issakov J, et al. Clinical activity of mTOR inhibition in combination with cyclophosphamide in the treatment of recurrent unresectable chondrosarcomas. Cancer Chemother Pharmacol. 2012;70:855–860. 28.
   Branstetter DG, Nelson SD, Manivel JC, et al. Denosumab induces tumor reduction and bone formation in patients with giant-cell tumor of bone. Clin Cancer Res. 2012 Aug 15; 18(16):4415–4424.
- Thomas D, Henshaw R, Skubitz K, et al. Denosumab in patients with giant-cell tumour of bone: an open-label, phase 2 study. Lancet Oncol. 2010 Mar;11(3):275–280.
- Kaiser U, Neumann K, Havemann K.Generalised giant-cell tumour of bone: successful treatment of pulmonary metastases with interferon alpha, a case report. J Cancer Res Clin Oncol. 1993;119(5):301–303.
- Kaban LB, Troulis MJ, Ebb DJ, et al. Antiangiogenic therapy with interferon alpha for giant cell lesions of the jaws. Oral Maxillofac Surg. 2002 Oct;60(10):1103–1111; discussion 1111–1113.
- Bramwell VH, Burgers M, Sneath R, et al. A comparison of two short intensive adjuvant chemotherapy regimens in operable osteosarcoma of limbs in children and young adults: the first study of the European Osteosarcoma Intergroup. J Clin Oncol. 1992;10(10):1579–1591
- Lewis IJ, Nooij MA, Whelan J, et al; MRC BO06 and EORTC 80931 collaborators; European Osteosarcoma Intergroup.
   Improvement in histologic response but not survival in osteosarcoma patients treated with intensified chemotherapy: a randomized phase III trial of the European Osteosarcoma Intergroup. J Natl Cancer Inst. 2007;99:112–128.
- Souhami RL, Craft AW, Van der Eijken JW, et al. Randomised trial of two regimens of chemotherapy in operable osteosarcoma: a study of the European Osteosarcoma Intergroup. Lancet. 1997 Sep 27;350(9082):911–917.
- Bacci G, Ferrari S, Bertoni F, et al. Long-term outcome for patients with nonmetastatic osteosarcoma of the extremity treated at the istituto ortopedico rizzoli according to the istituto ortopedico rizzoli/osteosarcoma-2 protocol: an updated report. J Clin Oncol. 2000;18:4016–4027.
- Winkler K, Beron G, Delling G, Neoadjuvant chemotherapy of osteosarcoma: results of a randomized cooperative trial (COSS-82) with salvage chemotherapy based on histological tumor response. J Clin Oncol. 1988 Feb;6(2):329–337.
- Bacci G, Briccoli A, Rocca M, et al. Neoadjuvant chemotherapy for osteosarcoma of the extremities with metastases at presentation: recent experience at the Rizzoli Institute in 57 patients treated with cisplatin, doxorubicin, and a high dose of methotrexate and ifosfamide. Ann Oncol. 2003 Jul;14(7): 1211–1134.
- Basaran M, Bavbek ES, Saglam S, et al. A phase II study of cisplatin, ifosfamide and epirubicin combination chemotherapy in adults with nonmetastatic and extremity osteosarcomas. Oncology. 2007;72:255–260.
- Grignani G, Palmerini E, Dileo P, et al. A phase II trial of sorafenib in relapsed and unresectable high-grade osteosarcoma after failure of standard multimodal therapy: an Italian Sarcoma Group study. Ann Oncol. 2012;23:508–516.
- Berger M, Grignani G, Ferrari S, et al. Phase 2 trial of two courses of cyclophosphamide and etoposide for relapsed highrisk osteosarcoma patients. Cancer. 2009;115:2980–2987.
- Maki RG, Wathen JK, Patel SR, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma alliance for research through collaboration study 002. J Clin Oncol. 2007;25:2755–2763.
- Le Deley MC, Guinebretiere JM, Gentet JC, et al. SFOP OS93: a randomised trial comparing preoperative high-dose methotrexate plus doxorubicin to high-dose methotrexate plus etoposide and ifosfamide in osteosarcoma patients. Eur J Cancer. 2007;43;752–761.





# Brain Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5393 Adjuvant Treatment for Supratentorial Astrocytoma or Oligodendroglioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Unresectable tumor;
- Status post resection (adjuvant) and recurrent disease.

## ASSOCIATED CHEMOTHERAPY REGIMENS

PCV

Temozolomide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 46 of 387



- Ind. 5393 Adjuvant Treatment for Supratentorial Astrocytoma or Oligodendroglioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Status post resection (adjuvant);
  - 1pQ19 deletion.

## Temozolomide

- Ind. 5394 Chemotherapy for Recurrent or Progressive, Low Grade Supratentorial Astrocytoma or Oligodendroglioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - First-line treatment; and EITHER of the following:
    - Securrent disease;
    - S Unresectable tumor.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin

Carboplatin + Teniposide

Carmustine

Cisplatin + Etoposide

Lomustine



PCV

Temozolomide

Ind. 5395 Systemic Adjuvant Therapy for Anaplastic Gliomas per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Age less than 70 years; and EITHER of the following:
  - S Adjuvant treatment post resection with 1pQ19 deletion;
  - S Recurrent disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

PCV

Temozolomide

Ind. 5396 Systemic Recurrent Therapy for Anaplastic Gliomas per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 70 years;
- Recurrent disease;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Bevacizumab



Bevacizumab + Carboplatin

Bevacizumab + Fotemustine

Bevacizumab + Irinotecan

Carboplatin

Carboplatin + Teniposide

Carmustine

Cisplatin + Etoposide

Cyclophosphamide

Etoposide

Irinotecan

Lomustine

PCV

Temozolomide

Ind. 5397 Systemic Adjuvant Therapy for Anaplastic Oligoastrocytoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

• Age less than 70 years;



• Adjuvant treatment post resection.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

PCV

- Ind. 5398 Systemic Adjuvant Therapy for Glioblastoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Age less than 70 years;
  - Adjuvant treatment post resection.

ASSOCIATED CHEMOTHERAPY REGIMENS

Temozolomide

- Ind. 5399 Systemic Recurrent Therapy for Glioblastoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Age less than 70 years;
  - Recurrent disease;
  - Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bevacizumab

Bevacizumab + Carboplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 50 of 387



Bevacizumab + Fotemustine

Bevacizumab + Irinotecan

Carboplatin

Carboplatin + Teniposide

Carmustine

Cisplatin + Etoposide

Cyclophosphamide

Lomustine

PCV

Temozolomide

Ind. 5400 Systemic Recurrent Treatment for Intracranial and Spinal Ependymoma (excluding Supependymoma) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 70 years;
- Recurrent or advanced disease;
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Bevacizumab



Carboplatin

Carboplatin + Teniposide

Cisplatin + Etoposide

Etoposide

Temozolomide

- Ind. 5401 Systemic Adjuvant Therapy for Adult Medulloblastoma and Supratentorial Primitive Neuroectodermal Tumor (PNET) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Age less than 70 years; and EITHER of the following:
  - Adjuvant treatment post resection;
    - § Recurrent disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Cyclophosphamide + Vincristine

Cisplatin + Lomustine + Vincristine

Ind. 5402 Systemic Recurrent Therapy for Adult Medulloblastoma and Supratentorial Primitive Neuroectodermal Tumor (PNET) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Age less than 70 years; and EITHER of the following:



- S Adjuvant treatment post resection;
- S Recurrent disease.

Carboplatin + Thiotepa + Etoposide

Etoposide

Temozolomide

Ind. 5403 Primary Treatment for CNS Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age 70 years or less;
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Glucarpidase

Methotrexate

Methotrexate + Cytarabine

Methotrexate + Ifosfamide + Mesna

Methotrexate + Vincristine + Procarbazine + Cytarabine

Methotrexate + Vincristine + Procarbazine + Rituximab + Cytarabine

Rituximab + Temozolomide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 53 of 387



Temozolomide

Methotrexate +Rituximab

Methotrexate + Vincristine + Procarbazine+ Cytarabine

Ind. 5404 For Recurrent or Progressive CNS Lymphoma, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 70 years;
- Recurrent disease;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cytarabine

Dexamethasone + Cisplatin + Cytarabine (DHAP)

Methotrexate

Pemetrexed

Rituximab

Rituximab + Temozolomide

Temozolomide

Topotecan

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 54 of 387



Ind. 5405 For Meningioma, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age less than 70 years;
- Recurrent disease;
- Unresectable.

## ASSOCIATED CHEMOTHERAPY REGIMENS

## Interferon-Alfa

## Octreotide acetate LAR

## Sunitinib

- Ind. 5406 Systemic Therapy for Metastatic Lesions per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Age less than 70 years;
  - Multiple sites of involvement;
  - Recurrent disease;
  - First-line treatment.

## ASSOCIATED CHEMOTHERAPY REGIMENS

## Capecitabine

## Capecitabine + Lapatinib



Capecitabine + Temozolomide

Cisplatin + Etoposide

Dabrafenib

Ipilimumab

Methotrexate

Methotrexate + Cytarabine + Procarbazine

Topotecan

Vemurafenib

Ind. 5407 Therapy for Leptomeningeal Metastases per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Age less than 70 years;
- Multiple sites of involvement.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cytarabine

Cytarabine + Rituximab

Cytarabine Liposomal

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 56 of 387



Erlotinib

Etoposide

Interferon-Alfa

Methotrexate

Topotecan

Trastuzumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 57 of 387



#### REFERENCES

- Shaw EG, Wang M, Coons SW, et al. Randomized trial of radiation therapy plus procarbazine, lomustine, and vincristine chemotherapy for supratentorial adult low-grade glioma: initial results of RTOG 902. J Clin Oncol. 2012;30:3065–3070.
- Kesari S, Schiff D, Drappatz J, et al. Phase II study of protracted daily temozolomide for low-grade gliomas in adults. Clin Cancer Res. 2009;15:330–337.
- Nicholson HS, Kretschmar CS, Krailo M, et al. Phase 2 study of temozolomide in children and adolescents with recurrent central nervous system tumors: a report from the Children's Oncology Group. Cancer. 2007;110:1542–1550.
- Pouratian N, Gasco J, Sherman JH, Shaffrey ME, Schiff D. Toxicity and efficacy of protracted low dose temozolomide for the treatment of low grade gliomas. J Neurooncol. 2007;82: 281–288.
- Perry JR, Rizek P, Cashman R, Morrison M, Morrison T. Temozolomide rechallenge in recurrent malignant glioma by using a continuous temozolomide schedule: the "rescue" approach. Cancer. 2008;113:2152–2157.
- Triebels VH, Taphoorn MJ, Brandes AA, et al. Salvage PCV chemotherapy for temozolomide-resistant oligodendrogliomas. Neurology. 2004;63:904–906.
- Brandes AA, Basso U, Vastola F, et al. Carboplatin and teniposide as third-line chemotherapy in patients with recurrent oligodendroglioma or oligoastrocytoma: a phase II study. Ann Oncol. 2003;14:1727–1731.
- Moghrabi A, Friedman HS, Ashley DM, et al. Phase II study of carboplatin (CBDCA) in progressive low-grade gliomas. Neurosurg Focus. 1998;4:e3.
- Massimino M, Spreafico F, Riva D, et al. A lower-dose, lower- toxicity cisplatin-etoposide regimen for childhood progressive low-grade glioma. J Neurooncol. 2010;100:65–71.
- Lomustine (CeeNU) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company. 2012.
- Carmustine (BiCNU) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company. 2011.
- Wick W, Hartmann C, Engel C, et al. NOA-04 randomized phased III trials of sequential radiochemotherapy of ana plastic glioma with procarbazine, lomustine, and vincristine or temozolamide. J Clin Oncol. 2009;27:5874–5880.
- Taliansky-Aronov A, Bokstein F, Lavon I, Siegal T. Temozolomide treatment for newly diagnosed anaplastic oligodendrogliomas: a clinical efficacy trial. J Neurooncol. 2006;79:153–157.
- Stupp R, Mason WP, van den Bent MJ, et al. European Organisation for Research and Treatment of Cancer Brain Tumor and Radiotherapy Groups; National Cancer Institute of Canada Clinical Trials Group. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med. 2005; 352:987–996.
- Perry JR, Bélanger K, Mason WP, et al. Phase II trial of continuous dose-intense temozolomide in recurrent malignant glioma: RESCUE study. J Clin Oncol. 2010;28:2051–2057.
- Wick W, Puduvalli VK, Chamberlain MC, et al. Phase III study of enzastaurin compared with lomustine in the treatment of recurrent intracranial glioblastoma. J Clin Oncol. 2010;28: 1168–1174.
- Chamberlain MC, Johnston S. Bevacizumab for recurrent alkylator-refractory anaplastic oligodendroglioma. Cancer. 2009;115:1734–1743.
- Chamberlain MC, Johnston S. Salvage chemotherapy with bevacizumab for recurrent alkylator-refractory anaplastic strocytoma. J Neurooncol. 2009;91:359–367.



- Norden AD, Young GS, Setayesh K, et al. Bevacizumab for recurrent malignant gliomas: efficacy, toxicity, and patterns of ecurrence. Neurology. 2008;70:779–787.
- Taillibert S, Vincent LA, Granger B, et al. Bevacizumab and irinotecan for recurrent oligodendroglial tumors. Neurology. 2009;72:1601–1606.
- Vredenburgh JJ, Desjardins A, Herndon JE 2nd, et al. Phase II trial of bevacizumab and irinotecan in recurrent malignant glioma. Clin Cancer Res. 2007;13:1253–1259.Soffietti R, Rudà R, Trevisan E, et al. Phase II study of bevacizumab and nitrosourea in patients with recurrent malignant glioma: a multicenter Italian study [abstract 2012] J Clin Oncol. 2009;27(Suppl 15):90s.
- Mrugala MM, Crew LK, Fink JR, Spence AM. Carboplatin and bevacizumab for recurrent malignant glioma. Oncol Lett. 2012;4:1082–1086.
- Thompson EM, Dosa E, Kraemer DF, Neuwelt EA. Treatment with bevacizumab plus carboplatin for recurrent malignant glioma. Neurosurgery. 2010;67:87–93.
- Chamberlain MC, Wei-Tsao DD, Blumenthal DT, Glantz MJ. Salvage chemotherapy with CPT-11 for recurrent temozolomide-refractory anaplastic astrocytoma. Cancer. 2008;112: 2038–2045.
- Chamberlain MC. Salvage chemotherapy with CPT-11 for recurrent oligodendrogliomas. J Neurooncol. 2002;59: 157– 163.
- Chamberlain MC, Tsao-Wei DD. Salvage chemotherapy with cyclophosphamide for recurrent, temozolomide-refractory glioblastoma multiforme. Cancer. 2004;100:1213–1220.
- Chamberlain MC, Tsao-Wei DD, Groshen S. Salvage chemotherapy with cyclophosphamide for recurrent temozolomiderefractory anaplastic astrocytoma. Cancer. 2006;106: 172–179.
- Fulton D, Urtasun R, Forsyth P. Phase II study of prolonged oral therapy with etoposide (VP16) for patients with recurrent malignant glioma. J Neurooncol. 1996;27:149–155.
- van den Bent MJ, Brandes AA, Taphoorn MJ, et al. Adjuvant procarbazine, Iomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: Iong-term follow-up of EORTC brain tumor group study 26951. J Clin Oncol. 2013;31:344–350.
- Malmström A, Grønberg BH, Marosi C, et al; Nordic Clinical Brain Tumour Study Group (NCBTSG). Temozolomide versus standard 6-week radiotherapy versus hypofractionated radiotherapy in patients older than 60 years with glioblastoma: the Nordic randomised, phase 3 trial. Lancet Oncol. 2012; 13:916–926.
- Cloughesy TF, Prados MD, Wen PY. A phase II randomized non-comparative clinical trial of the effect of bevacizumab
   alone or in combination with irinotecan on 6 month progression free survival (PFS6) in recurrent treatment-refractory
   glioblastoma (GBM) [abstract]. J Clin Oncol. 2008;26(suppl 15):2010b.
- Friedman HS, Prados MD, Wen PY, et al. Bevacizumab alone and in combination with irinotecan in recurrent glioblastoma. J Clin Oncol. 2009;27:4733–4740.
- Kreisl TN, Kim L, Moore K, et al. Phase II trial of single-agent bevacizumab followed by bevacizumab plus irinotecan at tumor progression in recurrent glioblastoma. J Clin Oncol. 2009;27:740–745.
- Yung WK, Prados MD, Yaya-Tur R, et al. Multicenter phase II trial of temozolomide in patients with anaplastic astrocytoma or anaplastic oligoastrocytoma at first relapse. Temodal Brain Tumor Group. J Clin Oncol. 1999;17:2762–2771.
- Packer RJ, Gajjar A, Vezina G, et al. Phase III study of craniospinal radiation therapy followed by adjuvant chemotherapy for newly diagnosed average-risk medulloblastoma. J Clin Oncol. 2006;24:4202–4208.



- Dunkel IJ, Gardner SL, Garvin JH Jr, Goldman S, Shi W, Finlay JL. High-dose carboplatin, thiotepa, and etoposide with autologous stem cell rescue for patients with previously irradiated recurrent medulloblastoma. Neuro Oncol. 2010; 12:297–303.
- Ashley DM, Meier L, Kerby T, et al. Response of recurrent medulloblastoma to low-dose oral etoposide. J Clin Oncol. 1996;14:1922–1927.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer.
   Version 1.2016. 25 July 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/cns.pdf
- Chamberlain MC, Kormanik PA. Chronic oral VP-16 for recurrent medulloblastoma. Pediatr Neurol. 1997;17:230–234.
- DeAngelis LM, Seiferheld W, Schold SC, Fisher B, Schultz CJ; Radiation Therapy Oncology Group Study 93-10.
   Combination chemotherapy and radiotherapy for primary central nervous system lymphoma: Radiation Therapy Oncology Group Study 93-10. J Clin Oncol. 2002;20:4643–4648.
- Ferreri AJ, Reni M, Foppoli M, et al; International Extranodal Lymphoma Study Group (IELSG). High-dose cytarabine plus high-dose methotrexate versus high-dose methotrexate alone in patients with primary CNS lymphoma: a randomised phase 2 trial. Lancet. 2009;374:1512–1520.
- Thiel E, Korfel A, Martus P, et al. High-dose methotrexate with or without whole brain radiotherapy for primary CNS lymphoma (G-PCNSL-SG-1): a phase 3, randomised, non-inferiority trial. Lancet Oncol. 2010;11:1036–1047.
- Shah GD, Yahalom J, Correa DD, et al. Combined immunochemotherapy with reduced whole-brain radiotherapy for newly diagnosed primary CNS lymphoma. J Clin Oncol. 2007; 25:4730–4735.
- Batchelor T, Carson K, O'Neill A, Grossman SA, Alavi J, New P, Hochberg F, Priet R. Treatment of primary CNS lymphoma with methotrexate and deferred radiotherapy: a report of NABTT 96–07. J Clin Oncol. 2003;21:1044–1049.
- Chamberlain MC, Johnson SK. High-dose methotrexate and rituximab with deferred radiotherapy for newly diagnosed primary B-cell CNS lymphoma. Neuro Oncol. 2010;12: 736–744.
- Wieduwilt MJ, Valles F, Issa S, et al. Immunotherapy with intensive consolidation for primary central nervous system lymphoma: a pilot study and prognostic assessment by diffusion-weighted MRI. Clin Cancer Res. 2012 Jan 6. [Epub ahead of print].
- Widemann BC, Balis FM, Kim A, et al. Glucarpidase, leucovorin, and thymidine for high-dose methotrexate-induced renal dysfunction: clinical and pharmacologic factors affecting outcome. J Clin Oncol. 2010;28:3979–3986.
- Enting RH, Demopoulos A, DeAngelis LM, Abrey LE. Salvage therapy for primary CNS lymphoma with a combination of rituximab and temozolomide. Neurology. 2004;63:901–903.
- Topotecan (Hycamtin) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline. 2015.
- De Angelis L, Kreis W, Chan K, et al. Pharmacokinetics of ara-C and ara-U in plasma and CSF after high-dose administration of cytosine arabinoside. Cancer Chemother Pharmacol. 1992; 29:173–177.
- McLaughlin P, Velasquez WS, Redman JR, et al. Chemotherapy with dexamethasone, high-dose cytarabine, and cisplatin for parenchymal brain lymphoma. J Natl Cancer Inst. 1988;80: 1408–1412.
- Raizer JJ, Rademaker A, Evens AM, et al. Pemetrexed in the treatment of relapsed/refractory primary central nervous system lymphoma. Cancer. 2012;118:3743–3748.
- Chamberlain MC, Glantz MJ. Interferon-alpha for recurrent World Health Organization grade 1 intracranial meningiomas. Cancer. 2008;113:2146–2151.



- Chamberlain MC, Glantz MJ, Fadul CE. Recurrent meningioma: salvage therapy with long-acting somatostatin analogue. Neurology. 2007;69:969–973.
- Kaley TJ, Wen P, Schiff D, et al. Phase II trial of sunitinib for recurrent and progressive atypical
- Ewend MG, Brem S, Gilbert M, et al. Treatment of single brain metastasis with resection, intracavity carmustine polymer wafers, and radiation therapy is safe and provides excellent local control. Clin Cancer Res. 2007;13:3637–3641.
- Lassman AB, Abrey LE, Shah GD, et al. Systemic high-dose intravenous methotrexate for central nervous system metastases. J Neurooncol. 2006;78:255–260.
- Bokstein F, Lossos A, Lossos IS, et al. Central nervous system relapse of systemic non-Hodgkin's lymphoma: Results of treatment based on high-dose methotrexate combination chemotherapy. Leuk Lymphoma. 2002;43:587–593.
- Metro G, Foglietta J, Russillo M, et al. Clinical outcome of patients with brain metastases from HER2-positive breast cancer treated with lapatinib and capecitabine. Ann Oncol. 2011;22:625–630.
- Sutherland S, Ashley S, Miles D, et al. Treatment of HER2-positive metastatic breast cancer with lapatinib and capecitabine in the lapatinib expanded access programme, including efficacy in brain metastases--the UK experience. Br J Cancer. 2010; 102:995–1002.
- Cocconi G, Lottici R, Gisagni G et al, Combination therapy with platinum and etoposide in brain metastases from breast carcinoma. Cancer Invest. 1990;8:327–334.
- Franciosi V, Cocconi G, Michiara M, et al. Front-line chemotherapy with cisplatin and etoposide for patients with brain metastases from breast carcinoma, nonsmall cell lung carcinoma, or malignant melanoma. Cancer. 1999;85:1599–1605.
- Rivera E, Meyers C, Groves M, et al. Phase I study of capecitabine in combination with temozolomide in the treatment of patients with brain metastases from breast carcinoma. Cancer. 2006;107:1348–1354.
- Fabi A, Vidiri A, Ferretti G, et al. Dramatic regression of multiple brain metastases from breast cancer with Capecitabine: another arrow at the bow? Cancer Invest. 2006;24:466-8.
- Siegelmann-Danieli N, Stein M, Bar-Ziv J. Complete response of brain metastases originating in breast cancer to capecitabine therapy. Isr Med Assoc J. 2003;5:833–834.
- Wang MLH, Yung AWK, Royce ME, et al. Capecitabine for 5-fluorouracil-resistant brain metastases from breast cancer. Am J Clin Oncol. 2001;24:421–424.
- Hikino H, Yamada T, Johbara K, et al. Potential role of chemo-radiation with oral capecitabine in a breast cancer patient with central nervous system relapse. Breast. 2006;15:97–99.
- Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. Lancet Oncol. 2012;13:459–465.
- Long GV, Trefzer U, Davies MA, et al. Dabrafenib in patients with Val600Glu or Val600Lys BRAF-mutant melanoma metastatic to the brain (BREAK-MB): a multicentre, open-label, phase 2 trial. Lancet Oncol. 2012;13:1087–1095.
- Dummer R, Goldinger SM, Turtschi CP, et al. Vemurafenib in patients with BRAF(V600) mutation-positive melanoma with symptomatic brain metastases: final results of an open-label pilot study. Eur J Cancer. 2014;50:611–621.
- Jaeckle KA, Phuphanich S, Bent MJ, et al Intrathecal treatment of neoplastic meningitis due to breast cancer with a slow-release formulation of cytarabine. Br J Cancer. 2001; 84:157–163.
- Chamberlain MC, Johnston S, Van Horn A, Glantz MJ. Recurrent lymphomatous meningitis treated with intra-CSF rituximab and liposomal ara-C. J Neurooncol. 2009;91: 271–277.



- Groves MD, Glantz MJ, Chamberlain MC, et al. A multicenter phase II trial of intrathecal topotecan in patients with meningeal malignancies. Neuro Oncol. 2008;10:208-215.
- Chamberlain MC, Tsao-Wei DD, Groshen S. Phase II trial of intracerebrospinal fluid etoposide in the treatment of neoplastic meningitis. Cancer. 2006;106:2021–2027.
- Zagouri F, Sergentanis TN, Bartsch R, et al. Intrathecal administration of trastuzumab for the treatment of meningeal carcinomatosis in HER2-positive metastatic breast cancer: a systematic review and pooled analysis. Breast Cancer Res Treat. 2013;139:13–22.
- Chamberlain MC. A phase II trial of intra-cerebrospinal fluid alpha interferon in the treatment of neoplastic meningitis. Cancer. 2002; 94:2675–2680.
- Grommes C, Oxnard GR, Kris MG et al. 'Pulsatile' high- dose weekly erlotinib for CNS metastases from EGFR mutant nonsmall cell lung cancer. Neuro Oncol. 2011;13: 1364–1369.



## Breast Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age 60 years or older;
- Metastatic disease is present;
- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Bilateral oophorectomy has been performed



Fulvestrant 1,2,3

Palbociclib + Letrozole 1,2,3

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease is present;Second-line endocrine therapy; Failed an aromatase inhibitor;Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer; Bilateral oophorectomy has been performed; and EITHER of the following:
  - Section Age 60 years or older;
  - S Amenorrhea for more than twelve (12) months in the absence of tamoxifen, chemotherapy, or ovarian suppression with Follicle Stimulating Hormone (FSH) and estradiol that are in postmenopausal range in a patient who is less than 60 years of age.

ASSOCIATED CHEMOTHERAPY REGIMENS

Megestrol Acetate

Everolimus + Exemestane

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Age less than 60 years;



- Metastatic disease is present;
- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Bilateral oophorectomy has been performed;
- Amenorrhea for more than twelve (12) months in the absence of tamoxifen, chemotherapy, or ovarian suppression;
- Follicle Stimulating Hormone (FSH) and estradiol are in the postmenopausal range.

## Fulvestrant

#### Palbociclib + Letrozole

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Metastatic disease is present;
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Negative HER2.

ASSOCIATED CHEMOTHERAPY REGIMENS

Albumin-bound Paclitaxel

Capecitabine

## Carboplatin



Cisplatin

Cyclophosphamide

Cyclophosphamide + Methotrexate + 5-Fluorouracil (CMF)

Docetaxel

Docetaxel + Capecitabine

Docetaxel + Cyclophosphamide

Eribulin

Gemcitabine

Gemcitabine + Carboplatin

Gemcitabine + Paclitaxel (GT)

Ixabepilone

Paclitaxel

Paclitaxel + Bevacizumab

Vinorelbine

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 66 of 387



- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Negative HER2;
- Standard chemotherapy regimen containing Doxorubicin + Cyclophosphamide;
- Subsequent treatment of Neoadjuvant/Adjuvant chemotherapy (maintenance regimen); and EITHER of the following:
  - **§** Metastatic disease is present;
  - **§** Recurrence occurred greater than twelve (12) months after treatment.

Paclitaxel

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease is present;
- Negative HER2;
- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Doxorubicin

Doxorubicin + Cyclophosphamide (AC)



Epirubicin

Epirubicin + Cyclophosphamide (EC)

Pegylated Liposomal Doxorubicin

Paclitaxel (subsequent cycles)

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- First-line treatment;
- Normal cardiac function;
- Hormone Receptor positive;
- HER2 positive;
- Patient is postmenopausal.
  - **§** And EITHER of the following:
    - Metastatic disease
    - Locally advanced disease

ASSOCIATED CHEMOTHERAPY REGIMENS

Anastrozole + Trastuzumab

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:



- First-line treatment;
- Normal cardiac function;
- HER2 positive;
- Patient is postmenopausal.
  - **§** And EITHER of the following:
    - Metastatic disease
    - Locally advanced disease

## Pertuzumab + Trastuzumab

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - First-line treatment;
  - Hormone Receptor positive;
  - HER2 negative;
  - Patient is postmenopausal
  - Failure of previous treatment with Letrozole or Anastrozole.
    - **§** And EITHER of the following:
      - Metastatic disease
      - Locally advanced disease

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 69 of 387



Everolimus + Exemestane

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- First-line treatment;
- Hormone Receptor positive;
- HER2 positive;
- Patient is postmenopausal.
  - **§** And EITHER of the following:
    - Metastatic disease
    - Locally advanced disease

## ASSOCIATED CHEMOTHERAPY REGIMENS

Lapatinib + Letrozole

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- First-line treatment;
- Hormone Receptor positive;
- HER2 negative;
- Patient is postmenopausal.
- Metastatic disease



Palbociclib + Letrozole

Ribociclib + Letrozole

Abemaciclib

Abemaciclib + Anastrozole

Abemaciclib + Letrozole

Abemaciclib + Exemestane

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Positive HER2;
  - Normal cardiac function and EITHER of the following;
    - S Recurrence that occurred greater than 12 months after treatment, and this is first line treatment;
    - Metastatic disease and this is third-line treatment (previous exposure to Trastuzumab and TDM-1

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel + Carboplatin + Trastuzumab

Paclitaxel + Trastuzumab



Pertuzumab + Trastuzumab + Paclitaxel Pertuzumab + Trastuzumab + Docetaxel Trastuzumab + Capecitabine Trastuzumab + Docetaxel Trastuzumab + Vinorelbine Trastuzumab + Eribulin Lapatinib + Capecitabine Trastuzumab + Lapatinib

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease is present;
- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Positive HER2;
- First-line treatment;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel + Carboplatin + Trastuzumab

Paclitaxel + Trastuzumab



Trastuzumab + Capecitabine Trastuzumab + Docetaxel Trastuzumab + Vinorelbine Trastuzumab + Eribulin

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Positive HER2;
- Recurrence occurred less than twelve (12) months after treatment;
- Second-line treatment (previous exposure to Trastuzumab);
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Ado-Trastuzumab Emtansine (T-DM1)

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Patient is experiencing osteoporosis related to breast cancer;
  - Patient is experiencing hypercalcemia related to breast cancer.



• Pathology is consistent with ductal, lobular, mixed or metaplastic breast cancer with metastasis to the bone.

## ASSOCIATED CHEMOTHERAPY REGIMENS

Zoledronic Acid

# Denosumab

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Completion of Endocrine therapy and ANY of the following:
    - S Hormone receptor (HR) positive;
    - **§** Locally advanced with negative HER2
    - Metastatic disease is present
  - Patient is post menopausal, with metastatic disease, is hormone receptor positive and has completed anti estrogen therapy

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Palbociclib + Fulvestrant

# Abemaciclib + Fulvestrant

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Patient is post menopausal;



- Metastatic disease is present;
- Hormone receptor (HR) positive;
- Anti estrogen treatment

- Palbociclib + Fulvestrant
- Abemaciclib + Fulvestrant

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient is post menopausal;
- Pathology is consistent with ductal, lobular, mixed or metaplastic breast cancer;
- Metastatic disease is present;
- Negative HER2;
- Hormone reception positive;
- Prior treatment with endocrine therapy;
- Subsequent treatment of Neoadjuvant/Adjuvant chemotherapy (maintenance regimen)

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Abemaciclib + Fulvestrant

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:



- Patient is post menopausal;
- Metastatic disease is present;
- Negative HER2;
- Hormone reception positive;
- Prior treatment with endocrine therapy;

## Abemaciclib

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease is present;
- Positive HER2;
- Subsequent treatment of Neoadjuvant/Adjuvant chemotherapy (maintenance regimen);
- Cardiac function is normal

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Trastuzumab-dkst

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Metastatic disease is present;
  - Negative HER2
  - Hormone receptor positive
  - Prior treatment with endocrine therapy;



• Subsequent treatment of Neoadjuvant/Adjuvant chemotherapy (maintenance regimen)

## ASSOCIATED CHEMOTHERAPY REGIMENS

# Olaparib

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Patient is post menopausal;
  - Metastatic disease is present;
  - Hormone receptor positive
  - Prior treatment with endocrine therapy;
  - Failed an aromatase inhibitor
  - First line treatment

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Abemaciclib + Anastrozole

- Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Patient is post menopausal;
  - Metastatic disease is present;
  - Hormone receptor positive
  - First line treatment



Abemaciclib + Letrozole

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient is postmenopausal
- Failed an aromatase inhibitor

ASSOCIATED CHEMOTHERAPY REGIMENS

Abemaciclib + Exemestane

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient is 60 years or older;
- Bilateral oophorectomy has been performed;
- Patient is postmenopausal;
- Failure of treatment with Letrozole or Anastrozole;
- Pathology is consistent with ductal, lobular, mixed or metaplastic breast cancer;
- Metastatic disease is present;
- Negative HER2



# • Hormone receptor positive

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Fulvestrant + Everolimus

Ind. 5527 Medical Oncology for Recurrent or Metastatic Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient is postmenopausal
- Failure of treatment with Letrozole or Anastrozole
- Metastatic disease
- Negative HER2
- Hormone receptor positive
- First line treatment

ASSOCIATED CHEMOTHERAPY REGIMENS

Tamoxifen + Everolimus

Ribociclib + Tamoxifen



Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- High risk score on validated recurrence score calculators;
- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Tumor 0.6-1.0 cm;
- Node positive;
- Negative HER2;
- Hormone receptor positive (estrogen or progesterone);
- Neoadjuvant chemotherapy;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dose-Dense Doxorubicin + Cyclophosphamide (AC)

Doxorubicin + Cyclophosphamide (AC)

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 80 of 387



- High risk score on validated recurrence score calculators;
- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Tumor 0.6-1.0 cm;
- Negative HER2;
- Hormone receptor positive (estrogen or progesterone);
- Adjuvant chemotherapy;
- Normal cardiac function.

5-Fluorouracil + Doxorubicin + Cyclophosphamide (FAC) + Paclitaxel

Cyclophosphamide + Methotrexate + 5-Fluorouracil (CMF)

Docetaxel + Cyclophosphamide (TC)

Dose-Dense Doxorubicin + Cyclophosphamide (AC) + Paclitaxel

Epirubicin + Cyclophosphamide (EC)

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Docetaxel

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Paclitaxel

- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - High risk score on validated recurrence score calculators;



- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Negative HER2;
- Normal cardiac function.

AC + Albumin-bound Paclitaxel

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Tumor greater than or equal to 0.5 cm;
- Node negative;
- Negative HER2;
- Hormone receptor negative (estrogen or progesterone);
- Neoadjuvant chemotherapy;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dose-Dense Doxorubicin + Cyclophosphamide (AC)

Doxorubicin + Cyclophosphamide (AC)



- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Tumor greater than or equal to 0.5 cm;
  - Node negative;
  - Negative HER2;
  - Adjuvant chemotherapy;
  - Normal cardiac function.

Doxorubicin + Cyclophosphamide (AC) + Docetaxel

Docetaxel + Doxorubicin + Cyclophosphamide (TAC)

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Tumor greater than or equal to 0.5 cm;
- Positive HER2;
- Adjuvant chemotherapy;



• Normal cardiac function.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel + Carboplatin + Trastuzumab (TCH)

Dose-Dense Doxorubicin + Cyclophosphamide (AC) + Paclitaxel + Trastuzumab

Doxorubicin + Cyclophosphamide (AC) + Docetaxel + Trastuzumab

Doxorubicin + Cyclophosphamide (AC) + Paclitaxel + Trastuzumab

Doxorubicin + Cyclophosphamide (AC) + Pertuzumab + Trastuzumab + Docetaxel

Doxorubicin + Cyclophosphamide (AC) + Pertuzumab + Trastuzumab + Paclitaxel

TCH + Pertuzumab

- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Tumor greater than or equal to 0.5 cm;
  - Positive HER2;
  - Neoadjuvant chemotherapy;
  - Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel + Cyclophosphamide + Trastuzumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 84 of 387



Doxorubicin + Cyclophosphamide (AC) + Docetaxel + Trastuzumab

Doxorubicin + Cyclophosphamide (AC) + Pertuzumab + Trastuzumab + Docetaxel

Doxorubicin + Cyclophosphamide (AC) + Paclitaxel + Trastuzumab

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Tumor greater than or equal to 0.5 cm;
- Negative HER2;
- Hormone receptor negative (estrogen or progesterone);
- Locally advanced or inflammatory breast cancer;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil + Doxorubicin + Cyclophosphamide (FAC) + Paclitaxel

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Paclitaxel

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:



- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Tumor greater than or equal to 0.5 cm;
- Negative HER2;
- Hormone receptor negative (estrogen or progesterone);
- Adjuvant chemotherapy;
- Normal cardiac function.

Cyclophosphamide + Methotrexate + 5-Fluorouracil (CMF)

Docetaxel + Cyclophosphamide (TC)

Dose-Dense Doxorubicin + Cyclophosphamide (AC)

Dose-Dense Doxorubicin + Cyclophosphamide (AC) + Paclitaxel

Doxorubicin + Cyclophosphamide (AC)

Epirubicin + Cyclophosphamide (EC)

Doxorubicin + Cyclophosphamide (AC) + Paclitaxel

Doxorubicin + Cyclophosphamide (AC) + Albumin Bound Paclitaxel



- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Tumor greater than or equal to 0.5 cm;
  - Negative HER2;
  - Hormone receptor negative (estrogen or progesterone);
  - Neoadjuvant chemotherapy;
  - Normal cardiac function.

5-Fluorouracil + Doxorubicin + Cyclophosphamide (FAC) + Paclitaxel

Cyclophosphamide + Methotrexate + 5-Fluorouracil (CMF)

Epirubicin + Cyclophosphamide (EC)

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Paclitaxel

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

> Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;



- Tumor greater than or equal to 0.5 cm;
- Negative HER2;
- Neoadjuvant chemotherapy;
- Normal cardiac function.

Doxorubicin + Cyclophosphamide (AC) + Docetaxel

Doxorubicin + Cyclophosphamide (AC) + Albumin Bound Paclitaxel

Docetaxel + Doxorubicin + Cyclophosphamide (TAC)

- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Node positive;
  - Positive HER2;
  - Normal cardiac function; and EITHER of the following:
    - **§** Adjuvant chemotherapy;
    - **§** Neoadjuvant chemotherapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel + Carboplatin + Trastuzumab (TCH)

Docetaxel + Cyclophosphamide + Trastuzumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 88 of 387



Dose-Dense Doxorubicin + Cyclophosphamide (AC) + Paclitaxel + Trastuzumab

Doxorubicin + Cyclophosphamide (AC) + Docetaxel + Trastuzumab

Doxorubicin + Cyclophosphamide (AC) + Paclitaxel + Trastuzumab

Doxorubicin + Cyclophosphamide (AC) + Pertuzumab + Trastuzumab + Docetaxel

Doxorubicin + Cyclophosphamide (AC) + Pertuzumab + Trastuzumab + Paclitaxel

Paclitaxel + Trastuzumab

TCH + Pertuzumab

Trastuzumab-dkst + Paclitaxel

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Node positive;
- Negative HER2;
- Adjuvant chemotherapy;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil + Doxorubicin + Cyclophosphamide (FAC) + Paclitaxel

Cyclophosphamide + Methotrexate + 5-Fluorouracil (CMF)



Docetaxel + Cyclophosphamide (TC)

Dose-Dense Doxorubicin + Cyclophosphamide (AC)

Dose-Dense Doxorubicin + Cyclophosphamide (AC) + Paclitaxel

Doxorubicin + Cyclophosphamide (AC)

Epirubicin + Cyclophosphamide (EC)

Doxorubicin + Cyclophosphamide (AC) + Albumin Bound Paclitaxel

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Paclitaxel

Ind. 5525Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Node positive;
- Negative HER2;
- Neoadjuvant chemotherapy;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil + Doxorubicin + Cyclophosphamide (FAC) + Paclitaxel

Cyclophosphamide + Methotrexate + 5-Fluorouracil (CMF)



Dose-Dense Doxorubicin + Cyclophosphamide (AC)

Doxorubicin + Cyclophosphamide (AC)

Doxorubicin + Cyclophosphamide (AC) + Docetaxel

Epirubicin + Cyclophosphamide (EC)

Doxorubicin + Cyclophosphamide (AC) + Albumin Bound Paclitaxel

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Docetaxel

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Paclitaxel

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Node negative;
- Negative HER2;
- Adjuvant chemotherapy;
- Normal cardiac function.

#### ASSOCIATED CHEMOTHERAPY REGIMENS



Doxorubicin + Cyclophosphamide (AC) + Docetaxel

Docetaxel + Doxorubicin + Cyclophosphamide (TAC)

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Negative HER2;
- Locally advanced or inflammatory breast cancer;
- Neoadjuvant chemotherapy;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil + Doxorubicin + Cyclophosphamide (FAC) + Paclitaxel

Docetaxel + Cyclophosphamide (TC)

Dose-Dense Doxorubicin + Cyclophosphamide (AC)

Dose-Dense Doxorubicin + Cyclophosphamide (AC) + Paclitaxel

Doxorubicin + Cyclophosphamide (AC)

Doxorubicin + Cyclophosphamide (AC) + Docetaxel

Epirubicin + Cyclophosphamide (EC)

AC + Albumin-bound Paclitaxel



5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Docetaxel

5-Fluorouracil + Epirubicin + Cyclophosphamide (FEC) + Paclitaxel

Docetaxel + Doxorubicin + Cyclophosphamide (TAC)

Doxorubicin + Cyclophosphamide (AC) + Paclitaxel

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Negative HER2;
- Subsequent treatment of Neoadjuvant/Adjuvant chemotherapy (maintenance regimen);
- Standard chemotherapy regimen containing 5-FU + Epirubicin + Cyclophosphamide;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel (Subsequent Cycles)



- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Positive HER2;
  - Subsequent treatment of Neoadjuvant/Adjuvant chemotherapy (maintenance regimen);
  - Normal cardiac function.

Trastuzumab (Subsequent cycles)

- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Negative HER2;
  - Subsequent treatment of Neoadjuvant/Adjuvant chemotherapy (maintenance regimen);
  - Standard chemotherapy regimen containing 5-FU + Doxorubicin + Cyclophosphamide;
  - Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel (Subsequent Cycles)



- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Positive HER2;
  - Neoadjuvant chemotherapy;
  - Normal cardiac function and EITHER of the following:
    - § Node positive;
    - S Tumor greater than or equal to 0.5 cm.

Pertuzumab + Trastuzumab

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Node positive;
- Positive HER2;
- Adjuvant chemotherapy
- Normal cardiac function

ASSOCIATED CHEMOTHERAPY REGIMENS

Trastuzumab-dkst + Docetaxel + Carboplatin

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:



- Positive HER2
- Hormone receptor positive (estrogen or progesterone)
- Adjuvant chemotherapy

# Neratinib

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Positive HER2
- Normal cardiac function and EITHER
  - **§** Node negative OR node positive, and ANY of the following:
    - Received treatment regimen consisting of Doxorubicin + Cyclophosphamide and either Paclitaxel or Docetaxel;
    - received treatment regimen of Docetaxel + Carboplatin;
    - This is a single agent therapy following multi modality anthracycline based therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Trastuzumab-dkst

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

• Adjuvant chemotherapy



- Normal cardiac function and EITHER
  - S Node positive
  - S Node negative

Trastuzumab-dkst + Docetaxel

- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - High risk score on validated recurrence score calculators;
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Tumor 0.6-1.0 cm;
  - Negative HER2;
  - Hormone receptor positive (estrogen or progesterone);
  - Adjuvant chemotherapy;
  - Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Doxorubicin + Cyclophosphamide (AC) + Paclitaxel

- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Positive HER2;
  - Hormone receptor positive (estrogen or progesterone);
  - Adjuvant chemotherapy;



• To follow adjuvant Trastuzumab based therapy

## ASSOCIATED CHEMOTHERAPY REGIMENS

# Neratinib

Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Node positive
- Positive HER2;
- Adjuvant chemotherapy;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Trastuzumab-dkst + Docetaxel + Carboplatin

- Ind. 5525 Adjuvant or Neoadjuvant Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Positive HER2
  - Neoadjuvant chemotherapy
  - Normal cardiac function and EITHER
    - S Node positive
    - S Tumor greater than or equal to 0.5 cm

ASSOCIATED CHEMOTHERAPY REGIMENS

Pertuzumab + Trastuzumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 98 of 387



Ind. 5413 Adjuvant Endocrine Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Amenorrhea for more than twelve (12) months in the absence of tamoxifen, chemotherapy, or ovarian suppression with Follicle Stimulating Hormone (FSH) and estradiol that are in postmenopausal range in a patient who is less than 60 years of age.
- Adjuvant therapy
- Bilateral oophorectomy has been performed;
- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer; AND EITHER:
  - § Node positive;
  - **§** Tumor greater than 0.5 cm;

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Anastrozole

Exemestane

## Letrozole

- Ind. 5413 Adjuvant Endocrine Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Patient has had a bilateral oopherectomy



- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Node positive;
- Adjuvant therapy;

Anastrozole

Exemestane

Letrozole

- Ind. 5413 Adjuvant Endocrine Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
  - Tumor greater than 0.5 cm;
  - Adjuvant therapy.

# ASSOCIATED CHEMOTHERAPY REGIMENS

Tamoxifen

# Toremifine

Ind. 5413 Adjuvant Endocrine Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:



- Patient is experiencing osteoporosis related to breast cancer;
- Patient is experiencing hypercalcemia related to breast cancer.
- Pathology is consistent with ductal, lobular, mixed or metaplastic breast cancer, this is adjuvant therapy, and FSH and estradiol are in the postmenopausal range

Zoledronic Acid

Denosumab

Ind. 5413 Adjuvant Endocrine Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Node positive;
- Adjuvant therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Anastrozole

Exemestane

Letrozole

Tamoxifen

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 101 of 387



# Toremifene

Ind. 5413 Adjuvant Endocrine Chemotherapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Pathology is consistent with ductal, lobular, mixed or metaplastic breast cancer
- Tumor greater than 0.5 cm
- Adjuvant therapy, and EITHER:
  - § 60 years old or greater
  - § Bilateral oophorectomy has been performed.

ASSOCIATED CHEMOTHERAPY REGIMENS

Anastrozole

Letrozole

Exemestane

Ind. 5526 GnRH Agonist Therapy for Breast Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Age 40 years or less;
- Premenopausal;

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 102 of 387



- Pathology is consistent with ductal, lobular, mixed, or metaplastic breast cancer;
- Adjuvant therapy; and EITHER of the following:
  - S Tumor greater than 0.5 cm;
  - § Node positive

Goserelin

Leuprolide Depot

Tamoxifen + Leuprolide Depot



#### UPDATED REFERENCES

 National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 1.2019. March 14, 2019. Please refer to the NCCN website for additional information, available at:

https://www.nccn.org/ professionals/physician\_gls/pdf/breast.pdf.

- Lee, CI, Goodwin A, Wilcken N. Fulvestrant for hormone-sensitive metastatic breast cancer. <u>Cochrane Database Syst Rev.</u> 2017 Jan 3;1:CD011093. doi: 10.1002/14651858.CD011093.pub2.
- Ellis, M. J., Llombart-Cussac, A., Feltl, D., Dewar, J. A., Jasiówka, M., Hewson, N., ... Robertson, J. F. (2015). Fulvestrant 500 mg Versus Anastrozole 1 mg for the First-Line Treatment of Advanced Breast Cancer: Overall Survival Analysis From the Phase II FIRST Study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 33*(32), 3781– 3787. doi:10.1200/JCO.2015.61.5831

#### REFERENCES

- Chan S, Friedrichs K, Noel D, et al. Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. J Clin Oncol. 1999;17(8):2341–2354.
- Gasparini G, Dal Fior S, Panizzoni GA, Favretto S, Pozza F. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinical trial. Am J Clin Oncol. 1991;14(1):38-44.
- O'Brien ME, Wigler N, Inbar M, et al. Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCI (CAELYX/Doxil) versus conventional doxorubicin for first-line treatment of metastatic breast cancer. Ann Oncol. 2004;15(3):440–449.
- Seidman AD, Tiersten A, Hudis C, et al. Phase II trial of paclitaxel by 3-hour infusion as initial and salvage chemotherapy for metastatic breast cancer. J Clin Oncol. 1995;13(10):2575–2581.
- Perez EA, Vogel CL, Irwin DH, et al. Multicenter phase II trial of weekly paclitaxel in women with metastatic breast cancer. JClin Oncol. 2001;19(22):4216–4223.
- Bajetta E, Procopio G, Celio L, et al. Safety and efficacy of two different doses of capecitabine in the treatment of advanced breast cancer in older women. J Clin Oncol. 2005;23(10):2155–2161.
- Seidman AD. Gemcitabine as single-agent therapy in the management of advanced breast cancer. Oncology. (Williston Park) 2001;15(2 suppl 3):11–14.
- Zelek L, Barthier S, Riofrio M, et al. Weekly vinorelbine is an effective palliative regimen after failure with anthracyclines and taxanes in metastatic breast carcinoma. Cancer. 2001;92(9):2267–2272.
- Cortes J, O'Shaughnessy J, Loesch O, et al. Eribulin monotherapy versus treatment of physicians choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomized study. Lancet. 2011;377(9769):914–923.
- Licchetta A, Correale P, Migali C, et al. Oral metronomic chemo- hormonal-therapy of metastatic breast cancer with cyclophosphamide and megestrol acetate. J Chemother. 2010;22(3):201–204.
- Isakoff S J, Goss PE, Mayer EL, et al. TBCRCOO9: A multi-center phase II study of cisplatin or carboplatin for metastatic triple-negative breast cancer and evaluation of p631p73 as a biomarker of response [abstract). J Clin Oncol. 2011;29 (15\_ suppl): Abstract 1025.
- Burris HA 3rd. Single-agent docetaxel (Taxotere) in randomized phase III trials. Semin Oncol. 1999;26(3 suppl 9):1–6.



- Harvey V, Mouridsen H, Semiglazov V, et al: Phase III trial comparing three doses of docetaxel for second-line treatment of advanced breast cancer. J Clin Oncol. 2006;24(31):4963–4970.
- Rivera E, Mejia JA, Arun BK, et al. Phase 3 study comparing the use of docetaxel on an every-3-week versus weekly schedule in the treatment of metastatic breast cancer. Cancer. 2008;112(7):1455–1461.
- Gradishar W, Tjulandin S. Davidson N, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. J Clin Oncol. 2005;23(31):7794–7803.
- Gradishar W, Dimitry K, Sergey C, et al. Significantly longer progression-free survival with nab-paclitaxel compared with docetaxel as first-line therapy for metastatic breast cancer. J Clin Oncol. 2009;27(22):3611–3619.
- Silver DR, Richardson AL, Eklund AC, et al. Efficacy of neoadjuvant cisplatin in triple-negative breast cancer. J Clin Oncol.2010;28(7):1145–1153.
- Bastholt L, Dalmark M, Gjedde SB, et al. Dose-response relationship of epirubicin in the treatment of postmenopausal patients with metastatic breast cancer a randomized study of epirubicin at four different dose levels performed by the Danish Breast Cancer Cooperative Group. J Clin Oncol. 1996;14(4):1146–1155.
- Perez E, Lerzo G, Pivot X, et al. Efficacy and safety of ixabepilone (BMS-247550) in a phase II study of patients with advanced breast cancer resistant to an anthracycline, a taxane, and capecitabine. J Clin Oncol. 2007;25(23):3407–3414.
- Bull JM, Tormey DC, Li SH, et al. A randomized comparative trial of adriamycin versus methotrexate in combination drug therapy. Cancer. 1978;41(5):1649–1657.
- Hortobagyi GN, Gutterman JU, Blumenschein GR, et al. Combination chemoimmunotherapy of metastatic breast cancer with 5-fluorouracil, adriamycin, cyclophosphamide, and BCG. Cancer. 1979;43(4):1225–33.
- Ackland SR, Anton A, Breithach GR, et al. Dose-intensive epirubicin-based chemotherapy is superior to an intensive intravenous cyclophosphamide, methotrexate, and fluorouracil regimen in metastatic breast cancer a randomized multinational study. J Clin Oncol. 2001;19(4):943–953.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 1.2017. 10 March 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/breast.pdf.
- Nabholtz JM, Falkson C, Campos O, et al. Docetaxel and doxorubicin compared with doxorubicin and cyclophosphamide as first-line chemotherapy for metastatic breast cancer results of a randomized, multicenter, phase III trial. J Clin Oncol. 2003;21(6):968–975.
- Langley RE, Carmichel J, Jones AL, et al. Phase III trial of epirubicin plus paclitaxel compared with epirubicin plus cyclophosphamide as first-line chemotherapy for metastatic breast cancer United Kingdom Cancer Research Institute. J Clin Oncol. 2005;23(33):8322–8330.
- Bonadonna G, Brusamolino E, Valagussa P, et al. Combination chemotherapy as an adjuvant treatment in operable breast cancer. N Engl J Med. 1976;294(8):405–410.
- Mavroudis D, Papakotoulas P, Ardavanis A, et al; Breast Cancer Investigators of the Hellenic Oncology Research Group.
   Randomized phase III trial comparing docetaxel plus epirubicin versus docetaxel plus capecitabine as first-line treatment in women with advanced breast cancer. Ann Oncol. 2010;21(1):48–54.
- Albain KS, Nag S, Calderillo-Ruiz G, et al. Gemcitabine plus paclitaxel versus paclitaxel monotherapy in patients with metastatic breast cancer and prior anthracycline treatment. J Clin Oncol. 2008;26(24):3950–3957.



- O'Shaughnessy J, Schwartzberg LS, Danso MA, et al. A randomized phase ill study of iniparib (BSI-201) in combination with gemcitabine/carboplatin (GIC) in metastatic triple-negative breast cancer (TNBC). [abstract]. J Clin Oncol. 2011; 29(Suppl\_15):Abstract 1007.
- Miller K, Wang M, Gralow J, et al. Paclitaxel plus bevacizurriab versus paclitaxel alone for metastatic breast cancer. N Engl J Med. 2007;357(26):2666–2676.
- Baselga J, Cones J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med. 2012;366(2):109–119.
- Datko F, D'Andrea G, Dickler M, et al. Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with metastatic HER2-overexpressing metastatic breast cancer [abstract]. Cancer Research. 2012;72: Abstract P5-18–20.
- Leyland-Jones B, Gelmon K, Ayoub JP, et al. Pharmacokinetics, safety, and efficacy of trastuzumab administered every three weeks in combination with paclitaxel. J Clin Oncol. 2003;21(21):3965–3971.
- Verma S, Miles O, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012;367(19):1783–1791.
- Robert N, Leyland-Jones B, Asmar L, et al. Randomized phase III study of trastuzumab, paclitaxel, and carboplatin compared with trastuzumab and paclitaxel in women with HER-2-overexpressing metastatic breast cancer. J Clin Oncol. 2006;24(18):2786–2792.
- Perez EA, Suman VJ, Rowland KM, et al. Two concurrent phase II trials of paclitaxel/carboplatin/trastuzumab (weekly or every-3-week schedule) as first-line therapy in women with HER2-overexpressing metastatic breast cancer: NCCTG study 983252. Clin Breast Cancer. 2005;6(5):425–432.
- Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med. 2001;344(11):783–792.
- Seidman A, Berry DA, Cirrincione C, et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all HER-2 overexpressors and random assignment to trastuzumab or not in HER-2 nonoverexpressors: final results of Cancer and Leukemia Group B protocol 9840. J Clin Oncol. 2008;26(10):1642–1649.
- Marty M, Cognetti F, Maraninchi O, et al. Randomized phase II trial of the efficacy and safety of trastuzumab combined with docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer administered as first- line treatment: the M77001 study group. J Clin Oncol. 2005;23(19):4265–4274.
- Esteva FJ, Valero V, Booser O, et al. Phase II study of weekly docetaxel and trastuzumab for patients with HER-2overexpressing metastatic breast cancer. J Clin Oncol. 2002;20(7):1800–1808.
- Burstein HJ, Keshaviah A, Baron AD, et al. Trastuzumab plus vinorelbine or taxane chemotherapy for HER2overexpressing metastatic breast cancer the trastuzumab and vinorelbine or taxane study. Cancer. 2007;110(5):965– 972.
- von Minckwitz G, du Bois A, Schmidt M, et al. Trastuzumab beyond progression in human epidermal growth factor receptor 2-positive advanced breast cancer a German breast group 26/breast international group 03-05 study. J Clin Oncol. 2009;27(12):1999–2006.
- Cobleigh MA, Vogel CL, Tripathy D, et al. Multinational study of the efficacy and safety of humanized anti-I-IER2
   ruonodonal antibody in women who have HER2- overexpressing metastatic breast cancer that has progressed after
   chemotherapy for metastatic disease. J Clin Oncol. 1999;17(9):2639–2648.



- Geyer C, Forster J, Undquist O, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med. 2006:355(26):2733–2743.
- Bartsch R, Wenzel C, Altorjai G, et al. Capecitabine and trastuzumab in heavily pretreated metastatic breast cancer. J Clin Oncol. 2007;25(25):3853–3858.
- Blackwell KL, Burstein H, Storniolo AM, et al. Randomized study of lapatinib alone or in combination with trastuzumab in women with ErbB2-positive. Trastuzumab-refractory metastatic breast cancer. J Clin Oncol. 2010;28(7):1124–1130.

# Cervical Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5528 First-Line Therapy for Recurrent or Metastatic Cervical Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Advanced disease.

ASSOCIATED CHEMOTHERAPY REGIMENS



Carboplatin + Paclitaxel

Cisplatin + Gemcitabine

Cisplatin + Paclitaxel + Bevacizumab

Cisplatin + Topotecan

Paclitaxel + Carboplatin + Bevacizumab

Paclitaxel + Cisplatin

Topotecan + Paclitaxel

Topotecan + Paclitaxel + Bevacizumab

Ind. 5528 First-Line Therapy for Recurrent or Metastatic Cervical Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Advanced disease;
- History of Cerebrovascular Accident (CVA) or Myocardial Infarction (MI).

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Paclitaxel

Cisplatin + Gemcitabine

Cisplatin + Topotecan

Paclitaxel + Cisplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 108 of 387



Ind. 5528 First-Line Therapy for Recurrent or Metastatic Cervical Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• History of Cerebrovascular Accident (CVA) or Myocardial Infarction (MI).

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin

Cisplatin

Paclitaxel

- Ind. 5529 Second-Line Therapy for Recurrent or Metastatic Cervical Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Advanced disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

Albumin-bound Paclitaxel

Bevacizumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 109 of 387



Docetaxel

Gemcitabine

lfosfamide + Mesna

Irinotecan

Leucovorin + 5-Fluorouracil (5-FU)

Mitomycin

Pemetrexed

Topotecan

Vinorelbine

- Ind. 5424 First-Line Therapy with Radiotherapy for Locally Advanced Cervical Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Stage 1B1, 2A1 with intermediate or high risk features, such as presence of positive nodes, positive surgical margins, or positive parametrium;
  - Stage 1B2, 2A2, 2B- 4A.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + 5-Fluorouracil (5-FU) + Hydroxyurea

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 110 of 387



Cisplatin + Gemcitabine

Ind. 5424 First-Line Therapy with Radiotherapy for Locally Advanced Cervical Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Stage 1B1, 2A1;
- Intermediate or high risk features, such as presence of positive nodes, positive surgical margins, or positive parametrium.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin

Cisplatin + 5-Fluorouracil (5-FU)



#### REFERENCES

- Keys HM, Bundy BN, Stehman FB, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med. 1999;340(15):1154–1161. Erratum in: N Engl J Med. 1999;341(9):708.
- Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for advanced cervical cancer. N Engl J Med. 1999;340(15):1144–1153. Erratum in: N Engl J Med. 1999;341(9):708.
- Morris M, Eifel PF, Lu J, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. N Engl J Med. 1999;340(15):1137–1143.
- Whitney CW, Sause W, Bundy BN, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol. 1999;17(5):1339–1348.
- Tewari KS1, Sill MW, Long HJ 3rd, et al. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014;370(8):734–43.
- Monk BJ, Sill MW, M cmeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a Gynecologic Oncology Group study. J Clin Oncol. 2009;27(28):4649–4655.
- Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22(15):3113–3119.
- Moore KN, Herzog TJ, Lewin S, et al. A comparison of cisplatin/paclitaxel and carboplatin/paclitaxel in stage IVB, recurrent or persistent cervical cancer. Gynecol Oncol. 2007;105(2):299–303.
- Kitagawa R, Katsumata N, Shibata T, et al. Paclitaxel plus carboplatin versus paclitaxel plus cisplatin in metastatic or recurrent cervical cancer: the open-label randomized phase iii trial JCOG0505. J Clin Oncol. 2015;33(19):2129–2135.
- Long HJ 3rd, Bundy BN, Grendys EC Jr, et al; Gynecologic Oncology Group Study. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol. 2005;23(21):4626–4633.
- Brewer CA, Blessing JA, Nagourney RA, et al. Cisplatin plus gemcitabine in previously treated squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2006;100(2):385–388.
- Weiss GR, Green S, Hannigan EV, et al. A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: a Southwest Oncology Group study. Gynecol Oncol. 1990;39(3):332–336.
- Kudelka AP, Winn R, Edwards CL, et al. An update of a phase II study of paclitaxel in advanced or recurrent squamous cell cancer of the cervix. Anticancer Drugs. 1997;8(7):657–661.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Cervical Cancer.
   Version 1.2017. 10 Oct 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.
   org/professionals/physician\_gls/pdf/cervical.pdf.
- Monk BJ, Sill MW, Burger RA, et al. Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27(7):1069–1074.



- Alberts DS, Blessing JA, Landrum LM, et al. Phase II trial of nab-paclitaxel in the treatment of recurrent or persistent advanced cervix cancer: a gynecologic oncology group study. Gynecol Oncol. 2012;127(3):451–455.
- Garcia AA, Blessing JA, Vaccarello L, et al. Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. Am J Clin Oncol. 2007;30(4):428–431.
- Look KY, Blessing JA, Gallup DG, Lentz SS. A phase II trial of 5-fluorouracil and high-dose leucovorin in patients with recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Am J Clin Oncol. 96;19(5):439– 441.
- Schilder RJ, Blessing J, Cohn DE. Evaluation of gemcitabine in previously treated patients with non-squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2005;96(1):103–107.
- RE, Harper PG, Gallagher C, et al. A phase II study of ifosfamide in advanced and relapsed carcinoma of the cervix. Cancer Chemother Pharmacol. 1986;18(3):280–283.
- Sutton GP, Blessing JA, McGuire WP, Patton T, Look KY. Phase II trial of ifosfamide and mesna in patients with advanced or recurrent squamous carcinoma of the cervix who had never received chemotherapy: a Gynecologic Oncology Group study. Am J Obstet Gynecol. 1993;168(3 Pt 1):805–807.
- Verschraegen CF, Levy T, Kudelka AP, et al. Phase II study of irinotecan in prior chemotherapy-treated squamous cell carcinoma of the cervix. J Clin Oncol. 1997;15(2):625–631.
- Wagenaar HC, Pecorelli S, Mangioni C, et al. Phase II study of mitomycin-C and cisplatin in disseminated, squamous cell carcinoma of the uterine cervix. A European Organization for Research and Treatment of Cancer (EORTC) Gynecological Cancer Group study. Eur J Cancer. 2001;37(13):1624–1628.
- Miller DS, Blessing JA, Bodurka DC, Bonebrake AJ, Schorge JO; Gynecologic Oncology Group. Evaluation of pemetrexed (Alimta, LY231514) as second line chemotherapy in persistent or recurrent carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2008;110(1):65–70.
- Bookman MA, Blessing JA, Hanjani P, Herzog TJ, Andersen WA. Topotecan in squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2000;77(3):446–449.
- Muderspach LI, Blessing JA, Levenback C, Moore JL Jr. A phase II study of topotecan in patients with squamous cell carcinoma of the cervix: a gynecologic oncology group study. Gynecol Oncol. 2001;81(2):213–215.
- Muggia FM, Blessing JA, Method M, et al; Gynecologic Oncology Group study. Evaluation of vinorelbine in persistent or recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Gynecol Oncol. 2004;92(2):639– 643.



# Chronic Myeloid Leukemia

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5492 Primary Therapy for Chronic Myeloid Leukemia (CML) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Ph positive or BCR-ABL1 positive and chronic phase CML.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dasatinib

Imatinib

## Nilotinib



Omacetaxine

# Omacetaxine (Maintenance Cycles)

Ponatinib

Ind. 5492 Primary Therapy for Chronic Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Ph positive or BCR-ABL1 positive and chronic phase CML;
- Cytogenetic relapse.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bosutinib

Dasatinib

Imatinib

Nilotinib

Omacetaxine

Omacetaxine (Maintenance Cycles)

Ponatinib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 115 of 387



Ind. 5492 Primary Therapy for Chronic Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Ph positive or BCR-ABL1 positive and accelerated phase.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Bosutinib

Dasatinib

Imatinib

Nilotinib

Ponatinib

Ind. 5492 Primary Therapy for Chronic Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Ph positive or BCR-ABL1 positive and chronic phase CML; and EITHER of the following:
  - **§** Blast Crisis-lymphoid;
  - Blast Crisis-myeloid.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Ponatinib



Ind. 5492 Primary Therapy for Chronic Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Ph positive or BCR-ABL1 positive and accelerated phase;
- Resistance and/or intolerance to tyrosine-kinase inhibitor (TKI);
- Post Allogenic Hematopoitic stem cell transplantation with or without CCyR (Complete Cytogenic Response);
- Unable to tolerate tyrosine-kinase inhibitor (TKI) as initial treatment (i.e., Imatinib, Nilotinib, Dasatinib, Bosutinib, Ponatinib).

ASSOCIATED CHEMOTHERAPY REGIMENS

Omacetaxine

## Omacetaxine (Maintenance Cycles)

- Ind. 5492 Primary Therapy for Chronic Myeloid Leukemia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates Ph positive or BCR-ABL1 positive and chronic phase CML and EITHER of the following:
  - Post Allogenic Hematopoitic stem cell transplantation with or without CCyR (Complete Cytogenic Response)
  - Unable to tolerate tyrosine-kinase inhibitor (TKI) as initial treatment (i.e., Imatinib, Nilotinib, Dasatinib, Bosutinib, Ponatinib)

ASSOCIATED CHEMOTHERAPY REGIMENS

Interferon alfa-2b



PEGinterferon alfa-2a/2b



#### REFERENCES

- Kantarjian HM, Shah NP, Hochhaus A, et al. Dasatinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med. 2010;28:398–404.
- Kantarjian HM, Shah NP, Cortes JE, et al. Dasatinib or imatinib in newly diagnosed chronic-phase chronic myeloid leukemia: 2-year follow-up from a randomized phase 3 trial (DASISION). Blood. 2012;119:1123–1129.
- Hochhaus A, Kim D-W, Shah NP, et al. Four-year (yr) follow-up of patients (pts) with newly diagnosed chronic myeloid leukemia in chronic phase (CML-CP) receiving dasatinib or imatinib: efficacy based on early response [abstract]. Blood. 2013;122:Abstract 653.
- Larson RA, Hochhaus A, Hughes TP, et al. Nilotinib vs imatinib in patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase: ENESTnd 3-year follow-up. Leukemia. 2012;26:2197– 2203.
- Hughes TP, Saglio G, Kantarjian HM, et al. Early molecular response predicts outcomes in patients with chronic myeloid leukemia in chronic phase treated with frontline nilotinib or imatinib. Blood. 2014;123:1353–1360.
- O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med. 2003;348:994–1004.
- Saglio G, Kim DW, Issaragrisil S, et al. Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. N Engl J Med. 2010;362:2251–2259.
- Cortes JE, Jones D, O'Brien S, et al. Results of dasatinib therapy in patients with early chronic-phase chronic myeloid leukemia. J Clin Oncol. 2010;28:398–404.
- Hanfstein B, Muller MC, Hehlmann R, et al. Early molecular and cytogenetic response is predictive for long-term progression- free and overall survival in chronic myeloid leukemia (CML). Leukemia. 2012;26:2096–2102.
- Jabbour E, Kantarjian HM, Saglio G, et al. Early response with dasatinib or imatinib in chronic myeloid leukemia: 3-year follow- up from a randomized phase 3 trial (DASISION). Blood. 2014;123:494–500.
- Yeung DT, Osborn MP, White DL, et al. Early switch to nilotinib does not overcome the adverse outcome for CML patients failing to achieve early molecular response on imatinib, despite excellent overall outcomes in the TIDEL II trial [abstract]. Blood. 2012;120:Abstract 3771.
- Kim DD, Lee H, Kamel-Reid S, Lipton JH. BCR-ABL1 transcript at 3 months predicts long-term outcomes following second generation tyrosine kinase inhibitor therapy in the patients with chronic myeloid leukaemia in chronic phase who failed imatinib. Br J Haematol. 2013;160:630–639.
- Falchi L, Kantarjian HM, Wang X, et al. Significance of deeper molecular responses in patients with chronic myeloid leukemia in early chronic phase treated with tyrosine kinase inhibitors. Am J Hematol. 2013;88:1024–1029.
- Talpaz M, Silver RT, Druker BJ, et al. Imatinib induces durable hematologic and cytogenetic responses in patients with accelerated phase chronic myeloid leukemia: results of a phase 2 study. Blood. 2002;99:1928–1937.
- Kantarjian HM, Cortes J, O'Brien S, et al. Imatinib mesylate (STI571) therapy for Philadelphia chromosome-positive chronic myelogenous leukemia in blast phase. Blood. 2002;99:3547–3553.
- Kantarjian HM, O'Brien S, Cortes JE, et al. Treatment of Philadelphia chromosome-positive, accelerated-phase chronic myelogenous leukemia with imatinib mesylate. Clin Cancer Res. 2002;8:2167–2176.
- Kantarjian HM, Cortes J, O'Brien S, et al. Imatinib mesylate (STI571) therapy for Philadelphia chromosome-positive chronic myelogenous leukemia in blast phase. Blood. 2002;99:3547–3553.



- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Chronic Myeloid Leukemia. Version 2.2017. 19 Jan 2017. Please refer to the NCCN website for additional information, available at: https:// www.nccn.org/professionals/physician\_gls/pdf/ cml.pdf.
- Kantarjian HM, O'Brien S, Cortes JE, et al. Treatment of Philadelphia chromosome-positive, accelerated-phase chronic myelogenous leukemia with imatinib mesylate. Clin Cancer Res. 2002;8:2167–2176.
- Sawyers CL, Hochhaus A, Feldman E, et al. Imatinib induces hematologic and cytogenetic responses in patients with chronic myelogenous leukemia in myeloid blast crisis: results of a phase II study. Blood. 2002;99:3530–3539.
- Palandri F, Castagnetti F, Testoni N, et al. Chronic myeloid leukemia in blast crisis treated with imatinib 600 mg: outcome of the patients alive after a 6-year follow-up. Haematologica. 2008;93:1792–1796.
- Palandri F, Castagnetti F, Alimena G, et al. The long-term durability of cytogenetic responses in patients with accelerated phase chronic myeloid leukemia treated with imatinib 600 mg: the GIMEMA CML Working Party experience after a 7-year follow-up. Haematologica. 2009;94:205–212.
- Silver RT, Cortes J, Waltzman R, et al. Sustained durability of responses and improved progression-free and overall survival with imatinib treatment for accelerated phase and blast crisis chronic myeloid leukemia: long-term follow-up of the STI571 0102 and 0109 trials. Haematologica. 2009;94:743–744.
- Rea D, Etienne G, Nicolini F, et al. First-line imatinib mesylate in patients with newly diagnosed accelerated phase-chronic myeloid leukemia. Leukemia. 2012;26:2254–2259.
- Ohanian M, Kantarjian HM, Quintas-Cardama A, et al. Tyrosine kinase inhibitors as initial therapy for patients with chronic myeloid leukemia in accelerated phase. Clin Lymphoma Myeloma Leuk. 2014;14:155–162 e151.
- Apperley JF, Cortes JE, Kim D-W, et al. Dasatinib in the treatment of chronic myeloid leukemia in accelerated phase after imatinib failure: the START A trial. J Clin Oncol. 2009;27:3472–3479.
- Cortes J, Kim DW, Raffoux E, et al. Efficacy and safety of dasatinib in imatinib-resistant or –intolerant patients with chronic myeloid leukiemia in blast phase. Leukemia. 2008;22:2176–2183.
- Kantarjian H, Cortes J, Kim DW, et al. Phase 3 study of dasatinib 140 mg once daily versus 70 mg twice daily in patients with chronic myeloid leukemia in accelerated phase resistant or intolerant to imatinib: 15-month median follow-up. Blood. 2009;113:6322–6329.
- Le Coutre PD, Giles FJ, Hochhaus A, et al. Nilotinib in patients with Ph+ chronic myeloid leukemia in accelerated phase following imatinib resistance or intolerance: 24-month follow-up results. Leukemia. 2012;26:1189–1194.
- Giles FJ, Kantarjian HM, le Coutre PD, et al. Nilotinib is effective in imatinib-resistant or –intolerant patients with chronic myeloid leukemia in blastic phase. Leukemia. 2012;26: 959–962.
- Gambacorti-Passerini C, Cortes JE, Khoury HJ, et al. Safety and efficacy of bosutinib in patients with AP and BP CML and ph+ ALL following resistance/intolerance to imatinib and other TKIs: Update from study SKI-200 [abstract]. J Clin Oncol. 2010;28(15\_suppl):Abstract 6509.
- Sokal JE, Baccarani M, Russo D, Tura S. Staging and prognosis in chronic myelogenous leukemia. Semin Hematol. 1988;25:49–61.
- Nicolini FE, Khoury HJ, Akard L, et al. Omacetaxine mepesuccinate for patients with accelerated phase chronic myeloid leukemia with resistance or intolerance to two or more tyrosine kinase inhibitors. Haematologica. 2013;98:e78–79.
- Cortes JE, Kim D-W, Pinilla-Ibarz J, et al. Long-term follow-up of ponatinib efficacy and safety in the phase 2 PACE trial [abstract]. Blood. 2014;124:Abstract 3135.



# Colon Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease is present;
- Unresectable metachronous metastases;
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin (LV5FU2)

## Capecitabine



Capecitabine + Bevacizumab

CapeOx

CapeOx + Bevacizumab

FOLFIRI

FOLFIRI + Bevacizumab

FOLFIRI + Cetuximab

FOLFIRI + Panitumumab

FOLFIRI + Ramucirumab

FOLFIRI + Ziv-Aflibercept

## FOLFOXIRI

FOLFOXIRI + Bevacizumab

Irinotecan

Irinotecan + Oxaliplatin (IROX)

Leucovorin + 5-Fluorouracil (5-FU) (Roswell Park)

## mFOLFOX6

## mFOLFOX6 + Bevacizumab

mFOLFOX6 + Panitumumab

## sLV5FU2

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 122 of 387



### FOLFOX + Cetuximab

Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- KRAS mutation;
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin (LV5FU2)

Capecitabine

Capecitabine + Bevacizumab

#### CapeOx

CapeOx + Bevacizumab

## FOLFIRI

FOLFIRI + Bevacizumab

FOLFIRI + Ramucirumab

FOLFIRI + Ziv-Aflibercept

#### FOLFOXIRI

FOLFOXIRI + Bevacizumab

Irinotecan

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 123 of 387



## Irinotecan + Oxaliplatin (IROX)

Leucovorin + 5-Fluorouracil (5-FU) (Roswell Park)

#### mFOLFOX6

mFOLFOX6 + Bevacizumab

sLV5FU2

#### MFOLFOX7

Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease is present;
- Unresectable metachronous metastases;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin (LV5FU2)

Capecitabine

Capecitabine + Bevacizumab

## CapeOx

#### CapeOx + Bevacizumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 124 of 387



FOLFIRI

FOLFIRI + Bevacizumab

FOLFIRI + Cetuximab

FOLFIRI + Panitumumab

FOLFIRI + Ramucirumab

FOLFIRI + Ziv-Aflibercept

FOLFOXIRI

FOLFOXIRI + Bevacizumab

Irinotecan

Irinotecan + Oxaliplatin (IROX)

Leucovorin + 5-Fluorouracil (5-FU) (Roswell Park)

mFOLFOX6

mFOLFOX6 + Bevacizumab

mFOLFOX6 + Cetuximab

mFOLFOX6 + Panitumumab

sLV5FU2

MFOLFOX7

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 125 of 387



Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- KRAS mutation;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin (LV5FU2)

Capecitabine

Capecitabine + Bevacizumab

CapeOx

CapeOx + Bevacizumab

FOLFIRI

FOLFIRI + Bevacizumab

FOLFIRI + Ramucirumab

FOLFIRI + Ziv-Aflibercept

## FOLFOXIRI

FOLFOXIRI + Bevacizumab

#### Irinotecan

Irinotecan + Oxaliplatin (IROX)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 126 of 387



Leucovorin + 5-Fluorouracil (5-FU) (Roswell Park)

## mFOLFOX6

#### mFOLFOX6 + Bevacizumab

sLV5FU2

## MFOLFOX7

Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease;
- RAS wild-type
- Progressive disease with Fluoropyrimidine, Oxaliplatin, and Irinotecan-based chemotherapy
- Third-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Regorafenib

Trifluridine + Tipiracil

Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:



- Metastatic disease;
- KRAS mutation;
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cetuximab

Cetuximab + Irinotecan

FOLFIRI + Cetuximab

FOLFIRI + Panitumumab

mFOLFOX6 + Panitumumab

Panitumumab

FOLFOX + Cetuximab

Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease;
- KRAS mutation;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 128 of 387



Cetuximab

Cetuximab + Irinotecan

FOLFIRI + Cetuximab

FOLFIRI + Panitumumab

FOLFOX + Cetuximab

mFOLFOX6 + Panitumumab

## Panitumumab

Ind. 5428 For Advanced or Metastatic Colon Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease
- Microsatellite instability-high (MSI-H) or mismatch repair deficient
- Progressive disease with Fluoropyrimidine, Oxaliplatin, and Irinotecan-based chemotherapy
- Unresectable metachronous metastases
- Second-line treatment

ASSOCIATED CHEMOTHERAPY REGIMENS

Pembrolizumab

Nivolumab



Ind. 5429 Neoadjuvant or Adjuvant Therapy for Colon Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Node positive; and ANY of the following:
  - Stage T1;
  - Stage T2;
  - Stage 3;
  - **§** Stage T4; and ANY of the following:
    - Bowel obstruction;
    - Less than 12 lymph nodes examined;
    - Perineural invasion;
    - Localized perforation;
    - Close, indeterminate, or positive margins.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

#### Capecitabine

#### CapeOx

#### FLOX

#### Leucovorin + 5-Fluorouracil (5-FU)

#### mFOLFOX6

#### sLV5FU2

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 130 of 387



- Ind. 5429 Neoadjuvant or Adjuvant Therapy for Colon Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Node positive;
  - Stage 4.

ASSOCIATED CHEMOTHERAPY REGIMENS

Capecitabine

CapeOx

# FLOX

Leucovorin + 5-Fluorouracil (5-FU)

## sLV5FU2

- Ind. 5429 Neoadjuvant or Adjuvant Therapy for Colon Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Stage T4; and EITHER of the following:
  - Poorly differentiated histology;
  - Lymphovascular invasion (LVI).

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## FLOX

# mFOLFOX6

## Capecitabine



CapeOx

Leucovorin + 5-Fluorouracil (5-FU)

sLV5FU2

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 132 of 387



#### REFERENCES

- deGramont A, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced rectal cancer. J Clin Oncol. 2000;18:2938–2947.
- Cheeseman SL, Joel SP, Chester JD, et al. A "modified deGramont" regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. Br J Cancer. 2002;87:393–399. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12177775.
- Maindrault-Goebel F, deGramont A, Louvet C, et al. Evaluation of oxaliplatin dose intensity in bimonthly leucovorin and 48-hour 5-fluorouracil continuous infusion regimens (FOLFOX) in pretreated metastatic colorectal cancer. Ann Oncol. 2000; 11:1477–1483.
- Emmanouilides C, Sfakiotaki G, Androulakis N, et al. Front-line bevacizumab in combination with oxaliplatin, leucovorin and 5-fluorouracil (FOLFOX) in patients with metastatic colorectal cancer: a multicenter phase II study. BMC Cancer. 2007;7:91.
- Douillard JY, Siena S, Cassidy J, et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol. 2010;28: 4697–4705.
- Venook AP, Niedzwiecki D, Lenz H-J, et al. CALGB/SWOG 80405: Phase III trial of irinotecan/5-FU/leucovorin (FOLFIRI) or oxaliplatin/5-FU/leucovorin (mFOLFOX6) with bevacizumab or cetuximab for patients with KRAS wild-type untreated metastatic adenocarcinoma of the colon or rectum [abstract]. ASCO Meeting Abstracts 2014;32:LBA3.
- Saltz LB, Clarke S, Diaz-Rubio E, et al. Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study. J Clin Oncol. 2008;26:2013–2019. Available at: http://www.ncbi. nlm.nih.gov/pubmed/18421054.
- Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. Eur J Cancer. 1999;35(9): 1343–1347.
- Fuchs CS, Marshall J, Mitchell E, et al. Randomized, controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C Study. J Clin Oncol. 2007;25: 4779–4786. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17947725.
- Cunningham D, Humblet Y, Siena 5, et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecanrefractory metastatic colorectal cancer. N Engl J Med. 2004;351:337–345.
- Martin-Martorell P, Rosellô S, Rodriguez-Braun E, et al. Biweekly cetuximab and irinotecan in advanced colorectal cancer patients progressing after at least one previous line of chemotherapy: results of a phase II single institution trial. Br J Cancer. 2008;99:455–458.
- Peeters M, Price TJ, Cervantes A, et al. Randomized phase III study of panitumumab with fluorouracil, leucovorin, and irinotecan (FOLFIRI) compared with FOLFIRI alone as second-line treatment in patients with metastatic colorectal cancer. J Gun Oncol. 2010;28:4706–4713. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20921462.
- Van Cutsem E, Tabernero J, Lakomy R, et al. Addition of Aflibercept to Fluorouracil, Leucovorin, and Irinotecan Improves Survival in a Phase III Randomized Trial in Patients With Metastatic Colorectal Cancer Previously Treated With an Oxaliplatin- Based Regimen. J Clin Oncol. 2012;30:3499–3506. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22949147.



- Tabernero J, Yoshino T, Cohn AL, et al. Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): a randomized, double-blind, multicentre, phase 3 study. Lancet Oncol. 2015;16:499–508.
- Van Cutsem E, Twelves C, Cassidy J, et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study. J Clin Oncol. 2001;19:4097–4106.
- Wolmark N. Rockette H, Fisher B, et al. The benefit of leucovorin-modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer: results from National Surgical Adjuvant Breast and Bowel Protocol C-03. J Clin Oncol. 1993;11: 1879–1887.
- Jäger E, Heike M, Bernhard H, et al. Weekly high-dose leucovorin versus low-dose leucovorin combined with fluorouracil in advanced colorectal cancer: results of a randomized multicenter trial. J Clin Oncol. 1996;14:2274–2279.
- Douillard JY, Cunningham D, Roth AD, et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomized trial. The Lancet. 2000;355:1041–1047.
- Haller DG, Rothenberg ML, Wong AO, et al. Oxaliplatin plus irinotecan compared with irinotecan alone as second-line treatment after single agent fluoropyrimidine therapy for metastatic colorectal carcinoma. J Clin Oncol. 2008;26:4544– 4550.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colon Cancer. Version 1.2017. 23 Nov 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/colon.pdf.
- Falcone A, Ricci S, Brunetti I, et al. Phase III trial of infusional fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI) compared with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) as first-line treatment for metastatic colorectal cancer: The Gruppo Oncologico Nord Ovest. J Clin Oncol. 2007; 25(13):1670–1676.
- Loupakis F, Cremolini C, Masi G, et al. FOLFOXIRI plus bevacizumab (bev) versus FOLFIRI plus bev as first-line treatment of metastatic colorectal cancer (MCRC): results of the phase III randomized TRIBE trial. J Clin Oncol. 2013;31(Suppl 4) Abstract 336.
- Cunningham D, Pyrhonen S, James R, et al. Randomized trial of irinotecan plus supportive care versus supportive care alone after fluorouracil failure for patients with metastatic colorectal cancer. The Lancet. 1998;352:1413–1418.
- Fuchs CS, Moore MR, Harker G, et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. J Clin Oncol. 2003;21:807–814.
- Van Cutsem E, Tejpar S, Vanbeckevoort D, et al. Intrapatient Cetuximab Dose Escalation in Metastatic Colorectal Cancer According to the Grade of Early Skin Reactions: The Randomized EVEREST Study. J Clin Oncol. 2012;30:2861–2868. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22753904.
- Van Custem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. J Clin Oncol. 2007;25:1658–1664.
- Grothey A, Van Cutsem E, Sobrero A, et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer
   (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial. Lancet. 2013;381:303–312.
   Available at: http://www.ncbi.nlm.nih.gov/pubmed/23177514.
- Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med. 2004;350:2343–51.



- Andre T, Boni C, Navarro M, et al. Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trail. J Clin Oncol. 2009;27:3109–16. Epub 2009 May 18.
  Kuebler JP, Wieand HS, O'Connell MJ, et al. Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. J Clin Oncol. 2007;25:2198–2204.
- Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. N Engl J Med. 2005; 352(26):2696–704.
- Tournigand C, André T, Bonnetain F, et al. Adjuvant therapy with fluorouracil and oxaliplatin in stage II and elderly (between ages 70 and 75 years) with colon cancer: a subgroup analyses of the Multicenter International Study of oxaliplatin, fluorouracil, and leucovorin in the adjuvant treatment of colon cancer trial. J Clin Oncol. 2012;published online ahead of print on August 20, 2012.
- Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med. 2004;350:2343–2351.
- Cheeseman SL, Joel SP, Chester JD, et al. A "modified deGramont" regimen of fluorouracil, alone and with oxaliplatin, for
   advanced colorectal cancer. Br J Cancer. 2002;87:393–399. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12177775.
- Maindrault-Goebel F, deGramont A, Louvet C, et al. Evaluation of oxaliplatin dose intensity in bimonthly leucovorin and 48- hour 5-fluorouracil continuous infusion regimens (FOLFOX) in pretreated metastatic colorectal cancer. Annals of Oncology. 2000;11:1477–1483.
- Kuebler JP, Wieand HS, O'Connell MJ, et al. Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. J Clin Oncol. 2007:25: 2198–2204.
- Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. N Eng J Med. 2005; 352:2696–2704.
- Schmoll HJ, Cartwright T, Tabernero J, et al. Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: a planned safety analysis in 1,864 patients. J Clin Oncol. 2007;25:102–109.
- Hailer DG, Tabernero J, Maroun J, et al. Capecitabine Plus Oxaliplatin Compared With Fluorouracil and Folinic Acid As
   Adjuvant Therapy for Stage III Colon Cancer. J Clin Oncol. 2011;29:1465–1471. Available at: http://www.ncbi.nlm.nih.gov/
   pubmed/21383294.
- Haller DG, Catalano PJ, Macdonald JS Mayer RJ. Phase III study of fluorouracil, leucovorin and levamisole in high risk stage II and III colon cancer: final report of Intergroup 0089. J Clin Oncol. 2005:23:8671–8678.
- Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. Eur J Cancer. 1999; 35(9):1343–1347.



# **Endometrial Cancer**

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5430 Systemic Chemotherapy for Recurrent, Metastatic, or High-Risk Endometrial Carcinoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Distant metastases.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bevacizumab

Carboplatin

## Carboplatin + Docetaxel



Carboplatin + Paclitaxel

Cisplatin

Cisplatin + Doxorubicin

Cisplatin + Doxorubicin + Paclitaxel

Cisplatin + Ifosfamide + Mesna

Doxorubicin

lfosfamide

Ifosfamide + Paclitaxel + Mesna

Liposomal Doxorubicin

Paclitaxel

Temsirolimus

Topotecan

Ind. 5430 Systemic Chemotherapy for Recurrent, Metastatic, or High-Risk Endometrial Carcinoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Local/regional recurrence.

ASSOCIATED CHEMOTHERAPY REGIMENS

#### Bevacizumab



Carboplatin

Carboplatin + Docetaxel

Carboplatin + Paclitaxel

Cisplatin

Cisplatin + Doxorubicin

Cisplatin + Doxorubicin + Paclitaxel

Doxorubicin

Liposomal Doxorubicin

Paclitaxel

Temsirolimus

Topotecan

Ind. 5430 Systemic Chemotherapy for Recurrent, Metastatic, or High-Risk Endometrial Carcinoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Adjuvant therapy; and ANY of the following:
  - Stage 1B, G3;
  - **§** Stage 2, G3;
  - Stage 3A;



- Stage 3B or 3C;
- Stage 4.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin

Carboplatin + Docetaxel

Carboplatin + Paclitaxel

Cisplatin

Cisplatin + Doxorubicin

Cisplatin + Doxorubicin + Paclitaxel

Ind. 5430 Systemic Chemotherapy for Recurrent, Metastatic, or High-Risk Endometrial Carcinoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Adjuvant therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Ifosfamide + Mesna

lfosfamide

Ifosfamide + Paclitaxel + Mesna

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 139 of 387



- Ind. 5431 Systemic Hormonal Therapy for Recurrent, Metastatic, or High-Risk Endometrial Carcinoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Endometriod histology, hormone receptor positive, and low grade; and EITHER of the following:
    - S Distant metastases;
    - **§** Local/regional recurrence.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

#### Anastrazole

Medroxyprogesterone Acetate

Medroxyprogesterone Acetate + Tamoxifen

Megestrol Acetate + Tamoxifen

Tamoxifen

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 140 of 387



#### REFERENCES

- Miller D, Filiaci V, Fleming G, et al. Randomized phase III non-inferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma: a Gynecologic Oncology Group study [abstract]. Gynecol Oncol. 2012:125:771.
- Sorbe B, Andersson H, Boman K, et al. Treatment of primary advanced and recurrent endometrial carcinoma with a combination of carboplatin and paclitaxel-long-term follow-up. Int J Gynecol Cancer. 2008;18(4):803–808.
- Fleming GF, Brunetto VL, Cella D, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. J Clin Oncol. 2004;22(11):2159–2166.
- Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. Gynecol Oncol. 2009;112(3):543–552.
- Scribner DR Jr, Puls LE, Gold MA. A phase II evaluation of docetaxel and carboplatin followed by tumor volume directed pelvic plus or minus paraaortic irradiation for stage III endometrial cancer. Gynecol Oncol. 2012;125(2):388–393.
- Geller MA, Ivy JJ, Ghebre R, et al. A phase II trial of carboplatin and docetaxel followed by radiotherapy given in a "Sandwich" method for stage III, IV, and recurrent endometrial cancer. Gynecol Oncol. 2011;121(1):112–117.
- Nomura H, Aoki D, Takahashi F, et al. Randomized phase II study comparing docetaxel plus cisplatin, docetaxel plus carboplatin, and paclitaxel plus carboplatin in patients with advanced or recurrent endometrial carcinoma: a Japanese Gynecologic Oncology Group study (JGOG2041). Ann Oncol. 2011;22(3):636–642.
- Homesley HO, Filiaci V, Markman M, et al. Phase III trial of ifosfamide with or without paclitaxel in advanced uterine carcinosarcoma: a Gynecologic Oncology Group Study. J Clin Oncol. 2007:25(5):526–531.
- Wolfson AH, Brady MF, Rocereto TF, et al. A gynecologic oncology group randomized trial of whole abdominal irradiation (WAI) vs cisplatin-ifosfamide-mesna (CIM) in optimally debulked stage I-IV carcinosarcoma (CS) of the uterus. J Clin Oncol. 2006;24(18S):5001.
- Thigpen JT, Blessing JA, Lagasse LD. Phase II trial of cisplatin as first-line chemotherapy in patients with advanced or recurrent endometrial carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol. 1989;33(1):68–70.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Uterine Neoplasms. Version 1.2017. 21 Nov 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/uterine.pdf
- Van Wijk FH, Lhomme C, Bolis G, et al. Phase II study of carboplatin in patients with advanced or recurrent endometrial carcinoma: a trial of the EORTC Gynaecological Cancer Group. Eur J Cancer. 2003;39(1):78–85.
- Aapro MS, van Wijk FH, Bolis G, et al. Doxorubicin versus doxorubicin and cisplatin in endometrial carcinoma: definitive results of a randomized study (55872) by the EORTC Gynaecological Cancer Group. Ann Oncol. 2003;14(3):441–448.
- Muggia FM, Blessing JA, Sorosky J, Reid GC. Phase II trial of the pegylated liposomal doxorubicin in previously treated metastatic endometrial cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2002;20(9):2360–2364.
- Lincoln S, Blessing JA, Lee RB, Rocereto TF. Activity of paclitaxel as second-line chemotherapy in endometrial carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol. 2003;88(3):277–281.



- Wadler S, Levy DE, Lincoln ST, et al. Topotecan is an active agent in the first-line treatment of metastatic or recurrent endometrial carcinoma: Eastern Cooperative Oncology Group Study E3E93. J Clin Oncol. 2003;21(11):2110–2114.
- Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial: a Gynecologic Oncology Group study. J Clin Oncol. 2011;29(16):2259–2265.
- Oza AM, Elit L, Tsao MS, et al. Phase II study of temsirolimus in women with recurrent or metastatic endometrial cancer: a trial of the NCIC Clinical Trials Group. J Clin Oncol. 2011;29(24):3278–3285.
- Garcia AA, Blessing JA, Nolte S, Mannel RS. A phase II evaluation of weekly docetaxel in the treatment of recurrent or persistent endometrial carcinoma: a study by the Gynecologic Oncology Group. Gynecol Oncol. 2008;111(1):22–26.
- Fiorica JV, Brunetto VL, Hanjani P, et al. Phase II trial of alternating courses of megestrol acetate and tamoxifen in advanced endometrial carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol. 2004;92(1):10–14.
- MF, Homesley HD, Soper JT, Bell J. Tamoxifen in the treatment of advanced or recurrent endometrial carcinoma: a Gynecologic Oncology Group study. J Clin Oncol. 2001;19(2):364–367.



# Esophageal Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5532 Preoperative Chemoradiation for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Neoadjuvant or Adjuvant therapy; and EITHER of the following:
  - Squamous cell carcinoma with the primary tumor located in the cervical esophagus;
  - Adenocarcinoma with the primary tumor located in the non-cervical esophagus.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin + Oxaliplatin (FOLFOX)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 143 of 387



Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Capecitabine

Irinotecan + Cisplatin

Oxaliplatin + 5-Fluorouracil (5-FU)

Oxaliplatin + Capecitabine

Paclitaxel + 5-Fluorouracil (5-FU)

Paclitaxel + Capecitabine

Paclitaxel + Carboplatin

Ind. 5532 Preoperative Chemoradiation for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Squamous cell carcinoma; and EITHER of the following:

- § Unresectable locally advanced or metastatic disease;
- S Neoadjuvant or Adjuvant therapy for a primary tumor located in the cervical esophagus.

ASSOCIATED CHEMOTHERAPY REGIMENS

Irinotecan + Cisplatin

Paclitaxel + 5-Fluorouracil (5-FU)

Paclitaxel + Capecitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 144 of 387



- Ind. 5532 Preoperative Chemoradiation for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Unresectable locally advanced or metastatic adenocarcinoma;
  - Neoadjuvant or Adjuvant therapy for a primary tumor located in the cervical esophagus.

Irinotecan + Cisplatin

Paclitaxel + 5-Fluorouracil (5-FU)

Paclitaxel + Capecitabine

- Ind. 5532 Preoperative Chemoradiation for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:
  - Neoadjuvant or Adjuvant therapy for the treatment of Adenocarcinoma;
  - Location of the primary tumor is in the cervical esophagus; and EITHER of the following:
    - **§** Unresectable locally advanced or metastatic disease;
    - Son-surgical candidate;
  - Location of the primary tumor is in the non-cervical esophagus; and EITHER of the following:
    - S Unresectable locally advanced or metastatic disease;
    - **§** Non-surgical candidate.



5-Fluorouracil (5-FU) + Leucovorin + Oxaliplatin (FOLFOX)

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Capecitabine

Oxaliplatin + 5-Fluorouracil (5-FU)

Oxaliplatin + Capecitabine

Paclitaxel + Carboplatin

- Ind. 5534 Perioperative Chemoradiation (including Esophagogastric junction) for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following: Adenocarcinoma; and EITHER of the following:
  - Unresectable locally advanced or metastatic disease;
  - Adjuvant/Neoadjuvant for treatment of primary tumor is in the non-cervical esophagus therapy StageT3-4, NO/N+, MO,RO resection;

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + 5-Fluorouracil (5-FU)

Epirubicin + Cisplatin + 5-Fluorouracil (5-FU) (ECF)

Epirubicin + Oxaliplatin + 5-Fluorouracil (5-FU) (EOF)

Epirubicin + Oxaliplatin + Capecitabine (ECX)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 146 of 387



- Ind. 5534 Perioperative Chemoradiation (including Esophagogastric junction) for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Adenocarcinoma treatment with Adjuvant/Neoadjuvant therapy when the primary tumor is in the non-cervical esophagus therapy StageT3-4, NO/N+, M0,R1/R2 resection.

Epirubicin + Cisplatin + 5-Fluorouracil (5-FU) (ECF)

- Ind. 5437 Postoperative Chemoradiation for Esophageal Cancer (Adenocarcinoma or Gastroesophageal Junction Only) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Adenocarcinoma;
  - Location of the primary tumor is in the non-cervical esophagus;
  - Adjuvant/Neoadjuvant therapy; and EITHER of the following:
    - § R1/R2 resection;
    - StageT3-4, NO/N+, M0, R0 resection.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) with radiation

5-Fluorouracil (5-FU) + Leucovorin



Capecitabine

Capecitabine with radiation

Ind. 5530 Definitive Chemoradiation (Non-Surgical) for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Squamous cell carcinoma;
- Non-surgical candidate; and EITHER of the following:
  - S Location of the primary tumor is in the cervical esophagus;
  - **§** Location of the primary tumor is in the non-cervical esophagus.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin + Oxaliplatin (FOLFOX)

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Capecitabine

Docetaxel + Cisplatin

Irinotecan + Cisplatin

Oxaliplatin + 5-Fluorouracil (5-FU)

Oxaliplatin + Capecitabine

Paclitaxel + 5-Fluorouracil (5-FU)

Paclitaxel + Capecitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 148 of 387



Paclitaxel + Carboplatin

Paclitaxel + Cisplatin

Ind. 5530 Chemoradiation (Non-Surgical) for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Adenocarcinoma;
- Location of the primary tumor is in the non-cervical esophagus;
- Non-surgical candidate.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin + Oxaliplatin (FOLFOX)

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Capecitabine

Docetaxel + Cisplatin

Irinotecan + Cisplatin

Oxaliplatin + 5-Fluorouracil (5-FU)

Oxaliplatin + Capecitabine

Paclitaxel + 5-Fluorouracil (5-FU)

Paclitaxel + Capecitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 149 of 387



Paclitaxel + Carboplatin

Paclitaxel + Cisplatin

Ind. 5531 First-Line Therapy for Metastatic or Locally Advanced Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Adenocarcinoma;
- Unresectable locally advanced or metastatic disease;
- Positive HER2.

ASSOCIATED CHEMOTHERAPY REGIMENS

Trastuzumab

Trastuzumab + Cisplatin + 5-Fluorouracil (5-FU)

Trastuzumab + Cisplatin + Capecitabine

Ind. 5531 First-Line Therapy for Metastatic or Locally Advanced Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Non-surgical candidate;
- Adenocarcinoma;
- Unresectable locally advanced or metastatic disease.

ASSOCIATED CHEMOTHERAPY REGIMENS



## 5-Fluorouracil (5-FU)

## 5-Fluorouracil (5-FU) + Leucovorin + Oxaliplatin (mFOLFOX6)

## Capecitabine

Capecitabine + Oxaliplatin (CapeOx)

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Capecitabine

Cisplatin + Leucovorin + 5-Fluorouracil (5-FU)

DCF

Docetaxel

Docetaxel + Cisplatin

Docetaxel + Irinotecan

ECF

ECX

EOF

EOX

Irinotecan + Leucovorin + 5-Fluorouracil (5-FU)

Leucovorin + 5-Fluorouracil (5-FU)

Modified DCF

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 151 of 387



Oxaliplatin + Leucovorin + 5-Fluorouracil (5-FU)

Paclitaxel

Paclitaxel + Carboplatin

Paclitaxel + Cisplatin

Ind. 5531 First-Line Therapy for Metastatic or Locally Advanced Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Non-surgical candidate;
- Squamous cell carcinoma;
- Unresectable locally advanced or metastatic disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU)

5-Fluorouracil (5-FU) + Leucovorin + Oxaliplatin (mFOLFOX6)

Capecitabine

Capecitabine + Oxaliplatin (CapeOx)

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Capecitabine

Cisplatin + Leucovorin + 5-Fluorouracil (5-FU)

DCF

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 152 of 387



Docetaxel

Docetaxel + Cisplatin

### Docetaxel + Irinotecan

ECF

ECX

EOF

EOX

Irinotecan + Leucovorin + 5-Fluorouracil (5-FU)

Leucovorin + 5-Fluorouracil (5-FU)

Modified DCF

Oxaliplatin + Leucovorin + 5-Fluorouracil (5-FU)

Paclitaxel

Paclitaxel + Carboplatin

Paclitaxel + Cisplatin

Trastuzumab

Trastuzumab + Cisplatin + 5-Fluorouracil (5-FU)

Trastuzumab + Cisplatin + Capecitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 153 of 387



Ind. 5533 Second-Line Therapy for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Adenocarcinoma;
- Second-line chemotherapy;
- Unresectable locally advanced or metastatic disease.

## ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel

Docetaxel + Irinotecan

Irinotecan

Irenotecan + Capecetabine

Irinotecan + Cisplatin

Irinotecan + Leucovorin + 5-Fluorouracil (5-FU) (FOLFIRI)

Mitomycin + Irintoecan

Mitomycin + Leucovorin + 5-FU

## Paclitaxel

## Ramucirumab

Ramucirumab + Paclitaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 154 of 387



Ind. 5533 Second-Line Therapy for Esophageal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Squamous cell carcinoma;
- Second-line chemotherapy;
- Unresectable locally advanced or metastatic disease.

## ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel

Docetaxel + Irinotecan

Irinotecan

Irinotecan + Cisplatin

## Irinotecan + Capecitabine

Irinotecan + Leucovorin + 5-Fluorouracil (5-FU) (FOLFIRI)

Mitomycin + Irintoecan

Mitomycin + Leucovorin + 5-FU

Paclitaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 155 of 387



### REFERENCES

- van Hagen P, Hulshof MC, van Lanschot JJ, et al; CROSS Group. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med. 2012;366:2074-2084.
- Tepper J, Krasna MJ, Niedzwiecki D, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. J Clin Oncol. 2008;26:1086–1092.
- Bedenne L, Michel P, Bouché O, et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. J Clin Oncol. 2007;25:1160–1168.
- Conroy T, Galais M-P, Raoul JL, et al; UNICANCER-GI/FFCD PRODIGE Intergroup. Phase III randomized trial of definitive chemoradiotherapy (CRT) with FOLFOX or cisplatin and fluorouracil in esophageal cancer (EC): Final results of the PRODIGE 5/ACCORD 17 trial [abstract]. J Clin Oncol. 2012; 30(Suppl 18):LBA4003.
- Lee HS, Choi Y, Hur WJ, et al. Pilot study of postoperative adjuvant chemoradiation for advanced gastric cancer: adjuvant 5-FU/cisplatin and chemoradiation with capecitabine. World J Gastroenterol. 2006;12:603–607.
- Khushalani NI, Leichman CG, Proulx G, et al. Oxaliplatin in combination with protracted-infusion fluorouracil and radiation: report of a clinical trial for patients with esophageal cancer. J Clin Oncol. 2002;20:2844–2850.
- Javle MM, Yang G, Nwogu CE, et al. Capecitabine, oxaliplatin and radiotherapy: a phase 1B neoadjuvant study for esophageal cancer with gene expression analysis. Cancer Invest. 2009;27:193–200
- Cunningham D, Allum WH, Stenning SP, et al. MAGIC Trial Participants. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med. 2006;355:11–20.
- Sumpter K, Harper-Wynne C, et al. Report of two protocol planned interim analyses in a randomised multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophagogastric cancer receiving ECF. Br J Cancer. 2005;92:1976–1983.
- Sharma R, Yang GY, Nava HR, et al. A single institution experience with neoadjuvant chemoradiation (CRT) with irinotecan (I) and cisplatin (C) in locally advanced esophageal carcinoma (LAEC). J Clin Oncol. 2009;27 (suppl 15): Abstract e15619.
- Ajani JA, Winter K, Okawara GS, et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. J Clin Oncol. 2006;24:3953–3958.
- Hihara J, Yoshida K, Hamai Y, et al. Phase I study of docetaxel (TXT) and 5-fluorouracil (5-FU) with concurrent radiotherapy in patients with advanced esophageal cancer. Anticancer Res. 2007;27:2597–2603.
- Minsky BD, Pajak TF, Ginsberg RJ, et al. INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combinedmodality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy. J Clin Oncol. 2002;20:1167– 1174.
- Conroy T, Galais P, Raoul JL, et al. Phase III randomized trial of definitive chemoradiotherapy (CRT) with FOLFOX or cisplatin and fluorouracil in esophageal cancer (EC): Final results of the PRODIGE 5/ACCORD 17 trial. J Clin Oncol. 30, 2012 (suppl: abstr LBA4003).
- Urba SG, Orringer MB, Ianettonni M, et al. Concurrent cisplatin, paclitaxel, and radiotherapy as preoperative treatment for patients with locoregional esophageal carcinoma. Cancer. 2003;98:2177–2183.
- Li QQ, Liu MZ, Hu YH, et al. Definitive concomitant chemoradiotherapy with docetaxel and cisplatin in squamous esophageal carcinoma. Dis Esophagus. 2010;23:253–259.



- Day FL, Leong T, Ngan S, et al. Phase I trial of docetaxel, cisplatin, and concurrent radical radiotherapy in locally advanced esophageal cancer. Br J Cancer. 2011;104:265–271.
- Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med. 2001;345:725–730.
- Jansen EP, Boot H, Saunders MP, et al. A phase I-II study of postoperative capecitabine-based chemoradiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys. 2007;69:1424–1428.
- Chua YJ, Barbachano Y, Cunningham D, et al. Neoadjuvant capecitabine and oxaliplatin before chemoradiotherapy and total mesorectal excision in MRI-defined poor-risk rectal cancer: a phase 2 trial. Lancet Oncol. 2010;11:241–248.
- André T, Quinaux E, Louvet C, et al. Phase III study comparing a semimonthly with a monthly regimen of fluorouracil and leucovorin as adjuvant treatment for stage II and III colon cancer patients: final results of GERCOR C96.1. J Clin Oncol. 2007;25:3732–3738.
- Leong T, Joon DL, Willis D, et al. Adjuvant chemoradiation for gastric cancer using epirubicin, cisplatin, and 5-fluorouracil before and after three-dimensional conformal radiotherapy with concurrent infusional 5-fluorouracil: a multicenter study of the Trans-Tasman Radiation Oncology Group. Int J Radiat. Oncol Biol Phys. 2011;79:690–695.
- Bang YJ, Van Cutsem E, Feyereislova A, et al; ToGA Trial Investigators. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet. 2010; 376(9742):687–697.
- Van Cutsem E, Moiseyenko VM, Tjulandin S, et al. V325 Study Group. Phase III study of docetaxel and cisplatin plus fluoro- uracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group. J Clin Oncol. 2006;24:4991–4997.
- Shah MA, Shibata S, Stoller RG, et al; MSKCC Gastric Cancer Consortium. Random assignment multicenter phase II study
   of modified docetaxel, cisplatin, fluorouracil (mDCF) versus DCF with growth factor support (GCSF) in metastatic
   gastroesophageal adenocarcinoma (GE). J Clin Oncol. 2010;28 (Suppl 15):4010.
- Ozal G, Dogan M, Akbulut H, et al., The safety and efficacy of modified-dose docetaxel, cisplatin, and 5-fluorouracil (mDCF) combination in the front-line treatment of advanced gastric cancer [abstract 113]. Presented at the 2010 Gastrointestinal Cancers Symposium.
- Roth AD, Fazio N, Stupp R, et al; Swiss Group for Clinical Cancer Research. Docetaxel, cisplatin, and fluorouracil; docetaxel and cisplatin; and epirubicin, cisplatin, and fluorouracil as systemic treatment for advanced gastric carcinoma: a randomized phase II trial of the Swiss Group for Clinical Cancer Research. J Clin Oncol. 2007;25:3217–3223.
- Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol. 2008;26:1435–1442.
- Shankaran V, Mulcahy MF, Hochster HS, et al. Docetaxel, oxaliplatin and 5-fluorouracil for the treatment of metastatic or unresectable gastric or gastroesophageal junction (GEJ) adenocarcinomas: preliminary results of a phase II study [abstract]. Presented at the Gastrointestinal Cancers Symposium 2009;Abstract 47.
- Elkerm YM, Elsaid A, Al-Batran S, et al. Final results of a phase II trial of docetaxel-carboplatin-FU in locally advanced gastric carcinoma [abstract]. Presented at the 2008 Gastrointestinal Cancers Symposium. Abstract 38.



- Ross P, Nicolson M, Cunningham D, et al. Prospective randomized trial comparing mitomycin, cisplatin, and protracted venous-infusion fluorouracil (PVI 5-FU) With epirubicin, cisplatin, and PVI 5-FU in advanced esophagogastric cancer. J Clin Oncol. 2002;20:1996–2004.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Esophageal and Esophagogastric Junction Cancers. Version 1.2017. 21 March 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/esophageal.pdf
- Cunningham D, Starling N, Rao S, et al. Capecitabine and oxaliplatin for advanced esophagogastric cancer. N Engl J Med. 2008;358:36–46.
- Lorenzen S, Brucher B, Zimmermann F, et al. Neoadjuvant continuous infusion of weekly 5-fluorouracil and escalatingdoses of oxaliplatin plus concurrent radiation in locally advanced oesophageal squamous cell carcinoma: results of a phase I/II trial. Br J Cancer. 2008;99:1020–1026.
- Bouché O, Raoul JL, Bonnetain F, et al; Fédération Francophone de Cancérologie Digestive Group. Randomized multicenter phase II trial of a biweekly regimen of fluorouracil and leucovorin (LV5FU2), LV5FU2 plus cisplatin, or LV5FU2 plus irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study—FFCD 9803. J Clin Oncol. 2004;22:4319–4328.
- Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III non- inferiority trial. Ann Oncol. 2009;20:666–673.Enzinger PC, Burtness B, Hollis D, et al. CALGB 80403/ECOG 1206: A randomized phase II study of three standard chemotherapy regimens (ECF, IC, FOLFOX) plus cetuximab in metastatic esophageal and GE junction cancer [abstract 4006]. J Clin Oncol. 2010; 28 (suppl 15):4007.
- Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine-oxaliplatin in advanced gastric cancer. Eur J Cancer. 2012;48:518–526.
- Dank M, Zaluski J, Barone C, et al. Randomized phase III study comparing irinotecan combined with 5-fluorouracil and folinic acid to cisplatin combined with 5-fluorouracil in chemotherapy naive patients with advanced adenocarcinoma of the stomach or esophagogastric junction. Ann Oncol. 2008;19:1450–1457.
- André T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. GERCOR. Eur J Cancer. 1999;35:1343–1347.
- Wolff K, Wein A, Reulbach U, et al. Weekly high-dose 5-fluorouracil as a 24-h infusion and sodium folinic acid (AIO regimen) plus irinotecan in patients with locally advanced nonresectable and metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus: a phase II trial. Anticancer Drugs. 2009;20:165–173.
- Ilson DH, Forastiere A, Arquette M, et al. A phase II trial of paclitaxel and cisplatin in patients with advanced carcinoma of the esophagus. Cancer J. 2000;6:316–323.
- Petrasch S, Welt A, Reinacher A, et al. Chemotherapy with cisplatin and paclitaxel in patients with locally advanced, recurrent or metastatic oesophageal cancer. Br J Cancer. 1998;78:511–514.
- Gadgeel SM, Shields AF, Heilbrun LK, et al. Phase II study of paclitaxel and carboplatin in patients with advanced gastric cancer. Am J Clin Oncol. 2003;26:37–41.
- Ajani JA, Fodor MB, Tjulandin SA, et al. Phase II multi-institutional randomized trial of docetaxel plus cisplatin with or without fluorouracil in patients with untreated, advanced gastric, or gastroesophageal adenocarcinoma. J Clin Oncol. 2005;23:5660–5667.



- Kim JY, Do YR, Park KU, et al. A multi-center phase II study of docetaxel plus cisplatin as first-line therapy in patients with metastatic squamous cell esophageal cancer. Cancer Chemother Pharmacol. 2010;66:31–36.
- Burtness B, Gibson M, Egleston B, et al. Phase II trial of docetaxel-irinotecan combination in advanced esophageal cancer. Ann Oncol. 2009;20:1242–1248.
- Ohtsu A, Shimada Y, Shirao K, et al. Randomized phase III trial of fluorouracil alone versus fluorouracil plus cisplatin versus uracil and tegafur plus mitomycin in patients with unresectable, advanced gastric cancer: The Japan Clinical Oncology Group Study (JCOG9205). J Clin Oncol. 2003;21:54–59.
- Hong YS, Song SY, Lee SI, et al. A phase II trial of capecitabine in previously untreated patients with advanced and/or metastatic gastric cancer. Ann Oncol. 2004;15:1344–1347.
- Albertsson M, Johansson B, Friesland S, et al. Phase II studies on docetaxel alone every third week, or weekly in combination with gemcitabine in patients with primary locally advanced, metastatic, or recurrent esophageal cancer. Med Oncol. 2007;24(4):407–412.
- Ajani JA, Ilson DH, Daugherty K, et al. Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophagus. J Natl Cancer Inst. 1994;86:1086–1091.
- Ilson DH, Wadleigh RG, Leichman LP, et al. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer. Ann Oncol. 2007;18:898–902.
- Wilke H, Muro K, Van Cutsem E, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-esophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. Lancet Oncol. 2014;1224–1235.
- Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastroesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2014;383:31–39.
- Ueda S, Hironaka S, Yasui H, et al; West Japan Oncology Group. Randomized phase III study of irinotecan (CPT-11) versus weekly paclitaxel (wPTX) for advanced gastric cancer (AGC) refractory to combination chemotherapy (CT) of fluoropyrimidine plus platinum (FP): WJOG4007 trial. J Clin Oncol. 2012;30:15s (suppl; abstr 4002).
- Thuss-Patience PC, Kretzschmar A, Deist T, et al. Irinotecan versus best supportive care (BSC) as second-line therapy in gastric cancer: A randomized phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO). J Clin Oncol. 2009;27:15s (suppl; abstr 4540).
- Fuchs CS, Moore MR, Harker G, et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. J Clin Oncol. 2003;21:807–814.
- Ilson DH. Phase II trial of weekly irinotecan/cisplatin in advanced esophageal cancer. Oncology (Williston Park).
   2004;18(14 Suppl 14):22–25.
- Leary A, Assersohn L, Cunningham D, et al. A phase II trial evaluating capecitabine and irinotecan as second line treatment in patients with oesophago-gastric cancer who have progressed on, or within 3 months of platinum-based chemotherapy. Cancer Chemother Pharmacol. 2009;64:455–462.
- Di Lauro L, Fattoruso SI, Giacinti L, et al. Second-line chemotherapy with FOLFIRI in patients with metastatic gastric cancer (MGC) not previously treated with fluoropyrimidines. J Clin Oncol. 2009;27:15s (suppl; abstr 4549).



- Lustberg MB, Bekaii-Saab T, Young D, et al. Phase II randomized study of two regimens of sequentially administered mitomycin C and irinotecan in patients with unresectable esophageal and gastroesophageal adenocarcinoma. J Thorac Oncol. 2010;5:713–718.
- Giuliani F, Molica S, Maiello E, et al. Irinotecan (CPT-11) and mitomycin-C (MMC) as second-line therapy in advanced gastric cancer: a phase II study of the Gruppo Oncologico dell' Italia Meridionale (prot. 2106). Am J Clin Oncol. 2005;28:581–585.
- Bamias A, Papamichael D, Syrigos K, et al. Phase II study of irinotecan and mitomycin C in 5-fluorouracil-pretreated patients with advanced colorectal and gastric cancer. J Chemother. 2003;15:275–281.
- Hofheinz RD, Hartung G, Samel S, et al. High-dose 5-fluorouracil/folinic acid in combination with three-weekly mitomycin C in the treatment of advanced gastric cancer. A phase II study. Onkologie. 2002;25:255–260.



# Gastric Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5442 Preoperative Chemoradiation for Gastric Cancer (Esophagogastric Junction and Gastric Cardia) may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Stage T2 or higher, any N;
  - Tumor is potentially resectable;

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin + Oxaliplatin (FOLFOX)

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Capecitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 161 of 387



Oxaliplatin + 5-Fluorouracil (5-FU)

Oxaliplatin + Capecitabine

Paclitaxel + 5-Fluorouracil (5-FU)

Paclitaxel + Capecitabine

Paclitaxel + Carboplatin

Ind. 5443 Perioperative Chemoradiation for Gastric Cancer (Esophagogastric Junction and Gastric Cardia) may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Stage T2 or higher, any N; and EITHER of the following

• Tumor is potentially resectable;

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Cisplatin

Epirubicin + Cisplatin + 5-Fluorouracil (5-FU) (ECF)

Epirubicin + Cisplatin + Capecitabine (ECX)

Epirubicin + Oxaliplatin + 5-Fluorouracil (5-FU) (EOF)

Epirubicin + Oxaliplatin + Capecitabine (EOX)

Oxaliplatin + Leucovorin +5FU



Capecitabine + Oxaliplatin

Ind. 5444 Postoperative Chemoradiation for Gastric Cancer (Including Esophagogastric Junction) may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Stage T3 or T4 or node positive;
- Stage T1s or T1 with a margin positive resection.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU)

5-Fluorouracil (5-FU) + Leucovorin

Capecitabine

Capecitabine + Oxaliplatin

Capecitabine + Cisplatin

Ind. 5534 First-Line Therapy for Metastatic or Locally Advanced Gastric Cancer may be reasonable and appropriate when the patient's medical record demonstrates the following:

• First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Cisplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 163 of 387



5-Fluorouracil (5-FU) + Cisplatin + Leucovorin

Capecitabine + Cisplatin

Capecitabine + Oxaliplatin (CapeOx)

Docetaxel + Carboplatin + 5-Fluorouracil (5-FU) (Modified DCF)

Docetaxel + Cisplatin + Leucovorin + 5-Fluorouracil (5-FU) (Modified DCF)

Docetaxel + Oxaliplatin + 5-Fluorouracil (5-FU) (Modified DCF)

Epirubicin + Cisplatin + 5-Fluorouracil (5-FU) (ECF)

Epirubicin + Cisplatin + Capecitabine (ECX)

Epirubicin + Oxaliplatin + 5-Fluorouracil (5-FU) (EOF)

Epirubicin + Oxaliplatin + Capecitabine (EOX)

Oxaliplatin + Leucovorin + 5-Fluorouracil (5-FU) (mFOLFOX6)

Trastuzumab + Cisplatin + 5-Fluorouracil (5-FU)

Trastuzumab + Cisplatin + Capecitabine

Ind. 5534 First-Line Therapy for Metastatic or Locally Advanced Gastric Cancer may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Evidence of measurable disease on imaging.

ASSOCIATED CHEMOTHERAPY REGIMENS



5-Fluorouracil (5-FU) + Leucovorin

Capecitabine

Docetaxel

Docetaxel + Cisplatin

Irinotecan + Leucovorin + 5-Fluorouracil (5-FU)

Paclitaxel

Paclitaxel + Carboplatin

Paclitaxel + Cisplatin

Ind. 5535 Second-Line Therapy for Metastatic or Locally Advanced Gastric Cancer may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Evidence of measurable disease on imaging.

ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel

Irinotecan

Paclitaxel

Ramucirumab

Ramucirumab + Paclitaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 165 of 387



Ind. 5535 Second-Line Therapy for Metastatic or Locally Advanced Gastric Cancer may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Evidence of measurable disease on imaging;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel + Irinotecan

Irinotecan + Cisplatin

Irinotecan + Leucovorin + 5-Fluorouracil (5-FU)

Irinotecan + Capecitabine

Ind. 5535 Second-Line Therapy Metastatic or Locally Advanced Gastric Cancer may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Progressive disease after two (2) or more prior lines of therapy includeing fluorophyrimidine and platinum based chemotherapy; and EITHER of the following:
  - Second or Third line therapy with deficient mismatched repair (dMMR) or microsatellite instability is high (MSI-H);
  - S Third line therapy with PD-L1 expression, combined positive score (CPS) greater than or equal to 1%.



## Pembrolizumab

### REFERENCES

- van Hagen P, Hulshof MC, van Lanschot JJ, et al. CROSS Group. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med. 2012;366:2074–2084.
- Tepper J, Krasna MJ, Niedzwiecki D, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. J Clin Oncol. 2008;26:1086–1092.
- Bedenne L, Michel P, Bouché O, et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. J Clin Oncol. 2007;25: 1160–1168.
- Conroy T, Galais M-P, Raoul JL, et al. UNICANCER-GI/FFCD PRODIGE Intergroup. Phase III randomized trial of definitive chemoradiotherapy (CRT) with FOLFOX or cisplatin and fluorouracil in esophageal cancer (EC): Final results of the PRODIGE 5/ACCORD 17 trial [abstract]. J Clin Oncol. 2012;30 (Suppl 18): LBA4003.
- Khushalani NI, Leichman CG, Proulx G, et al. Oxaliplatin in combination with protracted-infusion fluorouracil and radiation: report of a clinical trial for patients with esophageal cancer. J Clin Oncol. 2002;20:2844–2850.
- Lee SS, Kim SB, Park SI, et al. Capecitabine and cisplatin chemotherapy (XP) alone or sequentially combined chemoradiotherapy containing XP regiment in patients with three different settings of stage IV esophageal cancer. Jpn J Clin Oncol. 2007;37:829–835.
- Javle MM, Yang G, Nwogu CE, et al. Capecitabine, oxaliplatin and radiotherapy: a phase 1B neoadjuvant study for esophageal cancer with gene expression analysis. Cancer Invest. 2009;27:193–200.
- Sharma R, Yang GY, Nwogu CE at al. A single institution experience with neoadjuvant chemoradiation (CRT) with irinotecan (i) and cisplatin (C) in locally advanced esophageal carcinoma (LAEC) [abstract]. J Clin Oncol. 2009;27(Suppl 15): Abstract e15619.
- Ajani JA, Winter K, Okawara GS, et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. J Clin Oncol. 2006;24:3953–3958.
- Cunningham D, Allum WH, Stenning SP, et al. MAGIC Trial Participants. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med. 2006;355:11–20.
- Sumpter K, Harper-Wynne C, et al. Report of two protocol planned interim analyses in a randomised multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophagogastric cancer receiving ECF. Br J Cancer. 2005;92:1976–1983.
- Ychou M, Boige V, Pignon JP, et al. Perioperative chemotherapy compared with surgery alone for resectable gastroesophageal adenocarcinoma: an FNCLCC and FFCD multicenter phase III trial. J Clin Oncol. 2011;29:1715–1721.



- Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med. 2001;345:725–730.
- Jansen EP, Boot H, Saunders MP, et al. A phase I-II study of postoperative capecitabine-based chemoradiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys. 2007;69:1424–1428.
- André T, Quinaux E, Louvet C, et al. Phase III study comparing a semimonthly with a monthly regimen of fluorouracil and leucovorin as adjuvant treatment for stage II and III colon cancer patients: final results of GERCOR C96.1. J Clin Oncol. 2007;25:3732–3738.
- Leong T, Joon DL, Willis D, et al. Adjuvant chemoradiation for gastric cancer using epirubicin, cisplatin, and 5-fluorouracil before and after three-dimensional conformal radiotherapy with concurrent infusional 5-fluorouracil: a multicenter study of the Trans-Tasman Radiation Oncology Group. Int J Radiat Oncol Biol Phys. 2011;79:690–695.
- Lee HS, Choi Y, Hur WJ, et al. Pilot study of postoperative adjuvant chemoradiation for advanced gastric cancer: adjuvant 5-FU/cisplatin and chemoradiation with capecitabine. World J Gastroenterol. 2006;12:603–607.
- Bang YJ, Kim YW, Yang HK, et al. CLASSIC trial investigators. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. Lancet. 2012;379:315-321.
- Lee J, Lim do H, Kim S, et al. Phase III trial comparing capecitabine plus cisplatin versus capecitabine plus cisplatin with concurrent capecitabine radiotherapy in completely resected gastric cancer with D2 lymph node dissection: the ARTIST trial. J Clin Oncol. 2012;30:268–273.
- Bang YJ, Van Cutsem E, Feyereislova A, et al. ToGA Trial Investigators. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet. 2010;376(9742):687–697.
- Van Cutsem E, Moiseyenko VM, Tjulandin S, et al. V325 Study Group. Phase III study of docetaxel and cisplatin plus fluorouracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group. J Clin Oncol. 2006;24:4991–4997.
- Shah MA, Shibata S, Stoller RG, et al. MSKCC Gastric Cancer Consortium. Random assignment multicenter phase II study of modified docetaxel, cisplatin, fluorouracil (mDCF) versus DCF with growth factor support (GCSF) in metastatic gastroesophageal adenocarcinoma (GE). J Clin Oncol. 2010;28 (Suppl 15): 4010.
- Shankaran V, Mulcahy MF, Hochster HS, et al. Docetaxel, oxaliplatin, and 5-fluorouracil for the treatment of metastatic or unresectable gastric or gastroesophageal junction (GEJ) adenocarcinomas: Preliminary results of a phase II study [abstract 47]. Presented at the 2009 Gastrointestinal Cancers Symposium.
- Elkerm YM, Elsaid A, Al-Batran SE, et al. Final results of a phase II trial of docetaxel-carboplatin-FU in locally advanced gastric carcinoma. Presented at the Gastrointestinal Cancers Symposium, January 25–27, 2008, Orlando, FL.
- Ross P, Nicolson M, Cunningham D, et al. Prospective randomized trial comparing mitomycin, cisplatin, and protracted venous-infusion fluorouracil (PVI 5-FU) with epirubicin, cisplatin, and PVI 5-FU in advanced esophagogastric cancer. J Clin Oncol. 2002;20:1996–2004.
- Cunningham D, Starling N, Rao S, et al. Capecitabine and oxaliplatin for advanced esophagogastric cancer. N Engl J Med. 2008;358:36–46.
- Lorenzen S, Schuster T, Porschen R, et al. Cetuximab plus cisplatin-5-fluorouracil versus cisplatin-5-fluorouracil alone in first-line metastatic squamous cell carcinoma of the esophagus: a randomized phase II study of the Arbeitsgemeinschaft Internistische Onkologie. Ann Oncol. 2009;20:1667–1673.



- Al-Batran SE, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol. 2008;26:1435–1442.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Gastric Cancer. Version 1.2017. 21 Mar 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/gastric.pdf
- Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III non-inferiority trial. Ann Oncol. 2009;20:666–673.
- Bouché O, Raoul JL, Bonnetain F, et al. Fédération Francophone de Cancérologie Digestive Group. Randomized multicenter phase II trial of a biweekly regimen of fluorouracil and leucovorin (LV5FU2), LV5FU2 plus cisplatin, or LV5FU2 plus irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study—FFCD 9803. J Clin Oncol. 2004;22:4319–4328.
- Enzinger PC, Burtness B, Hollis D, et al. CALGB 80403/ECOG 1206: A randomized phase II study of three standard chemotherapy regimens (ECF, IC, FOLFOX) plus cetuximab in metastatic esophageal and GE junction cancer [abstract 4006]. J Clin Oncol. 2010; 28 (suppl 15):4007.
- Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine-oxaliplatin in advanced gastric cancer. Eur J Cancer. 2012;48:518–526.
- Dank M, Zaluski J, Barone C, et al. Randomized phase III study comparing irinotecan combined with 5-fluorouracil and folinic acid to cisplatin combined with 5-fluorouracil in chemotherapy naive patients with advanced adenocarcinoma of the stomach or esophagogastric junction. Ann Oncol. 2008;19: 1450–1457.
- Sym SJ, Hong J, Park J, et al. A randomized phase II study of biweekly irinotecan plus 5-fluorouracil/leucovorin (mFOLFIRI) in patients with metastatic gastric adenocarcinoma refractory to or progressive after first-line chemotherapy. Cancer Chemother Pharmacol. 2013;71:481–488.
- Wolff K, Wein A, Reulbach U, et al. Weekly high-dose 5-fluorouracil as a 24-h infusion and sodium folinic acid (AIO regimen) plus irinotecan in patients with locally advanced nonresectable and metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus: a phase II trial. Anticancer Drugs. 2009;20:165–173.
- Ilson DH, Forastiere A, Arquette M, et al. A phase II trial of paclitaxel and cisplatin in patients with advanced carcinoma of the esophagus. Cancer J. 2000;6:316–323.
- Petrasch S, Welt A, Reinacher A, et al. Chemotherapy with cisplatin and paclitaxel in patients with locally advanced, recurrent or metastatic oesophageal cancer. Br J Cancer. 1998;78:511–514.
- Gadgeel SM, Shields AF, Heilbrun LK, et al. Phase II study of paclitaxel and carboplatin in patients with advanced gastric cancer. Am J Clin Oncol. 2003;26:37–41.
- Ajani JA, Fodor MB, Tjulandin SA, et al. Phase II multi-institutional randomized trial of docetaxel plus cisplatin with or without fluorouracil in patients with untreated, advanced gastric, or gastroesophageal adenocarcinoma. J Clin Oncol. 2005;23:5660–5667.
- Kim JY, Do YR, Park KU, et al. A multi-center phase II study of docetaxel plus cisplatin as first-line therapy in patients with metastatic squamous cell esophageal cancer. Cancer Chemother Pharmacol. 2010;66:31–36.
- Burtness B, Gibson M, Egleston B, et al. Phase II trial of docetaxel-irinotecan combination in advanced esophageal cancer. Ann Oncol. 2009;20:1242–1248.



- Ohtsu A, Shimada Y, Shirao K, et al. Randomized phase III trial of fluorouracil alone versus fluorouracil plus cisplatin versus uracil and tegafur plus mitomycin in patients with unresectable, advanced gastric cancer: The Japan Clinical Oncology Group Study (JCOG9205). J Clin Oncol. 2003;21:54–59.
- Hong YS, Song SY, Lee SI, et al. A phase II trial of capecitabine in previously untreated patients with advanced and/or metastatic gastric cancer. Ann Oncol. 2004;15:1344–1347.
- Albertsson M, Johansson B, Friesland S, et al. Phase II studies on docetaxel alone every third week, or weekly in combination with gemcitabine in patients with primarily locally advanced, metastatic, or recurrent esophageal cancer. Med Oncol. 2007; 24:407–412.
- Ford HE, Marshall A, Bridgewater JA, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. Lancet Oncol. 2014;15:78–86.
- Ajani JA, Ilson DH, Daugherty K, et al. Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophague. J Natl Cancer Inst. 1994;86:1086–1091.
- Ilson DH, Wadleigh RG, Leichman LP, Kelsen DP. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer.
   Ann Oncol. 2007;18:898–902.
- Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastrooesophageal junction adenocarcinoma (REGARD): an international, randomized, multicentre, placebo-controlled, phase 3 trial. Lancet. 2014;383:31–39.
- Wilke H, Van Cutsem E, Oh SC, et al. RAINBOW: A global, phase III, randomized, double-blind study of ramucirumab plus paclitaxel versus placebo plus paclitaxel in the treatment of metastatic gastroesophageal junction (GEJ) and gastric. adenocarcinoma following disease progression on first-line platinum- and fluoropyrimidine-containing combination therapy rainbow IMCL COP12-0922 (I4T-IE-JVBE). J Clin Oncol. 2014;32 (3\_suppl):Abstract LBA7.
- Hironaka S, Ueda S, Yasui H, et al. Randomized, Open-Label, Phase III Study Comparing Irinotecan With Paclitaxel in Patients With Advanced Gastric Cancer Without Severe Peritoneal Metastasis After Failure of Prior Combination Using Fluoropyrimidine Plus Platinum: WJOG 4007 Trial. J Clin Oncol. 2013;31:4438–4444.
- Thuss-Patience PC, Kretzschmar A, Bichev D, et al. Survival advantage for irinotecan versus best supportive care as second- line chemotherapy in gastric cancer—a randomized phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO). Eur J Cancer. 2011;47:2306–2314.
- Fuchs CS, Moore MR, Harker G, et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. J Clin Oncol. 2003;21:807–814.
- Ilson DH. Phase II trial of weekly irinotecan/cisplatin in advanced esophageal cancer. Oncology (Williston Park).
   2004;18:22–25.
- Leary A, Assersohn L, Cunningham D, et al. A phase II trial evaluating capecitabine and irinotecan as second line treatment in patients with oesophago-gastric cancer who have progressed on, or within 3 months of platinum-based chemotherapy. Cancer Chemother Pharmacol. 2009;64: 455–462.
- Maugeri-Sacca M, Pizzuti L, Sergi D, et al. FOLFIRI as a second-line therapy in patients with docetaxel-pretreated gastric cancer: a historic cohort. J Exp Clin Cancer Res. 2013;32:67.
- Lustberg MB, Bekali-Saab T, Young D, et al. Phase II randomized study of two regimens of sequentially administered mitomycin C and irinotecan in patients with unresectable esophageal and gastroesophageal adenocarcinoma. J Thorac Oncol. 2010;5:713–718.



- Giuliani F, Molica S, Maiello E, et al. Irinotecan (CPT-11) and mitomycin-C (MMC) as second-line therapy in advanced gastric cancer: a phase II study of the Gruppo Oncologico dell' Italia Meridonale (prot. 2106). Am J Clin Oncol. 2005; 28:581–585.
- Barnias A, Papamichael D, Syrigos K, Pavlidis N. Phase II study of irinotecan and mitomycin C in 5-fluorouracil- pretreated patients with advanced colorectal and gastric cancer. J Chemother. 2003;15:275–281.
- Hofheinz RD, Hartung G, Samel S, et al. High-dose 5-fluorouracil/folinic acid in combination with three-weekly mitomycin C in the treatment of advanced gastric cancer: A phase II study. Onkologie. 2002;25:255–260.



## Growth Factor Support

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Growth Factor Support treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens.

- Ind. 5377 White Blood Cell Support for Primary Prophylaxis per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Febrile Neutropenia (FN) is greater than or equal to 20 percent;
  - ECOG performance status is rated as 2 or less or KPS is greater than or equal to 70.

ASSOCIATED CHEMOTHERAPY REGIMENS

Filgrastim (Neupogen)

PegFilgrastim (Neulasta)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 172 of 387



- Ind. 5377 White Blood Cell Support for Primary Prophylaxis per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Febrile Neutropenia (FN) is greater than or equal to 20 percent;
  - ECOG performance status is rated as 2 or less or KPS is greater than or equal to 70.

Tbo-Filgrastim (Granix)

Filgrastim Biosimilar (Zarxio)

- Ind. 5377 White Blood Cell Support for Primary Prophylaxis per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates Febrile Neutropenia (FN) between 10 and 20 percent and ANY of the following:
  - ECOG performance status is rated as greater than 2 or KPS is less than or equal to 60;
  - Age is 65 years old or older;
  - Documented neutropenic event on a previous cycle of chemotherapy;
  - Bone marrow involvement by tumor causing neutropenia.

ASSOCIATED CHEMOTHERAPY REGIMENS

Filgrastim (Neupogen)



## PegFilgrastim (Neulasta)

Ind. 5377 White Blood Cell Support for Primary Prophylaxis per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Febrile Neutropenia (FN) is between 10 and 20 percent and ANY of the following:
  - § Age is 65 years or older;
  - S Documented neutropenic event on a previous cycle of chemotherapy;
  - Sone marrow involvement by tumor causing neutropenia
  - § ECOG performance status is rated as greater t han 2 or KPS is less than or equal to 60.

ASSOCIATED CHEMOTHERAPY REGIMENS

Tbo-Filgrastim (Granix)

Filgrastim Biosimilar (Zarxio)

Ind. 5377 White Blood Cell Support for Primary Prophylaxis per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Febrile Neutropenia (FN) is between 10 and 20 percent; and ANY of the following:
  - **§** Poor nutritional status (Albumin less than 3.5 g/dL);



- § Poor renal function or liver dysfunction (increased total bilirubin);
- S Extensive prior treatment including large radiation therapy ports;
- S Other serious comorbidities (COPD, CVD).

Filgrastim (Neupogen)

PegFilgrastim (Neulasta)

- Ind. 5377 White Blood Cell Support for Primary Prophylaxis: Nutritional Status and Prior Treatment per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Febrile Neutropenia (FN) is between 10 and 20 percent and ANY of the following:
    - **§** Poor nutritional status (Albumin less than 3.5 g/dL);
    - **§** Poor renal function or liver dysfunction (increased total bilirubin);
    - **§** Extensive prior treatment including large radiation therapy ports;
    - S Other serious comorbidities (COPD, CVD).

ASSOCIATED CHEMOTHERAPY REGIMENS

Tbo-Filgrastim (Granix)

Filgrastim Biosimilar (Zarxio)

Ind. 5377 White Blood Cell Support for Primary Prophylaxis: Chemotherapy Treatment per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:



- Intermittent dosing in selected MDS patients with no del (5q) with severe neutropenia and recurrent infection with other serious comorbidities (COPD, CVD)
- Patient is being treated with dose-dense chemotherapy regimen;
- Patient has diffuse aggressive lymphoma and to receive curative intent regimen;
- Post-initial induction or first post-remission course of chemotherapy for Acute Lymphoblastic Leukemia
- Patient who older than 55 years of age is receiving post-induction or postremission chemotherapy for treatment of Acute Myeloid Leukemia (AML).

Filgrastim (Neupogen)

PegFilgrastim (Neulasta)

- Ind. 5377 White Blood Cell Support for Primary Prophylaxis: Chemotherapy Treatment per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the ANY of the following:
  - Intermittent dosing in selected MDS patients with no del (5q) with severe neutropenia and recurrent infection with other serious comorbidities (COPD, CVD);
  - Patient is being treated with dose-dense chemotherapy regimen;
  - Patient has diffuse aggressive lymphoma and to receive curative intent regimen;
  - Post-initial induction or first post-remission course of chemotherapy for Acute Lymphoblastic Leukemia;



 Patient who is greater than 55 years of age is receiving post-induction or post-remission chemotherapy for treatment of Acute Myeloid Leukemia (AML).

ASSOCIATED CHEMOTHERAPY REGIMENS

Tbo-Filgrastim (Granix)

Filgrastim Biosimilar (Zarxio)

Ind. 5377 White Blood Cell Support for Primary Prophylaxis: Chemotherapy Treatment per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:

- Febrile Neutropenia (FN) is between 10-20 percent and ANY of the following:
  - Patient's ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70;
  - **§** Patient age is greater than or equal to 65 years old;
  - S Documented neutropenic event on a previous cycle of chemotherapy;
  - **§** Bone marrow involvement by tumor causing neutropenia;
- Febrile Neutropenia (FN) is greater than or equal to 20 percent and Patient's ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70

### ASSOCIATED CHEMOTHERAPY REGIMENS

Pegfilgrastim-jmdb (Fulphila)

Filgrastim-aafi (Nivestym) Pegfilgrastim-cbqv (Udenyca)



- Ind. 5377 White Blood Cell Support for Secondary Prophylaxis per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates an ECOG performance status is rated as 2 or less, or KPS is greater than or equal to 70 and EITHER of the following:
  - Prior episode of neutropenia was dose-limiting (dose reduction on chemotherapy compromises patient's outcome and overall or disease-free survival);
  - Documented neutropenic event on a previous cycle of chemotherapy.

Filgrastim (Neupogen)

PegFilgrastim (Neulasta)

Pegfilgrastim-jmdb (Fulphila)

Filgrastim-aafi (Nivestym)

Pegfilgrastim-cbqv (Udenyca)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 178 of 387



- Ind. 5377 White Blood Cell Support for Secondary Prophylaxis per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - ECOG performance status rated as 2 or less or KPS is greater than or equal to 70, and EITHER of the following:
    - Prior episode of neutropenia was dose-limiting (dose reduction on chemotherapy compromises patient's outcome and overall or diseasefree survival);
    - S Documented neutropenic event on a previous cycle of chemotherapy;

Tbo-Filgrastim (Granix)

Filgrastim Biosimilar (Zarxio)

Ind. 5377 White Blood Cell Support for Therapeutic Use as Adjunctive Treatment of Febrile Neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:



- Patient is febrile with single temperature greater than or equal to 38.3
   Celsius or 100.9 Fahrenheit orally; or greater than or equal to 38.0 Celsius or 100.4 Fahrenheit sustained over 1 hour;
- Absolute Neutrophil Count (ANC) is less than 500/mcL or less than 1000/mcL with predicted decline to less than or equal to 500/mcL over the next 48 hours;
- Patient has one or more of the following risk factors for infectious related complications: hypotension; sepsis syndrome or multiorgan dysfunction; severe neutropenia with Absolute Neutrophil Count (ANC) less than 100/mcL; prolonged neutropenia greater than or equal to 10 days; invasive fungal infection or other documented infection; pneumonia; development of Febrile Neutropenia (FN) as inpatient; leukemia or lymphoma; uncontrolled malignancy.
- ECOG performance status is rated as 2 or less or KPS is greater than or equal to 70.

Filgrastim (Neupogen)

PegFilgrastim (Neulasta)

Ind. 5377 White Blood Cell Support for Therapeutic Use as Adjunctive Treatment of Febrile Neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 180 of 387



- Patient is febrile with single temperature greater than or equal to 38.3
   Celsius or 100.9 Fahrenheit orally; or greater than or equal to 38.0 Celsius or 100.4 Fahrenheit sustained over 1 hour;
- Absolute Neutrophil Count (ANC) is less than 500/mcL or less than 1000/mcL with predicted decline to less than or equal to 500/mcL over the next 48 hours;
- Patient has one or more of the following risk factors for infectious related complications: hypotension; sepsis syndrome or multiorgan dysfunction; severe neutropenia with Absolute Neutrophil Count (ANC) less than 100/mcL; prolonged neutropenia greater than or equal to 10 days; invasive fungal infection or other documented infection; pneumonia; development of Febrile Neutropenia (FN) as inpatient; leukemia or lymphoma; uncontrolled malignancy;
- ECOG performance status is rated as 2 or less or KPS is greater than or equal to 70.

Tbo-Filgrastim (Granix)

Filgrastim Biosimilar (Zarxio)

- Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Patient is receiving chemotherapy;
  - Hematocrit less than 30% at initiation of therapy.



Darbepoetin Alfa (Aranesp)

Epoetin Alfa (Epogen, Procrit)

Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Severe aplastic anemia (SAA) for patients who fail to respond adequately to at least 1 prior immunosuppressive therapy.
- ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70

ASSOCIATED CHEMOTHERAPY REGIMENS

Eltrombopag Olamine (Promacta)

- Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Chronic immune (Idiopathic) thrombocytopenia (ITP) with insufficient response to corticosteroids, immunoglobulins, or splenectomy.
  - ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70



## Eltrombopag Olamine (Promacta)

Romiplostim (Nplate)

Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Patient at severe risk of thrombocytopenia; AND
- Patient's platelet count is less than the normal 150,000/microL.
- ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Oprelvekin (Neumega)

- Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Patient is receiving chemotherapy
  - Hemoglobin increased by less than 1 g/dL and remains below 10 g/dL after 4 weeks of initial Epoetin Alfa therapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Epoetin Alfa (Epogen, Procrit) - dose escalation



Epoetin alfa-epbx (Retacrit) - dose escalation

Epoetin alfa-epbx (Retacrit) - [Pediatric =5 years] - dose escalation

Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Patient is receiving chemotherapy
- Hemoglobin increased by less than 1 g/dL and remains below 10 g/dL after
   6 weeks of initial Darbepoetin Alfa therapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Darbepoetin Alfa (Aranesp) - dose escalation

Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Severe aplastic anemia (SAA) for patients who fail to respond adequately to at least 1 prior immunosuppressive therapy
- Platelet count is less than 50 x 10^9/L following at least 2 weeks of initial Eltrombopag Olamine therapy

#### ASSOCIATED CHEMOTHERAPY REGIMENS



Eltrombopag Olamine (Promacta) - dose escalation

Ind. 5377 Red Blood Cell Support for Therapeutic use as adjunctive treatment of febrile neutropenia per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Chronic immune (Idiopathic) thrombocytopenia (ITP) with insufficient response to corticosteroids, immunoglobulins, or splenectomy
- Platelet count is less than 50 x 10<sup>9</sup>/L following at least 1 week of initial Romiplostim therapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Romiplostim (Nplate) - dose escalation

Ind. 5377 Stem Cell Transplant Support per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient has Non-Hodgkin Lymphoma or Multiple Myeloma;
- Patient is undergoing mobilization of hematopoietic stem cells to the pheripheral blood for collection and subsequent autologous transplantation;
- Patient concurrently will receive Filgrastim (Neupogen) or Filgrastin biosimilar (Zarxio) or Tbo-Filgrastim (Granix).
- ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70

ASSOCIATED CHEMOTHERAPY REGIMENS

Plerixafor (Mozobil)



- Ind. 5377 Stem Cell Transplant Support per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates an ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70 and ANY of the following:
  - Patient is undergoing mobilization of hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation;
  - Myeloid reconstitution following allogenic or autologous bone marrow transplant;
  - Post-initial induction or first post-remission course of chemotherapy for Acute Lymphoblastic Leukemia;

Sargramostim (Leukine)

- Ind. 5377 Stem Cell Transplant Support per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Patient has Non-Hodgkin Lymphoma or Multiple Myeloma;
  - Patient is undergoing mobilization of hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation.
  - ECOG Performance Status is rated as 2 or less OR KPS is greater than or equal to 70

ASSOCIATED CHEMOTHERAPY REGIMENS

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 186 of 387



Filgrastim (Neupogen) + Plerixafor (Mozobil)

Filgrastim Biosimilar (Zarxio) + Plerixafor (Mozobil)

Tbo-Filgrastim (Granix) + Plerixafor (Mozobil)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 187 of 387



#### REFERENCES

- Bohlius, Julia, Christine Herbst, Marcel Reiser, Guido Schwarzer, and Andreas Engert. "Granulopoiesis-stimulating factors to prevent adverse effects in the treatment of malignant lymphoma." Protocols, 2008. doi:10.1002/14651858.cd003189.pub4.
- Dale, David C. "Colony-Stimulating Factors for the Management of Neutropenia in Cancer Patients." Drugs 62, no.
   Supplement 1 (2002): 1-15. doi:10.2165/00003495-200262001-00001.
- Farese, Ann M., Melanie V. Cohen, Barry P. Katz, Cassandra P. Smith, Allison Gibbs, Daniel M. Cohen, and Thomas J.
   MacVittie. "Filgrastim Improves Survival in Lethally Irradiated Nonhuman Primates." Radiation Research 179, no. 1 (2013): 89-100. doi:10.1667/rr3049.1.
- Fortner, Barry V., Lee Schwartzberg, Kurt Tauer, Arthur C. Houts, James Hackett, and Brad S. Stolshek. "Impact of chemotherapy-induced neutropenia on quality of life: a prospective pilot investigation." Support Care Cancer 13, no. 7 (2005): 522-528. doi:10.1007/s00520-004-0757-4.
- Hidaka, Takao, Masaki Fujimura, Masatoshi Sakai, and Shigeru Saito. "Macrophage Colony-stimulating Factor Prevents Febrile Neutropenia Induced by Chemotherapy." Japanese Journal of Cancer Research 92, no. 11 (2001): 1251-1258. doi:10.1111/j.1349-7006.2001.tb02147.x.
- Lyman, Gary H., and Nicole M. Kuderer. "Epidemiology of Febrile Neutropenia." Supportive Cancer Therapy 1, no. 1 (2003): 23-35. doi:10.3816/sct.2003.n.002.
- Motoyoshi, Kazuo. "Macrophage Colony-Stimulating Factor for Cancer Therapy." Oncology 51, no. 2 (1994): 198-204. doi:10.1159/000227334.
- Sourgens, H., and F. Lefrère. "A systematic review of available clinical evidence filgrastim compared with lenograstim." Int. Journal of Clinical Pharmacology and Therapeutics 49, no. 08 (2011): 510-518. doi:10.5414/cp201537.
- Timmer-Bonte, J., E. Adang, T. De Boo, and V. Tjan-Heijnen. "P-848 Prevention of chemotherapy-induced febrile neutropenia (FN) by the addition of granulocyte-colony stimulating factor (G-CSF) to antibiotics in small cell lung cancer (SCLC) patients at risk of FN: A prospective economic evaluation along a Dutch randomised phase III trial." Lung Cancer 49 (2005): S342-S343. doi:10.1016/s0169-5002(05)81341-8.
- Vogel, C. L. "First and Subsequent Cycle Use of Pegfilgrastim Prevents Febrile Neutropenia in Patients With Breast Cancer: A Multicenter, Double-Blind, Placebo-Controlled Phase III Study." Journal of Clinical Oncology 23, no. 6 (2005): 1178-1184. doi:10.1200/jco.2005.09.102.



## Head and Neck Cancers

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5451 Primary Systemic Therapy with Concurrent Radiotherapy for Squamous Cell Cancer in the Head and Neck region per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Locally advanced disease; and EITHER of the following:
    - S Laryngeal cancer T3-T4, N0-3;
    - Stage T4b, unresectable, or unfit for surgery.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Hydroxyurea

Carboplatin + 5-Fluorouracil (5-FU)



Cetuximab

Cisplatin

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + Paclitaxel

Paclitaxel + Carboplatin

Ind. 5452 Primary Chemotherapy with Postoperative Chemoradiation for Squamous Cell Cancer in the Head and Neck region per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Locally advanced disease; and EITHER of the following:
  - S Laryngeal cancer T3-T4, N0-3;
  - Stage T4b, unresectable, or unfit for surgery;
  - Adjuvant chemoradiation with extracapsular spread or positive margins.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin

Ind. 5453 Induction Chemotherapy / Sequential Chemotherapy for Cancer in the Head and Neck region per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:



- Squamous cell Stage T4b, unresectable, or unfit for surgery;
- Squamous cell disease which is locally advanced.

Docetaxel + Cisplatin + 5-Fluorouracil (5-FU)

Paclitaxel + Cisplatin + 5-Fluorouracil (5-FU)

- Ind. 5453 Induction Chemotherapy / Sequential Chemotherapy for Cancer in the Head and Neck region per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Nasopharynx cell;
  - Locally advanced disease; and ANY of the following:
    - **§** Stage T1, N1-3;
    - Stage T2-T4, any N;
    - **§** Stage T4b, unresectable or unfit for surgery.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + 5- Fluorouracil (5-FU)

Docetaxel + Cisplatin

Docetaxel + Cisplatin + 5-Fluorouracil (5-FU)

Epirubicin + Paclitaxel + Cisplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 191 of 387



- Ind. 5454 Chemoradiation followed by Adjuvant Chemotherapy for Nasopharynx Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:
  - Locally advanced disease which is unresectable or unfit for surgery;
  - Adjuvant chemoradiation; and EITHER of the following:
    - **§** Stage T1, N1-3;
    - Stage T2-T4, any N;
  - Stage T1, N1-3;
  - Stage T2-T4, any N.

Carboplatin + 5- Fluorouracil (5-FU)

Cisplatin + 5-Fluorouracil (5-FU)

Ind. 5456 For Recurrent, Unresectable, or Metastatic Cancer in the Head and Neck region, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Locally advanced disease which is unresectable or unfit for surgery
- Metastatic disease; and EITHER of the following
  - § First-line treatment;
  - Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU)

## Bleomycin



Capecitabine

Carboplatin

Carboplatin + 5-Fluorouracil (5-FU) + Cetuximab

Cetuximab

Cetuximab (Maintenance Cycles)

Cetuximab + Carboplatin

Cisplatin

Cisplatin + 5-Fluorouracil (5-FU)

Cisplatin + 5-Fluorouracil (5-FU) + Cetuximab

Cisplatin + Cetuximab

Cisplatin + Cetuximab (Subsequent Cycles)

Cisplatin + Gemcitabine

Cisplatin + Paclitaxel

Cisplatin + Paclitaxel (Initial Cycles)

Docetaxel

Docetaxel + Carboplatin

Docetaxel + Cisplatin + Cetuximab (Initial Cycles)

Gemcitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 193 of 387



Gemcitabine + Vinorelbine

lfosfamide + Mesna

Methotrexate

Paclitaxel

Vinorelbine



#### REFERENCES

- Chen C, Wang FH, Wang ZQ, et al. Salvage gemcitabine-vinorelbine chemotherapy in patients with metastatic nasopharyngeal carcinoma pretreated with platinum-based chemotherapy. Oral Oncol. 2012;48:1146–1151.
- Forastiere AA, Zhang Q, Weber RS, et al. Long-term results of RTOG 91–11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer. J Clin Oncol. 2013;31:845–852.
- Haddad R, O'Neill A, Rabinowits G, et al. Induction chemotherapy followed by concurrent chemoradiotherapy (sequential chemoradiotherapy) versus concurrent chemoradiotherapy alone in locally advanced head and neck cancer (PARADIGM): a randomised phase 3 trial. Lancet Oncol. 2013;14:257–264.
- Jin Y, Cai XY, Shi YX, et al. Comparison of five cisplatin-based regimens frequently used as the first-line protocols in metastatic nasopharyngeal carcinoma. J Cancer Res Clin Oncol. 2012;138(10):1717–25.
- Martinez-Trufero J, Isla D, Adansa JC, et al. Phase II study of capecitabine as palliative treatment for patients with recurrent and metastatic squamous head and neck cancer after previous platinum-based treatment. Br J Cancer. 2010; 102:1687–1691.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Head and Neck Cancers. Version 1.2017. 6 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/head-and-neck.pdf.



## Hepatobiliary Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5458 For Gallbladder Cancer and Cholangiocarcinoma, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Adjuvant therapy
- First-line treatment; and EITHER of the following
  - **§** Unresectable and locally advanced disease;
  - **§** Metastatic disease;
  - S Adjuvant therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU)



Capecitabine

Gemcitabine

Gemcitabine + Cisplatin

GemOx

Oxaliplatin + Leucovorin + 5-Fluorouracil (5-FU)

Ind. 5459 For Hepatocellular Cardinoma (HCC), the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Tumor is locally advanced or metastatic.

ASSOCIATED CHEMOTHERAPY REGIMENS

Sorafenib



#### REFERENCES

- Hezel AF, Zhu AX. Systemic therapy for biliary tract cancers. Oncologist. 2008;13:415–423.
- Macdonald OK, Crane CH. Palliative and postoperative radiotherapy in biliary tract cancer. Surg Oncol Clin N Am. 2002
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary Cancers. Version 1.2017. 15 March 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn. org/professionals/physician\_gls/pdf/hepatobiliary.pdf. Oct;11(4):941–954.
- Valle J, Wasan H, Palmer DH, et al. ABC-02 Trial Investigators. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med. 2010;362:1273–1281.



# Hodgkin Lymphoma

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5501 First-Line Therapy for Classical Hodgkin Lymphoma per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich (LRHL); and EITHER of the following:
    - **§** Stage 1A or 2A with no unfavorable risk factors;
    - Stage 1 or 2, unfavorable and non-bulky.

ASSOCIATED CHEMOTHERAPY REGIMENS

## ABVD



- Ind. 5501 First-Line Therapy for Classical Hodgkin Lymphoma per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich (LRHL); and EITHER of the following:
    - Stage 1A or 2A with unfavorable risk factors: bulky mediastinal disease (greater than 10 cm), B symptoms, ESR greater than 50, or greater than 3 sites of disease;
    - Stage 3 or 4.

## ABVD

Escalated BEACOPP

Stanford V

- Ind. 5502 Second-Line Therapy for Classical Hodgkin Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Stage 3 or 4 Classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich (LRHL) with or without local/regional recurrence
  - Stage 1A or 2A Classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich (LRHL) with unfavorable risk factors: bulky mediastinal



disease (greater than 10 cm), B symptoms, ESR greater than 50, or greater than 3 sites of disease

- Classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich
- Local/regional recurrence with classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Brentuximab

C-MOPP

DHAP

ESHAP

#### Everlolimus

Gemcitabine + Carboplatin + Dexamethasone (GCD)

Gemcitabine + Vinorelobine + Liposomal Doxorubicin (GVD)

Ifosfomide + Carboplatin + Etoposide (ICE)

#### IGEV

## MINE

#### Mini-BEAM

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 201 of 387



- Ind. 5503 Third-Line Therapy for Classical Hodgkin Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich (LRHL); and EITHER of the following:
    - Stage 1A or 2A with unfavorable risk factors: bulky mediastinal disease (greater than 10 cm); B symptoms; ESR greater than 50; greater than 3 sites of disease;
    - Stage 3 or 4.

Bendamustine

Lenalidomide

Ind. 5503 Third-Line Therapy for Classical Hodgkin Lymphoma per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Classical Hodgkin Lymphoma including: nodular sclerosis (NSHL), mixed cellularity (MCHL), lymphocyte depleted (LDHL) and lymphocyte rich (LRHL);
- Local/regional recurrence.

ASSOCIATED CHEMOTHERAPY REGIMENS

Lenalidomide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 202 of 387



- Ind. 5503 Third-Line Therapy for Classical Hodgkin Lymphoma per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Local/regional recurrence.

## Bendamustine

- Ind. 5503 Third-Line Therapy for Classical Hodgkin Lymphoma per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - High-dose therapy with autologous stem cell rescue (HDT/ASCR) treatment failure;
  - At least two previous chemotherapy treatment failures and not a candidate for high-dose therapy with autologous stem cell rescue (HDT/ASCR).

ASSOCIATED CHEMOTHERAPY REGIMENS

## Brentuximab

- Ind. 5503 Third-Line Therapy for Classical Hodgkin Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Third-line treatment;
  - High-dose therapy with autologous stem cell rescue (HDT/ASCR) treatment failure;
  - Brentuximab vedotin therapy treatment failure.



Nivolumab

Pembrolizumab

Ind. 5504 First-Line Therapy for Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL);
- First-line treatment; and ANY of the following:
  - Stage 1A or 2A with unfavorable risk factors: bulky mediastinal disease (greater than 10 cm); B symptoms; ESR greater than 50; greater than 3 sites of disease;
  - Stage 1A or 2A with no unfavorable risk factors;
  - Stage 1 or 2, unfavorable and non-bulky.

ASSOCIATED CHEMOTHERAPY REGIMENS

ABVD

CHOP

Cyclophosphamide + Vinblasine + Prednisolone (CVP)

Ind. 5504 First-Line Therapy for Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 204 of 387



- Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL);
- Stage 3 or 4;
- Unfavorable risk factors: bulky mediastinal disease (greater than 10 cm); B symptoms; ESR greater than 50; greater than 3 sites of disease.

ABVD

СНОР

Ind. 5504 First-Line Therapy for Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL);
- Maintenance therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Rituximab



- Ind. 5504 First-Line Therapy for Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL).

Cyclophosphamide + Vinblasine + Prednisolone (CVP)

- Ind. 5514 Second-Line Therapy for Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL);
  - Second-line treatment; and ANY of the following:
    - § Local/regional recurrence;
    - Unfavorable risk factors: bulky mediastinal disease (greater than 10 cm);
       B symptoms; ESR greater than 50; greater than 3 sites of disease;
    - Stage 1 or 2, unfavorable and non-bulky;
    - Stage 1A or 2A;
    - Stage 3 or 4.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

C-MOPP + Rituximab

DHAP + Rituximab

ESHAP + Rituximab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 206 of 387



Gemcitabine + Carboplatin + Dexamethasone (GCD) + Rituximab

Gemcitabine + Vinorelobine + Liposomal Doxorubicin (GVD) + Rituximab

Ifosfomide + Carboplatin + Etoposide (ICE) + Rituximab

IGEV + Rituximab

MINE + Rituximab

Mini-BEAM + Rituximab

Ind. 5514 Second-Line Therapy for Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL) per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL);
- Maintenance therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Rituximab



#### REFERENCES

- Eich HT, Diehl V, Görgen H, et al. Intensified chemotherapy and dose-reduced involved-field radiotherapy in patients with early unfavorable Hodgkin's lymphoma: final analysis of the German Hodgkin Study Group HD11 trial. J Clin Oncol. 2010;28:4199– 4206.
- Engert A, Plutschow A, Eich HT, et al. Reduced treatment intensity in patients with early-stage Hodgkin's lymphoma. N Engl J Med. 2010;363:640–652.
- Meyer R, Gospodarowicz M, Connors J, et al. ABVD alone versus radiation based therapy in limited stage Hodgkin's lymphoma. N Engl J Med. 2012;366:399–408.
- Bonadonna G, Bonfante V, Viviani S, et al. ABVD plus subtotal nodal versus involved-field radiotherapy in early-stage Hodgkin's disease: long-term results. J Clin Oncol. 2004;22:2835–2841.
- Gordon LI, Hong F, Fisher RI, et al. Randomized phase III trial of ABVD versus Stanford V with or without radiation therapy in locally extensive and advanced-stage Hodgkin lymphoma: an intergroup study coordinated by the Eastern Cooperative Oncology Group (E2496). J Clin Oncol. 2013;31:684–691.
- Advani RH, Hoppe RT, Baer DM, et al. Efficacy of abbreviated Stanford V chemotherapy and involved field radiotherapy in early stage Hodgkin's disease: mature results of the G4 trial. Ann Oncol. 2013;24:1044–1048.
- Edwards-Bennett SM, Jacks LM, Moskowitz CH, et al. Stanford V program for locally extensive and advanced Hodgkin lymphoma: the Memorial Sloan-Kettering Cancer Center experience. Ann Oncol. 2010;21:574–581.
- von Tresckow B, Plutschow A, Fuchs M, et al. Dose-intensification in early unfavorable Hodgkin's lymphoma: final analysis of the German Hodgkin Study Group HD14 trial. J Clin Oncol. 2012;30:907–913.
- Engert A, Haverkamp H, Cobe C, et al. Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin's lymphoma (HD15 trial): a randomized, open-label, phase 3 non-inferiority trial. The Lancet. 2012;379(9828):1791–1799.
- Younes A, Bartlett NL, Leonard JP et al. Brentuximab vedotin (SGN-35) for relapsed CD30-positive lymphomas. N Engl J Med.2010;4;363:1812–1821.
- Adcetris [package insert]. Bothell, WA: Seattle Genetics, Inc; 2015.
- Montoto S, Camós M, López-Guillermo A, et al. Hybrid chemotherapy consisting of C-MOPP/ABV as first-line treatment forpatients with advanced Hodgkin disease. Cancer. 2000;88(9): 2142–2148.
- Takenaka T, Mikuni C, Miura A, et al. Alternating combination chemotherapy C-MOPP and ABVD in clinical stage II–IV Hodgkin's disease: a multicenter phase II study (JCOG 8905). The Lymphoma Study Group of the Japan Clinical Oncology Group. Jpn J Clin Oncol. 2000;30(3):146–152.
- Josting A, Rudolph C, Reiser M, et al. Time-intensified dexamethasone/cisplatin/cytarabine: an effective salvage therapy with low toxicity in patients with relapsed and refractory Hodgkin's disease. Ann Oncol. 2002;13(10):1628–1635.
- Abali H, Urün Y, Oksüzoğlu B, Budakoğlu B, et al. Comparison of ICE versus DHAP as salvage chemotherapy in patients with relapsed or refractory lymphoma. Cancer Invest. 2008;26(4):401–406.
- Aparicio J, Segura A, Garcera S, et al. ESHAP is an active regimen for relapsing Hodgkin's disease. Ann Oncol. 1999; 10(5):593–595.
- NCCN Clinical Practice Guidelines in Oncology<sup>™</sup>. Hodgkin Lymphoma.V.2.2015.Available at: http://www.nccn.org/ professionals/physician\_gls/pdf/hodgkins.pdf. Accessed February 10, 2016.



- Fernández de Larrea C, Martinez C, et al. Salvage chemotherapy with alternating MINE-ESHAP regimen in relapsed or refractory Hodgkin's lymphoma followed by autologous stem cell transplantation. Ann Oncol. 2010;21(6):1211–1216.
   Johnston PB, Inwards DJ, Colgan JP, et al. A phase II trial of the oral mTOR inhibitor everolimus in relapsed Hodgkin
  - lymphoma. Am J Hematol. 2010;85:320–324.
- Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. Leuk Lymphoma. 2010;51:1523–1529.
- Bartlett NL, Niedzwiecki D, JL Johnson JL et al. Gemcitabine, vinorelbine, and pegylated liposomal doxorubicin (GVD), a salvage regimen in relapsed Hodgkin's lymphoma: CALGB 59804. Ann Oncol. 2007;18:1071–1079.
- Moskowitz CH, Nimer SD, Zelenetz AD, et al. A 2-step comprehensive high-dose chemoradiotherapy second-line program for relapsed and refractory Hogdkin disease: analysis by intent to treat and development of a prognostic model. Blood. 2001;97(3):616–623.
- Santoro A, Magagnoli M, Spina M, et al. Ifosfamide, gemcitabine, and vinorelbine: a new induction regimen for refractory and relapsed Hodgkin's lymphoma. Haematologica. 2007;92(1):35–41.
- Colwill R, Crump M, Couture F, et al. Mini-BEAM as salvage therapy for relapsed or refractory Hodgkin's disease before intensive therapy and autologous bone marrow transplantation. J Clin Oncol. 1995;13:396–402.
- Martin A, Fernández-Jiménez MC, Caballero MD, et al. Long-term follow-up in patients treated with Mini-BEAM as salvage therapy for relapsed or refractory Hodgkin's disease. Br J Haematol. 2001;113(1):161–171.
- Rodriguez MA et al. A phase II trial of mesna/ifosfamide, mitoxantrone and etoposide for refractory lymphoma. Ann Oncol 1995;6:609-612.
- Moskowitz AJ, Hamlin PA, Perales M-A, et al. Phase II study of bendamustine in relapsed and refractory classical Hodgkin lymphoma. J Clin Oncol. 2013;31(4):450–460.
- Fehniger TA, Larson S, Trinkaus K, et al. A phase 2 multi- center study of lenalidomide in relapsed or refractory classical Hodgkin lymphoma. Blood. 2011;118:5119–5125.
- Moskowitz CH, Nademanee A, Masszi T, et al. Brentuximab vedotin as a consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, doubleblind, placebo-controlled, phase 3 trial. Lancet. 2015;385(9980)1853-1862.
- Savage KJ, Skinnider B, Al-Mansour M, et al. Treating limited stage nodular lymphocyte predominant Hodgkin lymphoma similarly to classical Hodgkin lymphoma with ABVD may improve outcome. Blood. 2011;118:4585–4590.
- Canellos GP, Mauch P. What is the appropriate systemic chemotherapy for lymphocyte-predominant Hodgkin's Lymphoma? JClin Oncol. 2010;28:e8.
- Advani RH, Hoppe RT. How I treat nodular predominant Hodgkin lymphoma. Blood. 2013;122(26):4182-418
- Advani RH, Horning SJ, Hoppe RT, et al. Mature results of a phase II study of rituximab therapy for nodular lymphocytepredominant Hodgkin lymphoma. J Clin Oncol. 2014;32(9):912-918.
- Fanale MA, Lai C-M, McLaughlin P, et al. Outcomes of nodular lymphocyte predominant Hodgkin's Lymphoma (NLPHL) patients treated with R-CHOP. ASH Annual Meeting Abstracts. 2010;116:2812.
- Schulz H, Rehwald U, Morschhauser F, et al. Rituximab in relapsed lymphocyte-predominant Hodgkin lymphoma: long-term results of a phase 2 trial by the German Hodgkin Lymphoma Study Group (GHSG). Blood. 2008;111:109–111.



Eichenauer DA, Fuchs M, Pluetschow A, et al. Phase 2 study of rituximab in newly diagnosed stage 1A nodular lymphocyte-predominant Hodgkin lymphoma: a report from the German Hodgkin Study Group. Blood. 2011;118:4363– 4365.



# Kidney Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5460 First-Line Therapy for Kidney Cancer with Clear Cell Histology per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Good risk (normal LDH and normal Hg);
- Clear cell histology.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Axitinib

Bevacizumab + Interferon Alfa

## Interleukin-2



Pazopanib

Sorafenib

Sunitinib

Ind. 5460 First-Line Therapy for Kidney Cancer with Clear Cell Histology per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Clear cell histology; and intermediate risk (elevated LDH but normal Hg).

ASSOCIATED CHEMOTHERAPY REGIMENS

Sunitinib

Ind. 5460 First-Line Therapy for Kidney Cancer with Clear Cell Histology per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Poor risk (elevated LDH and Low Hg or Ca higher than 10 mg/dL);
- Clear cell histology.

ASSOCIATED CHEMOTHERAPY REGIMENS

Temsirolimus



- Ind. 5461 Subsequent Therapy for Kidney Cancer with Clear Cell Histology per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Second-line treatment; and EITHER of the following:
    - S Patient has had prior tyrosine-kinase inhibitor (TKI);
    - S Patient previously treated with cytokine therapy.

## Axitinib

Bevacizumab

Cabozantinib

Everolimus

Interleukin-2

Lenvatinib + Everolimus

Nivolumab

Pazopanib

Sorafenib

Sunitinib

Temsirolimus

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 213 of 387



- Ind. 5461 Subsequent Therapy for Kidney Cancer with Clear Cell Histology per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Second-line treatment;
  - Patient has had prior tyrosine-kinase inhibitor (TKI); and EITHER of the following
    - S Patient has renal cell carcinoma (RCC) with predominant sarcomatoid features;
    - **§** Patient previously treated with cytokine therapy.

Gemcitabine + Doxorubicin

Gemcitabine + Sunitinib

- Ind. 5461 Subsequent Therapy for Kidney Cancer with Clear Cell Histology per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Bone metastases

ASSOCIATED CHEMOTHERAPY REGIMENS

Denosumab

Zoledronic Acid

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 214 of 387



- Ind. 5462 Systemic Therapy for Kidney Cancer with Non-Clear Cell Histology per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Good risk (normal LDH and normal Hg);
  - Non-clear cell histology;
  - First-line treatment.

## Axitinib

## Bevacizumab

Carboplatin + Paclitaxel

Erlotinib

## Everolimus

Gemcitabine + Carboplatin

Gemcitabine + Cisplatin

Gemcitabine + Doxorubicin

Gemcitabine + Sunitinib

Pazopanib

Sorafenib

Sunitinib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 215 of 387



## Temsirolimus

Ind. 5462 Systemic Therapy for Kidney Cancer with Non-Clear Cell Histology per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient received prior anti-angiogenic therapy
- Non-clear cell histology
- Second-line treatment

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Cabozantinib

## Nivolumab

Ind. 5462 Systemic Therapy for Kidney Cancer with Non-Clear Cell Histology per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient received prior anti-angiogenic therapy
- Non-clear cell histology
- Second-line treatment
- Advanced disease

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Lenvatinib + Everolimus

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 216 of 387





#### REFERENCES

- Sutent [package insert]. New York, NY: Pfizer Labs; 2015.
- Gore ME, Szczylik C, Porta C, et al. Safety and efficacy of sunitinib for metastatic renal-cell carcinoma: an expandedaccess trial. Lancet Oncol. 2009;10:757–763.
- Torisel [package insert]. Philadelphia, PA: Wyeth; 2015.
- Hudes G, Carducci M, Tomczak P, et al; Global ARCC Trial. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. N Engl J Med. 2007;356:2271–2281.
- Avastin [package insert]. San Francisco, CA: Genentech; 2015.
- Escudier B, Pluzanska A, Koralewski P, et al; AVOREN Trial investigators. Bevacizumab plus interferon alfa-2a for treatment of metastatic renal cell carcinoma: a randomised, double-blind phase III trial. Lancet. 2007;370:2103–2111.
- Rini BI, Halabi S, Rosenberg JE, et al. Phase III trial of bevacizumab plus interferon alfa versus interferon alfa monotherapy in patients with metastatic renal cell carcinoma: final results of CALGB 90206. J Clin Oncol. 2010;28:2137–2143.
- Votrient [package insert]. Research Triangle Park, NC: GSK; 2014.
- Sternberg CN, Davis ID, Mardiak J et al. Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. J Clin Oncol. 2010;28:1061–1068.
- Proleukin [package insert]. San Diego, CA: Prometheus Laboratories; 2015.
- McDermott DF, Regan MM, Clark JI, et al. Randomized phase III trial of high-dose interleukin-2 versus subcutaneous interleukin-and interferon in patients with metastatic renal cell carcinoma. J Clin Oncol. 2005;23:133–141.
- Inlyta [package insert]. New York, NY: Pfizer Inc; 2014.
- Rini BI, Escudier B, Tomczak P, et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomized phase 3 trial. Lancet. 2011;378:1931–1939.
- Escudier B, Szczylik C, Hutson TE, et al. Randomized phase II trial of first-line treatment with sorafenib versus interferon Alfa- 2a in patients with metastatic renal cell carcinoma. J Clin Oncol. 2009;27(8):1280–1289.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. Version
  2.2017. 31 Oct 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/
  professionals/physician\_gls/pdf/kidney.pdf.
- Choueiri TK, Escudier B, Powles T, et al; METEOR Investigators. Cabozantinib versus everolimus in advanced renal-cell carcinoma. N Engl J Med. 2015;373(19):1814–1823.
- Motzer RJ, Escudier B, McDermott DF, et al; CheckMate 025 Investigators. Nivolumab versus everolimus in advanced renal- cell carcinoma. N Engl J Med. 2015;373(19):1803–1813.
- Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2015.
- Afinitor [package insert]. East Hanover, NJ: Novartis; 2015.
- Motzer RJ, Escudier B, Oudard S, et al; RECORD-1 Study Group. Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomised, placebo-controlled phase III trial. Lancet. 2008;372:449–456.
- Nexavar [package insert]. Wayne, NJ: Bayer HealthCare; 2015.
- Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear cell renal-cell carcinoma. N Engl J Med. 2007;356:125– 134.



- Di Lorenzo G, Carteni G, Autorino R, et al. Phase II study of sorafenib in patients with sunitinib-refractory metastatic renal cell cancer. J Clin Oncol. 2009;27:4469–4474.
- Garcia JA, Hutson TE, Elson P, et al. Sorafenib in patients with metastatic renal cell carcinoma refractory to either sunitinib or bevacizumab. Cancer. 2010;116:5383–5390.
- Motzer RJ, Michaelson MD, Redman BG, et al. Activity of SU11248, a multitargeted inhibitor of vascular endothelial growth factor receptor and platelet-derived growth factor receptor, in patients with metastatic renal cell carcinoma. J Clin Oncol. 2006;24:16–24.
- Motzer RJ, Rini BI, Bukowski RM, et al. Sunitinib in patients with metastatic renal cell carcinoma. JAMA. 2006;295:2516–2524.
- Atkins MB, Hidalgo M, Stadler WM, et al. Randomized phase II study of multiple dose levels of CCI-779, a novel mammalian target of rapamycin kinase inhibitor, in patients with advanced refractory renal cell carcinoma. J Clin Oncol. 2004;22:909–918.
- Hutson TE, Escudier B, Esteban E, et al. Temsirolimus vs Sorafenib as Second Line Therapy in Metastatic Renal Cell Carcinoma: Results from the INTORSECT Trial [abstract]. Ann Oncol. 2012;23:Abstract: LBA22.
- Yang JC, Haworth L, Sherry RM, et al. A randomized trial of bevacizumab, an anti-vascular endothelial growth factor antibody, for metastatic renal cancer. N Engl J Med. 2003;349:427–434.
- Gordon MS, Hussey M, Nagle RB, et al. Phase II study of erlotinib in patients with locally advanced or metastatic papillary histology renal cell cancer: SWOG S0317. J Clin Oncol. 2009;27:5788–5793.



## Myelodysplastic Syndrome

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5491 For Myelodysplastic Syndrome, the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - International Prognostic Scoring System (IPSS) Low/Intermediate- less than or equal to 1;
  - 5q deletion present.

ASSOCIATED CHEMOTHERAPY REGIMENS

Lenalidomide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 220 of 387



Ind. 5491 For Myelodysplastic Syndrome, the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- International Prognostic Scoring System (IPSS) Low/Intermediate- less than or equal to 1;
- International Prognostic Scoring System (IPSS) High/Intermediate- greater than or equal to 2.

ASSOCIATED CHEMOTHERAPY REGIMENS

Azacitadine

Decitabine



#### REFERENCES

- List A, Dewald G, Bennett J, et al. Lenalidomide in the myelodysplastic syndrome with chromosome 5q deletion. N Engl J Med. 2006;355(14):1456–1465.
- Revlimid [package insert]. Summit, NJ: Celgene Corporation; 2015.
- Revicki DA, Brandenburg NA, Muus P, et al. Health-related quality of life outcomes of lenalidomide in transfusiondependent patients with low- or intermediate-1-risk myelodysplastic syndromes with a chromosome 5q deletion: results from a randomized clinical trial. Leuk Res. 2013;37(3): 259–265.
- Oliva EN, Latagliata R, Laganà C, et al. Lenalidomide in International Prognostic Scoring System Low and Intermediate-1 risk myelodysplastic syndromes with del(5q): an Italian phase II trial of health-related quality of life, safety and efficacy. Leuk Lymphoma. 2013;54(11):2458–2465.
- Greenberg P. The role of hemopoietic growth factors in the treatment of myelodysplastic syndromes. Int J Ped Hem-Onc. 1997;4:231–238.
- Hellström-Lindberg E. Efficacy of erythropoietin in the myelodysplastic syndromes: a meta-analysis of 205 patients from 17 studies. Br J Haematol. 1995;89(1):67–71.
- Negrin RS, Stein R, Doherty K, et al. Maintenance treatment of the anemia of myelodysplastic syndromes with recombinant human granulocyte colony-stimulating factor and erythropoietin: evidence for in vivo synergy. Blood. 1996;87(10): 076–4081.
- Hellström-Lindberg E, Ahlgren T, Beguin Y, et al. Treatment of anemia in myelodysplastic syndromes with granulocyte colony-stimulating factor plus erythropoietin: results from a randomized phase II study and long-term follow-up of 71 patients. Blood. 1998;92(1):68–75.
- Casadevall N, Durieux P, Dubois S, et al. Health, economic, and quality-of-life effects of erythropoietin and granulocyte colony-stimulating factor for the treatment of myelodysplastic syndromes: a randomized, controlled trial. Blood. 2004;104(2):321–327.
- Hellström-Lindberg E, Negrin R, Stein R, et al. Erythroid response to treatment with G-CSF plus erythropoietin for the anaemia of patients with myelodysplastic syndromes: proposal for a predictive model. Br J Haematol. 1997;99(2):344– 351.
- Mannone L, Gardin C, Quarre MC, et al. High-dose darbepoetin alpha in the treatment of anaemia of lower risk myelodysplastic syndrome results of a phase II study. Br J Haematol. 2006;133(5):513–519.
- Musto P, Lanza F, Balleari E, et al. Darbepoetin alpha for the treatment of anaemia in low-intermediate risk myelodysplastic syndromes. Br J Haematol. 2005;128(2):204–209.
- Giraldo P, Nomdedeu B, Loscertales J, et al; Aranesp in Myelodysplastic Syndromes (ARM) Study Group. Darbepoetin alpha for the treatment of anemia in patients with myelodysplastic syndromes. Cancer. 2006;107(12):2807–2816.
- Stasi R, Abruzzese E, Lanzetta G, Terzoli E, Amadori S. Darbepoetin alfa for the treatment of anemic patients with lowand intermediate-1-risk myelodysplastic syndromes. Ann Oncol. 2005;16(12):1921–1927.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Myelodysplastic Syndromes. Version 2.2017. 10 Nov 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/mds.pdf.
- Sloand EM, Wu CO, Greenberg P, Young N, Barrett J. Factors affecting response and survival in patients with myelodysplasia treated with immunosuppressive therapy. J Clin Oncol. 2008; 26(15):2505–2511.



- Passweg JR, Giagounidis AA, Simcock M, et al. Immunosuppressive therapy for patients with myelodysplastic syndrome: a
  prospective randomized multicenter phase III trial comparing antithymocyte globulin plus cyclosporine with best
  supportive care—SAKK 33/99. J Clin Oncol. 2011;29(3):303–309.
- Molldrem JJ, Caples M, Mavroudis D, et al. Antithymocyte globulin for patients with myelodysplastic syndrome. Br J Haematol. 1997;99(3):699–705.
- Deeg HJ, Gotlib J, Beckham C, et al. Hematologic responses of patients with MDS to antithymocyte globulin plus entanercept correlated with improved flow scores of marrow cells. Leuk Res. 2004;28(11):1177–1180.
- Vidaza [package insert]. Summit, NJ: Celgene Corporation; 2015.
- Silverman LR, Fenaux P, Mufti GJ, et al. Continued azacitidine therapy beyond time of first response improves quality of response in patients with higher-risk myelodysplastic syndromes. Cancer. 2011;117(12):2697–2702.
- Fenaux P, Mufti GJ, Hellstrom-Lindberg E, et al; International Vidaza High-Risk MDS Survival Study Group. Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: a randomised, open-label, phase III study. Lancet Oncol. 2009;10(3):223–232.
- Silverman LR, McKenzie DR, Peterson BL, et al. Further analysis of trials with azacitidine in patients with myelodysplastic syndrome: studies 8421, 8921, and 9221 by the Cancer and Leukemia Group B. J Clin Oncol. 2006;24(24):3895–3903.
- Dacogen [package insert]. Woodcliff Lake, NJ: Eisai Inc.; 2014.
- Kantarjian HM, O'Brien S, Shan J, et al. Update of the decitabine experience in higher risk myelodysplastic syndrome and analysis of prognostic factors associated with outcome. Cancer. 2007;109(2):265–273.
- Kantarjian H, Oki Y, Garcia-Manero G, et al. Results of a randomized study of 3 schedules of low-dose decitabine in higher-risk myelodysplastic syndrome and chronic myelomonocytic leukemia. Blood. 2007;109(1):52–57.
- Alyea EP, Kim HT, Ho V, et al. Comparative outcome of nonmyeloablative and myeloablative allogeneic hematopoietic cell transplantation for patients older than 50 years of age. Blood. 2005;105(4):1810–1814.
- Laport GG, Sandmaier BM, Storer BE, et al. Reduced-intensity conditioning followed by allogeneic hematopoietic cell transplantation for adult patients with myelodysplastic syndrome and myeloproliferative disorders. Biol Blood Marrow Transplant. 2008;14(2):246–255.
- Sorror ML, Sandmaier BM, Storer BE, et al. Long-term outcomes among older patients following nonmyeloablative conditioning and allogeneic hematopoietic cell transplantation for advanced hematologic malignancies. JAMA. 2011;306(17):1874–1883.
- Beran M, Shen Y, Kantarjian H, et al. High-dose chemotherapy in high-risk myelodysplastic syndrome: covariate-adjusted comparison of five regimens. Cancer. 2001;92(8):1999–2015.



## Melanoma

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5478 For Advanced or Metastatic Melanoma, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Advanced and unresectable disease with measurable lesions on imaging;
  - First-line treatment.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Vinblastine + Dacarbazine + Interleukin-2 + Interferon Alpha-2b

Cisplatin + Vinblastine + Temozolomide + Interleukin-2 + Interferon Alpha-2b

## Dacarbazine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 224 of 387



Interleukin-2

Ipilimumab

Nab-Paclitaxel

Nivolumab

Paclitaxel

Paclitaxel + Carboplatin

Pembrolizumab

Temozolomide

Ind. 5478 For Advanced or Metastatic Melanoma, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced and unresectable disease with measurable lesions on imaging;
- First-line treatment;
- BRAF mutation.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dabrafenib

Dabrafenib + Trametinib

Trametinib

Vemurafenib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 225 of 387



Ind. 5478 For Advanced or Metastatic Melanoma, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced and unresectable disease with measurable lesions on imaging;
- First-line treatment;
- C-KIT mutation.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Imatinib

Ind. 5497 Adjuvant Therapy for Melanoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Adjuvant therapy; and EITHER of the following:
  - Stage 2B or 2C;
  - Stage 3 with a wide local excision including or excluding lymph nodes having been performed.

ASSOCIATED CHEMOTHERAPY REGIMENS

Interferon Alfa-2b (low and high dose)

## Peginterferon Alfa-2b

#### REFERENCES

- Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. Lancet Oncol. 2012;13:459–465.
- Weber JS, Kahler KC, Hauschild A. Management of Immune-Related Adverse Events and Kinetics of Response With Ipilimumab. J Clin Oncol. 2012.



- Hodi FS, O'Day SJ, McDermott DF, Weber RW, et al. Improved survival with ipilimumab in patients with metastatic melanoma. N Eng J Med. 2010;363:711–723.
- Robert C, Thomas L, Bondarenko I, et al. Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. N Engl J Med. 2011;364:2517–2526.
- Long GV, Stroyakovskiy D, Gogas H, et al. Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma.
   N Eng J Med. 2014 Sep 29. [Epub ahead of print].
- Robert C, Karaszewska B, Schachter J, et al. COMBI-v: A randomised, open-label, phase III study comparing the combination of dabrafenib (D) and trametinib (T) to vemurafenib (V) as first-line therapy in patients (pts) with unresectable or metastatic BRAF V600E/K mutation-positive cutaneous melanoma [abstract]. Ann Oncol. 2014;25(Suppl 4):Abstract LBA4.
- Flaherty KT, Infante JR, Daud A, et al. Combined BRAF and MEK Inhibition in Melanoma with BRAF V600 Mutations. N Eng J Med. 2012;367:1694–1703.
- Robert C, Ribas A, Wolchok JD, et al. Anti-programmed-death-receptor-1 treatment with pembrolizumab in ipilimumabrefractory advanced melanoma: a randomised dose-comparison cohort of a phase 1 trial. Lancet. 2014;384:1109–1117.
- Hamid O, Robert C, Daud A, et al. Safety and Tumor Responses with Lambrolizumab (Anti-PD-1) in Melanoma. N Eng J Med.2013;369:134–144.
- Sosman JA, Kim KB, Schuchter L, et al. Survival in BRAF V600-mutant advanced melanoma treated with vemurafenib. N Engl J Med. 2012;366:707–714.
- Weber JS, Minor DR, D'Angelo SP, et al. Phase 3 randomized, open-label study of nivolumab (anti-PD-1; BMS-936558, ONO- 4538) versus investigator's choice chemotherapy (ICC) in patients with advanced melanoma after prior anti-CTLA4 therapy [Abstract LBA3\_PRA]. Ann Oncol. 2014;25 (Suppl 4).
- Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation.
   N Engl J Med. 2011;2507–2516.
- Long GV, Trefzer U, Davies MA, et al. Dabrafenib in patients with Val600Glu or Val600Lys BRAF-mutant melanoma metastatic to the brain (BREAK-MB): a multicentre, open-label, phase 2 trial. Lancet Oncol. 2012;13:1087–1095.
- Hauschild A, Grob JJ, Demidov LV, et al. Dabrafenib in BRAF-mutated metastatic melanoma: a multicentre, open-label, phase 3 randomised controlled trial. Lancet. 2012;380: 358–365.
- Flaherty KT, Robert C, Hersey P, et al. Improved Survial with MEK Inhibition in BRAF-mutated melanoma. N Eng J Med.2012;367:107–114.
- Hodi FS1, Corless CL, Giobbie-Hurder A, et al. Imatinib for melanomas harboring mutationally activated or amplified KIT arising on mucosal, acral, and chronically sun-damaged skin. J Clin Oncol. 2013;31:3182–3190.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Melanoma. Version 1.2017. 10 Nov 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/melanoma.pdf.18. Carvajal RD, Antonescu CR, Wolchok, JD, et al. KIT as a therapeutic target in metastatic melanoma. JAMA. 2011;395:2327–2334.
- Serrone L, Zeuli M, Sega FM, et al. Dacarbazine-based chemotherapy for metastatic melanoma: thirty-year experience overview. J Exp Clin Cancer Res. 2000;19:21–34.
- Middleton MR, Grob JJ, Aaronson N, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. J Clin Oncol. 2000;18:158–166



- Hersh EM, O'Day SJ, Ribas A, et al. A phase 2 Clinical trial of nab-Paclitaxel in previously treated and chemotherapy-naïve patients with metastatic melanoma. Cancer. 2010;116:155–163.
- Kottschade LA, Suman VJ, Amatruda T, et al. A phase II trial of nab-paclitaxel (ABI-007) and carboplatin in patients with unresectable stage iv melanoma: a north central cancer treatment group study, N057E(1). Cancer. 2011;117:1704–1710.
- Rosenberg SA, Yang JC, Topalian SL, et al. Treatment of 283 consecutive patients with metastatic melanoma or renal cell cancer using high-dose bolus interleukin 2. JAMA. 1994;271:907–913.
- Atkins MB, Lotze MT, Dutcher JP, et al. High-dose recombinant interleukin 2 therapy for patients with metastatic melanoma: analysis of 270 patients treated between 1985 and 1993. J Clin Oncol. 1999;17:2105–2116.
- Atkins MB, Kunkel L, Sznol M, Rosenberg SA. High-dose recombinant interleukin-2 therapy in patients with metastatic melanoma: long-term survival update. Cancer J Sci Am. 2000;6 Suppl 1:S11–14.
- Smith FO, Downey SG, Klapper JA, et al. Treatment of metastatic melanoma using interleukin-2 alone or in conjunction with vaccines. Clin Cancer Res. 2008;14(17):5610–5618.
- Legha SS, Ring S, Eton O, et al. Development of a biochemotherapy regimen with concurrent administration of cisplatin, vinblastine, dacarbazine, interferon alfa, and interleukin-2 for patients with metastatic melanoma. J Clin Oncol. 1998;16: 1752–1759.
- Eton O, Legha SS, Bedikian AY, et al. Sequential biochemotherapy versus chemotherapy for metastatic melanoma: results from a phase III randomized trial. J Clin Oncol. 2002;20:2045–2052.
- Atkins MB, Hsu J, Lee S, et al. Phase III trial comparing concurrent biochemotherapy with cisplatin, vinblastine, dacarbazine, interleukin-2, and interferon alfa-2b with cisplatin, vinblastine, and dacarbazine alone in patients with metastatic malignant melanoma (E3695): a trial coordinated by the eastern cooperative oncology group. J Clin Oncol. 2008 Dec 10;26(35):5746–5754.
- Wiernik PH and Einzig AI. Taxol in malignant melanoma. J Natl Cancer Inst Monogr. 1993;15:185–187.
- Rao RD, Holtan SG, Ingle JN, et al. Combination of paclitaxel and carboplatin as second-line therapy for patients with metastatic melanoma. Cancer. 2006;106(2):375–382.
- Agarwala SS, Keilholz U, Hogg D, et al. Randomized phase III study of paclitaxel plus carboplatin with or without sorafenib as second-line treatment in patients with advanced melanoma. J Clin Oncol. (Meeting Abstracts). 2007;25(18\_suppl):8510.
- Hauschild A, Agarwala SS, Trefzer U, et al. Results of a phase III, randomized, placebo-controlled study of sorafenib in combination with carboplatin and paclitaxel as second-line treatment in patients with unresectable stage III or stage IV melanoma. J Clin Oncol. 2009;27:2823–2830.
- Flaherty KT, Lee SJ, Schuchter LM, et al. Final results of E2603: A double-blind, randomized phase III trial comparing carboplatin (C)/paclitaxel (P) with or without sorafenib (S) in metastatic melanoma. J Clin Oncol. (ASCO Meeting Abstracts) 2010. 28:(suppl; abstr):8511.

## Mesothelioma



HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5347 First-Line Therapy for Mesothelioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Patient is receiving chemotherapy alone; and ANY of the following:
  - **§** Medically inoperable;
  - Stage 4;
  - Sarcomatoid histology.

ASSOCIATED CHEMOTHERAPY REGIMENS

Gemcitabine + Cisplatin

Pemetrexed

Pemetrexed + Carboplatin

Pemetrexed + Cisplatin

Pemetrexed + Cisplatin + Bevacizumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 229 of 387



#### Vinorelbine

Ind. 5347 First-Line Therapy for Mesothelioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Maintenance therapy following Pemetrexed + Cisplatin + Bevacizumab treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bevacizumab Maintenance

Ind. 5348 Subsequent Therapy for Mesothelioma per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Extensive stage disease;
- Second line treatment
- Chemotherapy previously administered as first-line treatment;
- Relapse greater than 6 months.

ASSOCIATED CHEMOTHERAPY REGIMENS

Pemetrexed

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 230 of 387



Ind. 5348 Subsequent Therapy for Mesothelioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Extensive stage disease;
- Progression of disease while on Pemetrexed and Platinum-based therapy;
- Unresectable lesion;
- PD-L1 expression, tumor proportion score (TPS) greater than or equal to 1%, and EITHER of the following:
  - Second line therapy
  - S Third line therapy

ASSOCIATED CHEMOTHERAPY REGIMENS

## Nivolumab

Nivolumab + Ipilimumab

Ind. 5348 Subsequent Therapy for Mesothelioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Extensive stage disease;
- Second line therapy
- PD-L1 expression, tumor proportion score (TPS) greater than or equal to 1%.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Pembrolizumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 231 of 387



Ind. 5348 Subsequent Therapy for Mesothelioma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Extensive stage disease
- Second line therapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Gemcitabine

Vinorelbine



#### REFERENCES

- Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol. 2003;21:2636–2644.
- Castagneto B, Botta M, Aitini E, et al. Phase II study of pemetrexed in combination with carboplatin in patients with malignant pleural mesothelioma. Ann Oncol. 2008;19:370–373.
- Ceresoli GL, Zucali PA, Favaretto AG, et al. Phase II study of pemetrexed plus carboplatin in malignant pleural mesothelioma. J Clin Oncol. 2006;24:1443–1448.
- Santoro A, O'Brien ME, Stahel RA, et al. Pemetrexed plus cisplatin or pemetrexed plus carboplatin for chemonaive patients with malignant pleural mesothelioma. J Thorac Oncol. 2008;3:756–763.
- Nowak AK, Byrne MJ, Willianson R, et al. A multicentre phase II study of cisplatin and gemcitabine for malignant mesothelioma. Br J Cancer. 2002;87:491–496.
- Van Haarst JM, Baas J, Manegold CH, et al. Multicentre phase II study of gemcitabine and cisplatin in malignant pleural mesothelioma. Br J Cancer. 2002; 86:342–345.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Malignant Pleural Mesothelioma. Version 1.2017. 2 March 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/nscl.pdf.
- Taylor P, Castagneto B, Dark G, et al. Single-agent pemetrexed for chemonaive and pretreated patients with malignant pleural mesothelioma: results of an International Expanded Access Program. J Thorac Oncol. 2008;3:764–771.
- Muers MF, Stephens RJ, Fisher P, et al. Active symptom control with or without chemotherapy in the treatment of patients with malignant pleural mesothelioma (MS01): a multicentre randomised trial. Lancet. 2008;371:1685–1694.
- Jassem J, Ramlau R, Santoro A, et al. Phase III trial of pemetrexed plus best supportive care compared with best supportive care in previously treated patients with advanced malignant pleural mesothelioma. J Clin Oncol. 2008;26: 1698–1704.
- Zucal PA, Simonelli M, Michetti G, et al. Second-line chemotherapy in malignant pleural mesothelioma: results of a retrospective multicenter survey. Lung Cancer. 2012;75:360–367.
- Stebbing J, Powles T, McPherson K, et al. The efficacy and safety of weekly vinorelbine in relapsed malignant pleural mesothelioma. Lung Cancer. 2009;63:94–97.
- van Meerbeeck JP, Baas P, Debruyne C, et al. A phase II study of gemcitabine in patients with malignant pleural mesothelioma. European Organization for Research and Treatment of Cancer Lung Cancer Cooperative Group. Cancer. 1999;85:2577–2582.



## Multiple Myeloma

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5505 Primary Therapy for Multiple Myeloma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient has smoldering symptomatic myeloma;
- Patient is transplant candidate; \
- Clonal bone marrow plasma cells less than or equal to 10% or biopsy proven bony or extramedullary plasmacytoma; and ANY of the following:
  - S Clonal bone marrow plasma cells greater than 60%;
  - Sone or more osteolytic bone lesions on skeletal imaging;
  - **§** More than one focal lesions on MRI studies greater than 5 mm;
  - S Abnormal serum free light chain (FLC) ratio;



- **§** Patient has anemia;
- S Calcium greater than 0.25 mmol/L higher than the upper limit of normal or less than 2.75 mmol/L (greater than 11 mg/dl);
- **§** Renal inefficiency or creatinine clearance is less than 40 mL/min.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bortezomib + Cyclophosphamide + Dexamethosone (BCD)

Bortezomib + Dexamethasone

Bortezomib + Doxorubicin + Dexamethasone

Bortezomib + Lenalidomide + Desamethasone (RVD)

Bortezomib + Thalidomide + Dexamethasone

Carfilzomib + Lenalidomide + Desamethasone (CRD)

Lenalidomide + Dexamethasone

Ind. 5505 Primary Therapy for Multiple Myeloma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient has smoldering symptomatic myeloma;
- Patient is not transplant candidate;
- Clonal bone marrow plasma cells less than or equal to 10% or biopsy proven bony or extramedullary plasmacytoma; and ANY of the following
  - S Clonal bone marrow plasma cells greater than 60%;
  - S One or more osteolytic bone lesions on skeletal imaging;



- More than one focal lesions on MRI studies greater than 5 mm;
- S Abnormal serum free light chain (FLC) ratio;
- **§** Patient has anemia;
- S Calcium greater than 0.25 mmol/L higher than the upper limit of normal or less than 2.75 mmol/L (greater than 11 mg/dl);
- **§** Renal inefficiency or creatinine clearance is less than 40 mL/min.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bortezomib + Dexamethasone

Ixazomib + Lenalidomide + Dexamethasone

Lenalidomide + Low Dose Dexamethasone

- Ind. 5505 Primary Therapy for Multiple Myeloma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates one or more osteolytic bone lesions on skeletal imaging and EITHER of the following:
  - Patient has smoldering symptomatic myeloma
  - Patient has smoldering asymptomatic myeloma

ASSOCIATED CHEMOTHERAPY REGIMENS

Zoledronic Acid



Ind. 5506 Maintenance Therapy for Multiple Myeloma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Good response after initial therapy; and EITHER of the following:
  - Stable disease;
  - **§** Patient waiting for stem cell transplant;
- Stable disease, Post stem cell transplant with Relapsed Disease.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Bortezomib

## Lenalidomide

Ind. 5507 For Prior Line of Therapy Ineffective for Multiple Myeloma, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:

- Relapsed Multiple Myeloma after initial therapy or after stem cell transplant;
- Patient has symptomatic Myeloma with no response to initial therapy;
- Patient has received at least three prior lines of therapy including a proteasome inhibitor (PI) and immunomodulatory agent or doublerefractory PI and immunomodulatory agent;
- Patient has received between one and three prior therapies.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Bendamustine

## Bendamustine + Bortezomib + Dexamethasone



Bendamustine + Lenalidomide + Dexamethasone

Bortezomib + Cyclophosphamide + Dexamethasone (BCD)

Bortezomib + Dexamethasone

Bortezomib + Lenalidomide + Dexamethasone

Bortezomib + Liposomal Doxorubicin

Carfilzomib + Lenalidomide + Dexamethasone (Initial Cycle)

Carfilzomib + Lenalidomide + Dexamethasone (Subsequent Cycles 12+)

Carfilzomib + Lenalidomide + Dexamethasone (Subsequent Cycles)

Cyclophosphamide (Initial Cycles)

Cyclophosphamide (Subsequent Cycles)

Cyclophosphamide + Lenalidomide + Dexamethosone

Daratumumab + Bortezomib + Dexamethasone

Daratumumab + Lenalidomide + Dexamethasone

DCEP

## DT-PACE

Elotuzumab + Bortezomib + Dexamethasone

Elotuzumab + Lenalidomide + Dexamethasone (Initial Cycles)

Elotuzumab + Lenalidomide + Dexamethasone (Subsequent Cycles)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 238 of 387



Lenalidomide + Dexamethasone

Panobinostat + Bortezomib + Dexamethasone (Subsequent Cycles)

Panobinostat + Bortezomib + Dexamethasone (Initial Cycles)

Panobinostat + Carfilzomib

Pomalidomide + Bortezomib + Dexamethasone

Pomalidomide + Carfilzomib + Dexamethasone

Pomalidomide + Cyclophosphamide + Dexamethasone

Pomalidomide + Dexamethasone

VTD-PACE (Consolidation 1)

VTD-PACE (Consolidation 2)

VTD-PACE (Induction)

VTD-PACE Interim Cycle



#### REFERENCES

- Alchalby H, Kröger N. Allogeneic stem cell transplant vs. Janus kinase inhibition in the treatment of primary myelofibrosis or myelofibrosis after essential thrombocythemia or polycythemia vera. Clinical Lymphoma Myeloma and Leukemia. 2014; 14 Suppl:S36-S41. doi: 10.1016/j.clml.2014.06.012. PMID: 25486953
- Alexander D, Mink P, Olov Adami H, et al. Multiple myeloma: A review of the epidemiologic literature. Int. J. Cancer. 2007; 120: 40-61. PMID: 17405120
- Badros A, Barlogie B, Morris C, et al. High response rate in refractory and poor-risk multiple myeloma after allotransplantation using a nonmyeloablative conditioning regimen and donor lymphocyte infusions. Blood. 2001; 97: 2574. PMID: 11313244
- Barlogia B, Kyle RA, Anderson KC, et al. Standard Chemotherapy coupled with high-dose chemoradiotherapy for multiple myeloma: Final results of phase III U.S. Intergroup Trial S9321. J Clin. Oncol. 2006; 24: 929-36. PMID: 16432076
- Barosi G, Tefferi A, Besses C, et al. Clinical end points for drug treatment trials in BCR-ABL1-negative classic myeloproliferative neoplasms: consensus statements from European LeukemiaNET (ELN) and Internation Working Group- Myeloproliferative Neoplasms Research and Treatment (IWG-MRT). Leukemia. 2015; 29(1): 20-26. doi: 10.1038/leu.2014.250. PMID: 25151955
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 3.2017. 28 Nov 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/myeloma.pdf
- Durie BG, Kyle RA, Belch A, et al. Myeloma management guidelines: a consensus report from the Scientific Advisors of the International Myeloma Foundation. Hematol J. 2003; 4: 379-98. PMID: 14671610
- Durie BG and Salmon SE. A clinical staging system for multiple myeloma correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. Cancer. 1975; 36: 842–54. doi: 10.1002/1097-0142(197509)36:3<842::AID-CNCR2820360303>3.0.CO;2-U. PMID: 1182674
- Lynch HT, Ferrara K, Barlogie B, at al. Familial Myeloma: Study of a Unique Family. N Engl J Med. 2008 July 10; 359(2): 152–157. doi:10.1056/NEJMoa0708704. PMCID: PMC2775509
- Lynch HT, Sanger WG, Pirruccello S, et al. Familial multiple myeloma: a family study and review of the literature. J Natl Cancer Inst. 2001; 93: 1479. PMID:11584064
- Rajkumar S. Multiple myeloma: 2012 update on diagnosis, risk-stratification, and management. Am J Hematol. 2012 Jan; 87(1): 78-88. PMID: 22180161
- Waxman AJ, Mink PJ, Devesa SS, et al. Racial disparities in incidence and outcome in multiple myeloma: a populationbased study. Blood. 2010; 116(25): 5501. PMID: 20823456



# Non-Hodgkin: Adult T-Cell Leukemia/Lymphoma

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5508 Adult-T-Cell Therapy per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - First-line treatment;
  - Normal cardiac function;
  - ALK-positive ALCL (Anaplastic Lymphoma Kinase positive Anaplastic Large Cell Lymphoma).

ASSOCIATED CHEMOTHERAPY REGIMENS

## CHOEP



## CHOP

Ind. 5508 Adult-T-Cell Therapy per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- First-line treatment;
- Normal cardiac function; and ANY of the following:
  - **§** Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS);
  - S Angioimmunoblastic T-cell lymphoma (AITL);
  - S Natural killer (NK)/T-cell lymphoma, Adult T-cell leukemia/lymphoma (ATTL);
  - ALK-negative ALCL (Anaplastic Lymphoma Kinase negative Anaplastic Large Cell Lymphoma);
  - Senteropathy-associated T-cell lymphoma (EATL).

## ASSOCIATED CHEMOTHERAPY REGIMENS

## CHOEP

## CHOP

## DA-EPOCH

## HyperCVAD (Even Cycles)

## HyperCVAD (Odd Cycles)



Ind. 5508 Adult-T-Cell Therapy per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- First-line treatment; and ANY of the following:
  - **§** Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS);
  - S Angioimmunoblastic T-cell lymphoma (AITL);
  - S Natural killer (NK)/T-cell lymphoma, Adult T-cell leukemia/lymphoma (ATTL).

ASSOCIATED CHEMOTHERAPY REGIMENS

Zidovudine + Interferon alpha (Induction Therapy)

Zidovudine + Interferon alpha (Maintenence Therapy)



#### REFERENCES

- Goede V, Fischer K, Humphrey K, et al. Obinutuzumab (GA101) plus chlorambucil (Clb) or rituximab plus Clb versus Clb
  alone in patients with chronic lymphocytic leukemia (CLL) and preexisting medical conditions (comorbidities): final stage
  1 results of the CLL (BO21004 phase III trial [abstract]. J Clin Oncol. 2013;31:Abstract 7004.
- Hillmen P, Robak T, Janssens A, et al. Ofatumumab + chlorambucil versus chlorambucil alone in patients with untreated chronic lymphocytic leukemia (CLL): Results of the phase III study Complement 1 (OMB110911) [abstract]. Blood. 2013;122:Abstract 528.
- Foa R, Alietti A, Guarini A, et al. A phase II study of chlorambucil rituximab (CLB-R) followed by R maintenance vs observation in elderly patients with previously untreated chronic lymphocytic leukemia (CLL): induction phase results [abstract]. Haematologica. 2011;96:Abstract 532.
- Fischer K, Cramer P, Busch R, et al. Bendamustine combined with rituximab for previously untreated patients with chronic lymphocytic leukemia: a multicenter phase II trial of the German Chronic Lymphocytic Leukemia Study Group. J Clin Oncol. 2012;30:3209–3216.
- Knauf WU, Lissitchkov T, Aldaoud A, et al. Phase III randomized study of bendamustine compared with chlorambucil in previously untreated patients with chronic lymphocytic leukemia. J Clin Oncol. 2009;27:4378–4384.
- Knauf WU, Lissitchkov T, Aldaoud A, et al. Bendamustine in the treatment of chronic lymphocytic leukemia–consistent superiority over chlorambucil in elderly patients and across clinically defined risk groups [abstract]. Blood. 2009;114: Abstract 2367.
- Flynn JM, Byrd JC, Kipps TJ, et al. Obinutuzumab (GA101) 1,000 mg versus 2,000 mg in patients with chronic lymphocytic leukemia (CLL): results of the phase II GAGE (GAO4768g) trial [abstract]. J Clin Oncol. 2014;32(15\_suppl):Abstract 7083.
- Huhn D, von Schilling C, Wilhelm M, et al. Rituximab therapy of patients with B-cell chronic lymphocytic leukemia. Blood. 2001;98(5):1326–1331.
- Byrd JC, Peterson BL, Morrison VA, et al. Randomized phase 2 study of fludarabine with concurrent versus sequential treatment with rituximab in symptomatic, untreated patients with B-cell chronic lymphocytic leukemia: results from Cancer and Leukemia Group B 9712 (CALGB 9712). Blood. 2003;101:6–14.
- Robak T, Blonski JZ, Kasznicki M, et al. Cladribine with or without prednisone in the treatment of previously treated and untreated B-cell chronic lymphocytic leukemia—updated results of the multicentre study of 378 patients. Br J Haematol. 2000;108(2):357–368.
- Eichhorst BF, Busch R, Stilgenbauer S, et al. First-line therapy with fludarabine compared with chlorambucil does not result in a major benefit for elderly patients with advanced chronic lymphocytic leukemia. Blood. 2009;114:3382–3391
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. T-cell Lymphomas. Version 2.2017. 21 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/t-cell.pdf.
- Rai KR, Peterson BL, Applebaum FR, et al. Fludarabine compared with chlorambucil as primary therapy for chronic lymphocytic leukemia. N Engl J Med. 2000;343:1750–1757.
- Keating MJ O'Brien S, Albitar M, et al. Early results of a chemoimmunotherapy regimen of fludarabine, cyclophosphamide, and rituximab as initial therapy for chronic lymphocytic leukemia. J Clin Oncol. 2005;23:4079–4088.
- Tam CS, O'Brien S, Wierda W, et al. Long-term results of the fludarabine, cyclophosphamide, and rituximab regimen as initial therapy of chronic lymphocytic leukemia. Blood. 2008;112:975–980.



- Hallek M, Fischer K, Fingerle-Rowson G, et al. Addition of rituximab to fludarabine and cyclophosphamide in patients with chronic lymphocytic leukemia: a randomized, open-label, phase 3 trial. Lancet. 2010;376:1164–1174.
- Kay NE, Geyer SM, Call TG, et al. Combination chemoimmunotherapy with pentostatin, cyclophosphamide, and rituximab shows significant clinical activity with low accompanying toxicity in previously untreated B chronic lymphocytic leukemia.Blood. 2007;109:405–411.
- Faderl S, Thomas DA, O'Brien S, et al. Experience with alemtuzumab plus rituximab in patients with relapsed and refractory lymphoid malignancies. Blood. 2003;101:3413–3415.
- Castro JE, James DF, Sandoval-Sus JD, et al. Rituximab in combination with high-dose methylprednisolone for the treatment of chronic lymphocytic leukemia. Leukemia. 2009;23:1779–1789.
- Thornton PD, Matutes E, Bosanquet AG, et al. High dose methylprednisolone can induce remissions in CLL patients with p53 abnormalities. Ann Hematol. 2003;82:759–765.
- Byrd JC, Furman RR, Coutre SE, et al. Targeting BTK with ibrutinib in relapsed chronic lymphocytic leukemia. N Engl J Med. 2013;369:32–42.
- Hillmen P, Gribben JG, Follows GA, et al. Rituximab plus chlorambucil (R-Chlorambucil) as first-line treatment chronic lymphocytic leukemia (CLL): Final analysis of an open-label phase II study [abstract]. Ann Oncol. 2011;22:Abstract 120.
- Raphael B, Andersen JW, Silber R, et al. Comparison of chlorambucil and prednisone versus cyclophosphamide, vincristine, and prednisone as initial treatment for chronic lymphocytic leukemia: long-term follow-up of an Eastern Cooperative Oncology Group randomized clinical trial. J Clin Oncol. 1991;9(5):770–776.
- Foon KA, Boviadzis M, Land, SR, et al. Chemoimmunotherapy with low-dose fludarabine and cyclophosphamide and high dose rituximab in previously untreated patients with chronic lymphocytic leukemia. J Clin Oncol. 2009;27(4):498–503.



# Non-Hodgkin: Diffuse Large B-Cell Lymphoma

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

CAR-T Requests: All requests for CAR-T are reviewed by the Medical Director and Health Plan for medical necessity against the most recent evidence based medicine on an individual basis.

Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Induction therapy; and ANY of the following:
  - Stage 1 or 2, non-bulky disease;



Stage 1 or 2, bulky disease (>10 cm);

Stage 3 or 4.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dose-Adjusted R-EPOCH

RCHOP

## RCHOP-14

Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Induction therapy;
- HIV positive.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dose-Adjusted R-EPOCH

Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Poor left ventricular function or very frail;
- Induction therapy;
- Poor candidate for high-dose therapy; and ANY of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 247 of 387



- Stage 1 or 2, non-bulky disease;
- Stage 1 or 2, bulky disease (greater than 10cm);
- Stage 3 or 4.

ASSOCIATED CHEMOTHERAPY REGIMENS

CDOP + Rituximab

CEPP + Rituximab

Dose-Adjusted R-EPOCH

#### RCEOP

Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Induction therapy;
- Poor candidate for high-dose therapy; and ANY of the following:
  - Stage 1 or 2, non-bulky disease;
  - Stage 1 or 2, bulky disease (greater than 10cm);
  - Stage 3 or 4.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## Mini-RCHOP



Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Central nervous system (CNS) involvement;
- Parenchymal disease;
- Induction therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

RCHOP + Methotrexate

- Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Paranasal sinus, testicular, or epidural involvement; bone marrow with large cell lymphoma; HIV lymphoma (especially EBER+); greater than or equal to two (2) extra-nodal sites and elevated LDH;
  - Leptomeningeal.

ASSOCIATED CHEMOTHERAPY REGIMENS

Methotrexate + Cytarabine



Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Primary Mediastinal Large B-Cell Lymphoma;
- Induction therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

ICE

Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Poor left ventricular function or very frail.

ASSOCIATED CHEMOTHERAPY REGIMENS

## RGCVP

Ind. 5512 First-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Central nervous system (CNS) involvement;
- Leptomeningeal;
- Induction therapy.

#### ASSOCIATED CHEMOTHERAPY REGIMENS



Methotrexate + Cytarabine

Ind. 5513 Second-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Intent to proceed with autologous stem cell transplant.

ASSOCIATED CHEMOTHERAPY REGIMENS

DHAP + Rituximab

ESHAP + Rituximab

GDP + Rituximab

GemOx + Rituximab

ICE + Rituximab

MINE + Rituximab

Ind. 5513 Second-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Poor candidate for high-dose therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

CEPP + Rituximab

Dose-Adjusted R-EPOCH

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 251 of 387



GDP + Rituximab

GemOx + Rituximab

## Lenalidomide + Rituximab

RCEOP

Rituximab

Ind. 5513 Second-Line Systemic Therapy for DLBCL per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Poor candidate for high-dose therapy;
- CD30 positive lymphoma (CD 30+).

ASSOCIATED CHEMOTHERAPY REGIMENS

Bendamustine + Rituximab

Brentuximab Vedotin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 252 of 387



#### REFERENCES

- Coiffier B, Thieblemont C, Van Den Neste E, et al. Long-term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemo- therapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. Blood. 2010;116:2040–2045.
- Feugier P, Van Hoof A, Sebban C, et al, Long-term results of the R-CHOP study in the treatment of elderly patients with diffuse large B-cell lymphoma: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. J Clin Oncol. 2005;23:4117–4211.
- Pfreundschuh M, Trumper L, Osterborg A, et al. CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis diffuse large-B-cell lymphoma: a randomised controlled trial by the MabThera International Trial (MINT) Group. Lancet Oncol. 2006;7:379–391.
- Pfreundschuh M, Schubert J, Ziepert M, et al. Six versus eight cycles of bi-weekly CHOP-14 with or without rituximab in elderly patients with aggressive CD20+ B-cell lymphomas: a randomized controlled trial (RICOVER-60). Lancet Oncol. 2008;9:105–116.
- Cunningham D, Hawkes EA, Jack A, et al. Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone in patients with newly diagnosed diffuse large B-cell non-Hodgkin lymphoma: a phase 3 comparison of dose intensification with 14-day versus 21-day cycles. Lancet. 2013;381:1817–1826.
- Purroy N, Lopez A, Vallespi T, et al. Dose-adjusted EPOCH plus rituximab (DA-EPOCH-R) in untreated patients with poor risk large B-cell lymphoma. A phase 2 study conducted by the Spanish PETHEMA Group [Abstract]. Blood. 2009;114:Abstract 2701.
- Wilson WH, Dunleavy K, Pittaluga S, et al. Phase II study of dose-adjusted EPOCH and rituximab in untreated diffuse large B-cell lymphoma with analysis of germinal center and post-germinal center biomarkers. J Clin Oncol. 2008;26:2717– 2724.
- Wilson WH, Jung SH, Porcu P, et al. A Cancer and Leukemia Group B multi-center study of DA-EPOCH-rituximab in untreated diffuse large B-cell lymphoma with analysis of outcome by molecular subtype. Haematologica. 2012;97:758– 765.
- Chao NJ, Rosenberg SA, Horning SJ. CEPP(B): An effective and well-tolerated regimen in poor-risk, aggressive non-Hodgkin's lymphoma. Blood. 1990;76:1293–1298.
- Martino R, Perea G, Caballero MD, et al. Cyclophosphamide, pegylated liposomal doxorubicin (Caelyx), vincristine and prednisone (CCOP) in elderly patients with diffuse large B- cell lymphoma: results from a prospective phase II study. Haematologica. 2002;87:822–827.
- Zaja F, Tomadini V, Zaccaria A, et al. CHOP-rituximab with pegylated liposomal doxorubicin for the treatment of elderly patients with diffuse large B-cell lymphoma. Leuk Lymphoma. 2006;47:2174–2180.
- Bessell EM, Burton A, Haynes AP, et al. A randomized multicentre trial of modified CHOP versus MCOP in patients aged 65 years and over with aggressive non-Hodgkin's lymphoma. Ann Oncol. 2003;14:258–267.
- Bezwoda W, Rastogi RB, Erazo Valla A, et al. Long-term results of a multicentre randomised, comparative phase III trial of CHOP versus CNOP regimens in patients with intermediate- and high-grade non-Hodgkin's lymphomas. Novantrone International Study Group. Eur J Cancer. 1995;31:903–911.



- Sonneveld P, de Ridder M, van der Lelie H, et al. Comparison of doxorubicin and mitoxantrone in the treatment of elderly patients with advanced diffuse non-Hodgkin's lymphoma using CHOP versus CNOP chemotherapy. J Clin Oncol. 1995;13:2530–2539.
- Garcia-Suarez J, Banas H, Arribas I, et al. Dose-adjusted EPOCH plus rituximab is an effective regimen in patients with poor-prognostic untreated diffuse large B-cell lymphoma: results from a prospective observational study. British Journal of Haematology. 2006;211:276–285.
- Moccia AA, Schaff K, Hoskins P, et al. R-CHOP with etoposide substituted for doxorubicin (R-CEOP): excellent outcome in diffuse large B cell lymphoma for patients with a contraindi- cation to anthracyclines. Presented at: 51st American Society of Hematology Annual Meeting and Exposition; December 7, 2009; New Orleans, LA. Blood. 2009;114: Abstract 408.
- Peyrade F, Jardin F, Thieblemont C, et al. Attenuated immunochemotherapy regimen (R-miniCHOP) in elderly patients older than 80 years with diffuse large B-cell lymphoma: a multicentre, single-arm, phase 2 trial. Lancet Oncol. 2011;12:460–468.
- Stiff PJ, Unger JM, Cook J, et al. Randomized phase III U.S./Canadian intergroup trial (SWOG S9704) comparing CHOP {+/-} R for eight cycles to CHOP {+/-} R for six cycles followed by autotransplant for patients with high-intermediate (H-Int) or high IPI grade diffuse aggressive non-Hodgkin lymphoma (NHL). J Clin Oncol. 2011;29:8001.
- Velasquez WS, Cabanillas F, Salvador P, et al. Effective salvage therapy for lymphoma with cisplatin in combination with high-dose Ara-C and dexamethasone (DHAP). Blood. 1988;71:117–122.
- Mey UJ, Orlopp KS, Flieger D, et al. Dexamethasone, high-dose cytarabine, and cisplatin in combination with rituximab as salvage treatment for patients with relapsed or refractory aggressive non-Hodgkin's lymphoma. Cancer Invest. 2006;24:593–600.
- Gisselbrecht C, Glass B, Mounier N, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol. 2010;28:4184–4190.
- Velasquez WS, McLaughlin P, Tucker S, et al. ESHAP—an effective chemotherapy regimen in refractory and relapsing lymphoma: a 4-year follow-up study. J Clin Oncol. 1994;12:1169–1176.
- Martin A, Conde E, Arnan M, et al. R-ESHAP as salvage therapy for patients with relapsed or refractory diffuse large B-cell lymphoma: the influence of prior exposure to rituximab on outcome. A GEL/TAMO study. Haematologica. 2008;93:1829– 1836.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. B-cell Lymphomas. Version 2.2017. 21 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/b-cell.pdf
- Crump M, Baetz T, Couban S, et al. Gemcitabine, dexamethasone, and cisplatin in patients with recurrent or refractory
   aggressive histology B-cell non-Hodgkin lymphoma: a Phase II study by the National Cancer Institute of Canada Clinical
   Trials Group (NCIC-CTG). Cancer. 2004;101:1835–1842.
- Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. Leuk Lymphoma. 2010;51:1523–1529.
- Lopez A, Gutierrez A, Palacios A, et al. GEMOX-R regimen is a highly effective salvage regimen in patients with refractory/ relapsing diffuse large-cell lymphoma: a phase II study. Eur J Haematol. 2008;80:127–132.



- Zelenetz AD, Hamlin P, Kewalramani T, et al. Ifosfamide, carboplatin, etoposide (ICE)-based second-line chemotherapy for the management of relapsed and refractory aggressive non-Hodgkin's lymphoma. Ann Oncol. 2003;14:5–10.
- Kewalramani T, Zelenetz AD, Nimer SD, et al. Rituximab and ICE (RICE) as second-line therapy prior to autologous stem cell transplantation for relapsed or primary refractory diffuse large B-cell lymphoma. Blood. 2004;103:3684–3688.
- Gisselbrecht C, Glass B, Mounier N, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol. 2010;28:4184–4190.
- Dincol D, Buyukcelik A, Dogan M, et al. Long-term outcome of mesna, ifosfamide, mitoxantrone, etoposide (MINE) regimen as a consolidation in patients with aggressive non-Hodgkin lymphoma responding to CHOP. Med Oncol. 2010;27:942–945.
- Emmanouilides C, Lill M, Telatar M, et al. Mitoxantrone/ifosfamide/etoposide salvage regimen with rituximab for in vivo purging in patients with relapsed lymphoma. Clin Lymphoma. 2002;3:111–116.
- Weidmann E, Kim SZ, Rost A, et al. Bendamustine is effective in relapsed or refractory aggressive non-Hodgkin's lymphoma. Ann Oncol. 2002;13:1285–1289.
- Vacirca J, Tabbara I, Acs P, Shumaker G. Bendamustine + rituximab as treatment for elderly patients with relapsed or refractory diffuse large B-cell lymphoma [abstract]. Blood. 2010;116: Abstract 2806.
- Ohmachi K, Niitsu N, Uchida T, et al. Multicenter phase II study of bendamustine plus rituximab in patients with relapsed or refractory diffuse large B-cell lymphoma. J Clin Oncol. 2013;31:2103–2109.
- Bartlett N, Sharman J, Oki Y, et al. A phase 2 study of brentuximab vedotin in patients with relapsed or refractory CD30positive non-Hodgkin lymphomas: interim results in patients with DLBCL and other B-cell lymphomas [abstract]. Blood. 2013;122; Abstract:848.
- Yan L, Yimamu M, Wang X, et al. Addition of rituximab to a CEOP regimen improved the outcome in the treatment of non-germinal center immunophenotype diffuse large B cell lymphoma cells with high Bcl-2 expression. Int J Hematol. 2014:99:79–86.
- Gutierrez M, Chabner BA, Pearson D, et al. Role of a doxorubicin-containing regimen in relapsed and resistant lymphomas: An 8-year follow-up study of EPOCH. J Clin Oncol. 2000;18:3633–3642.
- Jermann M, Jost LM, Taverna C, et al. Rituximab-EPOCH, an effective salvage therapy for relapsed, refractory or transformed B-cell lymphomas: Results of a phase II study. Ann Oncol. 2004;15:511–516.
- Hou Y, Wang H, Ba Y. Rituximab, gemcitabine, cisplatin, and dexamethasone in patients with refractory or relapsed or aggressive B-cell lymphoma. Med Oncol. 2012;29:2409–2416.
- Gopal A, Press O, Pagel J. Efficacy and Safety of Gemcitabine (G), Carboplatin ©, Dexamethasone (D), and Rituximab in Patients with Relapsed/Refractory Lymphoma: A Prospective Multi-center Phase II Study of by the Puget Sound Oncology Consortium (PSOC). Leuk Lymphoma. 2010;51:1523–1529.
- Corazzelli G, Capobianco G, Arcamone M, et al. Long-term results of gemcitabine plus oxaliplatin with and without rituximab as salvage treatment for transplant-ineligible patients with refractory/relapsing B-cell lymphoma. Cancer Chemother Pharmacol. 2009;64:907–916.
- El Gnaoui T, Dupuis J, Belhadj K, et al. Rituximab, gemcitabine and oxaliplatin: An effective salvage regimen for patients with relapsed or refractory B-cell lymphoma not candidates for high-dose therapy. Ann Oncol. 2007;18:1363–1368.
- Witzig TE, Vose JM, Zinzani PL, et al. An international phase II trial of single-agent lenalidomide for relapsed or refractory aggressive B-cell non-Hodgkin's lymphoma. Ann Oncol. 2011;22:1622–1627.



- Wiernik PH, Lossos IS, Tuscano JM, et al. Lenalidomide monotherapy in relapsed or refractory aggressive Non-Hodgkin's lymphoma. J Clin Oncol. 2008;26:4952–4957.
- Wang M, Fowler N, Wagner-Bartak N, et al. Oral lenalidomide with rituximab in relapsed or refractory diffuse large cell, follicular, and transformed lymphoma: a phase II clinical trial. Leukemia. 2013.
- Rituxan® (rituximab) [package insert]. Genentech, Inc. South San Francisco, CA.



# Non-Hodgkin: Follicular Lymphoma

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

CAR-T Requests: All requests for CAR-T are reviewed by the Medical Director and Health Plan for medical necessity against the most recent evidence based medicine on an individual basis.

- Ind. 5537 First-Line, Consolidation, or Extended Dosing for Follicular Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Grade 1 or 2; and ANY of the following:
    - Symptoms attributable to follicular lymphoma;
    - **§** Threatened end-organ function;
    - S Cytopenia secondary to lymphoma;



Bulky disease (1 greater than 7 cm, or 3 or more greater than 3 cm);

Steady progression of disease; and ANY of the following:

- Stage 2 bulky disease;
- Stage 3;
- Stage 4.

ASSOCIATED CHEMOTHERAPY REGIMENS

90Yttrium-Ibritumomab-Tiuxetan

Bendamustine + Rituximab

Chlorambucil + Rituximab

Lenalidomide

Lenalidomide + Rituximab

RCHOP

RCVP

## Rituximab

Ind. 5537 First-Line, Consolidation, or Extended Dosing for Follicular Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Stage 2;
- Grade 1 or 2; and ANY of the following:
  - Symptoms attributable to follicular lymphoma;
  - S Threatened end-organ function;
  - S Cytopenia secondary to lymphoma;



- Sulky disease (1 greater than 7 cm, or 3 or more greater than 3 cm);
- Steady progression of disease.

90Yttrium-Ibritumomab-Tiuxetan

Chlorambucil + Rituximab

- Ind. 5537 First-Line, Consolidation, or Extended Dosing for Follicular Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Partial or complete response to first-line treatment; and ANY of the following:
    - Symptoms attributable to follicular lymphoma;
    - **§** Threatened end-organ function;
    - S Cytopenia secondary to lymphoma;
    - Sulky disease (1 greater than 7 cm, or 3 or more greater than 3 cm);
    - Steady progression of disease; and ANY of the following:
      - Stage 2 bulky disease;
      - Stage 3;
      - Stage 4.

### ASSOCIATED CHEMOTHERAPY REGIMENS

Rituximab + 90Yttrium-Ibritumomab-Tiuxetan

Rituximab Maintenance



Ind. 5537 First-Line, Consolidation, or Extended Dosing for Follicular Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Grade 3 or 4; and ANY of the following:
  - Symptoms attributable to follicular lymphoma;
  - § Threatened end-organ function;
  - S Cytopenia secondary to lymphoma;
  - Sulky disease (1 greater than 7 cm, or 3 or more greater than 3 cm);
  - **§** Steady progression of disease.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

## RCHOP

Ind. 5538 Second-Line, Subsequent, or Extended Dosing for Follicular Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Partial or complete response to second-line treatment; and ANY of the following:
  - Symptoms attributable to follicular lymphoma;
  - **§** Threatened end-organ function;
  - S Cytopenia secondary to lymphoma;
  - Sulky disease (1 greater than 7 cm, or 3 or more greater than 3 cm);
  - **§** Steady progression of disease; and ANY of the following:
    - Stage 2 bulky disease;
    - Stage 3;
    - Stage 4.



Rituximab Maintenance

Ind. 5538 Second-Line, Subsequent, or Extended Dosing for Follicular Lymphoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:

- Symptoms attributable to follicular lymphoma;
- Threatened end-organ function;
- Cytopenia secondary to lymphoma;
- Bulky disease (1 greater than 7 cm, or 3 or more greater than 3 cm);
- Steady progression of disease; and ANY of the following:
  - Stage 2 bulky disease;
  - Stage 3;
  - Stage 4.

ASSOCIATED CHEMOTHERAPY REGIMENS

Fludarabine + Rituximab

FND + Rituximab

Idelalisib

Lenalidomide

Lenalidomide + Rituximab

Rituximab

Rituximab + 90Yttrium-Ibritumomab-Tiuxetan

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 261 of 387





#### REFERENCES

- Rummel M, Niederle N, Maschmeyer G, et al. Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial. Lancet. 2013;381:1203–1210.
- Czuczman M, Weaver R, Alkuzweny B, et al. Prolonged clinical and molecular remission in patients with low-grade or follicular non-Hodgkin's lymphoma treated with rituximab plus CHOP chemotherapy: 9-year follow-up. J Clin Oncol. 2004;22:4711–4716.
- Hiddemann W, Kneba M, Dreyling M, et al. Frontline therapy with rituximab added to the combination of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) significantly improves the outcome for patients with advanced-stage follicular lymphoma compared with therapy with CHOP alone: results of a prospective randomized study of the German Low-Grade Lymphoma Study Group. Blood.2005;106:3725–3732.
- Marcus R, Imrie K, Solal-Celigny P, et al. Phase III study of R-CVP compared with cyclophosphamide, vincristine, and prednisonealone in patients with previously untreated advanced follicular lymphoma. J Clin Oncol. 2008;26:4579–4586.
- Marcus R, Imrie K, Belch A et al. CVP chemotherapy plus rituximab compared with CVP as first-line treatment for advanced follicular lymphoma. Blood. 2005;105:1417–1423.
- Hainsworth JD, Litchy S, Burris HA, III, et al. Rituximab as first-line and maintenance therapy for patients with indolent Non-Hodgkin's lymphoma. J Clin Oncol. 2002;20:4261–4267.
- Colombat P, Salles G, Brousse N, et al. Rituximab (anti-CD20 monoclonal antibody) as single first-line therapy for patients with follicular lymphoma with a low tumor burden: Clinical and molecular evaluation. Blood. 2001;97:101–106.
- Martin P, Jung S-H, Johnson JL, et al. CALGB 50803 (Alliance): a phase II trial of lenalidomide plus rituximab in patients with previously untreated follicular lymphoma [abstract]. J Clin Oncol. 2014;32:Abstract 8521.
- Fowler N, Davis R, Rawal S, et al. Safety and activity of lenalidomide and rituximab in untreated indolent lymphoma: an open-label, phase 2 trial. Lancet Oncol. 2014;15:1311–1318.
- Scholz CW, Pinto A, Linkesch W, et al. 90Yttrium ibritumomab tiuxetan as first line treatment for follicular lymphoma. first results from an international phase II clinical trial [abstract]. Blood. 2010;116:Abstract 593.
- Rigacci L, Nassi L, Puccioni M, et al. Rituximab and chlorambucil as first-line treatment for low-grade ocular adnexal lymphomas. Ann Hematol. 2007;86:565–568.
- Morschhauser F, Radford J, Van Hoof A, et al. Phase III trial of consolidation therapy with Yttrium-90–Ibritumomab Tiuxetan compared with no additional therapy after first remission in advanced follicular lymphoma. J Clin Oncol. 2008;26:5156–5164.
- Hagenbeek A, Radford J, Van Hoof A, et al. 90Y-Ibritumomab tiuxetan (Zevalin®) consolidation of first remission in advanced- stage follicular non-hodgkin's lymphoma: Updated results after a median follow-up of 66.2 months from the international, randomized, phase III First-Line Indolent Trial (FIT) in 414 Patients [abstract]. Blood. 2010;116:Abstract 594.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. B-cell Lymphomas.
   Version 2.2017. 21 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/b-cell.pdf
- Morschhauser F, Radford J, Van Hoof A, et al. 90Yttrium-ibritumomab tuxetan consolidation of first remission in advanced- stage follicular non-Hodgkin lymphoma: Updated results after a median follow-up of 7.3 years from the international, randomized, phase III first-line indolent trial. J Clin Oncol. 2013;31:1977–1983.



- Salles GA, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): A phase 3, randomized controlled trial. Lancet. 2011;377:42–51.
- Ghielmini M, Schmitz SH, Cogliatti SB, et al. Prolonged treatment with rituximab in patients with follicular lymphoma significantly increases event-free survival and response duration compared with the standard weekly × 4 schedule.Blood. 2004;103:4416–4423.
- Czuczman MS, Koryzna A, Mohr A, et al. Rituximab in combination with fludarabine chemotherapy in low-grade of follicular lymphoma. J Clin Oncol. 2005;23:694–704.
- Leonard J, Jung S-H, Johnson JL, et al. CALGB 50401: A randomized trial of lenalidomide alone versus lenalidomide plus rituximab in patients with recurrent follicular lymphoma [abstract]. J Clin Oncol. 2012;30:Abstract 8000.
- Witzig TE, Wiernik PH, Moore T, et al. Lenalidomide oral monotherapy produces durable responses in relapsed or refractory indolent non-Hodgkin's Lymphoma. J Clin Oncol. 2009;27:5404–5409.
- Witzig TE, Flinn IW, Gordon LI, et al. Treatment with ibritumomab tiuxetan radioimmunotherapy in patients with rituximab- refractory follicular non-Hodgkin's lymphoma. J Clin Oncol. 2002;20: 3262–3269.
- Witzig TE, Gordon LI, Cabanillas F, et al. Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy versus rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. J Clin Oncol. 2002;20:2453–2463.
- McLaughlin P, Grillo-Lopez AJ, Link BK, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. J Clin Oncol. 1998;16:2825–2833.
- Ghielmini M, Schmitz SH, Cogliatti SB, et al. Prolonged treatment with rituximab in patients with follicular lymphoma significantly increases event-free survival and response duration compared with the standard weekly x 4 schedule. Blood. 2004;103:4416–4423.
- McLaughlin P, Hagemeister FB, Rodriguez MA, et al. Safety of fludarabine, mitoxantrone, and dexamethasone combined with rituximab in the treatment of stage IV indolent lymphoma. Semin Oncol. 2000;27:37–41.
- Gopal A, Kahl B, De Vos S, et al. PI3Kδ inhibition by idelalisib in patients with relapsed indolent lymphoma. N Engl J Med.2014;370:1008–1018.
- van Oers MHJ, Van Glabbeke M, Giurgea L, et al. Rituximab maintenance treatment of relapsed/resistant follicular nonhodgkin's lymphoma: Long-term outcome of the EORTC 20981 Phase III randomized Intergroup Study. J Clin Oncol. 2010;28:2853–2858.
- Forstpointer R, Unterhalt M, Dreyling M, et al. Maintenance therapy with rituximab leads to a significant prolongation of response duration after salvage therapy with a combination of rituximab, fludarabine, cyclophosphamide, and mitoxantrone (R-F CM) in patients with recurring and refractory follicular and mantle cell lymphomas: Results of a prospective randomized study of the German Low Grade Lymphoma Study Group (GLSG). Blood. 2006;108:4003–400.



# Non-Small Cell Lung Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5349 Neoadjuvant or Adjuvant Chemotherapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Stage 1B with high risk features: poorly differentiated tumors, lymphovascular invasion, wedge resection, tumors greater than 4 cm, visceral pleural involvement, incomplete lymph node sampling;
  - Adjuvant chemotherapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Pemetrexed

Cisplatin + Vinorelbine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 265 of 387



- Ind. 5349 Neoadjuvant or Adjuvant Chemotherapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Stage 2 or 3a;
  - Adjuvant chemotherapy.

Cisplatin + Docetaxel

Cisplatin + Etoposide

Cisplatin + Gemcitabine

Cisplatin + Pemetrexed

Cisplatin + Vinblastine

Cisplatin + Vinorelbine

- Ind. 5349 Neoadjuvant or Adjuvant Chemotherapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Stage 3 or locally advanced;
  - Adjuvant chemotherapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Docetaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 266 of 387



Cisplatin + Gemcitabine Cisplatin + Pemetrexed Cisplatin + Vinblastine Cisplatin + Vinorelbine

- Ind. 5349 Neoadjuvant or Adjuvant Chemotherapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Preoperative chemotherapy; and EITHER of the following:
    - Stage 2 or 3a;
    - **§** Stage 3 or locally advanced.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Docetaxel

Cisplatin + Gemcitabine

Cisplatin + Pemetrexed

- Ind. 5349 Neoadjuvant or Adjuvant Chemotherapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Adjuvant chemotherapy for a patient with Cisplatin intolerance; and EITHER of the following:



- Stage 1B with high risk features: poorly differentiated tumors, lymphovascular invasion, wedge resection, tumors greater than 4 cm, visceral pleural involvement, incomplete lymph node sampling;
- Stage 2 or 3a.
- Preoperative chemotherapy for a patient with Cisplatin intolerance; and EITHER of the following:
  - Stage 2 or 3a;
  - **§** Stage 3 or locally advanced.

Paclitaxel + Carboplatin

- Ind. 5349 Neoadjuvant or Adjuvant Chemotherapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Mediastinoscopy reveals N2 (ipsilateral mediastinal or subcarinal lymph nodes).

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Vinorelbine

Ind. 5350 Concurrent Chemoradiation Therapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 268 of 387



- Adjuvant chemotherapy for Stage 2 or 3a with positive margins
- Stage 2 or 3a Preoperative chemotherapy;
- Stage 3 or locally advanced.

Cisplatin + Etoposide

Cisplatin + Vinblastine

- Ind. 5350 Concurrent Chemoradiation Therapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Stage 2 or 3a with Non-Squamous histology; and EITHER of the following:
    - **§** Preoperative chemotherapy;
    - S Adjuvant chemotherapy with positive margin;
  - Preoperative chemotherapy for Stage 3 or locally advanced disease with Non-Squamous histology.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Pemetrexed

Cisplatin + Pemetrexed

- Ind. 5351 Sequential Chemoradiation Therapy for NSCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Stage 2 or 3a; and EITHER of the following:



- **§** Preoperative chemotherapy;
- S Adjuvant chemotherapy with positive margin;
- Preoperative chemotherapy for Stage 3 or locally advanced disease.

Cisplatin + Vinblastine

Paclitaxel + Carboplatin

Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Positive Epidermal Growth Factor Receptor (EGFR);
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Afatinib

Erlotinib

Gefitinib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 270 of 387



Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Positive Anaplastic Lymphoma Kinase (ALK);
- Second-line treatment.
- Advanced or metastatic disease

### ASSOCIATED CHEMOTHERAPY REGIMENS

## Ceritinib

## Crizotinib

- Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Advanced or metastatic disease;
  - Positive Anaplastic Lymphoma Kinase (ALK);
  - Third-line treatment.

### ASSOCIATED CHEMOTHERAPY REGIMENS

# Ceritinib



Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Second-line treatment;
- Squamous histology.

ASSOCIATED CHEMOTHERAPY REGIMENS

Ramucirumab + Docetaxel

Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- First-line treatment;
- Non-Squamous histology.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bevacizumab

Bevacizumab + Paclitaxel + Carboplatin

Bevacizumab + Pemetrexed + Carboplatin

Bevacizumab + Pemetrexed + Cisplatin

Cisplatin + Pemetrexed



Docetaxel

Pemetrexed

Pemetrexed + Bevacizumab

Pemetrexed + Carboplatin

Pembrolizumab + Carboplatin + Pemetrexed

Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Advanced or metastatic disease;
- Second-line treatment.
- Epidermal Growth Factor Receptor (EGFR) is positive

ASSOCIATED CHEMOTHERAPY REGIMENS

Afatinib

Albumin-bound Paclitaxel

Albumin-bound Paclitaxel + Cisplatin

Carboplatin + Gemcitabine

Cisplatin + Docetaxel

Cisplatin + Etoposide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 273 of 387



Cisplatin + Gemcitabine

Cisplatin + Vinorelbine

Docetaxel

Docetaxel + Carboplatin

Erlotinib

Etoposide + Carboplatin

Gefitinib

Gemcitabine

Gemcitabine + Docetaxel

Paclitaxel

Paclitaxel + Cisplatin

Vinorelbine + Gemcitabine

Carboplatin + Albumin-bound Paclitaxel

Paclitaxel + Carboplatin

Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

• Advanced or metastatic disease;

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 274 of 387



• First-line treatment.

#### ASSOCIATED CHEMOTHERAPY REGIMENS

#### Albumin-bound Paclitaxel

Albumin-bound Paclitaxel + Cisplatin

Carboplatin + Gemcitabine

Cisplatin + Docetaxel

Cisplatin + Etoposide

Cisplatin + Gemcitabine

Cisplatin + Vinorelbine

Docetaxel + Carboplatin

Etoposide + Carboplatin

Gemcitabine + Docetaxel

Paclitaxel

Paclitaxel + Cisplatin

Vinorelbine + Gemcitabine

Paclitaxel + Carboplatin

Carboplatin + Albumin-bound Paclitaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 275 of 387



Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Advanced or metastatic disease;
- Third-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Gemcitabine

- Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Stage 4 or 3B with malignant pleural effusion;
  - Positive Epidermal Growth Factor Receptor (EGFR).

ASSOCIATED CHEMOTHERAPY REGIMENS

Erlotinib

## Gefitinib

- Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Advanced or metastatic disease;



- Positive Anaplastic Lymphoma Kinase (ALK);
- Disease progression on or intolerant to Crizotinib (TKI) therapy;

Alectinib

Brigatinib

Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Disease progression during or after platinum-based chemotherapy;
- Second-line treatment.

### ASSOCIATED CHEMOTHERAPY REGIMENS

Atezolizumab

Nivolumab

Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Positive Epidermal Growth Factor Receptor (EGFR);



- Disease progression on FDA approved therapy for Epidermal Growth Factor Receptor (EGFR) or Anaplastic Lymphoma Kinase (ALK) genomic tumor aberrations;
- Second-line treatment.

Afatinib + Cetuximab

Atezolizumab

Nivolumab

Osimertinib

Ind. 5542 For Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Positive Anaplastic Lymphoma Kinase (ALK);
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Crizotinib



Ind. 5542 Advanced Disease NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- Positive Anaplastic Lymphoma Kinase (ALK);
- Disease progression on FDA approved therapy for Epidermal Growth Factor Receptor (EGFR) or Anaplastic Lymphoma Kinase (ALK) genomic tumor aberrations;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Atezolizumab

Nivolumab

Ind. 5542 For Advanced NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metastatic disease;
- First-line treatment;
- No EGFR or ALK genomic tumor aberrations;
- High PD-L1 expression, TPS score greater than or equal to 50%.

ASSOCIATED CHEMOTHERAPY REGIMENS

# Pembrolizumab



Ind. 5542 For Advanced NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates of the following:

- Second-line treatement; and ANY of the following:
  - Disease progression during or after platinum based chemotherapy with
     PD-L1 expression, TPS greater than or equal to 1%;
  - S Disease progression on FDA approved therapy for EGFR or ALK genomic tumor aberrations and either EGFR is positive or ALK rearrangement is present with PD-L1 expression, TPS greater than or equal to 1%.

ASSOCIATED CHEMOTHERAPY REGIMENS

Pembrolizumab

Ind. 5542 For Advanced NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Stage III or locally advanced NSCLC;
- No disease progression after two (2) or more cycles of definitive chemoradiation.

ASSOCIATED CHEMOTHERAPY REGIMENS

### Durvalumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 280 of 387



Ind. 5542 For Advanced NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Advanced or metstatic disease;
- BRAF V600E positive;
- First-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dabrafenib + Trametinib

Dabrafenib

Vemurafenib

Ind. 5542 For Advanced NSCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Osteoporosis related to NSCLC;
- Hypercalcemia related to NSCLC.
- Advanced or mestatic disease with bone metastases

ASSOCIATED CHEMOTHERAPY REGIMENS

Zoledronic Acid

Denosumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 281 of 387





#### REFERENCES

- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015;65:5-29. Available at: http://www.ncbi.nlm.nih.
  gov/pubmed/25559415.
- Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2012, based on November 2014 SEER data submission, posted to the SEER web site, April 2015. Bethesda, MD: National Cancer Institute; 2015. Available at: http://seer.cancer.gov/csr/1975\_2012/.
- Johnson DH, Schiller JH, Bunn PA, Jr. Recent clinical advances in lung cancer management. J Clin Oncol 2014;32:973-982.
   Available at: http://www.ncbi.nlm.nih.gov/pubmed/24567433.
- Reck M, Heigener DF, Mok T, et al. Management of non-small-cell lung cancer: recent developments. Lancet 2013;382:709-719. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23972814.
- Forde PM, Ettinger DS. Targeted therapy for non-small-cell lung cancer: past, present and future. Expert Rev Anticancer Ther 2013;13:745-758. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23773106.
- Ettinger DS. Ten years of progress in non-small cell lung cancer. J Natl Compr Canc Netw 2012;10:292-295. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22393190.
- Simoff MJ, Lally B, Slade MG, et al. Symptom management in patients with lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e455S- 497S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23649452.
- Alberg AJ, Brock MV, Ford JG, et al. Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e1S-29S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23649439.
- Subramanian J, Govindan R. Lung cancer in never smokers: a review. J Clin Oncol 2007;25:561-570. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17290066.
- The Health Consequences of Smoking: A Report of the Surgeon General. (ed 2010/07/30). Atlanta (GA): U.S. Department of Health and Human Services. Centers for Disease Control and Prevention (US); 2004.
- Secretan B, Straif K, Baan R, et al. A review of human carcinogens -Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. Lancet Oncol 2009;10:1033-1034. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19891056.
- Doll R, Peto R. Mortality in relation to smoking: 20 years' observations on male British doctors. Br Med J 1976;2:1525-1536. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1009386.
- Taylor R, Najafi F, Dobson A. Meta-analysis of studies of passive smoking and lung cancer: effects of study type and continent. Int J Epidemiol 2007;36:1048-1059. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17690135.
- The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General. (ed 2010/07/30). Atlanta (GA): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2006.
- Hackshaw AK, Law MR, Wald NJ. The accumulated evidence on lung cancer and environmental tobacco smoke. BMJ 1997;315:980-988. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9365295.
- Wald NJ, Nanchahal K, Thompson SG, Cuckle HS. Does breathing other people's tobacco smoke cause lung cancer? Br Med J (Clin Res Ed) 1986;293:1217-1222. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3096439.
- Fraumeni JF, Jr. Respiratory carcinogenesis: an epidemiologic appraisal. J Natl Cancer Inst 1975;55:1039-1046. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1107567.



- Janerich DT, Thompson WD, Varela LR, et al. Lung cancer and exposure to tobacco smoke in the household. N Engl J Med 1990;323:632-636. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2385268.
- Straif K, Benbrahim-Tallaa L, Baan R, et al. A review of human carcinogens--part C: metals, arsenic, dusts, and fibres.
   Lancet Oncol 2009;10:453-454. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19418618.
- Driscoll T, Nelson DI, Steenland K, et al. The global burden of disease due to occupational carcinogens. Am J Ind Med 2005;48:419-431. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16299703.
- Humans IWGotEoCRt. Arsenic, metals, fibres, and dusts. IARC Monogr Eval Carcinog Risks Hum 2012;100:11-465.
   Available at: <u>http://www.ncbi.nlm.nih.gov/pubmed/23189751</u>.
- Carney DN. Lung cancer--time to move on from chemotherapy. N Engl J Med 2002;346:211-128. Available at: http://www.ncbi. nlm.nih.gov/pubmed/11784881.
- Chute JP, Chen T, Feigal E, et al. Twenty years of phase III trials for patients with extensive-stage small-cell lung cancer: perceptible progress. J Clin Oncol 1999;17:1794-1801. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10561217.
- Travis WD, Brambilla E, Noguchi M, et al. International association for the study of lung cancer/american thoracic society/ European respiratory society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol 2011;6:244-285. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21252716.
- Finkelstein DM, Ettinger DS, Ruckdeschel JC. Long-term survivors in metastatic non-small-cell lung cancer: an Eastern Cooperative Oncology Group Study. J Clin Oncol 1986;4:702-709. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3701389.
- Gould MK, Donington J, Lynch WR, et al. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e93S-120S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23649456.
- Naidich DP, Bankier AA, Ma cmahon H, et al. Recommendations for the management of subsolid pulmonary nodules detected at CT: a statement from the Fleischner Society. Radiology 2013;266:304-317. Available at: http://www.ncbi.nlm.nih.gov/ pubmed/23070270.
- Ma cmahon H, Austin JH, Gamsu G, et al. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. Radiology 2005;237:395-400. Available at: http://www.ncbi.nlm.nih.gov/ pubmed/16244247.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. Version 4.2017. 18 Jan 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/nscl.pdf.
- Gardiner N, Jogai S, Wallis A. The revised lung adenocarcinoma classification-an imaging guide. J Thorac Dis 2014;6:S537-546. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25349704.
- Seidelman JL, Myers JL, Quint LE. Incidental, subsolid pulmonary nodules at CT: etiology and management. Cancer Imaging 2013;13:365-373. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24061063.
- Hansell DM, Bankier AA, Ma cmahon H, et al. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008;246:697-722. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18195376.
- Travis WD, Brambilla E, Noguchi M, et al. Diagnosis of lung cancer in small biopsies and cytology: implications of the 2011
   International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society
   classification. Arch Pathol Lab Med 2013;137:668-684. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22970842.



- Kim HY, Shim YM, Lee KS, et al. Persistent pulmonary nodular ground-glass opacity at thin-section CT: histopathologic comparisons. Radiology 2007;245:267-275. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17885195.
- Howington JA, Blum MG, Chang AC, et al. Treatment of stage I and II non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e278S-313S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23649443.
- Martins RG, D'Amico TA, Loo BW, Jr., et al. The management of patients with stage IIIA non-small cell lung cancer with N2 mediastinal node involvement. J Natl Compr Canc Netw 2012;10:599-613. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22570291.
- Arriagada R, Bergman B, Dunant A, et al. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. N Engl J Med 2004;350:351-360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14736927.
- Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. N Engl J Med 2005;352:2589-2597. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15972865.
- Douillard JY, Rosell R, De Lena M, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely
  resected stage IB-IIIA non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a
  randomised controlled trial. Lancet Oncol 2006;7:719-727. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16945766.
- Song WA, Zhou NK, Wang W, et al. Survival benefit of neoadjuvant chemotherapy in non-small cell lung cancer: an updated meta-analysis of 13 randomized control trials. J Thorac Oncol 2010;5:510-516. Available at: http://www.ncbi.nlm.nih.gov/ pubmed/20107424.
- Scagliotti GV, Pastorino U, Vansteenkiste JF, et al. Randomized phase III study of surgery alone or surgery plus preoperative cisplatin and gemcitabine in stages IB to IIIA non-small-cell lung cancer. J Clin Oncol 2012;30:172-178. Available at: http:// www.ncbi.nlm.nih.gov/pubmed/22124104.
- Depierre A, Milleron B, Moro-Sibilot D, et al. Preoperative chemotherapy followed by surgery compared with primary surgery in resectable stage I (except T1N0), II, and IIIa non-small-cell lung cancer. J Clin Oncol 2002;20:247-253. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11773176.
- Rosell R, Gomez-Codina J, Camps C, et al. Preresectional chemotherapy in stage IIIA non-small-cell lung cancer: a 7-year assessment of a randomized controlled trial. Lung Cancer 1999;26:7-14. Available at: http://www.ncbi.nlm.nih.gov/ pubmed/10574676.
- Roth JA, Fossella F, Komaki R, et al. A randomized trial comparing perioperative chemotherapy and surgery with surgery alone in resectable stage IIIA non-small-cell lung cancer. J Natl Cancer Inst 1994;86:673-680. Available at: http://www.ncbi. nlm.nih.gov/pubmed/8158698.
- Felip E, Rosell R, Maestre JA, et al. Preoperative chemotherapy plus surgery versus surgery plus adjuvant chemotherapy versus surgery alone in early-stage non-small-cell lung cancer. J Clin Oncol 2010;28:3138-3145. Available at: http://www.ncbi. nlm.nih.gov/pubmed/20516435.
- Pisters KM, Vallieres E, Crowley JJ, et al. Surgery with or without preoperative paclitaxel and carboplatin in early-stage non-small-cell lung cancer: Southwest Oncology Group Trial S9900, an intergroup, randomized, phase III trial. J Clin Oncol 2010;28:1843-1849. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20231678.
- Group NM-aC. Preoperative chemotherapy for non-small-cell lung cancer: a systematic review and meta-analysis of individual participant data. Lancet 2014;383:1561-1571. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24576776.



- Curran WJ, Jr., Paulus R, Langer CJ, et al. Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410. J Natl Cancer Inst 2011;103:1452-1460. Available at: http://www.ncbi.nlm.nih.gov/ pubmed/21903745.
- Auperin A, Le Pechoux C, Rolland E, et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally
   advanced non-small-cell lung cancer. J Clin Oncol 2010;28:2181-2190. Available at: http://www.ncbi.nlm.nih.gov/
   pubmed/20351327.
- Socinski MA, Rosenman JG, Halle J, et al. Dose-escalating conformal thoracic radiation therapy with induction and concurrent carboplatin/paclitaxel in unresectable stage IIIA/B nonsmall cell lung carcinoma: a modified phase I/II trial. Cancer 2001;92:1213-1223. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11571735.
- Furuse K, Fukuoka M, Kawahara M, et al. Phase III study of concurrent versus sequential thoracic radiotherapy in combination with mitomycin, vindesine, and cisplatin in unresectable stage III non-smallcell lung cancer. J Clin Oncol 1999;17:2692-2699. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10561343.
- Socinski MA, Evans T, Gettinger S, et al. Treatment of stage IV non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e341S-368S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23649446.
- Azzoli CG, Temin S, Aliff T, et al. 2011 Focused Update of 2009 American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non-Small-Cell Lung Cancer. J Clin Oncol 2011;29:3825-3831. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21900105.
- Azzoli CG, Baker S, Jr., Temin S, et al. American Society of Clinical Oncology Clinical Practice Guideline update on chemotherapy for stage IV non-small-cell lung cancer. J Clin Oncol 2009;27:6251-6266. Available at: http://www.ncbi.nlm.nih. gov/pubmed/19917871.
- Group NM-AC. Chemotherapy in addition to supportive care improves survival in advanced non-small-cell lung cancer: a systematic review and meta-analysis of individual patient data from 16 randomized controlled trials. J Clin Oncol 2008;26:4617-4625. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18678835.
- Souquet PJ, Chauvin F, Boissel JP, et al. Polychemotherapy in advanced non small cell lung cancer: a meta-analysis.
   Lancet 1993;342:19-21. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8100290.
- Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomised clinical trials. Non-small Cell Lung Cancer Collaborative Group. BMJ 1995;311:899-909. Available at: http://www.ncbi.nlm.nih. gov/pubmed/7580546.
- Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small cell lung cancer. N Engl. J Med 2010;363:733-742. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20818875.
- Yates P, Schofield P, Zhao I, Currow D. Supportive and palliative care for lung cancer patients. J Thorac Dis 2013;5 Suppl 5:S623-628. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24163753.
- Ford DW, Koch KA, Ray DE, Selecky PA. Palliative and end-of-life care in lung cancer: Diagnosis and management of lung cancer, 3rd ed:
- American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e498S-512S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23649453.



# Occult Primary Tumors

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5490 For Adenocarcinoma, Squamous Cell Carcinoma, and Unspecified Occult Primary Tumors, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Squamous cell carcinoma
- Advanced or unresectable with distant metastases; and EITHER of the following:
  - **§** First-line treatment;
  - Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 287 of 387



СареОХ

Cisplatin + 5-Fluorouracil (5-FU)

Docetaxel + Carboplatin

Docetaxel + Cisplatin

Docetaxel + Cisplatin + 5-Fluorouracil (5-FU)

Gemcitabine + Cisplatin

Gemcitabine + Docetaxel

mFOLFOX6

Paclitaxel + Carboplatin

Paclitaxel + Carboplatin + Etoposide

Paclitaxel + Cisplatin

Ind. 5490 For Adenocarcinoma, Squamous Cell Carcinoma, and Unspecified Occult Primary Tumors, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Adenocarcinoma;
- Advanced or unresectable with distant metastases;
- First-line treatment

ASSOCIATED CHEMOTHERAPY REGIMENS

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 288 of 387



СареОХ

Cisplatin + 5-Fluorouracil (5-FU)

Docetaxel + Carboplatin

Docetaxel + Cisplatin

Docetaxel + Cisplatin + 5-Fluorouracil (5-FU)

Gemcitabine + Cisplatin

Gemcitabine + Docetaxel

Irinotecan + Carboplatin

Irinotecan + Gemcitabine

mFOLFOX6

Paclitaxel + Carboplatin

Paclitaxel + Carboplatin + Etoposide

Paclitaxel + Cisplatin

Ind. 5490 For Adenocarcinoma, Squamous Cell Carcinoma, and Unspecified Occult Primary Tumors, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Adenocarcinoma;
- Advanced or unresectable with distant metastases;
- Second-line treatment.

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 289 of 387



# СареОХ

### Cisplatin + 5-Fluorouracil (5-FU)

Docetaxel + Carboplatin

Docetaxel + Cisplatin

Gemcitabine + Cisplatin

Gemcitabine + Docetaxel

Irinotecan + Carboplatin

Irinotecan + Gemcitabine

mFOLFOX6

Paclitaxel + Carboplatin

Paclitaxel + Carboplatin + Etoposide

Paclitaxel + Cisplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 290 of 387



### REFERENCES

- Briasoulis E, Kalofonos H, Bafaloukos D, et al. Carboplatin plus paclitaxel in unknown primary carcinoma: A phase II Hellenic Cooperative Oncology Group Study. J Clin Oncol. 2000;18:3101–3107.
- Greco F, Burris, H, Erland J, et al. Carcinoma of unknown primary site: Long term follow-up after treatment with paclitaxel, carboplatin, and etoposide. Cancer. 2000;89:2655–2660.
- Greco F, Erland J, Morrissey H, et al. Carcinoma of unknown primary site: Phase II trials with docetaxel plus cisplatin or carboplatin. Ann Oncol. 2000;11:211–215.
- Demirci U, Coskun U, Karaca H, et al. Docetaxel and cisplatin in first line treatment of patients with unknown primary cancer: a multicenter study of the anatolian society of medical oncology. Asian Pac J Cancer Prev. 2014;15(4):1581–1584.
- Gross-Goupil M, Fourcade A, Blot E, et al. Cisplatin alone or combined with gemcitabine in carcinomas of unknown primary: Results of the randomised GEFCAPI 02 trial. Eur J Cancer. 2012;48:721–727.
- Pouessel D, Culine S, Becht C, et al. Gemcitabine and docetaxel as front-line chemotherapy in patients with carcinoma of an unknown primary site. Cancer. 2004;100:1257–2111.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Occult Primary (Cancer of Unknown Primary [CUP]). Version 2.2017. 17 Oct 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/occult.pdf
- Cassidy J, Clarke S, Diaz Rubio E, et al. Randomized phase III study of capecitabine plus oxaliplatin compared with fluorouracil/folinic acid plus oxaliplatin as first-line therapy for metastatic colorectal cancer. J Clin Oncol. 2008;26:2006–2012.
- Cheeseman SL, Joel SP, Chester JD, et al. A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. Br J Cancer. 2002;87:393–399.
- Pointreau Y, Garaud P, Chapet S, et al. Randomized trial of induction chemotherapy with cisplatin and 5-fluorouracil with or without docetaxel for larynx preservation. J Natl Cancer Inst. 2009;101:498–506.
- Park YH, Ryoo BY, Choi SJ, et al. A phase II study of paclitaxel plus cisplatin chemotherapy in an unfavourable group of patients with cancer of unknown primary site. Jpn J Clin Oncol. 2004;34:681–685.
- Pantheroudakis G, Briasoulis E, Kalofonos HP, et al. Docetaxel and carboplatin combination chemotherapy as outpatient palliative therapy in carcinoma of unknown primary: a multicenter Hellenic Cooperative Oncology Group phase II study. Acta Oncol. 2008;47:1148–1155.
- Mukai H, Katsumata N, Ando M, et al. Safety and efficacy of a combination of docetaxel and cisplatin in patients with unknown primary cancer. Am J Clin Oncol. 2010;33:32–35.
- Kusaba H, Shibata Y, Arita S, et al. Infusional 5-fluorouracil and cisplatin as first-line chemotherapy in patients with carcinoma of unknown primary site. Med Oncol. 2007;24:259–264.



# Ovarian Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Mucinous ovarian tumor; and ANY of the following:
    - Stage 1C;
    - Stage 1A or 1B Grade 2;
    - Stage 1A or 1B Grade 3.

ASSOCIATED CHEMOTHERAPY REGIMENS

Capecitabine + Oxaliplatin

Leucovorin + Oxaliplatin + 5-Fluorouracil (5-FU)



Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Stage 1C;
- Borderline epithelial carcinoma and low grade (-1) serous endometrial.

ASSOCIATED CHEMOTHERAPY REGIMENS

Anastrozole

Tamoxifen

- Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Malignant germ cell and Findings: Malignant sex cord stromal tumor of ovary; and ANY of the following:
    - Stage 1C;
    - Stage 1A or 1B Grade 2;
    - Stage 1A or 1B Grade 3.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bleomycin + Etoposide + Cisplatin (BEP)

Paclitaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 293 of 387



- Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Malignant germ cell tumor of ovary; and ANY of the following:
    - Stage 1C;
    - Stage 1A or 1B Grade 2;
    - Stage 1A or 1B Grade 3.

Carboplatin + Etoposide

- Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:
  - Stage 1A or 1B; and ANY of the following:
    - **§** Grade 2;
    - **§** Grade 3;
    - S Clear cell histology;
  - Stage 1C;
  - Stage 2;
  - Stage 3;
  - Stage 4;
  - Optimally debulked with no mass greater than 1 cm.

ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel + Carboplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 294 of 387



Dose-dense Paclitaxel + Carboplatin

Paclitaxel + Carboplatin

Paclitaxel + Cisplatin

Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Ovarian carcinosarcoma; and EITHER of the following:
  - Stage 1C;
  - **§** Stage 1A or 1B; and EITHER of the following:
    - Grade 2;
    - Grade 3.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Ifosfamide + Mesna

Cisplatin + Ifosfamide + Mesna

Paclitaxel + Ifosfamide + Mesna

Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:



- Stage 1A or 1B;
- Grade 2;
- Borderline epithelial carcinoma and low grade (-1) serous endometrial.

### Anastrozole

Leuprolide Acetate

Tamoxifen

Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Stage 1A or 1B;
- Grade 3;
- Borderline epithelial carcinoma and low grade (-1) serous endometrial.

ASSOCIATED CHEMOTHERAPY REGIMENS

Anastrozole

Letrozole

Leuprolide Acetate

Tamoxifen

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 296 of 387



- Ind. 5493 Primary or Adjuvant Therapy for Ovarian Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Stage 4 Grade 3.

Paclitaxel + Carboplatin + Bevacizumab

- Ind. 5494 For Recurrent Ovarian Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Relapse greater than 6 months after platinum therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin

Carboplatin + Gemcitabine + Bevacizumab

Cisplatin

Docetaxel + Carboplatin

Dose-dense Paclitaxel + Carboplatin

Gemcitabine + Carboplatin

Gemcitabine + Cisplatin

Liposomal Doxorubicin + Carboplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 297 of 387



Paclitaxel + Carboplatin

Paclitaxel + Carboplatin + Bevacizumab

Paclitaxel + Cisplatin

Ind. 5494 For Recurrent Ovarian Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Relapse less than 6 months after platinum therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Albumin-bound Paclitaxel

Altretamine

Bevacizumab

Capecitabine

Cyclophosphamide

Docetaxel

Doxorubicin

Etoposide

Gemcitabine

Ifosfamide + Mesna

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 298 of 387



Irinotecan

Liposomal Doxorubicin

Liposomal Doxorubicin + Bevacizumab

Melphalan

Olaparib

Oxaliplatin

Paclitaxel

Paclitaxel + Bevacizumab

Paclitaxel + Pazopanib

Pemetrexed

Topotecan

Topotecan + Bevacizumab

Vinorelbine

Ind. 5494 For Recurrent Ovarian Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 299 of 387



- Relapse greater than 6 months after platinum therapy; and EITHER of the following:
  - S Malignant germ cell tumor;

Leuprolide Acetate

Megestrol Acetate

Pazopanib

Tamoxifen

Ind. 5494 For Recurrent Ovarian Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Malignant germ cell tumor.

ASSOCIATED CHEMOTHERAPY REGIMENS

Anastrozole

Cisplatin + Etoposide

Etoposide + Ifosfamide + Cisplatin (VIP) + Mesna

Paclitaxel + Gemcitabine

Paclitaxel + Ifosfamide + Cisplatin (TIP) + Mesna

Paclitaxel + Ifosfamide + Mesna

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 300 of 387



Vinblastine + Ifosfamide + Cisplatin (VeIP) + Mesna

Vincristine + Dactinomycin + Cyclophosphamide (VAC)

- Ind. 5494 For Recurrent Ovarian Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Malignant sex cord stromal tumor.

ASSOCIATED CHEMOTHERAPY REGIMENS

Letrozole



### REFERENCES

- Ozols RF, Bundy BN, Greer BE, et al. Gynecologic Oncology Group. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2003;21:3194–3200.
- Armstrong DK, Bundy B, Wenzel L, et al. Gynecologic Oncology Group. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med. 2006;354:34–43.
- Pignata S, Scambia G, Ferrandina G, et al. Carboplatin plus paclitaxel versus carboplatin plus pegylated liposomal doxorubicin as first-line treatment for patients with ovarian cancer: the MITO-2 randomized phase III trial. J Clin Oncol. 2011;29(27):3628–3635.
- Katsumata N, Yasuda M, Takahashi F, et al. Japanese Gynecologic Oncology Group. Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovarian cancer: a phase 3, open-label, randomized controlled trial. Lancet. 2009;374:1331–1338.
- Pignata S, Scambia G, Katsaros D, et al; Multicentre Italian Trials in Ovarian cancer (MITO-7); Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens et du sein (GINECO); Mario Negri Gynecologic Oncology (MaNGO); European Network of Gynaecological Oncological Trial Groups (ENGOT-OV-10); Gynecologic Cancer InterGroup (GCIG) Investigators. Carboplatin plus paclitaxel once a week versus every 3 weeks in patients with advanced ovarian cancer (MITO-7): a randomised, multicentre, open-label, phase 3 trial. Lancet Oncol. 2014;15:396-405.
- Vasey PA, Jayson GC, Gordon A, et al. Scottish Gynecological Cancer Trials Group. Phase III randomized trial of docetaxel carboplatin versus paclitaxel-carboplatin as first-line chemotherapy for ovarian carcinoma. J Natl Cancer Inst. 2004;96:1682–1691.
- Burger RA, Brady MF, Bookman MA, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med. 2011;365:2473–2483.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Ovarian Cancer Including Fallopian Tube Cancers and Primary Peritoneal Cancers. Version 1.2016. 30 Jun 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/ovarian.pdf.
- Hall M, Gourley C, McNeish I, et al. Targeted anti-vascular therapies for ovarian cancer: current evidence. Br J Cancer. 2013;108:250–258.
- Perren TJ, Swart AM, Pfisterer J, et al. A phase 3 trial of bevacizumab in ovarian cancer. N Engl J Med 2011;365:2484–2496.
- Morgan RJ Jr, Alvarez RD, Armstrong DK, et al. Ovarian cancer, version 3.2012. J Natl Compr Canc Netw 2012:10:1339– 1349.
- Stark D, Nankivell M, Pujade-Lauraine E, et al. Standard chemotherapy with or without bevacizumab in advanced ovarian cancer: quality-of-life outcomes from the International Collaboration on Ovarian Neoplasms (ICON7) phase 3 randomized trial. Lancet Oncol 2013;14:236–243.
- Monk BJ, Huang HQ, Burger RA, et al. Patient reported outcomes of a randomized, placebo-controlled trial of bevacizumab in the front-line treatment of ovarian cancer: a Gynecologic Oncology Group Study. Gynecol Oncol 2013;128:573–578.
- Friedlander ML, Stockier MR, Butow P, et al. Clinical trials of palliative chemotherapy in platinum-resistant or –refractory ovarian cancer: time to think differently? J Clin Oncol 2013:31:2362.



Barlin JN, Dao F, Bou Zgheib N, et al. Progression-free and overall survival of a modified outpatient regimen of primary intravenous/intraperitoneal paclitaxel and intraperitoneal cisplatin in ovarian, fallopian tube, and primary peritoneal cancer. Gynecol Oncol. 2012;125(3):621–624.



# Penile Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5571 Primary Adjuvant Therapy for Penile Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- High risk (T1b or greater);
- Adjuvant therapy;
- Palpable bulky or non-bulky inguinal lymph node with prior inguinal lymph node dissection (ILND) or pelvic lymph node dissection (PLND);

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel + Mesna + Ifosfamide + Cisplatin (TIP)

Cisplatin + 5FU

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 304 of 387



- Ind. 5571 Primary Neoadjuvant Therapy for Penile Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Tumor is potentially resectable;
  - Neoadjuvant chemotherapy and EITHER of the following:
    - **§** Palpable bulky inguinal lymph node with no prior ILND or PLND;
    - **§** Enlaged pelvic lymph node.

Paclitaxel + Mesna + Ifosfamide + Cisplatin (TIP)

- Ind. 5572 Recurrent Penile Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - First or Second-line therapy;
  - Prior ILND or PLND.

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel + Mesna + Ifosfamide + Cisplatin (TIP)

Cisplatin + 5FU

Paclitaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 305 of 387



Ind. 5572 Recurrent Penile Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Chemoradiation;
- Prior ILND or PLND

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel

Ind. 5572 Metastatic Penile Cancer per the drug regimens shown in the table below may be reasonable and appropriate.

ASSOCIATED CHEMOTHERAPY REGIMENS

Paclitaxel + Mesna + Ifosfamide + Cisplatin (TIP)

Cisplatin + 5FU

Paclitaxel

Ind. 5570 Chemoradiation for Penile Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:

- High-risk (T1b or greater) with palpable non-bulky inguinal lymph node and prior ILND or PLND;
- Unresectable tumorwith enlarged pelvic lymph node and no prio ILND or PLND;



- Recurrent disease with prior ILND or PLND;
- Metastatic disease.

Cisplatin

Cisplatin + 5FU (chemoradiation)

Mitomycin + 5FU

Capecitabine



### REFERENCES

- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Penile Cancer
   Guidelines version 1.2018-January 8,2018. Please refer to the NCCN website for additional information, available at:
   https://www.nccn.org/professionals/physician\_gls/pdf/penile.pdf
- Kossow JH, Hotchkiss RS, Morales PA. Carcinoma of penis treated surgically. Analysis of 100 cases. Urology 1973; 2:169.
- American Joint Committee on Cancer.. Penis.. In: American Joint Committee on Cancer, 7, Edge SB, Byrd DR, Compton CC (Eds), Springer, New York 2010. p.447.
- Buechner SA. Common skin disorders of the penis. BJU Int 2002; 90:498.
- Leis-Dosil VM, Alijo-Serrano F, Aviles-Izquierdo JA, et al. Angiokeratoma of the glans penis: clinical, histopathological and dermoscopic correlation. Dermatol Online J 2007; 13:19.
- Micali G, Innocenzi D, Nasca MR, et al. Squamous cell carcinoma of the penis. J Am Acad Dermatol 1996; 35:432.
- Jensen MO. Cancer of the penis in Denmark 1942 to 1962 (511 cases). Dan Med Bull 1977; 24:66.
- Boxer RJ, Skinner DG. Condylomata acuminata and squamous cell carcinoma. Urology 1977; 9:72.
- Smotkin D. Virology of human papillomavirus. Clin Obstet Gynecol 1989; 32:117.
- Maden C, Sherman KJ, Beckmann AM, et al. History of circumcision, medical conditions, and sexual activity and risk of penile cancer. J Natl Cancer Inst 1993; 85:19.
- Mikhail GR. Cancers, precancers, and pseudocancers on the male genitalia. A review of clinical appearances, histopathology, and management. J Dermatol Surg Oncol 1980; 6:1027.
- Graham JH, Helwig EB. Erythroplasia of Queyrat. A clinicopathologic and histochemical study. Cancer 1973; 32:1396.
- Wieland U, Jurk S, Weissenborn S, et al. Erythroplasia of queyrat: coinfection with cutaneous carcinogenic human papillomavirus type 8 and genital papillomaviruses in a carcinoma in situ. J Invest Dermatol 2000; 115:396.
- Ikenberg H, Gissmann L, Gross G, et al. Human papillomavirus type-16-related DNA in genital Bowen's disease and in Bowenoid papulosis. Int J Cancer 1983; 32:563.
- Lucia MS, Miller GJ. Histopathology of malignant lesions of the penis. Urol Clin North Am 1992; 19:227.
- Schellhammer PF, Jordan GH, Robey EL, Spaulding JT. Premalignant lesions and nonsquamous malignancy of the penis and carcinoma of the scrotum. Urol Clin North Am 1992; 19:131.
- Gross G, Hagedorn M, Ikenberg H, et al. Bowenoid papulosis. Presence of human papillomavirus (HPV) structural antigens and of HPV 16-related DNA sequences. Arch Dermatol 1985; 121:858.
- Bonnekoh B, Mahrle G, Steigleder GK. [Transition to cutaneous squamous cell carcinoma in 2 patients with bowenoid papulomatosis]. Z Hautkr 1987; 62:773.
- Yoneta A, Yamashita T, Jin HY, et al. Development of squamous cell carcinoma by two high-risk human papillomaviruses (HPVs), a novel HPV-67 and HPV-31 from bowenoid papulosis. Br J Dermatol 2000; 143:604.
- Endo M, Yamashita T, Jin HY, et al. Detection of human papillomavirus type 16 in bowenoid papulosis and nonbowenoid tissues. Int J Dermatol 2003; 42:474.
- Patterson JW, Kao GF, Graham JH, Helwig EB. Bowenoid papulosis. A clinicopathologic study with ultrastructural observations. Cancer 1986; 57:823.
- Schwartz RA, Janniger CK. Bowenoid papulosis. J Am Acad Dermatol 1991; 24:261.



- Campus GV, Alia F, Bosincu L. Squamous cell carcinoma and lichen sclerosus et atrophicus of the prepuce. Plast Reconstr Surg 1992; 89:962.
- Pride HB, Miller OF 3rd, Tyler WB. Penile squamous cell carcinoma arising from balanitis xerotica obliterans. J Am Acad Dermatol 1993; 29:469.
- Barbagli G, Palminteri E, Mirri F, et al. Penile carcinoma in patients with genital lichen sclerosus: a multicenter survey. J Urol 2006; 175:1359.
- Depasquale I, Park AJ, Bracka A. The treatment of balanitis xerotica obliterans. BJU Int 2000; 86:459.



# Pancreatic Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5485 Adjuvant Therapy for Pancreatic Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:

- Adjuvant therapy;
- Borderline resectable/locally advanced;
- First-line treatment for metastatic disease;
- Second-line treatment for metastatic disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU)

5-Fluorouracil (5-FU) + Leucovorin



Capecitabine

Gemcitabine

Ind. 5486 Concurrent Chemotherapy or Radiation Therapy for Pancreatic Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Adjuvant therapy;
- Borderline resectable/locally advanced; and EITHER of the following:
  - **§** First-line treatment;
  - Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU)

Capecitabine

Gemcitabine

Ind. 5487 Chemotherapy for Advanced or Metastatic Pancreatic Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Metastatic disease; and EITHER of the following:
  - **§** First-line treatment;
  - Second-line treatment;
- Borderline resectable/locally advanced; and EITHER of the following:



- **§** First-line treatment;
- Second-line treatment.

Albumin-bound Paclitaxel + Gemcitabine

CapeOX

FOLFIRINOX

Gemcitabine

Gemcitabine + Capecitabine

Gemcitabine + Cisplatin

Gemcitabine + Docetaxel + Capecitabine (GTX)

Gemcitabine + Erlotinib

Leucovorin + 5-Fluorouracil (5-FU) + Oxaliplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 312 of 387



### REFERENCES

- Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med.2011;364:1817–1825.
- Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med. 2013;369:1691–1703.
- Moore MJ, Goldstein D, Hamm J, et al. Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer. A phase III trial of the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol. 2007;25:1960–1966.
- Cunningham D, Chau I, Stocken D D, et al. Phase III randomized comparison of gemcitabine (GEM) versus gemcitabine plus capecitabine (GEM-CAP) in patients with advanced pancreatic cancer. J Clin Oncol. 2009;27:5513–5518.
- Oliver GR, Sugar E, Laheru D, et al. Family history of cancer and sensitivity to platinum chemotherapy in pancreatic adenocarcinoma [abstract]. Presented at: 2010 ASCO Gastrointestinal Cancers Symposium; January 22–24, 2010; Orlando, Florida. Abstract 180.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma. Version 1.2017. 24 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/professionals/physician\_gls/pdf/pancreatic.pdf
- Fine RL, Fogelman DR, Schreibman SM, et al. The gemcitabine, docetaxel, and capecitabine (GTX) regimen for metastatic pancreatic cancer: a retrospective analysis. Cancer Chemother Pharmacol. 2008;61:167–175.
- Pelzer U, Schwaner I, Stieler J, et al. Best supportive care (BSC) versus oxaliplatin, folinic acid and 5-fluorouracil (OFF) plus BSC in patients for second-line advanced pancreatic cancer: a phase III-study from the German CONKO-study group. Eur J Cancer. 2011;47:1676–1681.
- Xiong HQ, Varadhachary GR, Blais JC, et al. A phase II trial of oxaliplatin plus capecitabine (xelox) as second-line therapy for patients with advanced pancreatic cancer. 2008;113:2046–2052.
- Oettle H, Neuhaus P, Hochhaus A, et al. Adjuvant Chemotherapy With Gemcitabine and Long-term Outcomes Among
  Patients With Resected Pancreatic Cancer: The CONKO-001 Randomized Trial. JAMA. 2013;310(14):1473–1481.
- Neoptolemos J, Buchler M, Stocken DD, Bassi C, et al. Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. JAMA. 2010;304:1073–1081.
- Regine, WF Winter KA, Abrams RA et al. Fluorouracil vs. gemcitabine chemotherapy before and after fluorouracil-based chemoradiation after resection of pancreatic adenocarcinoma. A randomized controlled trial. JAMA. 2008;299:1019– 1026.



# Prostate Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5539 First-Line Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Symptomatic bone metastases and bone predominant disease;
- Metastatic disease;
- No known visceral metastasis;
- Castration resistant.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Radium-223



Ind. 5539 First-Line Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Metastatic disease;
- Castration resistant.

ASSOCIATED CHEMOTHERAPY REGIMENS

Abiraterone Acetate + Prednisone

Docetaxel + Prednisone

Enzalutamide

Ind. 5539 First-Line Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease;
- Castration resistant;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Mitoxantrone + Prednisone

Ind. 5539 First-Line Therapy for Prostate Cancer per the drug regimens shown in the



table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Metastatic disease;
- Not castration resistant.

ASSOCIATED CHEMOTHERAPY REGIMENS

Leuprolide

Bicalutamide

Degarelix

Triptorelin

Histrelin

Goserelin

Goserelin + Nilutamide

Histrelin + Nilutamide

Leuprolide + Niluatmide

Triptorelin + Niluatmide

Goserelin + Fluatmide

Histrelin + Flutamide

Leuprolide + Flutamide

Triptorelin + Flutamide



Goserelin + Bicalutamide Histrelin + Bicalutamide Leuprolide + Bicalutamide Triptorelin + Bicalutamide Goserelin + Enzalutamide Histrelin + Enzalutamide Leuprolide + Enzalutamide Triptorelin + Enzalutamide Abiraterone + Enzalutamide

- Ind. 5539 First-Line Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Patient is low risk (T1c-T2a, Gleason less than or equal to 6);
  - Life expectancy of greater than 5 years;
  - Not castration resistant.

ASSOCIATED CHEMOTHERAPY REGIMENS

# Triptorelin



Ind. 5539 First-Line Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Adjuvant/Neoadjuvant therapy;
- Not castration resistant; and ANY of the following:
  - **§** Patient is intermediate risk (T2b-T2c, Gleason 7);
  - **§** Patient is high risk (T3a, Gleason 8-10);
  - **§** Patient is very high risk (T3b-T4).

### ASSOCIATED CHEMOTHERAPY REGIMENS

### Leuprolide

Triptorelin

Histrelin

Goserelin

Goserelin + Nilutamide

Histrelin + Nilutamide

Leuprolide + Niluatmide

Triptorelin + Niluatmide

Goserelin + Fluatmide

Histrelin + Flutamide

Leuprolide + Flutamide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 318 of 387



Triptorelin + Flutamide Goserelin + Bicalutamide Histrelin + Bicalutamide Leuprolide + Bicalutamide Triptorelin + Bicalutamide Goserelin + Enzalutamide Histrelin + Enzalutamide Leuprolide + Enzalutamide Triptorelin + Enzalutamide Abiraterone + Enzalutamide

Ind. 5539 First-Line Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient is intermediate risk (T2b-T2c, Gleason 7);
- Life expectancy of greater than 5 years;
- Not castration resistant.

ASSOCIATED CHEMOTHERAPY REGIMENS

Leuprolide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 319 of 387



### Histrelin

### Goserelin

Goserelin + Nilutamide

Histrelin + Nilutamide

Leuprolide + Niluatmide

Triptorelin + Niluatmide

Goserelin + Fluatmide

Histrelin + Flutamide

Leuprolide + Flutamide

Triptorelin + Flutamide

Goserelin + Bicalutamide

Histrelin + Bicalutamide

Leuprolide + Bicalutamide

Triptorelin + Bicalutamide

Goserelin + Enzaluatmide

Histrelin + Enzalutamide

Leuprolide + Enzalutamide

Triptorelin + Enzalutamide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 320 of 387



Abiraterone + Enzalutamide

Ind. 5539 First-Line Therpay for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Surgical Castration;
- Metastatic Disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

Goserelin + Nilutamide

Histrelin + Nilutamide

Leuprolide + Nilutamide

Triptorelin + Nilutamide

Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Symptomatic bone metastases and bone predominant disease; and EITHER of the following:
  - High-volume metastatic disease (4 or more sites of bone metastasis);
  - **§** Low-volume metastatic disease (less than 4 sites of bone metastasis)
- Castration resistant; and EITHER of the following:
  - **§** Previously treated with Enzalutamide or Abiraterone;



**§** Previously treated with Docetaxel

### ASSOCIATED CHEMOTHERAPY REGIMENS

# Radium-223

Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- High-volume metastatic disease (4 or more sites of bone metastasis);
- Castration resistant;
- Previously treated with Enzalutamide or Abiraterone.

ASSOCIATED CHEMOTHERAPY REGIMENS

Abiraterone Acetate + Prednisone

Docetaxel + Prednisone

Enzalutamide

Radium-223

Sipuleucel-T

Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- High-volume metastatic disease (4 or more sites of bone metastasis);
- Castration resistant;



• Previously treated with Docetaxel.

### ASSOCIATED CHEMOTHERAPY REGIMENS

## Abiraterone Acetate + Prednisone

Cabazitaxel + Prednisone

Docetaxel + Prednisone

Enzalutamide

Radium-223

Sipuleucel-T

Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Normal cardiac function;
- Castration resistant;
- Previously treated with Docetaxel; and EITHER of the following:
  - **§** High-volume metastatic disease (4 or more sites of bone metastasis);
  - S Low-volume metastatic disease (less than 4 sites of bone metastasis).

ASSOCIATED CHEMOTHERAPY REGIMENS

Mitoxantrone + Prednisone



Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Low-volume metastatic disease (less than 4 sites of bone metastasis);
- Castration resistant;
- Previously treated with Enzalutamide or Abiraterone.

ASSOCIATED CHEMOTHERAPY REGIMENS

Abiraterone Acetate + Prednisone

Docetaxel + Prednisone

Enzalutamide

Sipuleucel-T

- Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Symptomatic bone metastases and bone predominant disease
  - Hypercalcemia

ASSOCIATED CHEMOTHERAPY REGIMENS

Zoledronic Acid

Denosumab



Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates Osteoporosis:

ASSOCIATED CHEMOTHERAPY REGIMENS

Alendronate

Zoledronic Acid

Denosumab

Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates surgical castration and EITHER of the following:

- High- volume metastatic disease (4 or more sites of bone metastasis);
- Low-volume metastatic disease (less than 4 sites of bone metastasis).

ASSOCIATED CHEMOTHERAPY REGIMENS

# Nilutamide

Goserelin + Nilutamide

Histrelin + Nilutamide

Leuprolide + Niluatmide

Triptorelin + Niluatmide



Goserelin + Fluatmide Histrelin + Flutamide Leuprolide + Flutamide Triptorelin + Flutamide

Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates castration resistance and EITHER of the following:

- High- volume metastatic disease (4 or more sites of bone metastasis);
- Low-volume metastatic disease (less than 4 sites of bone metastasis).

ASSOCIATED CHEMOTHERAPY REGIMENS

Enzalutamide

Histrelin

Goserelin

Goserelin + Enzalutamide

Histrelin + Enzalutamide

Leuprolide + Enzalutamide

Triptorelin + Enzalutamide

Abiraterone + Enzalutamide



Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimes shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- High- volume metastatic disease (4 or more sites of bone metastasis);
- Low-volume metastatic disease (less than 4 sites of bone metastasis).

### ASSOCIATED CHEMOTHERAPY REGIMENS

Bicalutamide

Flutamide

Goserelin + Bicalutamide

Histrelin + Bicalutamide

Leuprolide + Bicalutamide

Triptorelin + Bicalutamide

Ind. 5540 Subsequent Therapy for Prostate Cancer per the drug regimes shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Low volume metastatic disease (less than 4 sites of bone metastasis)
- Castration resistant
- Previously treated with Docetaxel

ASSOCIATED CHEMOTHERAPY REGIMENS

## Enzalutamide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 327 of 387



Abiraterone Actetate + Prednisone

Sipuleucel-T

Cabazitaxel + Prednisone

Docetaxel + Prednisone

Ind. 5495 For Small Cell Carcinoma Prostate Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Small cell histology on biopsy;
- Metastatic disease;
- Disease progression on medical or surgical castration.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Etoposide

Cisplatin + Etoposide

Docetaxel + Carboplatin

Docetaxel + Prednisone

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 328 of 387



- Ind. 5496 Castration-Sensitive Metastatic Therapy for Prostate Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Patient has visceral metastases;
  - High-volume metastatic disease (4 or more sites of bone metastasis).

### ASSOCIATED CHEMOTHERAPY REGIMENS

### Docetaxel

#### REFERENCES

- Xtandi [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc.; 2015.
- Scher HI, Fizazi K, Saad F, et al; AFFIRM Investigators. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012;367:1187–1197.
- Beer TM, Armstrong AJ, Rathkopf DE, et al; PREVAIL Investigators. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med. 2014;371:424–433.
- Zytiga [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; 2015.
- de Bono JS, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med.2011;364:1995–2005.
- Fizazi K, Scher HI, Molina A, et al. Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. Lancet Oncol. 2012;13:983–992.
- Logothetis CJ, Basch E, Molina A, et al. Effect of abiraterone acetate and prednisone compared with placebo and prednisone on pain control and skeletal-related events in patients with metastatic castration-resistant prostate cancer: exploratory analysis of data from the COU-AA-301 randomised trial. Lancet Oncol. 2012;13:1210–1217.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer. Version 2.2017. 21 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/prostate.pdf
- Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med. 2004;351:1502–1512.
- Berthold DR, Pond GR, Soban F, de Wit R, Eisenberger M, Tannock IF. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study. J Clin Oncol. 2008;26:242–245.
- Xofigo [prescribing information]. Wayne, NJ: Bayer HealthCare Pharmaceuticals Inc.; 2013.



- Parker C, Nilsson S, Heinrich D, et al; ALSYMPCA Investigators. Alpha emitter radium-223 and survival in metastatic prostate cancer. N Engl J Med. 2013;369:213–223.
- Provenge [prescribing information]. Seattle, WA: Dandreon Corp.; 2011.
- Kantoff PW, Higano CS, Shore ND, et al; IMPACT Study Investigators. Sipuleucel-T immunotherapy for castrationresistant prostate cancer. N Engl J Med. 2010;363:411–422.
- Jevtana [prescribing information] Bridgewater, NJ: sanofiaventis US LLC; 2014.
- de Bono JS, Oudard S, Ozguroglu M, et al; TROPIC Investigators. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet. 2010;376:1147–1154.
- Bahl A, Oudard S, Tombal B, et al; TROPIC Investigators. Impact of cabazitaxel on 2-year survival and palliation of tumourrelated pain in men with metastatic castration-resistant prostate cancer treated in the TROPIC trial. Ann Oncol. 2013;24:2402–2408.

# Rectal Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.



- Ind. 5475 For Advanced or Metastatic Rectal Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Unresectable metachronous metastatic disease previously treated with neoadjuvant therapy; and EITHER of the following:
    - **§** First-line treatment;
    - Second-line treatment.
  - First-line treatment where KRAS mutation is present;

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin

5-Fluorouracil (5-FU) + Leucovorin (LV5FU2)

5-Fluorouracil (5-FU) + Leucovorin (sLV5FU2)

Capecitabine

Capecitabine + Bevacizumab

СареОХ

CapeOX + Bevacizumab

# FOLFIRI

FOLFIRI + Bevacizumab

FOLFIRI + Cetuximab

FOLFIRI + Panitumumab



FOLFIRI + Ramucirumab

FOLFIRI + Ziv-Aflibercept

FOLFOXIRI

FOLFOXIRI + Bevacizumab

Irinotecan

Irinotecan + Oxaliplatin (IROX)

mFOLFOX6

mFOLFOX6 + Bevacizumab

mFOLFOX6 + Cetuximab

mFOLFOX6 + Panitumumab

MFOLFOX7

Ind. 5475 For Advanced or Metastatic Rectal Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Second-line treatment where KRAS mutation is present.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin

5-Fluorouracil (5-FU) + Leucovorin (LV5FU2)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 332 of 387



5-Fluorouracil (5-FU) + Leucovorin (sLV5FU2)

Capecitabine

Capecitabine + Bevacizumab

СареОХ

CapeOX + Bevacizumab

# FOLFIRI

FOLFIRI + Bevacizumab

FOLFIRI + Ramucirumab

FOLFIRI + Ziv-Aflibercept

FOLFOXIRI

FOLFOXIRI + Bevacizumab

Irinotecan

Irinotecan + Oxaliplatin (IROX)

mFOLFOX6

mFOLFOX6 + Bevacizumab

# MFOLFOX7

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 333 of 387



- Ind. 5475 For Advanced or Metastatic Rectal Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Third-line treatment for metastatic disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

Regorafenib

Ind. 5475 For Advanced or Metastatic Rectal Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Metastatic disease;
- KRAS mutation;
- Patient previously received neoadjuvant therapy; and EITHER of the following:
  - Second-line treatment;
  - S Third-line treatment

ASSOCIATED CHEMOTHERAPY REGIMENS

## Cetuximab

Cetuximab + Irinotecan

FOLFIRI + Cetuximab

FOLFIRI + Panitumumab

mFOLFOX + Cetuximab



mFOLFOX6 + Panitumumab

Panitumumab

- Ind. 5475 For Advanced or Metastatic Rectal Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Third-line treatment for metastatic disease when patient was previously treated with either fluoropyrimidine-oxaliplatin (FOLFOX) or irinotecan (FOLFIRI) based chemotherapy and received vascular endothelial growth factor (VEGF) therapy
  - KRAS mutation present, with third-line treatment for metastatic disease when patient was previously treated with either fluoropyrimidine-oxaliplatin (FOLFOX) or irinotecan (FOLFIRI) based chemotherapy and received vascular endothelial growth factor (VEGF) therapy
  - RAS wild type colorectal cancer with metastatic disease present when the patient was previously treated with either fluoropyrimidine-oxaliplatin (FOLFOX) or irinotecan (FOLFIRI) based chemotherapy and has received antiepidermal growth factor receptor (EGFR) therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Trifluridine + Tipiracil

- Ind. 5475 For Advanced or Metastatic Rectal Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Unresectable metachronous metastatic disease



- Microsatellite instability-high (MSI-H) or mismatch repair deficient
- Second-line treatment
- Patient previously treated with either fluoropyrimidine-oxaliplatin (FOLFOX) or irinotecan (FOLFIRI) based chemotherapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Pembrolizumab

Nivolumab

Ind. 5476 Post-Operative Adjuvant Chemotherapy for Patients with Rectal Cancer Not Receiving Preoperative Therapy per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:

- Node positive; and ANY of the following:
  - Stage T1;
  - Stage T2;
  - Stage T3;
  - Stage T4;
  - **§** Stage T4; and ANY of the following:
    - Poorly differentiated histology;
    - Lymphovascular invasion (LVI);
    - Bowel obstruction;
    - Less than 12 lymph nodes examined;
    - Perineural invasion;
    - Localized perforation;
    - Close, indeterminate, or positive margins.



### ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin (sLV5FU2)

Capecitabine

CapeOX

mFOLFOX6

- Ind. 5477 Neoadjuvant or Concurrent Therapy for Rectal Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Nodal involvement;
  - Stage T3 or T4.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU)

5-Fluorouracil (5-FU) + Leucovorin

Capecitabine

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 337 of 387



#### REFERENCES

- Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med. 2004;350:2343–2351.
- Cheeseman SL, Joel SP, Chester JD, et al. A "modified deGramont" regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. Br J Cancer. 2002;87(4):393–399.
- Maindrault-Goebel F, deGramont A, Louvet C, et al. Evaluation of oxaliplatin dose intensity in bimonthly leucovorin and 48-hour 5-fluorouracil continuous infusion regimens (FOLFOX) in pretreated metastatic colorectal cancer. Oncology Multidisciplinary Research Group (GERCOR). Ann Oncol. 2000;11(11):1477–1483.
- Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. N Engl J Med. 2005;354(26):2696–2704.
- Schmoll HJ, Cartwright T, Tabernero J, et al. Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: a planned safety analysis in 1,864 patients. J Clin Oncol. 2007;25(1):102–109.
- Haller DG, Tabernero J, Maroun J, et al. Capecitabine plus oxaliplatin compared with fluorouracil and folinic acid as adjuvant therapy for stage III colon cancer. J Clin Oncol. 2011;29(11):1465–1471.
- André T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. GERCOR. Eur J Cancer. 1999;35(9):1343–1347.
- Petrelli N, Douglass HO Jr, Herrare L, et al. The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: a prospective randomized phase III trial. Gastrointestinal Tumor Study Group. J Clin Oncol. 1989;7(10):1419– 1426. Erratum in: J Clin Oncol. 1990;8(1):185.
- O'Connell MJ, Martenson JA, Wieand HS, et al. Improving adjuvant therapy for rectal cancer by combining protractedinfusion fluorouracil with radiation therapy after curative surgery. N Engl J Med. 1994;331(8):502–507.
- Tepper JE, O'Connell M, Niedzwiecki D, et al. Adjuvant therapy in rectal cancer: analysis of stage, sex, and local control final report of intergroup 0114. J Clin Oncol. 2002;20(7):1744–1750.
- O'Connell MJ, Colangelo LH, Beart RW, et al. Capecitabine and oxaliplatin in the preoperative multimodality treatment of rectal cancer: surgical end points from National Surgical Adjuvant Breast and Bowel Project trial R-04. J Clin Oncol. 2014;32(18):1927–1934.
- Hofheinz R, Wenz FK, Post S et al. Capecitabine (Cape) versus 5-fluorouracil (5-FU)-based (neo)adjuvant chemotherapy (CRT) for locally advanced rectal cancer (LARC): long-term results of a randomized, phase III trial [abstract]. J Clin Oncol. 2011;29(suppl):3504.
- Emmanouilides C, Sfakiotaki G, Androulakis N, et al. Front-line bevacizumab in combination with oxaliplatin, leucovorin and 5-fluorouracil (FOLFOX) in patients with metastatic colorectal cancer: a multicenter phase II study. BMC Cancer. 2007;7:91.
- Douillard JY, Siena S, Cassidy J, et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol. 2010;28(31):4697–4705.
- Venook AP, Niedzwiecki D, Lenz H-J, et al. CALGB/SWOG 80405: Phase III trial of irinotecan/5-FU/leucovorin (FOLFIRI) or oxaliplatin/5-FU/leucovorin (mFOLFOX6) with bevacizumab or cetuximab for patients with KRAS wild-type untreated



metastatic adenocarcinoma of the colon or rectum [abstract]. ASCO Meeting Abstracts 2014;32:LBA3. Available at: http:// meeting.ascopubs.org/cgi/content/abstract/32/15\_suppl/LBA3.

- Saltz LB, Clarke S, Diaz-Rubio E, et al. Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study. J Clin Oncol. 2008;26(12):2013–2019.
- Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. Eur J Cancer. 1999;35(9):1343–1347.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Rectal Cancer. Version 3.2017. 13 Mar 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/rectal.pdf.
- Fuchs CS, Marshall J, Mitchell E, et al. Randomized, controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C Study. J Clin Oncol. 2007;25(30):4779–4786.
- Cunningham D, Humblet Y, Siena S, et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. N Engl J Med. 2004;351(4):337–345.
- Martin-Martorell P, Roselló S, Rodriguez-Braun, et al. Biweekly cetuximab and irinotecan in advanced colorectal cancer patients progressing after at least one previous line of chemotherapy: results of a phase II single institution trial. Br J Cancer. 2008; 99(3):455–458.
- Peeters M, Price TJ, Cervantes A, et al. Randomized phase III study of panitumumab with fluorouracil, leucovorin, and irinotecan (FOLFIRI) compared with FOLFIRI alone as second-line treatment in patients with metastatic colorectal cancer. J Clin Oncol. 2010;28(31):4706–4713.
- Van Cutsem E, Tejpar S, Vanbeckevoort D, et al. Intrapatient cetuximab dose escalation in metastatic colorectal cancer according to the grade of early skin reactions: the randomized EVEREST study. J Clin Oncol. 2012;30(23):2861–2868.
- Van Cutsem E, Twelves C, Cassidy J, et al; Xeloda Colorectal Cancer Study Group. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study. J Clin Oncol. 2001;19(21):4097–4106.
- Wolmark N, Rockette H, Fisher B, et al. The benefit of leucovorin-modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer: results from National Surgical Adjuvant Breast and Bowel Protocol C-03. J Clin Oncol. 1993;11(10):1879–1887
- Jager E, Heike M, Bernhard H, et al. Weekly high-dose leucovorin versus low-dose leucovorin combined with fluorouracil in advanced colorectal cancer: results of a randomized multicenter trial. Study Group for Palliative Treatment of Metastatic Colorectal Cancer Study Protocol 1. J Clin Oncol. 1996;14(8):2274–2279.
- Douillard JY, Cunningham D, Roth AD, et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multi-centre randomised trial. Lancet. 2000;355(9209):1041–1047.
- Haller DG, Rothenberg ML, Wong AO, et al. Oxaliplatin plus irinotecan compared with irinotecan alone as second-line treatment after single-agent fluoropyrimidine therapy for metastatic colorectal carcinoma. J Clin Oncol.2008;26(28):4544–4550.
- Loupakis, F., Cremolini, C., Masi, G., Lonardi, S., Zagonel, V., Trenta, P. Falcone, A. (2013). FOLFOXIRI plus bevacizumab (bev) versus FOLFIRI plus bev as first-line treatment of metastatic colorectal cancer (MCRC): Results of the phase III randomized TRIBE trial. Journal of Clinical Oncology, 31(4\_suppl), 336-336.



- Falcone A, Ricci S, Brunetti I, et al. Gruppo Oncologico Nord Ovest. Phase III trial of infusional fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI) compared with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) as first-line treatment for metastatic colorectal cancer: the Gruppo Oncologico Nord Ovest. J Clin Oncol. 2007;25(13):1670–1676.
- Cunningham D, Pyrhönen S, James RD, et al. Randomised trial of irinotecan plus supportive care versus supportive care alone after fluorouracil failure for patients with metastatic colorectal cancer. Lancet. 1998;352(9138):1413–1418.
- Fuchs CS, Moore MR, Harker G, Villa L, Rinaldi D, Hecht JR. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. J Clin Oncol. 2003;21(5):807–814.
- Van Cutsem E, Tabernero J, Lakomy R, et al. Addition of aflibercept to fluorouracil, leucovorin, and irinotecan improves survival in a phase III randomized trial in patients with metastatic colorectal cancer previously treated with an oxaliplatin-based regimen. J Clin Oncol. 2012;30(28):3499–3506.
- Van Cutsem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. J Clin Oncol. 2007;25(13):1658–1664.
- Grothey A, Van Cutsem E, Sobrero A, et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial. Lancet. 2013;381(9863):303– 312.Mayer RJ, Van Cutsem E, Falcone A, et al. RECOURSE Study Group. Randomized trial of TAS-102 for refractory metastatic



# Small Cell Lung Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5543 Primary or Adjuvant Therapy for SCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Patient has extensive stage disease;
- Patient is receiving chemotherapy alone; and EITHER of the following:
  - **§** First-line treatment;
  - Second-line treatment for relapse after more than 6 months.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Etoposide

Carboplatin + Irinotecan

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 341 of 387



Cisplatin + Etoposide

Cisplatin + Irinotecan

Ind. 5543 Primary or Adjuvant Therapy for SCLC per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Patient has limited stage disease;
- First-line treatment; and EITHER of the following:
  - § Patient is receiving chemotherapy alone;
  - **§** Patient undergoing concurrent radiation therapy

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin + Etoposide

Cisplatin + Etoposide

Ind. 5536 For Relapse of SCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient has limited stage disease;
- Relapse is greater than or equal to 6 months;
- Patient is receiving chemotherapy alone;
- Second-line treatment.

ASSOCIATED CHEMOTHERAPY REGIMENS

## Carboplatin + Etoposide

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 342 of 387



# Cisplatin + Etoposide

Ind. 5536 For Relapse of SCLC, the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient has extensive stage disease;
- Relapse is less than 6 months;
- Patient is receiving chemotherapy alone;
- Second-line treatment;
- Normal cardiac function.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cyclophosphamide + Doxorubicin + Vincristine (CAV)

Ind. 5536 For Relapse of SCLC, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

- Patient has extensive stage disease;
- Relapse is less than 6 months;
- Patient is receiving chemotherapy alone;
- Second-line treatment.

## ASSOCIATED CHEMOTHERAPY REGIMENS

Bendamustine

# Carboplatin + Etoposide



Cisplatin + Etoposide

Docetaxel

Etoposide

Gemcitabine

Irinotecan

Nivolumab

Nivolumab + Ipilimumab

Paclitaxel

Paclitaxel + Cisplatin

Temozolomide

Topotecan

Vinorelbine

Ind. 5536 For Relapse of SCLC, the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Continuation therapy after Nivolumab + Iplimumab treatment completion.

ASSOCIATED CHEMOTHERAPY REGIMENS

Nivolumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 344 of 387



#### REFERENCES

- Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-lung cancer. N Engl JMed. 2005;352:2589–2597.
- Arriagada R, Bergman B, Dunant A, et al. The International Adjuvant Lung Cancer Trial Collaborative Group. Cisplatinbased adjuvant chemotherapy in patients with completely resected non-small cell lung cancer. N Engl J Med. 2004;350:351–360.
- Douillard JY, Rosell R, De Lena M, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIA non-small cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a randomised controlled trial. Lancet Oncol. 2006;7:719–727.
- Sandler AB, Nemunaitis J, Denham C, et al. Phase III trial of gemcitabine plus cisplatin versus cisplatin alone in patients with locally advanced or metastatic non-small cell lung cancer. J Clin Oncol. 2000;18:122–130.
- Fossella F, Pereira JR, von Pawel J, et al. Randomized, multi- national, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small cell lung cancer: the TAX 326 study group. J Clin Oncol. 2003;21:3016–3024.
- Hanna NH, Sheperd FA, Fossella FV, et al. Randomized phase III study of pemetrexed versus docetaxel in patients with non- small cell lung cancer previously treated with chemotherapy. J Clin Oncol. 2004;22:1589–1597.
- Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage NSCLC. J Clin Oncol. 2008;26:3543–3551.
- Strauss GM, Herndon JE III, Maddaus MA, et al. Adjuvant paclitaxel plus carboplatin compared with observation in stage
   IB non-small cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group,
   and North Central Cancer Treatment Group Study groups. J Clin Oncol. 2008;26:5043–5051.
- Albain KS, Crowley JJ, Turrisi AT III, et al. Concurrent cisplatin, etoposide, and chest radiotherapy in pathologic stage IIIB non- small cell lung cancer: a Southwest Oncology Group phase II study, SWOG 9019. J Clin Oncol. 2002;20:3454–3460.
- Curran WJ, Scott CB, Langer CJ, et al. Long-term benefit is observed in a phase III comparison of sequential vs concurrent chemoradiation for patients with unresectable stage III NSCLC:RTOG 94–10. Proc Am Soc Clin Oncol. 22:621a,2003 (abstr 2499).
- Govindan R, Bogart J, Stinchcombe T, et al. Randomized phase II study of pemetrexed, carboplatin, and thoracic radiation
  with or without cetuximab in patients with locally advanced unresectable non-small cell lung cancer: Cancer and
  Leukemia Group B trial 30407. J Clin Oncol. 2011;29:3120–3125.



- Belani CP, Choy H, Bonomi P, et al. Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non-small cell lung cancer: a randomized phase II locally advanced multi-modality protocol. J Clin Oncol. 2005;23:5883–5891.
- Bonomi P, Kim K, Fairclough D, et al. Comparison of survival and quality of life in advanced non-small cell lung cancer patients treated with two dose levels of paclitaxel combined with cisplatin versus etoposide with cisplatin: results of an Eastern Cooperative Oncology Group trial. J Clin Oncol. 2000;18:623–631.
- Wozniak AJ, Crowley JJ, Balcerzak SP, et al. Randomized trial comparing cisplatin with cisplatin plus vinorelbine in the treatment of advanced non-small cell lung cancer: A Southwest Oncology Group Study. J Clin Oncol. 1998;16:2459–2465.
- Cardenal F, Lopez-Cabrerizo MP, Anton A, et al. Randomized phase III study of gemcitabine-cisplatin versus etoposidecisplatin in the treatment of locally advanced or metastatic non-small cell lung cancer. J Clin Oncol. 1999;17:12–18.
- Belani CP, Lee JS, Socinski MA, et al. Randomized phase III trial comparing cisplatin-etoposide to carboplatin-paclitaxel in advanced or metastatic non-small cell lung cancer. Ann Oncol. 2005;16:1069–1075.
- Smit EF, van Meerbeeck JR Lianes P, et al. Three-arm randomized study of two cisplatin-based regimens and paclitaxel plus gemcitabine in advanced non-small cell lung cancer: a phase III trial of the European Organization for Research and Treatment of Cancer Lung Cancer Group-EORTC 08975. J Clin Oncol. 2003;21:3909–3917.
- Schiller JH, Harrington D, Belani CR et al. Comparison of four chemotherapy regimens for advanced non-small cell lung cancer. N Engl J Med. 2002;346:92–98.
- Ohe Y, Ohashi Y, Kubota K, et al. Randomized phase III study of cisplatin plus irinotecan versus carboplatin plus paclitaxel, cisplatin plus gemcitabine, and cisplatin plus vinorelbine for advanced non-small cell lung cancer: Four-Arm Cooperative Study in Japan. Ann Oncol. 2007;18:317–323.
- Kelly K, Crowley J, Bunn PA, et al. Randomized phase III trial of paclitaxel plus carboplatin versus vinorelbine plus cisplatin in the treatment of patients with advanced non-small cell lung cancer: A Southwest Oncology Group trial. J Clin Oncol. 2001;19:3210–3218.
- Belani CP, Ramalingam S, Perry MC, et al. Randomized, phase III study of weekly paclitaxel in combination with carboplatin versus standard every-3-weeks administration of carboplatin and paclitaxel for patients with previously untreated advanced non-small cell lung cancer. J Clin Oncol. 2008;26:468–473.
- Fossella FV, DeVore R, Kerr RN, et al. Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small cell lung cancer previously treated with platinum- containing chemotherapy regimens. The TAX 320 Non- Small Cell Lung Cancer Study Group. J Clin Oncol. 2000;18:2354–2362.
- Pujol JL, Breton JL, Gervais R, et al. Gemcitabine-docetaxel versus cisplatin-vinorelbine in advanced or metastatic nonsmall cell lung cancer: a phase III study addressing the case for cisplatin. Ann Oncol. 2005;16:602–610.
- Shepherd FA, Pereira JR, Ciuleanu T, et al. Erlotinib in previously treated non-small cell lung cancer. N Engl J Med.2005;353:123–132.
- Sandler AB, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small cell lung cancer. N Engl J Med. 2006;355:2542–2550.
- Pirker R, Periera JR, Szczesna A, et al. Cetuximab plus chemotherapy in patients with advanced non-small cell lung cancer (FLEX): an open label randomised phase III trial. Lancet. 2009;373:1525–1531.
- Green M, Manikhas G, Orlov S, et al. Abraxane<sup>®</sup>, a novel Cremophor<sup>®</sup> -free, albumin-bound particle form of paclitaxel for the treatment of advanced non-small cell lung cancer. Ann Oncol. 2006;17:2113–2118.



- Rizvi N, Riely G, Azzoli, C, et al. Phase I/II Trial of Weekly Intravenous 130-nm Albumin-Bound Paclitaxel As Initial Chemotherapy in Patients With Stage IV Non-small cell Lung Cancer. J Clin Oncol. 2008;26:639–643.
- Socinski MA, Bondarenko I, Karaseva NA, et al. Weekly nab-paclitaxel in combination with carboplatin versus solventbased paclitaxel plus carboplatin as first-line therapy in patients with advanced non-small cell lung cancer: final results of a phase III trial. J Clin Oncol. 2012:30:2055–2062.
- Shaw AT, Yeap BY, Solomon BJ, et al. Effect of crizotinib on overall survival in patients with advanced non-small cell lung cancer harbouring ALK gene rearrangement: a retrospective analysis. Lancet Oncol. 2011;12:1004–1012.
- Sequist LV, Yang JC-H, Yamamoto N, et al. Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. J Clin Oncol. 2013;31(27):3327–3334.
- Shaw AT, Kim D-W, Mehra R, et al. Ceritinib in ALK-rearranged non-small-cell lung cancer. N Engl J Med. 2014;370:1189– 1197.
- Garon EB, Cieleanu TE, Arrieta O, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, double- blind, randomised phase 3 trial. Lancet. 2014;384:665–673.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Small Cell Lung Cancer.
   Version 3.2017. 23 Feb 2017. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/sclc.pdf.
- Rizvi NA, Mazieres J, Planchard D, et al. Activity and safety of nivolumab, an anti-PD-1 immune checkpoint inhibitor, for patients with advanced, refractory squamous non-small-cell lung cancer (CheckMate 063): a phase 2, single-arm trial. Lancet Oncol. 2015;16:257–65.
- Avastin [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2011.
- Cappuzzo F, Ciuleanu T, Stelmakh L, et al. SATURN investigators. Erlotinib as maintenance treatment in advanced nonsmall-cell lung cancer: a multicentre, randomised, placebo-controlled phase 3 study. Lancet Oncol. 2010;11:521–529.
- Tarceva [prescribing information]. S. San Francisco, CA: Genentech, Inc.; 2011.
- Alimta® [prescribing information]. Indianapolis, IN: Eli Lilly & Co.; 2011.
- Xalkori [prescribing information]. New York, NY: Pfizer, Inc.; 2011.
- Hanna N, Bunn PA Jr, Langer C, et al. Randomized phase III trial comparing irinotecan/cisplatin with etoposide/cisplatin in patients with previously untreated extensive-stage disease small-cell lung cancer. J Clin Oncol. 2006;24:2038–2043.
- Turrisi AT 3rd, Kim K, Blum R, et al. Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. N Eng J Med. 1999;340:265–271.
- Saito H, Takada Y, Ichinose Y, et al. Phase II study of etoposide and cisplatin with concurrent twice-daily thoracic radiotherapy followed by irinotecan and cisplatin in patients with limited- disease small-cell lung cancer: West Japan Thoracic Oncology Group 9902. J Clin Oncol. 2006;24(33):5247–5252.
- Skarlos DV, Samantas E, Briassoulis E, et al. Randomized comparison of early versus late hyperfractionated thoracic irradiation concurrently with chemotherapy in limited disease small-cell lung cancer: a randomized phase II study of the Hellenic Cooperative Oncology Group (HeCOG). Ann Oncol. 2001;12:1231–1238.
- Ihde DC, Mulshine JL, Kramer BS, et al. Prospective random- ized comparison of high-dose and standard-dose etoposide and cisplatin chemotherapy in patients with extensive-stage small-cell lung cancer. J Clin Oncol. 1994;12:2022–2034.



- Sundstrom S, Bremnes RM, Kaasa S, et al. Cisplatin and etoposide regimen is superior to cyclophosphamide, epirubicin, and vincristine regimen in small-cell lung cancer: results from a randomized phase III trial with 5 years' follow-up. J Clin Oncol. 2002;20:4665–4672.
- Evans WK, Shepherd FA, Feld R, et al. VP-16 and cisplatin as first line therapy for small-cell lung cancer. J Clin Oncol.1985;3:1471–1477.
- Natale RB et al. S0124: a randomized phase III trial comparing irinotecan/cisplatin (IP) with etoposide/cisplatin (EP) in patients (pts) with previously untreated extensive stage small-cell lung cancer (E-SCLC) [Abstract 7512]. 2008 ASCO annual meeting.
- Noda K, Nishiwaki Y, Kawahara M, et al. Irinotecan plus cisplatin compared with etoposide plus cisplatin for extensive small- cell lung cancer. N Engl J Med. 2002;346:85–91.
- Schmittel A, Sebastian M, Fischer von Weikersthal L, et al. For the Arbeitsgemeinschaft Internistische Onkologie thoracic oncology study group. A German multicenter, randomized phase III trial comparing irinotecan-carboplatin with etoposide- carboplatin as first-line therapy for extensive-disease small-cell lung cancer. Ann Oncol. 2011;22(8):1798– 1804.
- Okamoto H, Watanabe K, Nishiwaki Y, et al. Phase II study of area under the plasma-concentration-versus-time curvebased carboplatin plus standard-dose intravenous etoposide in elderly patients with small-cell lung cancer. J Clin Oncol. 1999;17:3540–3545.
- Yamamoto, N., Tsurutani, J., Yoshimura, N., et al. Phase II study of weekly paclitaxel for relapsed and refractory small cell lung cancer. Anticancer Res,2006;26(1b):777–781Smyth JF, Smith IE, Sessa C, et al. Activity of docetaxel (Taxotere) in small cell lung cancer. Eur J Cancer 1994;30A:1058–1060.
- von Pawel J, Schiller JH, Shepherd FA, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol. 1999;17(2):658–667.
- Eckardt JR, von Pawel J, Pujol JL, et al. Phase III study of oral compared with intravenous topotecan as second-line therapy in small-cell lung cancer. J Clin Oncol. 2007;25:2086–2092.
- O'Brien M, Ciuleanu TE, Tsekov H, et al. Phase III trial comparing supportive care alone with supportive care with oraltopotecan in patients with relapsed small-cell lung cancer. J Clin Oncol. 2006;24:5441–5447.
- Ardizzoni A, et al. Topotecan, a new active drug in the second-line treatment of small-cell lung cancer: a phase II study in
  patients with refractory and sensitive disease. The European Organization for Research and Treatment of Cancer Early
  Clinical Studies Group and New Drug Development Office, and the Lung Cancer Cooperative Group. J Clin Oncol.
  1997;15:2090–2096.
- Masuda N, Fukuoka M, Kusunoki Y, et al. CPT-11: a new derivative of camptothecin for the treatment of refractory or relapsed small-cell lung cancer. J Clin Oncol. 1992;10:1225–1229.
- Pietanza MC, Kadota K, Huberman K, et al. Phase II trial of temozolomide with relapsed sensitive or refractory small cell lung cancer, with assessment of methylguanine-DNA methyltransferase as a potential biomarker. Clin Cancer Res. 2012;18:1138–1145.
- Van der Lee I, Smit EF, van Putten JW, et al. Single-agent gemcitabine in patients with resistant small-cell lung cancer. Ann Oncol. 2001;12:557–561.
- Masters GA, Declerck L, Blanke C, et al. Phase II trial of gemcitabine in refractory or relapsed small-cell lung cancer. J Clin Oncol. 2003;21:1550–1555.



- Cantwell BM, Bozzino JM, Corns P, et al. The multidrug resistant phenotype in clinical practice; evaluation of cross resistance to ifosfamide and mesna after VPI6-213, doxorubicin and vincristine (VPAV) for small cell lung cancer. Eur J Cancer Clin Oncol. 1988;24:123–129.
- Jassem J, Karnicka-Mlodkowska H, van Pottelsberghe C, et al. Phase II study of vinorelbine (Navelbine) in previously treated small cell lung cancer patients. Eur J Cancer 1993;29A:1720–1722.
- Furuse K, Kuboa K, Kawahara M, et al. Phase II study of vinorelbine in heavily previously treated small cell lung cancer. Oncology. 1996;53:169–172.
- Einhorn LH, Pennington K, McClean J. Phase II trial of daily oral VP-16 in refractory small cell lung cancer. Semin Oncol.1990;17:32–35.
- Johnson DH, Greco FA, Strupp J, et al. Prolonged administration of oral etoposide in patients with relapsed or refractory small-cell lung cancer: a phase II trial. J Clin Oncol. 1990;8:1613–1617.
- Postmus PE, Berendsen HH, van Zandwijk N, et al. Retreatment with the induction regimen in small cell lung cancer relapsing after an initial response to short term chemotherapy. Eur J Cancer Clin Oncol. 1987;23:1409–1411.
- Giaccone G, Ferrati P, Donadio M, et al. Reinduction chemotherapy in small cell lung cancer. Eur J Cancer Clin Oncol.1987;23:1697–1699.



# Testicular Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5479 Primary Therapy for Germ Cell Tumor per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Primary chemotherapy;
  - Stage 1A/1B Seminoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 350 of 387



- Ind. 5479 Primary Therapy for Germ Cell Tumor per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ANY of the following:
  - Primary chemotherapy for Retroperitoneal Lymph Node Dissection (RPLND) with positive nodes; and EITHER of the following:
    - **§** Stage 1B Non-Seminoma;
    - **§** Stage 2 Non-Seminoma;
  - Primary chemotherapy for Retroperitoneal Lymph Node Dissection (RPLND) with negative nodes, Stage 2 Non-Seminoma;
  - Primary chemotherapy; and EITHER of the following:
    - Stage 2A Seminoma;
    - Stage 2B Seminoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bleomycin + Etoposide + Cisplatin (BEP)

Etoposide + Cisplatin (EP)

- Ind. 5479 Primary Therapy for Germ Cell Tumor per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Primary chemotherapy;
  - Stage 2C/3 Seminoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bleomycin + Etoposide + Cisplatin (BEP)

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 351 of 387



Ind. 5479 Primary Therapy for Germ Cell Tumor per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Primary chemotherapy;
- Good risk/prognosis; and EITHER of the following:
  - Stage 3B Non-Seminoma;
  - Stage 3C Non-Seminoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Bleomycin + Etoposide + Cisplatin (BEP)

Etoposide + Cisplatin (EP)

Etoposide + Ifosfamide + Cisplatin (VIP) + Mesna

- Ind. 5480 For Metastatic Germ Cell Tumor, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - Failed first-line chemotherapy;
  - Second-line therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Carboplatin

Carboplatin + Etoposide

# Etoposide



Etoposide + Cisplatin (EP)

Etoposide + Ifosfamide + Cisplatin (VIP) + Mesna

Gemcitabine + Oxaliplatin (GemOX)

Gemcitabine + Paclitaxel

Gemcitabine + Paclitaxel + Oxaliplatin

Paclitaxel + Ifosfamide + Cisplatin (TIP) + Mesna

Paclitaxel + Ifofamide + Mesna + Carboplatin + Etoposide

Vinblastine + Ifosfamide + Cisplatin (VeIP) + Mesna

Ind. 5480 For Metastatic Germ Cell Tumor, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Residual therapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

Etoposide + Cisplatin (EP)

Etoposide + Ifosfamide + Cisplatin (VIP) + Mesna

Paclitaxel + Ifofamide + Cisplatin (TIP) + Mesna

Vinblastine + Ifosfamide + Cisplatin (VeIP) + Mesna





#### REFERENCES

- Xiao H, Mazumdar M, Bajorin DF, et al. Long-term follow-up of patients with good-risk germ cell tumors treated with etoposide and cisplatin. J Clin Oncol. 1997;15(7):2553–2558.
- Saxman SB, Finch D, Gonin R, Einhorn LH. Long-term follow-up of a phase III study of three versus four cycles of bleomycin, etoposide, and cisplatin in favorable-prognosis germ-cell tumors: the Indiana University experience. J Clin Oncol. 1998;16(2):702–706.
- Nichols CR, Catalano PJ, Crawford ED, et al. Randomized comparison of cisplatin and etoposide and either bleomycin or ifosfamide in treatment of advanced disseminated germ cell tumors: an Eastern Cooperative Oncology Group, Southwest Oncology Group, and Cancer and Leukemia Group B Study. J Clin Oncol. 1998;16(4):1287–1293.
- Loehrer PJ Sr, Lauer R, Roth BJ, et al. Salvage therapy in recurrent germ cell cancer: ifosfamide and cisplatin plus either vinblastine or etoposide. Ann Intern Med. 1988;109(7): 540–546. Erratum in: Ann Intern Med. 1988;109(10):846.
- Kondagunta GV, Bacik J, Donadio A, et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. J Clin Oncol. 2005;23(27):6549–6555.
- Einhorn LH, Williams SD, Chamness A, et al. High-dose chemotherapy and stem-cell rescue for metastatic germ-cell tumors. N Engl J Med. 2007;357(4):340–348.
- Feldman DR, Sheinfeld J, Bajorin DF, et al. TI-CE high-dose chemotherapy for patients with previously treated germ cell tumors: results and prognostic factor analysis. J Clin Oncol. 2010; 28(10):1706–1713. Erratum in: J Clin Oncol. 2010;28(34):5211.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Testicular Cancer. Version 2.2017. 8 Dec 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/testicular.pdf.
- Pectasides D, Pectasides M, Farmakis D, et al. Gemcitabine and oxaliplatin (GEMOX) in patients with cisplatin-refractory germ cell tumors: a phase II study. Ann Oncol. 2004;15(3):493–497.
- Kollmannsberger C, Beyer J, Liersch R, et al. Combination chemotherapy with gemcitabine plus oxaliplatin in patients with intensively pretreated or refractory germ cell cancer: a study of the German Testicular Cancer Study Group. J Clin Oncol. 2004;22(1):108–114.
- De Giorgi U, Rosti G, Aieta M, et al. Phase II study of oxaliplatin and gemcitabine salvage chemotherapy in patients with cisplatin-refractory nonseminomatous germ cell tumor. Eur Urol. 2006;50(5):1032–1039.
- Einhorn LH, Brames MJ, Juliar B, Williams SD. Phase II study of paclitaxel plus gemcitabine salvage chemotherapy for germ cell tumors after progression following high-dose chemotherapy with tandem transplant. J Clin Oncol. 2007;25(5):513–516.
- Mulherin B, Brames MJ, Einhorn L. Long-term survival with paclitaxel and gemcitabine for germ cell tumors after progression following high-dose chemotherapy with tandem transplants. J Clin Oncol. 2011;29(Suppl):Abstract 4562.
- Bokemeyer C, Oechsle K, Honecker F, et al. Combination chemotherapy with gemcitabine, oxaliplatin, and paclitaxel in patients with cisplatin-refractory or multiply relapsed germ-cell tumors: a study of the German Testicular Cancer Study Group. Ann Oncol. 2008;19(3):448–453.
- Miller JC, Einhorn LH. Phase II study of daily oral etoposide in refractory germ cell tumors. Semin Oncol. 1990;17 (1 Supp 2):36–39.



# Thymoma

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

Ind. 5482 First Line Therapy for Thymoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- First-line treatment for unresectable locally advanced or metastatic;
- Adjuvant therapy; and EITHER of the following:
  - § R1 Resection;
  - § R2 Resection.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cisplatin + Doxorubicin + Cyclophosphamide (CAP)

Cisplatin + Doxorubicin + Cyclophosphamide (CAP) + Prednisone

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 356 of 387



Cisplatin + Doxorubicin + Vincristine + Cyclophosphamide (ADOC)

Cisplatin + Etoposide (PE)

Etoposide + Ifosfamide + Cisplatin (VIP) + Mesna

Carboplatin + Paclitaxel

Ind. 5483 Second Line Therapy for Thymoma per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Unresectable locally advanced or metastatic;
- Second-line chemotherapy.

ASSOCIATED CHEMOTHERAPY REGIMENS

5-Fluorouracil (5-FU) + Leucovorin

Etoposide

Everolimus

Gemcitabine

lfosfamide + Mesna

Octreotide

Octreotide + Prednisone

Octreotide LAR

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 357 of 387



Paclitaxel

Pemetrexed

Sunitinib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 358 of 387



#### REFERENCES

- Loehrer P, Kim K, Aisner S, et al. Cisplatin plus doxorubicin plus cyclophosphamide in metastatic or recurrent thymoma: final results of an intergroup trial. The Eastern Cooperative Oncology Group, Southwest Oncology Group, and Southeastern Cancer Study Group. J Clin Oncol. 1994;12:1164–1168.
- Kim E, Putnam J, Komaki R, et al. Phase II study of a multidisciplinary approach with induction chemotherapy, followed by surgical resection, radiation therapy, and consolidation chemotherapy for unresectable malignant thymomas: final report. Lung Cancer. 2004;44:369–379.
- Fornasiero A, Daniele O, Ghiotto C, et al. Chemotherapy for invasive thymoma. A 13-year experience. Cancer. 1991;68:30–33.
- Giaccone G, Ardizzoni A, Kirkpatrick A, et al. Cisplatin and etoposide combination chemotherapy for locally advanced or metastatic thymoma. A phase II study of the European Organization for Research and Treatment of Cancer Lung Cancer Cooperative Group. J Clin Oncol. 1996;14:814–820.
- Loehrer P, Jiroutek M, Aisner S, et al. Combined etoposide, ifosfamide, and cisplatin in the treatment of patients with advanced thymoma and thymic carcinoma: an intergroup trial. Cancer. 2001;91:2010–2015.
- Lemma G, Lee J, Aisner S, et al. Phase II study of carboplatin and paclitaxel in advanced thymoma and thymic carcinoma. JClin Oncol. 2011;29:2060–2065.
- Highley M, Underhill C, Parnis F, et al. Treatment of invasive thymoma with single-agent ifosfamide. J Clin Oncol. 1999;17:2737–2744.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Thymomas and Thymic Carcinomas. Version 3.2016. 22 Jun 2016. Please refer to the NCCN website for additional information, available at: https:// www.nccn.org/professionals/physician\_gls/pdf/thymic.pdf.
- Loehrer P, Yiannoutsos C, Dropcho S, et al. A phase II trial of pemetrexed in patients with recurrent thymoma or thymic carcinoma [abstract]. J Clin Oncol. 2006;24(Suppl 18): Abstract 7079.
- Loehrer P, Wang W, Johnson D, et al. Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: an Eastern Cooperative Oncology Group Phase II Trial. J Clin Oncol. 2004;22:293–299.
- Stewart D, Dahrouge S, Soltys K, Evans W. A phase II study of 5-fluorouracil plus high-dose folinic acid in the treatment of recurrent small cell lung cancer. Am J Clin Oncol. 1995;18:130–132.
- Masters G, Declerck L, Blanke C, et al. Phase II trial of gemcitabine in refractory or relapsed small-cell lung cancer: Eastern Cooperative Oncology Group Trial 1597. J Clin Oncol. 2003;21:1550–1555.
- Yamamoto N, Tsurutani J, Yoshimura N, et al. Phase II study of weekly paclitaxel for relapsed and refractory small cell lung cancer. Anticancer Res. 2006;26:777–781.
- Thomas A, Rajan A, Berman AW, et al. Phase II trial of sunitinib in patients with thymic epithelial tumors (TET) [abstract]. J Clin Oncol. 2014;32(suppl 5): Abstract 7525.
- Zucali PA, De Pas TM, Palmieri G, et al. Phase II study of everolimus in patients with thymoma and thymic carcinoma previously treated with cisplatin-based chemotherapy [abstract]. J Clin Oncol. 2014;32(suppl 5):Abstract 7527.



# Thyroid Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5488 Primary Therapy for Thyroid Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:
  - Symptomatic or progressive metastatic disease; and EITHER of the following:
    - § Medullary carcinoma;
    - **§** Dedifferentiated carcinoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Cabozantinib

# Sorafenib



# Vandetanib

Ind. 5488 Primary Therapy for Thyroid Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Symptomatic or progressive metastatic disease;
- Not amenable to Radioactive Iodine (RAI) therapy; and ANY of the following:
  - **§** Papillary Carcinoma;
  - **§** Follicular Carcinoma;
  - S Hürthle Carcinoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Sorafenib

Ind. 5488 Primary Therapy for Thyroid Cancer per the drug regimen shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

• Symptomatic or progressive metastatic disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

Denosumab

Pamidronate

Zoledronic Acid

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 361 of 387



Ind. 5489 For Recurrent Thyroid Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates the following:

- Symptomatic or progressive metastatic disease; and ANY of the following:
  - **§** Papillary carcinoma;
  - **§** Follicular carcinoma;
  - S Hürthle carcinoma;
  - **§** Dedifferentiated carcinoma.

# ASSOCIATED CHEMOTHERAPY REGIMENS

#### Axitinib

Axitinib + Denosumab

Axitinib + Pamidronate

Axitinib + Zoledronic Acid

Lenvatinib

Lenvatinib + Denosumab

Lenvatinib + Pamidronate

Pamidronate

Pazopanib

Pazopanib + Denosumab

Pazopanib + Pamidronate

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 362 of 387



Pazopanib + Zoledronic Acid

Sorafenib + Denosumab

Sorafenib + Pamidronate

Sorafenib + Zoledronic Acid

Sunitinib

Sunitinib + Denosumab

Sunitinib + Pamidronate

Sunitinib + Zoledronic Acid

Vandetanib + Denosumab

Vandetanib + Pamidronate

Vandetanib + Zoledronic Acid

Lenvatinib + Zoledronic Acid

Zoledronic Acid

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 363 of 387



Ind. 5489 For Recurrent Thyroid Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Symptomatic or progressive metastatic disease;
- Medullary carcinoma.

ASSOCIATED CHEMOTHERAPY REGIMENS

Pamindronate

Vandetanib + Denosumab

Vandetanib + Pamidronate

Vandetanib + Zoledronic Acid

Zoledronic Acid

Ind. 5489 For Recurrent Thyroid Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Symptomatic or progressive metastatic disease;
- Medullary carcinoma with disease progression while on ANY of the following:
  - S Vandetinib;
  - S Cabozentinib;
  - Sorafenib;
  - Sunitinib;
  - Se Pazopanib.



Dacarbazine + 5-Fluorouracil (5-FU)

Ind. 5489 For Recurrent Thyroid Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- Symptomatic or progressive metastatic disease;
- Dedifferentiated carcinoma; and EITHER of the following
  - Stage 4A or 4B (IVA or IVB) and post surgical adjuvant therapy;
  - Stage 4C (IVC).

ASSOCIATED CHEMOTHERAPY REGIMENS

Docetaxel + Doxorubicin

Doxorubicin

Paclitaxel

Paclitaxel + Carboplatin

Ind. 5489 For Recurrent Thyroid Cancer, the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates symptomatic or progressive metastatic disease with bone metastases.

ASSOCIATED CHEMOTHERAPY REGIMENS

Denosumab

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 365 of 387





#### REFERENCES

- Caprelsa [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals, LP. 2011.
- Cometriq [package insert]. San Francisco, CA: Exelixis Inc. 2012.
- Schoffski, et al. An international, double-blind, randomized, placebo-controlled phase III trial (EXAM) of cabozantinib (XL 184) in medullary thyroid carcinoma (MTC) patients (pts) with documented RECIST progression at baseline [abstract]. J Clin Oncol. 2012;30(Supl 15): Abstract 5508.
- Traynor K. Cabozantinib approved for advanced medullary thyroid cancer. Am J Health Syst Pharm. 2013;70(2):88.
- Ravaud A, et al. Efficacy of sunitinib in advanced medullary thyroid carcinoma: intermediate results of phase II THYSU.Oncologist. 2010;15(2):212–213.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Thyroid Carcinoma. Version 1.2016. 7 Aug 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/thyroid.pdf.
- Sherman SI. Advances in chemotherapy of differentiated epithelial and medullary thyroid cancers. J Clin Endocrinol Metab. 2009;94(5):1493–1499.
- Nocera M, et al. Treatment of advanced medullary thyroid cancer with an alternating combination of doxorubicinstreptozocin and 5 FU-dacarbazine. Groupe d'Etude des Tumeurs à Calcitonine (GETC). Br J Cancer. 2000;83(6):715–718.
- Smallridge RC, et al. American thyroid association guidelines for management of patients with anaplastic thyroid cancer. Thyroid. 2012;22(11):1104-1139.
- Ain KB, et al. Treatment of anaplastic thyroid carcinoma with paclitaxel: phase 2 trial using ninety-six-hour infusion. Collaborative Anaplastic Thyroid Cancer Health Intervention Trials (CATCHIT) Group. Thyroid. 2000;10(7):587–594.
- Shimaoka K, et al. A randomized trial of doxorubicin versus doxorubicin plus cisplatin in patients with advanced thyroid carcinoma. Cancer. 1985;56(9):2155–2160.



# Uterine Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.

- Ind. 5484 Systemic Therapy for Uterine Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:
  - High grade endometrial stromal sarcoma (ESS), undifferentiated uterine sarcoma (UUS), uterine leiomyosarcoma (ULMS);
  - Metastatic disease with measurable lesions.

ASSOCIATED CHEMOTHERAPY REGIMENS

Dacarbazine

Docetaxel

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 368 of 387



Docetaxel + Gemcitabine

Doxorubicin

Doxorubicin + Dacarbazine

Doxorubicin + Ifosfamide + Mesna

Doxorubicin + Olaratumab

Epirubicin

Gemcitabine

Gemcitabine + Dacarbazine

Gemcitabine + Vinorelbine

lfosfamide + Mesna

Liposomal Doxorubicin

Pazopanib

Temozolomide

Ind. 5484 Systemic Therapy for Uterine Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

 High grade endometrial stromal sarcoma (ESS), undifferentiated uterine sarcoma (UUS), uterine leiomyosarcoma (ULMS);

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 369 of 387



- Stage 2, 3, or 4;
- Adjuvant therapy after surgery.

Dacarbazine

Docetaxel + Gemcitabine

Doxorubicin

Doxorubicin + Dacarbazine

Doxorubicin + Ifosfamide + Mesna

Doxorubicin + Olaratumab

Epirubicin

Gemcitabine

Gemcitabine + Dacarbazine

Gemcitabine + Vinorelbine

lfosfamide + Mesna

Liposomal Doxorubicin

Ind. 5484 Systemic Therapy for Uterine Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 370 of 387



- High grade endometrial stromal sarcoma (ESS), undifferentiated uterine sarcoma (UUS), uterine leiomyosarcoma (ULMS);
- Relapsed disease;
- Extrapelvic disease.

Dacarbazine

Docetaxel

Docetaxel + Gemcitabine

Doxorubicin

Doxorubicin + Dacarbazine

Doxorubicin + Ifosfamide + Mesna

Doxorubicin + Olaratumab

Epirubicin

Gemcitabine

Gemcitabine + Dacarbazine

Gemcitabine + Vinorelbine

lfosfamide + Mesna

Liposomal Doxorubicin

Pazopanib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 371 of 387



Temozolomide

Vinorelbine

Ind. 5484 Systemic Therapy for Uterine Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates BOTH of the following:

- High grade endometrial stromal sarcoma (ESS), undifferentiated uterine sarcoma (UUS), uterine leiomyosarcoma (ULMS);
- Normal cardiac function; and ANY of the following:
  - § Metastatic disease with measurable lesions;
  - Stage 2, 3, or 4 with Adjuvant therapy after surgery;
  - § Relapsed disease with Extrapelvic disease.

ASSOCIATED CHEMOTHERAPY REGIMENS

Doxorubicin

Doxorubicin + Dacarbazine

Doxorubicin + Ifosfamide + Mesna

Doxorubicin + Olaratumab

Epirubicin

Liposomal Doxorubicin

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 372 of 387



- Ind. 5484 Systemic Therapy for Uterine Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates ALL of the following:
  - Metastatic disease with measurable lesions;
  - Patient has Liposarcoma and has completed anthracvcline containing therapy;
  - Unresectable metastases.

## Eribulin

#### REFERENCES

- Hensley ML, Blessing JA, Mannel R, Rose PG. Fixed-dose rate gemcitabine plus docetaxel as first-line therapy for metastatic uterine leiomyosarcoma: a Gynecologic Oncology Group phase II trial. Gynecol Oncol. 2008;109(3):329–334.
- Sutton G, Blessing JA, Malfetano JH. Ifosfamide and doxorubicin in the treatment of advanced leiomyosarcomas of the uterus: a Gynecologic Oncology Group study. Gynecol Oncol. 1996;62(2):226–229.
- Zalupski M, Metch B, Balcerzak S, et al. Phase III comparison of doxorubicin and dacarbazine given by bolus versus infusion in patients with soft-tissue sarcomas: a Southwest Oncology Group study. J Natl Cancer Inst. 1991;83(13):926– 932.
- Garcia-Del-Muro X, Lopez-Pousa A, Maurel J, et al. Randomized phase II study comparing gemcitabine plus dacarbazine versus dacarbazine alone in patients with previously treated soft tissue sarcoma: a Spanish Group for Research on Sarcomas study. J Clin Oncol. 2011;29(18):2528–2533.
- Dileo P, Morgan J, Zahrieh D, et al. Gemcitabine and vinorelbine combination chemotherapy for patients with advanced soft tissue sarcomas. Cancer. 2007;109(9):1863–1869.
- Judson I, Radford JA, Harris M, et al. Randomized phase II trial of pegylated liposomal doxorubicin (DOXIL/CAELYX) versus doxorubicin in the treatment of advanced or metastatic soft tissue sarcoma: a study by the EORTC Soft Tissue and Bone Sarcoma Group. Eur J Cancer. 2001;37(7):870–877.
- Mouridsen HT, Bastholt L, Somers R, et al. Adriamycin versus epirubicin in advanced soft tissue sarcomas. A randomized phase II/phase III study of the EORTC Soft Tissue and Bone Sarcoma Group. Eur J Cancer Clin Oncol. 1987;23(10):1477– 1483.



- Schöffski P, Maki RG, Italiano A, et al. Randomized, open-label, multicenter, phase III study of eribulin versus dacarbazine in patients (pts) with leiomyosarcoma (LMS) and adipocytic sarcoma (ADI). J Clin Oncol. 2015;33(18\_suppl):LBA10502.
- Look KY, Sandler A, Blessing JA, et al. Phase II trial of gemcitabine as second-line chemotherapy of uterine leiomyosarcoma:a Gynecologic Oncology Group (GOG) Study. Gynecol Oncol. 2004;92(2):644–647.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Uterine Neoplasms. Version 1.2017. 21 Nov 2016. Please refer to the NCCN website for additional information, available at: https://www.nccn.org/ professionals/physician\_gls/pdf/uterine.pdf.
- Sutton GP, Blessing JA, Barrett RJ, et al. Phase II trial of ifosfamide and mesna in leiomyosarcoma of the uterus: a Gynecologic Oncology Group study. Am J Obstet Gynecol. 1992;166(2):556–559.
- Amant F, Coosemans A, Debiec-Rychter M, et al. Clinical management of uterine sarcomas. Lancet Oncol. 2009;10(12):1188–1198.
- van der Graaf WT, Blay JY, Chawla SP, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2012;379(9829):1879–1886.
- Gajdos C, Elias A. Trabectedin: safety and efficacy in the treatment of advanced sarcoma. Clin Med Insights Oncol.2011;5:35–43.
- Demetri GD, Chawla SP, von Mehren M, et al. Efficacy and safety of trabectedin in patients with advanced or metastatic liposarcoma or leiomyosarcoma after failure of prior anthracyclines and ifosfamide: results of a randomized phase II study of two different schedules. J Clin Oncol. 2009;27(25):4188–4196.
- Fayette J, Boyle H, Chabaud S, et al. Efficacy of trabectedin for advanced sarcomas in clinical trials versus compassionate use programs: analysis of 92 patients treated in a single institution. Anticancer Drugs. 2010;21(1):113–119.
- Pautier P, Floquet A, Chevreau C, et al; French Sarcoma Group. Trabectedin in combination with doxorubicin for first-line treatment of advanced uterine or soft-tissue leiomyosarcoma (LMS-02): a non-randomised, multicentre, phase 2 trial. Lancet Oncol. 2015;16(4):457–464.
- Muggia F, Blessing JA, Method M. Evaluation of vinorelbine in persistent or recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Gynecol Oncol. 2004;92(2):639–643.
- Garcia AA, Blessing JA, Nolte S, Mannel RS. A phase II evaluation of weekly docetaxel in the treatment of recurrent or persistent endometrial carcinoma: a study by the Gynecologic Oncology Group. Gynecol Oncol. 2008;111(1):22–26.



# Vulvar Cancer

HealthHelp utilizes internal Medical Oncology Regimen codes to identify guideline-supported standard regimens. Regimen codes and their description details can be viewed through HealthHelp's WebConsult online tool. If you do not have access to HealthHelp's WebConsult, please contact HealthHelp's Program Support Team at 1-800-546-7092.

Medical Oncology treatments may be medically appropriate and supported by evidence to improve patient outcomes for the following indications and regimens. Unless otherwise stated, patients should demonstrate physical capability and appropriate clinical status as evidenced by either an Eastern Cooperative Oncology Group (ECOG) Performance Status Grade of 2 or less OR a Karnofsky Performance Status (KPS) Grade of 70 or greater.



- Ind. 5573 Systemic Therapy for Vulvar Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Locally Advanced cancer; and EITHER of the following:
    - **§** Node negative with positive margins;
    - **§** Node positive and tumor is unresectable;
  - Metastatic disease; and EITHER of the following:
    - Sequest is for primary treatment;
    - **§** Recurrent therapy for previously irradiated, node negative disease.

Cisplatin

Cisplatin + Vinorelbine

Paclitaxel + Cisplatin

Carboplatin

Carboplatin + Paclitaxel

Paclitaxel

Erlotinib

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 376 of 387



- Ind. 5574 Chemoradiation Therapy for Vulvar Cancer per the drug regimens shown in the table below may be reasonable and appropriate when the patient's medical record demonstrates EITHER of the following:
  - Early Stage; and EITHER of the following:
    - **§** Request is for primary treatment;
    - **§** Request is for adjuvant therapy for node positive disease.
  - Locally Advanced cancer; and EITHER of the following:
    - **§** Request is for primary treatment;
    - S Recurrent therapy for node negative disease, in an area that was not previously irradiated.

Cisplatin

Cisplatin + 5FU

Mitomycin + 5FU



#### REFERENCES

- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology.Vulvar Cancer
   (Squamous Cell Carcinoma). Version 1.2018. 27 October 2017. Please refer to the NCCN website for additional
   information, available at: https://www.nccn.org/ https://www.nccn.org/professionals/physician\_gls/pdf/vulvar.pdf.
- Greer BE, Koh WJ. New NCCN Guidelines for Vulvar Cancer. J Natl Compr Canc Netw 2016; 14:656.
- Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet 2009; 105:103.
- Hacker NF, Barlow EL. Staging for vulvar cancer. Best Pract Res Clin Obstet Gynaecol 2015; 29:802.
- Gibb RK, Olawaiye AB, Chen LM, et al. Vulva. In: AJCC Cancer Staging Manual, 8th ed, Amin MB (Ed), AJCC, Chicago 2017. p.633.
- Homesley HD, Bundy BN, Sedlis A, et al. Prognostic factors for groin node metastasis in squamous cell carcinoma of the vulva (a Gynecologic Oncology Group study). Gynecol Oncol 1993; 49:279.
- Shanbour KA, Mannel RS, Morris PC, et al. Comparison of clinical versus surgical staging systems in vulvar cancer. Obstet Gynecol 1992; 80:927.
- Burger MP, Hollema H, Emanuels AG, et al. The importance of the groin node status for the survival of T1 and T2 vulval carcinoma patients. Gynecol Oncol 1995; 57:327.
- Maggino T, Landoni F, Sartori E, et al. Patterns of recurrence in patients with squamous cell carcinoma of the vulva. A multicenter CTF Study. Cancer 2000; 89:116.
- Vulva. In: American Joint Committee on Cancer Staging Manual, 7th, Edge SB, Byrd DR, Compton CC, et al (Eds), Springer, New York 2010. p.379.
- Tan J, Chetty N, Kondalsamy-Chennakesavan S, et al. Validation of the FIGO 2009 staging system for carcinoma of the vulva. Int J Gynecol Cancer 2012; 22:498.
- Chao H, Sun J. [Metastatic tumors of the vulva: a report of 78 cases]. Zhonghua Fu Chan Ke Za Zhi 1999; 34:297.
- Kataoka MY, Sala E, Baldwin P, et al. The accuracy of magnetic resonance imaging in staging of vulvar cancer: a retrospective multi-centre study. Gynecol Oncol 2010; 117:82.
- Cohn DE, Dehdashti F, Gibb RK, et al. Prospective evaluation of positron emission tomography for the detection of groin node metastases from vulvar cancer. Gynecol Oncol 2002; 85:179.
- Lin G, Chen CY, Liu FY, et al. Computed tomography, magnetic resonance imaging and FDG positron emission tomography in the management of vulvar malignancies. Eur Radiol 2015; 25:1267.
- Fuh KC, Berek JS. Current management of vulvar cancer. Hematol Oncol Clin North Am 2012; 26:45.
- Heaps JM, Fu YS, Montz FJ, et al. Surgical-pathologic variables predictive of local recurrence in squamous cell carcinoma of the vulva. Gynecol Oncol 1990; 38:309.
- Andersen BL, Hacker NF. Psychosexual adjustment after vulvar surgery. Obstet Gynecol 1983; 62:457.
- DiSaia PJ, Creasman WT, Rich WM. An alternate approach to early cancer of the vulva. Am J Obstet Gynecol 1979; 133:825.
- Podratz KC, Symmonds RE, Taylor WF, Williams TJ. Carcinoma of the vulva: analysis of treatment and survival. Obstet Gynecol 1983; 61:63.



- Barton DP. The prevention and management of treatment related morbidity in vulval cancer. Best Pract Res Clin Obstet Gynaecol 2003; 17:683.
- Tyring SK. Vulvar squamous cell carcinoma: guidelines for early diagnosis and treatment. Am J Obstet Gynecol 2003; 189:S17.
- Stehman FB, Look KY. Carcinoma of the vulva. Obstet Gynecol 2006; 107:719.



### APPENDIX A: CPT AND HCPCS CODES ASSOCIATED WITH THIS POLICY

Any CPT or HCPCS codes that have been associated with this HealthHelp Clinical Guideline are for informational use only. The inclusion of a code in this guideline does not guarantee coverage or reimbursement by the individual health plan.

#### MEDICAL ONCOLOGY

HCPCS	CODES:
INDIUM IN-111 IBRITUMOMAB TIUXETAN, DIAGNOSTIC, PER STUDY	A9542
DOSE, UP TO 5 MILLICURIES	A7J4Z
YTTRIUM Y-90 IBRITUMOMAB TIUXETAN, THERAPEUTIC, PER TREATMENT	A9543
DOSE, UP TO 40 MILLICURIES	A7J4J
RADIUM RA-223 DICHLORIDE, THERAPEUTIC, PER MICROCURIE	A9606
RADIOPHARMACEUTICAL, THERAPEUTIC, NOT OTHERWISE CLASSIFIED	A9699
INJECTION, TRIPTORELIN EXTENDED RELEASE, 3.75 MG	C9016
INJECTION, LIPOSOMAL, 1 MG DAUNORUBICIN AND 2.27 MG	C9024
CYTARABINE	09024
INJECTION, INOTUZUMAB OZOGAMICIN, 0.1 MG	C9028
INJECTION, BEVACIZUMAB, 0.25 MG	C9257
INJECTION, GLUCARPIDASE, 10 UNITS	C9293
UNCLASSIFIED DRUGS OR BIOLOGICALS	C9399
INJECTION, DURVALUMAB, 10 MG	C9492
INJECTION, ALEMTUZUMAB, 1 MG	J0202
INJECTION, AMIFOSTINE, 500 MG	J0207
INJECTION, BUSULFAN, 1 MG	J0594
INJECTION, LEUCOVORIN CALCIUM, PER 50 MG	J0640
INJECTION, LEVOLEUCOVORIN CALCIUM, 0.5 MG	J0641
INJECTION, PROCHLORPERAZINE, UP TO 10 MG	J0780
INJECTION, DARBEPOETIN ALFA, 1 MICROGRAM (NON-ESRD USE)	J0881
INJECTION, EPOETIN ALFA, (FOR NON-ESRD USE), 1000 UNITS	J0885
INJECTIN, EPOETIN BETA, 1 MICROGRAM, (FOR NON ESRD USE)	J0888
INJECTION, DECITABINE, 1 MG	J0894
INJECTION, DENOSUMAB, 1 MG	J0897
INJECTION, MEDROXYPROGESTERONE ACETATE, 1 MG	J1050

Clinical Guidelines for Medical Necessity Review of Medical Oncology Services. http://www.healthhelp.com | © 2019 HealthHelp. All rights reserved. 16945 Northchase Dr #1300, Houston, TX 77060 (281) 447-7000

Page 380 of 387



INJECTION, DEXAMETHASONE ACETATE, 1 MG	J1094
INJECTION, DEXAMETHASONE SODIUM PHOSPHATE, 1 MG	J1100
INJECTION, DOLASETRON MESYLATE, 10 MG	J1260
INJECTION, FILGRASTIM (G-CSF), EXCLUDES BIOSIMILARS, 1 MICROGRAM	J1442
INJECTION, TBO-FILGRASTIM, 1 MICROGRAM	J1447
INJECTION, FOSAPREPITANT, 1 MG	J1453
INJECTION, IMMUNE GLOBULIN, (GAMMAPLEX), INTRAVENOUS, NON- LYOPHILIZED (E.G. LIQUID), 500 MG	J1557
INJECTION, IMMUNE GLOBULIN, (GAMUNEX-C/GAMMAKED), NON- LYOPHILIZED (E.G. LIQUID), 500 MG	J1561
INJECTION, IMMUNE GLOBULIN, INTRAVENOUS, LYOPHILIZED (E.G. POWDER), NOT OTHERWISE SPECIFIED, 500 MG	J1566
INJECTION, IMMUNE GLOBULIN, (GAMMAGARD LIQUID), NON- LYOPHILIZED, (E.G. LIQUID), 500 MG	J1569
INJECTION, GANCICLOVIR SODIUM, 500 MG	J1570
INJECTION, IMMUNE GLOBULIN, (FLEBOGAMMA/FLEBOGAMMA DIF), INTRAVENOUS, NON-LYOPHILIZED (E.G. LIQUID), 500 MG	J1572
INJECTION, GRANISETRON HYDROCHLORIDE, 100 MCG	J1626
INJECTION, GRANISETRON, EXTENDED-RELEASE, 0.1 MCG	J1627
INJECTION, HALOPERIDOL, UP TO 5 MG	J1630
INJECTION, HISTRELIN ACETATE, 10 MICROGRAMS	J1675
INJECTION, LANREOTIDE, 1 MG	J1930
INJECTION, LEUPROLIDE ACETATE (FOR DEPOT SUSPENSION), PER 3.75 MG	J1950
INJECTION, LORAZEPAM, 2 MG	J2060
INJECTION, OCTREOTIDE, DEPOT FORM FOR INTRAMUSCULAR INJECTION, 1 MG	J2353
INJECTION, OCTREOTIDE, NON-DEPOT FORM FOR SUBCUTANEOUS OR INTRAVENOUS INJECTION, 25 MCG	J2354
INJECTION, OPRELVEKIN, 5 MG	J2355
INJECTION, OLANZAPINE, LONG-ACTING, 1 MG	J2358
INJECTION, ONDANSETRON HYDROCHLORIDE, PER 1 MG	J2405
INJECTION, PAMIDRONATE DISODIUM, PER 30 MG	J2430
INJECTION, PALONOSETRON HCL, 25 MCG	J2469
INJECTION, PEGFILGRASTIM, 6 MG	J2505



INJECTION, PROMETHAZINE HCL, UP TO 25 MG	J2550
INJECTION, PLERIXAFOR, 1 MG	J2562
INJECTION, METOCLOPRAMIDE HCL, UP TO 10 MG	J2765
INJECTION, ROMIPLOSTIM, 10 MICROGRAMS	J2796
INJECTION, SARGRAMOSTIM (GM-CSF), 50 MCG	J2820
INJECTION, SILTUXIMAB, 10 MG	J2860
INJECTION, TOCILIZUMAB, 1 MG	J3262
INJECTION, TRIPTORELIN PAMOATE, 3.75 MG	J3315
INJECTION, VEDOLIZUMAB, 1 MG	J3380
INJECTION, ZIDOVUDINE, 10 MG	J3485
INJECTION, ZOLEDRONIC ACID, 1 MG	J3489
UNCLASSIFIED DRUGS	J3490
UNCLASSIFIED BIOLOGICS	J3590
LYMPHOCYTE IMMUNE GLOBULIN, ANTITHYMOCYTE GLOBULIN, EQUINE, PARENTERAL, 250 MG	J7504
LYMPHOCYTE IMMUNE GLOBULIN, ANTITHYMOCYTE GLOBULIN, RABBIT, PARENTERAL, 25 MG	J7511
SIROLIMUS, ORAL, 1 MG	J7520
EVEROLIMUS, ORAL, 0.25 MG	J7527
PRESCRIPTION DRUG, ORAL, NON CHEMOTHERAPEUTIC, NOS	J8499
APREPITANT, ORAL, 5 MG	J8501
BUSULFAN; ORAL, 2 MG	J8510
CABERGOLINE, ORAL, 0.25 MG	J8515
CAPECITABINE, ORAL, 150 MG	J8520
CAPECITABINE, ORAL, 500 MG	J8521
CYCLOPHOSPHAMIDE; ORAL, 25 MG	J8530
DEXAMETHASONE, ORAL, 0.25 MG	J8540
ETOPOSIDE; ORAL, 50 MG	J8560
FLUDARABINE PHOSPHATE, ORAL, 10 MG	J8562
GEFITINIB, ORAL, 250 MG	J8565
ANTIEMETIC DRUG, ORAL, NOT OTHERWISE SPECIFIED	J8597
MELPHALAN; ORAL, 2 MG	J8600
METHOTREXATE; ORAL, 2.5 MG	J8610
NABILONE, ORAL, 1 MG	J8650
NETUPITANT 300 MG AND PALONOSETRON 0.5 MG	J8655



ROLAPITANT, ORAL, 1 MG	J8670
TEMOZOLOMIDE, ORAL, 5 MG	J8700
TOPOTECAN, ORAL, 0.25 MG	J8705
PRESCRIPTION DRUG, ORAL, CHEMOTHERAPEUTIC, NOS	J8999
INJECTION, DOXORUBICIN HYDROCHLORIDE, 10 MG	J9000
INJECTION, ALDESLEUKIN, PER SINGLE USE VIAL	J9015
INJECTION, ARSENIC TRIOXIDE, 1 MG	J9017
INJECTION, ASPARAGINASE (ERWINAZE), 1,000 IU	J9019
INJECTION, ASPARAGINASE, NOT OTHERWISE SPECIFIED, 10,000 UNITS	J9020
INJECTION, ATEZOLIZUMAB, 10 MG	J9022
INJECTION, AVELUMAB, 10 MG	J9023
INJECTION, AZACITIDINE, 1 MG	J9025
INJECTION, CLOFARABINE, 1 MG	J9027
BCG (INTRAVESICAL) PER INSTILLATION	J9031
INJECTION, BELINOSTAT, 10 MG	J9032
INJECTION, BENDAMUSTINE HCL, 1 MG	J9033
INJECTION, DENDAMUSTINE HCL (BENDEKA), 1 MG	J9034
INJECTION, BEVACIZUMAB, 10 MG	J9035
INJECTION, BLINATUMOMAB, 1 MICROGRAM	J9039
INJECTION, BLEOMYCIN SULFATE, 15 UNITS	J9040
INJECTION, BORTEZOMIB, 0.1 MG	J9041
INJECTION, BRENTUXIMAB VEDOTIN, 1 MG	J9042
INJECTION, CABAZITAXEL, 1 MG	J9043
INJECTION, CARBOPLATIN, 50 MG	J9045
INJECTION, CARFILZOMIB, 1 MG	J9047
INJECTION, CARMUSTINE, 100 MG	J9050
INJECTION, CETUXIMAB, 10 MG	J9055
INJECTION, CISPLATIN, POWDER OR SOLUTION, 10 MG	J9060
INJECTION, CLADRIBINE, PER 1 MG	J9065
CYCLOPHOSPHAMIDE, 100 MG	J9070
INJECTION, CYTARABINE LIPOSOME, 10 MG	J9098
INJECTION, CYTARABINE, 100 MG	J9100
INJECTION, DACTINOMYCIN, 0.5 MG	J9120
DACARBAZINE, 100 MG	J9130
INJECTION, DARATUMUMAB, 10 MG	J9145



INJECTION, DAUNORUBICIN, 10 MG	J9150
INJECTION, DAUNORUBICIN CITRATE, LIPOSOMAL FORMULATION, 10 MG	J9151
INJECTION, DEGARELIX, 1 MG	J9155
INJECTION, DENILEUKIN DIFTITOX, 300 MICROGRAMS	J9160
INJECTION, DIETHYLSTILBESTROL DIPHOSPHATE, 250 MG	J9165
INJECTION, DOCETAXEL, 1 MG	J9171
INJECTION, ELLIOTTS' B SOLUTION, 1 ML	J9175
INJECTION, ELOTUZUMAB, 1 MG	J9176
INJECTION, EPIRUBICIN HCL, 2 MG	J9178
INJECTION, ERIBULIN MESYLATE, 0.1 MG	J9179
INJECTION, ETOPOSIDE, 10 MG	J9181
INJECTION, FLUDARABINE PHOSPHATE, 50 MG	J9185
INJECTION, FLUOROURACIL, 500 MG	J9190
INJECTION, FLOXURIDINE, 500 MG	J9200
INJECTION, GEMCITABINE HYDROCHLORIDE, 200 MG	J9201
GOSERELIN ACETATE IMPLANT, PER 3.6 MG	J9202
INJECTION, GEMTUZUMAB OZOGAMICIN, 0.1 MG	J9203
INJECTION, IRINOTECAN LIPOSOME, 1 MG	J9205
INJECTION, IRINOTECAN, 20 MG	J9206
INJECTION, IXABEPILONE, 1 MG	J9207
INJECTION, IFOSFAMIDE, 1 GRAM	J9208
INJECTION, MESNA, 200 MG	J9209
INJECTION, IDARUBICIN HYDROCHLORIDE, 5 MG	J9211
INJECTION, INTERFERON ALFACON-1, RECOMBINANT, 1 MICROGRAM	J9212
INJECTION, INTERFERON, ALFA-2A, RECOMBINANT, 3 MILLION UNITS	J9213
INJECTION, INTERFERON, ALFA-2B, RECOMBINANT, 1 MILLION UNITS	J9214
INJECTION, INTERFERON, ALFA-N3, (HUMAN LEUKOCYTE DERIVED),	J9215
250,000 IU	J9215
INJECTION, INTERFERON, GAMMA 1-B, 3 MILLION UNITS	J9216
LEUPROLIDE ACETATE (FOR DEPOT SUSPENSION), 7.5 MG	J9217
LEUPROLIDE ACETATE, PER 1 MG	J9218
LEUPROLIDE ACETATE IMPLANT, 65 MG	J9219
HISTRELIN IMPLANT (VANTAS), 50 MG	J9225
HISTRELIN IMPLANT (SUPPRELIN LA), 50 MG	J9226
INJECTION, IPILIMUMAB, 1 MG	J9228



INJECTION, MECHLORETHAMINE HYDROCHLORIDE, (NITROGEN MUSTARD), 10 MG	J9230
INJECTION, MELPHALAN HYDROCHLORIDE, 50 MG	J9245
METHOTREXATE SODIUM, 5 MG	J9250
METHOTREXATE SODIUM, 50 MG	J9260
INJECTION, NELARABINE, 50 MG	J9261
INJECTION, OMACETAXINE MEPESUCCINATE, 0.01 MG	J9262
INJECTION, OXALIPLATIN, 0.5 MG	J9263
INJECTION, PACLITAXEL PROTEIN-BOUND PARTICLES, 1 MG	J9264
INJECTION, PEGASPARGASE, PER SINGLE DOSE VIAL	J9266
INJECTION, PACLITAXEL, 1 MG	J9267
INJECTION, PENTOSTATIN, 10 MG	J9268
INJECTION, PLICAMYCIN, 2.5 MG	J9270
INJECTION, PEMBROLIZUMAB, 1 MG	J9271
INJECTION, MITOMYCIN, 5 MG	J9280
INJECTION, OLARATUMAB, 10 MG	J9285
INJECTION, MITOXANTRONE HYDROCHLORIDE, PER 5 MG	J9293
INJECTION, NECITUMUMAB, 1 MG	J9295
INJECTION, NIVOLUMAB, 1 MG	J9299
INJECTION, OBINUTUZUMAB, 10 MG	J9301
INJECTION, OFATUMUMAB, 10 MG	J9302
INJECTION, PANITUMUMAB, 10 MG	J9303
INJECTION, PEMETREXED, 10 MG	J9305
INJECTION, PERTUZUMAB, 1 MG	J9306
INJECTION, PRALATREXATE, 1 MG	J9307
INJECTION, RAMUCIRUMAB, 5 MG	J9308
INJECTION, RITUXIMAB, 100 MG	J9310
INJECTION, ROMIDEPSIN, 1 MG	J9315
INJECTION, STREPTOZOCIN, 1 GRAM	J9320
INJECTION, TALIMOGENE LAHERPAREPVEC, 1 MILLION PLAQUE FORMING UNITS (PFU)	J9325
INJECTION, TEMOZOLOMIDE, 1 MG	J9328
INJECTION, TEMSIROLIMUS, 1 MG	J9330
INJECTION, THIOTEPA, 15 MG	J9340
INJECTION, TOPOTECAN, 0.1 MG	J9351



INJECTION, TRABECTEDIN, 0.1 MG	J9352
INJECTION, ADO-TRASTUZUMAB EMTANSINE, 1 MG	J9354
INJECTION, TRASTUZUMAB, 10 MG	J9355
INJECTION, VALRUBICIN, INTRAVESICAL, 200 MG	J9357
INJECTION, VINBLASTINE SULFATE, 1 MG	J9360
VINCRISTINE SULFATE, 1 MG	J9370
INJECTION, VINCRISTINE SULFATE LIPOSOME, 1 MG	J9371
INJECTION, VINORELBINE TARTRATE, 10 MG	J9390
INJECTION, FULVESTRANT, 25 MG	J9395
INJECTION, ZIV-AFLIBERCEPT, 1 MG	J9400
INJECTION, PORFIMER SODIUM, 75 MG	J9600
NOT OTHERWISE CLASSIFIED, ANTINEOPLASTIC DRUGS	J9999
ONDANSETRON 1 MG, ORAL	Q0162
PROCHLORPERAZINE MALEATE, 5 MG, ORAL	Q0164
GRANISETRON HYDROCHLORIDE, 1 MG, ORAL	Q0166
DRONABINOL, 2.5 MG, ORAL	Q0167
PROMETHAZINE HYDROCHLORIDE, 12.5 MG, ORAL	Q0169
DOLASETRON MESYLATE, 100 MG, ORAL, FDA APPROVED PRESCRIPTION	
ANTI-EMETIC, FOR USE AS A COMPLETE THERAPEUTIC SUBSTITUTE FOR	Q0180
AN IV ANTI-EMETIC AT THE TIME OF CHEMOTHERAPY TREATMENT, NOT	20100
TO EXCEED A 24 HOUR DOSAGE REGIMEN	
INJECTION, TENIPOSIDE, 50 MG	Q2017
TISAGENLECLEUCEL, UP TO 250 MILLION CAR-POSITIVE VIABLE T CELLS,	
INCLUDING LEUKAPHERESIS AND DOSE PREPARATION PROCEDURES, PER	Q2040
INFUSION	
SIPULEUCEL-T, MINIMUM OF 50 MILLION AUTOLOGOUS CD54+ CELLS	
ACTIVATED WITH PAP-GM-CSF, INCLUDING LEUKAPHERESIS AND ALL	Q2043
OTHER PREPARATORY PROCEDURES, PER INFUSION	
INJECTION, DOXORUBICIN HYDROCHLORIDE, LIPOSOMAL, IMPORTED	Q2049
LIPODOX, 10 MG	02017
INJECTION, DOXORUBICIN HYDROCHLORIDE, LIPOSOMAL, NOT	Q2050
OTHERWISE SPECIFIED, 10MG	
INJECTION, FILGRASTIM (G-CSF), BIOSIMILAR, 1 MICROGRAM	Q5101
IMATINIB, 100 MG	S0088
GRANISETRON HYDROCHLORIDE, 1 MG	S0091



ZIDOVUDINE, ORAL, 100 MG	S0104
MERCAPTOPURINE, ORAL, 50 MG	S0108
ONDANSETRON, ORAL, 4 MG	S0119
INJECTION, PEGYLATED INTERFERON ALFA-2A, 180 MCG PER ML	S0145
INJECTION, PEGYLATED INTERFERON ALFA-2B, 10 MCG	S0148
EXEMESTANE, 25 MG	S0156
INJECTION, OLANZAPINE, 2.5 MG	S0166
ANASTROZOLE, ORAL, 1MG	S0170
CHLORAMBUCIL, ORAL, 2MG	S0172
DOLASETRON MESYLATE, ORAL 50MG	S0174
FLUTAMIDE, ORAL, 125MG	S0175
HYDROXYUREA, ORAL, 500MG	S0176
LOMUSTINE, ORAL, 10MG	S0178
MEGESTROL ACETATE, ORAL, 20MG	S0179
PROCARBAZINE HYDROCHLORIDE, ORAL, 50MG	S0182
PROCHLORPERAZINE MALEATE, ORAL, 5MG	S0183
TAMOXIFEN CITRATE, ORAL, 10MG	S0187