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2025 Gastrointestinal (GI) Cancer

Medical Oncology

Table 1. Gastrointestinal (GI) Cancer

Guideline	Protocol ID	Previous Review Date	Last Review Date
Anal Cancer	P_7586, P_7587	01/18/2024	**11/29/2024**
Colon Cancer	P_6866, P_7333	01/03/2024	**11/29/2024**
Esophageal Cancer	P_7591, P_7602, P_7606, P_7607, P_7608, P_7612	01/03/2024	**11/29/2024**
Gastric Cancer	P_7603, P_7604, P_7605, P_7610, P_7611	01/03/2024	**11/29/2024**
Rectal Cancer	P_6870, P_7348, P_7349, P_7350	01/03/2024	**11/29/2024**

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Anal Cancer Guideline

Anal cancer treatment is considered medically appropriate when the documentation demonstrates **ANY** of the following:

1. Anal cancer-specific chemotherapy for **ANY** of the following: [25] [17] [9]
    a. Metastatic anal cancer chemotherapy with **ANY** of the following:
        i. 5-Fluorouracil (5-FU) + cisplatin [18] [2] [3]
        ii. Paclitaxel + carboplatin [1] [6]
    b. Anal cancer chemotherapy with 5-FU + cisplatin [2] [3]
2. Anal cancer chemotherapy is considered medically appropriate when the documentation demonstrates **ALL** of the following: [18] [25] [17] [9]
    a. Associated-cancer chemotherapy medication regimens per the *National Comprehensive Cancer Network (NCCN) Guidelines*, approved by the United States (US) Food and Drug Administration (FDA), clinically prescribed and as authorized by the payor.
    b. Physical ability and clinical status of **ANY** of the following:
        A. Eastern Cooperative Oncology Group (ECOG) Performance Status grade of 2 or less
        B. Karnofsky Performance Status (KPS) grade of 70 or more
    c. Treatment is for **ANY** of the following:
        i. Inguinal node recurrence
        ii. Localized therapy
        iii. Locally recurrent prior to abdominoperineal resection (APR)
        iv. Metastatic local control
        v. Metastatic subsequent therapy
        vi. Metastatic therapy

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Colon Cancer Guideline

Colon cancer treatment is considered medically appropriate when the documentation demonstrates **ANY** of the following:

1. Advanced or metastatic colon cancer chemotherapy with **ANY** of the following: [14] [10]
    a. Irinotecan [15] [4]
    b. Irinotecan + oxaliplatin (IROX) [4] [5]
2. Colon cancer chemotherapy is considered medically appropriate when the documentation demonstrates **ALL** of the following: [14] [24] [15] [10]
    a. Associated-cancer chemotherapy medication regimens per the *National Comprehensive Cancer Network (NCCN) Guidelines*, approved by the United States (US) Food and Drug Administration (FDA), clinically prescribed and as authorized by the payor.
    b. Physical ability and clinical status of **ANY** of the following:
        A. Eastern Cooperative Oncology Group (ECOG) Performance Status grade of 2 or less
        B. Karnofsky Performance Status (KPS) grade of 70 or more
    c. Treatment is for **ANY** of the following: [10]
        i. Adjuvant or neoadjuvant chemotherapy with **ANY** of the following:
            A. Stage T1, T2, T3 or T4 disease, **AND** node positive
            B. Stage 4 disease and **ANY** of the following:

I. Bowel obstruction
II. Localized perforation
III. Lymph nodes: less than 12 examined
IV. Lymphovascular invasion (LVI)
V. Margins are close, indeterminate or positive.
VI. Peri-neural invasion
VII. Poorly differentiated histology

ii. Advanced or metastatic colon cancer and **ANY** of the following: [14] [24] [15]

A. Kirsten rat sarcoma viral oncogene homolog (KRAS) mutation, for first- or second-line treatment. [14]

B. Metastasis and **ANY** of the following:

I. Metachronus metastasis that is unresectable, for first or second-line treatment

II. Microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR) tumor

III. Progressive disease with fluoropyrimidine, oxaliplatin and irinotecan-based chemotherapy and **ALL** of the following:

1. Metachronus metastasis is unresectable for second-line treatment.
2. Metastasis
3. MSI-H/dMMR tumor

IV. Rat sarcoma (RAS) wild-type and **ALL** of the following:

1. Progressive disease with fluoropyrimidine, oxaliplatin and irinotecan-based chemotherapy
2. Third-line treatment

C. V-raf murine sarcoma viral oncogene homolog B1 (BRAF) V600E positive, for second-line treatment

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Esophageal Cancer Guideline

Esophageal cancer treatment is considered medically appropriate when the documentation demonstrates **ANY** of the following:

1. Esophageal cancer-specific chemotherapy for **ANY** of the following:
    a. Definitive chemoradiation (non-surgical) with **ANY** of the following: [7]
        i. Cisplatin + 5-Fluorouracil (5-FU) [20] [13] [2] [3]
        ii. Irinotecan + cisplatin [2] [4]
        iii. Oxaliplatin + 5-FU [20] [3] [5]
        iv. Paclitaxel + carboplatin [20] [1] [6]
        v. Paclitaxel + cisplatin [2] [6]
        vi. Paclitaxel + 5-FU [3] [6]
    b. First-line therapy for metastatic or locally advanced esophageal cancer with **ANY** of the following: [7]
        i. Cisplatin + 5-FU [20] [13] [2] [3]

ii. 5-FU [3]

iii. Paclitaxel [6]

iv. Paclitaxel + carboplatin [1] [6]

v. Paclitaxel + cisplatin [2] [6]

c. Peri-procedural for **ANY** of the following:

i. Peri-operative chemoradiation for esophageal cancer that includes the esophagogastric junction, with cisplatin + 5-FU. [20] [2] [3] [7]

ii. Post-operative chemoradiation for esophageal adenocarcinoma or gastroesophageal junction cancer (only) with 5-FU and radiation. [3] [7]

iii. Pre-operative chemoradiation for esophageal cancer with **ANY** of the following: [7]

A. Cisplatin + 5-FU [13] [2] [3]

B. Irinotecan + cisplatin [2] [4]

C. Oxaliplatin + 5-FU [3] [5]

D. Paclitaxel + 5-FU [3] [6]

E. Paclitaxel + carboplatin [1] [6]

d. Second-line therapy for esophageal cancer with **ANY** of the following: [20] [7]

i. Irinotecan [4]

ii. Irinotecan + cisplatin [2] [4]

iii. Paclitaxel [6]

2. Esophageal cancer chemotherapy is considered medically appropriate when the documentation demonstrates **ALL** of the following:

a. Associated-cancer chemotherapy medication regimens per the *National Comprehensive Cancer Network (NCCN) Guidelines*, approved by the United States (US) Food and Drug Administration (FDA), clinically prescribed and as authorized by the payor.

b. Physical ability and clinical status of **ANY** of the following:

A. Eastern Cooperative Oncology Group (ECOG) Performance Status grade of 2 or less

B. Karnofsky Performance Status (KPS) grade of 70 or more

c. Treatment is for **ANY** of the following:

i. Definitive chemoradiation and is **NOT** a surgical candidate, for **ANY** of the following: [13] [29] [20] [27] [28] [7]
   A. Adenocarcinoma and primary tumor is in the non-cervical esophagus
   B. Squamous cell carcinoma

ii. Metastatic or locally advanced esophageal cancer is unresectable, for **ANY** of the following: [29] [20] [7]
   A. First-line treatment and **ANY** of the following:
      I. Adenocarcinoma and positive human epidermal growth factor receptor 2 (HER-2), or is **NOT** a surgical candidate.
      II. Squamous cell carcinoma and is **NOT** a surgical candidate.
   B. Second-line treatment and **ANY** of the following:
      I. Adenocarcinoma
      II. Squamous cell carcinoma

iii. Peri-procedure chemoradiation for **ANY** of the following:
   A. Peri-operative chemoradiation that includes esophagogastric junction, and **ANY** the following: [29] [7]
      I. Adenocarcinoma with unresectable locally advanced or metastatic disease
      II. Primary tumor in the non-cervical esophagus and **ALL** of the following: [20] [13]
         1. Adjuvant/neoadjuvant therapy
         2. R0 or R1/2 resection
         3. Stage T3-4, N0/N+, M0
   B. Post-operative chemoradiation with primary tumor in the non-cervical esophagus, and **ALL** of the following: [29] [7]
      I. Adenocarcinoma
      II. Adjuvant/neoadjuvant therapy and **ANY** of the following:
         1. R1/R2 resection
         2. Stage T3-4, N0/N+, M0, R0 resection
   C. Pre-operative chemoradiation for esophageal cancer **ANY** of the following: [20] [29] [13] [7]

I. Adenocarcinoma and **ANY** of the following:

1. Adjuvant or neoadjuvant therapy
2. Unresectable, locally advanced or metastatic disease

II. Primary tumor is in the cervical esophagus and **ANY** of the following:

1. Adjuvant or neoadjuvant therapy
2. Unresectable, locally advanced or metastatic disease
3. **NOT** a surgical candidate

III. Primary tumor is in the non-cervical esophagus and **ANY** of the following:

1. Unresectable, locally advanced or metastatic disease
2. **NOT** a surgical candidate

IV. Squamous cell carcinoma with **ANY** of the following:

1. Primary tumor is in the cervical esophagus.
2. Unresectable, locally advanced or metastatic disease

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Gastric Cancer Guideline

Gastric cancer treatment is considered medically appropriate when the documentation demonstrates **ANY** of the following:

1. Gastric cancer-specific chemotherapy for **ANY** of the following:
    a. Metastatic or locally advanced gastric cancer treatment for **ANY** of the following:
        i. First-line therapy with **ANY** of the following: [8]
            A. 5-Fluorouracil (5-FU) + cisplatin [22] [21] [26] [16] [2] [3]
            B. Paclitaxel [6]
            C. Paclitaxel + carboplatin [1] [6]
            D. Paclitaxel + cisplatin [2] [6]
        ii. Second-line therapy with **ANY** of the following: [22] [21] [8]
            A. Irinotecan [4]
            B. Irinotecan + cisplatin [2] [4]
            C. Paclitaxel [26] [16] [6]
    b. Peri-procedure chemoradiation for **ANY** of the following:
        i. Peri-operative chemoradiation for esophagogastric junction and gastric cardia gastric cancer treatment with 5-FU + cisplatin. [21] [2] [3] [8]
        ii. Post-operative chemoradiation for gastric cancer that includes the esophagogastric junction, with 5-FU. [21] [26] [16] [3] [8]
        iii. Pre-operative chemoradiation for esophagogastric junction and gastric cardia gastric cancer treatment with **ANY** of the following: [8]
            A. Cisplatin + 5-FU [21] [2] [3]
            B. Oxaliplatin + 5-FU [3] [5]
            C. Paclitaxel + 5-FU [3] [6]
            D. Paclitaxel + carboplatin [1] [6]
2. Gastric cancer chemotherapy is considered medically appropriate when the documentation demonstrates **ALL** of the following:
    a. Associated-cancer chemotherapy medication regimens per the *National Comprehensive Cancer Network (NCCN) Guidelines*, approved by the United States (US) Food and Drug Administration (FDA), clinically prescribed and as authorized by the payor.

b. Physical ability and clinical status of **ANY** of the following:
   A. Eastern Cooperative Oncology Group (ECOG) Performance Status grade of 2 or less
   B. Karnofsky Performance Status (KPS) grade of 70 or more

c. Treatment is for **ANY** of the following:
   i. Metastatic or locally advanced gastric cancer for **ANY** of the following:
      A. First-line therapy [22] [21] [26] [16] [8]
      B. Second-line therapy and **ANY** of the following: [22] [21] [26] [16] [8]
         I. Progressive disease after 2 or more prior lines of therapy, including fluorophyrimidine and platinum based chemotherapy, and **ANY** of the following:
            1. Second or third-line treatment with deficient mismatched repair (dMMR) or microsatellite instability is high (MSI-H).
            2. Third-line treatment with programmed death-ligand 1 (PD-L1) expression, combined positive score (CPS) 1% or higher
         II. Second-line treatment with evidence of measurable disease on imaging
   ii. Peri-procedure chemotherapy for **ANY** of the following:
      A. Peri-operative chemotherapy for esophagogastric junction and gastric cardia gastric cancer and **ALL** of the following: [22] [21] [26] [16] [8]
         I. Stage T2 or higher (any N)
         II. Tumor is potentially resectable.
      B. Post-operative chemoradiation for gastric cancer that includes the esophagogastric junction and **ANY** of the following: [21] [26] [8]
         I. Node positive
         II. Stage T1s or T1 with a margin positive resection
         III. Stage T3 or T4
      C. Pre-operative chemoradiation for esophagogastric junction and gastric cardia gastric cancer and **ALL** of the following: [21] [8]

I. Stage T2 or higher (any N)

II. Tumor is potentially resectable.

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Rectal Cancer Guideline

Rectal cancer treatment is considered medically appropriate when the documentation demonstrates **ANY** of the following:

I. Rectal cancer-specific chemotherapy for **ANY** of the following:

A. Advanced or metastatic rectal cancer treatment with **ANY** of the following: [19] [12] [4] [5] [11]

1. Irinotecan

2. Irinotecan + oxaliplatin (IROX)

B. Neoadjuvant or concurrent chemotherapy with 5-fluorouracil (5-FU). [19] [12] [3] [11]

C. Post-operative adjuvant chemotherapy, when **NOT** receiving pre-operative therapy, with 5-FU. [3] [11]

II. Rectal cancer chemotherapy is considered medically appropriate when the documentation demonstrates **ALL** of the following:

A. Associated-cancer chemotherapy medication regimens per the *National Comprehensive Cancer Network (NCCN) Guidelines*, approved by the United States (US) Food and Drug Administration (FDA), clinically prescribed and as authorized by the payor.

B. Physical ability and clinical status of **ANY** of the following:

A. Eastern Cooperative Oncology Group (ECOG) Performance Status grade of 2 or less

B. Karnofsky Performance Status (KPS) grade of 70 or more

C. Treatment is for **ANY** of the following: [11]

1. Advanced or metastatic rectal cancer, with Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) mutation, for first **OR** second-line treatment.

2. Metastatic disease and **ANY** of the following:

i. KRAS mutation, for second **OR** third-line treatment after neoadjuvant therapy

ii. KRAS mutation for third-line treatment with rat sarcoma (RAS) wild type colorectal cancer, after anti-epidermal growth factor receptor (EGFR) therapy **AND** after **EITHER** fluoropyrimidine-oxaliplatin (FOLFOX) or fluoropyrimidine-irinotecan (FOLFIRI)

3. Metastatic disease and **ANY** of the following: [19] [12]

i. First, second **OR** third-line treatment

ii. Metachronous metastasis is unresectable, after neoadjuvant therapy and for first **OR** second-line treatment.

iii. Microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) and **ALL** of the following:

a. Metachronous metastasis is unresectable.

b. Previous treatment with **EITHER** FOLFOX or FOLFIRI

c. Second-line treatment

d. V-raf murine sarcoma viral oncogene homolog B1 (BRAF) V-600E mutation **AND** second-line treatment

iv. RAS wild type colorectal cancer, after EGFR therapy **AND** after **EITHER** FOLFOX **OR** FOLFIRI

4. Neoadjuvant/adjuvant or post-operative adjuvant chemotherapy for rectal cancer and **ANY** of the following: [12] [11]
    i. Node positive and Stage T1, T2 or T3 [19]
    ii. Stage T4 and **ANY** of the following:
        a. Bowel obstruction
        b. Close, indeterminate or positive margins
        c. Less than 12 lymph nodes examined
        d. Localized perforation
        e. Lymphovascular invasion (LVI)
        f. Node positive
        g. Peri-neural invasion
        h. Poorly differentiated histology
5. Neoadjuvant or concurrent chemotherapy for rectal cancer and **ANY** of the following: [19] [11]
    i. Nodal involvement
    ii. Stage T3 or T4

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GI Cancer Procedure Codes

Table 1. GI Cancer Associated Procedure Codes

CODE	DESCRIPTION
J8999	PRESCRIPTION DRUG, ORAL, CHEMOTHERAPEUTIC, NOS
J9228	INJECTION, IPILIMUMAB, 1 MG
J9190	INJECTION, FLUOROURACIL, 500 MG
J9060	INJECTION, CISPLATIN, POWDER OR SOLUTION, 10 MG
J0640	INJECTION, LEUCOVORIN CALCIUM, PER 50 MG
J9263	INJECTION, OXALIPLATIN, 0.5 MG
J9299	INJECTION, NIVOLUMAB, 1 MG
J9267	INJECTION, PACLITAXEL, 1 MG
J9045	INJECTION, CARBOPLATIN, 50 MG
J9271	INJECTION, PEMBROLIZUMAB, 1 MG
J8520	CAPECITABINE, ORAL, 150 MG
J8521	CAPECITABINE, ORAL, 500 MG
J9280	INJECTION, MITOMYCIN, 5 MG
J9035	INJECTION, BEVACIZUMAB, 10 MG
C9257	INJECTION, BEVACIZUMAB, 0.25 MG
J9206	INJECTION, IRINOTECAN, 20 MG
J9303	INJECTION, PANITUMUMAB, 10 MG
J9308	INJECTION, RAMUCIRUMAB, 5 MG
J9055	INJECTION, CETUXIMAB, 10 MG
J9400	INJECTION, ZIV-AFLIBERCEPT, 1 MG
J9171	INJECTION, DOCETAXEL, 1 MG
J9355	INJECTION, TRASTUZUMAB, EXCLUDES BIOSIMILAR, 10 MG
J9178	INJECTION, EPIRUBICIN HCL, 2 MG
J9354	INJECTION, ADO-TRASTUZUMAB EMTANSINE, 1 MG
J9356	INJECTION, TRASTUZUMAB, 10 MG AND HYALURONIDASE-OYSK
Q5116	INJECTION, TRASTUZUMAB-QYYP, BIOSIMILAR, (TRAZIMERA), 10 MG
Q5117	INJECTION, TRASTUZUMAB-ANNS, BIOSIMILAR, (KANJINTI), 10 MG
Q5113	INJECTION, TRASTUZUMAB-PKRB, BIOSIMILAR, (HERZUMA), 10 MG
Q5112	INJECTION, TRASTUZUMAB-DTTB, BIOSIMILAR, (ONTRUZANT), 10 MG
Q5114	INJECTION, TRASTUZUMAB-DKST, BIOSIMILAR, (OGIVRI), 10 MG
Q5118	INJECTION, BEVACIZUMAB-BVZR, BIOSIMILAR, (ZIRABEV), 10 MG
Q5107	INJECTION, BEVACIZUMAB-AWWB, BIOSIMILAR, (MVASI), 10 MG
Q5126	INJECTION, BEVACIZUMAB-MALY, BIOSIMILAR (ALYMSYS), 10 MG
Q5129	INJECTION, BEVACIZUMAB-ADCD (VEGZELMA), BIOSIMILAR, 10 MG

GI Cancer Summary of Changes

GI Cancer clinical guidelines from 2024 to 2025 had the following version changes:

- Citations updated per the evidence.
- Evidence reviewed and indications remained the same.

GI Cancer Definitions

Abdominoperineal resection is a surgical procedure in which the anus, rectum, and part of the sigmoid colon are removed to treat certain types of cancer, such as rectal cancer. This procedure involves creating a permanent opening (colostomy) in the abdominal wall for the elimination of waste.
Adenocarcinoma is a malignant tumor originating in glandular epithelium.
Adjuvant refers to enhancing the effectiveness of medical treatment.
Advanced disease is also called end-stage or terminal cancer. Advanced disease can occur when there are few signs that remission is possible.
Anal cancer is a disease in which malignant (cancer) cells form in the tissues of the anus
BRAF V600E mutation is a specific mutation (change) in the BRAF gene (a gene that provides instructions for making a protein that helps transmit chemical signals from outside the cell to the cell's nucleus), which makes a protein that is involved in sending signals in cells and in cell growth. This BRAF gene mutation may be found in some types of cancer, including melanoma and colorectal cancer. It may increase the growth and spread of cancer cells.
Chemotherapy is a treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. Chemotherapy may be given by mouth, injection, infusion or on the skin depending on the type and stage of the cancer being treated. It may be given alone or with other treatments, such as surgery, radiation therapy or biologic therapy.
Combined positive score is a robust, reproducible PD-L1 scoring method that predicts response to pembrolizumab in patients with G/GEJ cancer.
Deficient mismatched repair (dMMR) can be due to germline mutations in DNA mismatch repair genes (MLH1, MSH2, MSH6, or PMS2) or somatic epigenetic silencing of MLH1, which result in unrepaired repetitive DNA sequences. These altered sequences increase the risk of multiple cancers, but are most commonly associated with colorectal cancer.
Definitive treatment is the treatment plan for a disease or disorder that has been chosen as the best one for a patient after all other choices have been considered.
Eastern Cooperative Oncology Group (ECOG) scale describes an individual's level of functioning in terms of the ability to care for one's self, daily activity and physical ability (eg, walking, working).

Table 1. ECOG Performance Status Scale

Grade	ECOG PERFORMANCE STATUS
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

Source: https://ecog-acrin.org/resources/ecog-performance-status/

Esophageal cancer is cancer that forms in tissues lining the esophagus (the muscular tube through which food passes from the throat to the stomach).

First-line (primary) treatment is the first treatment given for a disease, and is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. When used by itself, first-line therapy is the one accepted as the best treatment.

Gastric cardia is the part of the stomach that is closest to the esophagus.

HER-2 positive describes cells that have a protein called HER2 on their surface. In normal cells, HER2 helps control cell growth. Cancer cells that make too much HER2 may grow more quickly and are more likely to spread to other parts of the body.

Indeterminate findings are inconclusive or insufficient for treatment planning.

Inguinal is situated in the region of the groin or in either of the lowest lateral regions of the abdomen.

Karnofsky performance status (KPS) is an assessment tool for functional impairment. It can be used to compare effectiveness of different therapies and to assess the prognosis in individual patients. In most serious illnesses, the lower the Karnofsky score, the worse the likelihood of survival.

Table 2. KARNOFSKY PERFORMANCE STATUS SCALE

Score	Status
100	Normal, no complaints; no evidence of disease
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort, some signs or symptoms of disease
70	Cares for self but unable to carry on normal activity or to do active work
60	Requires occasional assistance but is able to care for most of personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalization is indicated although death not imminent
20	Very ill; hospitalization and active supportive care necessary

Score	Status
10	Moribund
0	Dead

Source: https://ecog-acrin.org/resources/ecog-performance-status/

Kirsten rat sarcoma viral oncogene homolog (KRAS) mutation is an error in a protein in normal cells. It is called KRAS because it was first identified as causing cancer in Kirsten RAt Sarcoma virus. Normally, KRAS serves as an information hub for signals in the cell that lead to cell growth.

Localized disease describes disease that is limited to a certain part of the body. For example, localized cancer is usually found only in the tissue or organ where it began, and has not spread to nearby lymph nodes or to other parts of the body. Some localized cancers can be completely removed by surgery.

Lymphovascular invasion (LVI) indicates the presence or absence of tumor cells in lymphatic channels (not lymph nodes) or blood vessels within the primary tumor as noted microscopically by the pathologist.

Margin is the edge or border of the tissue removed in cancer surgery.

Metachronous describes something that is not functioning or occurring synchronously (at the same time).

Metastasis is the spread of a disease-producing agency (such as cancer cells) from the initial or primary site of disease to another part of the body.

Microsatellite instability-high (MSI-H) is a type of cancer cell that has a high number of mutations (changes) within microsatellites. For example, microsatellite testing that shows mutations in 30% or more microsatellites is called microsatellite instability-high.

Neoadjuvant treatment is treatment (such as chemotherapy or hormone therapy) administered before primary cancer treatment (such as surgery) to enhance the outcome of primary treatment.

Programmed cell death ligand 1 (PD-L1) expression is a protein that acts as a kind of "brake" to keep the body's immune responses under control. PD-L1 may be found on some normal cells and in higher-than-normal amounts on some types of cancer cells. Cancer cells that have a high amount of PDL1 may benefit from immunotherapy.

Perineural invasion (PNI) refers to the invasion of cancer to the space surrounding a nerve. It is common in head and neck cancer, prostate cancer and colorectal cancer.

Poorly differentiated histology describes tumor cells that don't look like normal cells. They're disorganized under the microscope and tend to describe high grade or grade III tumors that grow and spread faster than grade I tumors.

Progressive disease is cancer that is growing, spreading or getting worse.

Rat Sarcoma (RAS) wild-type is a term used to describe a gene called KRAS when it is found in its natural, non-mutated (unchanged) form. The KRAS gene makes a protein that is involved in cell signaling pathways that control cell growth, cell maturation and cell death. Mutated (changed)

forms of the KRAS gene have been found in some types of cancer, including non-small cell lung cancer, colorectal cancer and pancreatic cancer. Knowing whether a patient's tumor has a wild-type or mutated KRAS gene may help plan cancer treatment.

Recurrent disease is characterized by repeated alternations between acute relapse and long remission. Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumor or to another place in the body. Also called recurrence.

Second-line treatment is treatment for a disease or condition after the initial treatment (first-line treatment) has failed, stopped working or has side effects that are not tolerated.

Squamous cell carcinoma (SCC) is carcinoma that is made up of or arises from squamous cells (stratified epithelium that consists at least in its outer layers of small scale like cells) and usually occurs in areas of the body exposed to strong sunlight over many years.

Staging in cancer is the process of determining how much cancer is within the body (tumor size) and if it has metastasized (spread).

Subsequent treatment is treatment given after the main treatment to reduce the chance of cancer coming back by destroying any remaining cancer cells. It usually refers to chemotherapy, radiation therapy, hormone therapy and/or immunotherapy given after surgery.

Third-line treatment is treatment that is given when both initial treatment (first-line therapy) and subsequent treatment (second-line therapy) don't work, or stop working.

TNM staging system is a system to describe the amount and spread of cancer in a person's body. T describes the size of the tumor and any spread of cancer into nearby tissue; N describes the spread of cancer to nearby lymph nodes; and M describes metastasis (spread of cancer to other parts of the body).

Table 3. TNM Staging System

T describes the original Primary Tumor	N category describes whether or not the cancer has reached nearby lymph nodes	M category tells whether there are distant metastases (spread of cancer to other parts of the body).
TX Primary tumor cannot be evaluated	**NX** Regional lymph nodes cannot be evaluated	
T0 No evidence of primary tumor	**N0** No regional lymph node involvement (no cancer found in the lymph nodes)	**M0** No distant metastasis (cancer has not spread to other parts of the body)
Tis Carcinoma in situ (early cancer that has not spread to neighboring tissue)		
T1 to T4 Size and/or extent of the primary tumor	**N1 to N3** Involvement of regional lymph nodes (number and/or extent of spread)	**M1** Distant metastasis (cancer has spread to distant parts of the body)

Unresectable initial disease is cancer that is not capable of being surgically removed.

GI Cancer (ALL) References

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Disclaimer section

Purpose

The purpose of the HealthHelp's clinical guidelines is to assist healthcare professionals in selecting the medical service that may be appropriate and supported by evidence to safely improve outcomes. Medical information is constantly evolving, and HealthHelp reserves the right to review and update these clinical guidelines periodically. HealthHelp reserves the right to include in these guidelines the clinical indications as appropriate for the organization's program objectives. Therefore the guidelines are not a list of all the clinical indications for a stated procedure, and associated Procedure Code Tables may not represent all codes available for that state procedure or that are managed by a specific client-organization.

Clinician Review

These clinical guidelines neither preempt clinical judgment of trained professionals nor advise anyone on how to practice medicine. Healthcare professionals using these clinical guidelines are responsible for all clinical decisions based on their assessment. All Clinical Reviewers are instructed to apply clinical indications based on individual patient assessment and documentation, within the scope of their clinical license.

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The use of these clinical guidelines does not provide authorization, certification, explanation of benefits, or guarantee of payment; nor do the guidelines 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.

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National and Local Coverage Determination (NCD and LCD)

NOTICE
To ensure appropriate review occurs to the most current NCD and/or LCD, always defer to https://www.cms.gov/medicare-coverage-database/search.aspx.

Background

National Coverage Determinations (NCD) and Local Coverage Determinations (LCD) are payment policy documents outlined by the Centers for Medicare and Medicaid Services (CMS) and the government's delegated Medicare Audit Contractors (MACs) that operate regionally in jurisdictions.
CMS introduced variation between different jurisdictions/Medicare Audit Contractors (MACs) and their associated covered code lists with the transition to ICD 10. The variation resulted in jurisdictions independently defining how codes are applied for exclusions, limitations, groupings, ranges, etc. for the medical necessity indications outlined in the NCD and LCD. Due to this variation, there is an inconsistent use/application of codes and coverage determinations across the United States between the different MACs.
In addition, **WITHOUT** notice, CMS can change the codes that indicate medical necessity and the format of the coverage determinations/associated documents (eg, Articles). This is an additional challenge for organizations to keep up with ongoing, unplanned changes in covered codes and medical necessity indications.

Medical Necessity Codes

Due to the variation in code application between jurisdictions/MACs and that updates can happen without notification, HealthHelp is not able to guarantee full accuracy of the codes listed for any Coverage Determination, and advises that prior to use, the associated Coverage Determination Articles are reviewed to ensure applicability to HealthHelp's programs and any associated NCDs and LCDs.

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