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Genetics, Decoded.

Preimplantation Testing, Prenatal Cell-Free DNA Screening and Prenatal Diagnosis

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Table of Contents

Scope	3
State Biomarker Legislation.....	3
Guideline Coverage Criteria	3
General Testing.....	3
Preimplantation Genetic Testing of Embryos.....	4
Prenatal Cell-Free DNA Screening.....	5
Prenatal Molecular Testing of a Fetus.....	6
Key Terms and Definitions	7
CPT® Codes	8
Change Summary	11

Scope

This evidence-based guideline addresses preimplantation genetic testing, non-invasive prenatal screening, and prenatal molecular testing of a fetus including chromosomal microarray analysis/genome wide copy number variant analysis. The criteria in this guideline do not apply to cytogenetic chromosome analysis (karyotype) or fluorescence in situ hybridization (FISH).

This guideline's coverage criteria delineate medically necessary clinical scenarios for molecular testing and may include specific situations when testing is considered never medically necessary. In general, molecular testing is considered never medically necessary when evidence demonstrating its ability to improve diagnosis, management, or clinical outcomes is lacking in peer-reviewed literature.

- Please refer to the Whole Exome Sequencing, Whole Genome Sequencing and Genome Wide Copy Number Variant Analysis coverage guideline for fetal sequencing criteria.

State Biomarker Legislation

Medical necessity determinations must also take into consideration controlling state coverage mandates that may supersede these guidelines when applicable. When state biomarker legislation requirements impact coverage decisions, this guideline will initially be applied to determine if criteria are met for approval. If an approval cannot be granted based on the criteria in this guideline, some or all of the following sources will be reviewed, as defined by applicable state legislation, to determine if test coverage is supported in a manner that is consistent with the state biomarker legislation requirements:

- Medicare National Coverage Determinations (NCDs)
- Medicare Local Coverage Determinations (LCDs)
- U.S. Food and Drug Administration (FDA) approved or cleared tests
- Tests indicated for an FDA-approved drug
- Nationally recognized clinical practice guidelines
- Consensus statements

Guideline Coverage Criteria

General Testing

Testing is medically necessary when all of the following criteria are met (*see additional indication-specific testing criteria listed below*):

- The test is customarily recognized as clinically reasonable:
 - Symptoms and presentation are consistent with the suspected condition
 - Results are expected to lead to a change in medical management

- If testing guidelines exist, the clinical scenario falls within those recommendations
- The clinical benefit of testing outweighs the potential risk of psychological or medical harm to the individual being tested
- The clinical presentation warrants testing of multiple genes when a multi-gene panel is requested
- The test is customarily recognized as technically appropriate:
 - The test has established clinical validity/utility in the diagnosis and/or treatment of the suspected condition
 - The test is as targeted as possible for the clinical situation (e.g., familial pathogenic or likely pathogenic (P/LP) variant testing, common variants, genes related to phenotype)
 - The testing methodology* has been clinically validated and is the most accurate method-unless technical limitations (e.g., poor sample quality) necessitate the need for alternate testing strategies

Criteria listed above are based primarily on the following resources. Publications issued after this guideline's effective date will be evaluated on an individual basis until criteria are incorporated in the next iteration of this guideline.

- a. Bean LJH, Funke B, Carlston CM, et al. Diagnostic gene sequencing panels: from design to report-a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2020 Mar;22(3):453-461. doi: 10.1038/s41436-019-0666-z. Epub 2019 Nov 16. PMID: 31732716.
- b. Holtzman NA. Promoting safe and effective genetic tests in the United States: work of the task force on genetic testing. *Clin Chem.* 1999 May;45(5):732-8. PMID: 10222375.
- c. Matalon DR, Zepeda-Mendoza CJ, Aarabi M, et al. Electronic address: documents@acmg.net. Clinical, technical, and environmental biases influencing equitable access to clinical genetics/genomics testing: A points to consider statement of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2023 Jun;25(6):100812. doi: 10.1016/j.gim.2023.100812. Epub 2023 Apr 14. PMID: 37058144.
- d. Rehder C, Bean LJH, Bick D, et al. Next-generation sequencing for constitutional variants in the clinical laboratory, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2021 Aug;23(8):1399-1415. doi: 10.1038/s41436-021-01139-4. Epub 2021 Apr 29. PMID: 33927380.

Preimplantation Genetic Testing of Embryos

Preimplantation genetic testing, including the embryo biopsy procedure if applicable, is medically necessary for the following indications:

Preimplantation Genetic Testing for Monogenic Disease (PGT-M)

- Both biologic parents are carriers of an autosomal recessive disorder
- One biologic parent is a known carrier of an autosomal dominant disorder or an X-linked disorder
- One biologic parent is a potential carrier, based on family history, of an autosomal dominant disorder or X-linked disorder and is requesting non-disclosure testing
- A previous pregnancy or child has been diagnosed with a genetic disorder and familial pathogenic/likely pathogenic (P/LP) variant(s) are known
- A previous child has been diagnosed with a disorder requiring a stem cell transplant and human leukocyte antigen (HLA) typing of an embryo for a future matched sibling is needed to identify a compatible donor

Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR)

- One biologic parent is a carrier of a chromosomal rearrangement

Preimplantation genetic testing is never medically necessary for any other indication, including but not limited to the following:

- nonmedical gender selection
- nonmedical traits
- preimplantation genetic testing for polygenic risk scores (PGT-P)
- preimplantation genetic testing for aneuploidy (PGT-A) by any testing methodology for any indication
- testing solely to determine if an embryo is a carrier of an autosomal recessive disorder
- testing for a multifactorial condition

Criteria listed above are based primarily on the following resources. Publications issued after this guideline's effective date will be evaluated on an individual basis until criteria are incorporated in the next iteration of this guideline.

- Ethics Committee of the American Society for Reproductive Medicine. Electronic address: asrm@asrm.org. Use of reproductive technology for sex selection for nonmedical reasons: an Ethics Committee opinion. *Fertil Steril*. 2022 Apr;117(4):720-726. doi: 10.1016/j.fertnstert.2021.12.024. Epub 2022 Jan 31. PMID: 35105444.
- Grebe TA, Khushf G, Greally JM, T et al. Clinical utility of polygenic risk scores for embryo selection: A points to consider statement of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2024 Apr;26(4):101052. doi: 10.1016/j.gim.2023.101052. Epub 2024 Feb 23. PMID: 38393332.
- Practice Committee of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. The use of preimplantation genetic testing for aneuploidy: a committee opinion. *Fertil Steril*. 2024 May 18:S0015-0282(24)00241-3. doi: 10.1016/j.fertnstert.2024.04.013. Epub ahead of print. PMID: 38762806.
- Practice Committee and Genetic Counseling Professional Group of the American Society for Reproductive Medicine, American Society for Reproductive Medicine, Washington, D.C.. Electronic address: asrm@asrm.org. Indications and management of preimplantation genetic testing for monogenic conditions: a committee opinion. *Fertil Steril*. 2023 Jul;120(1):61-71. doi: 10.1016/j.fertnstert.2023.03.003. Epub 2023 May 10. PMID: 37162432.
- Preimplantation Genetic Testing: ACOG Committee Opinion, Number 799. *Obstet Gynecol*. 2020 Mar;135(3):e133-e137. [Reaffirmed 2023] doi: 10.1097/AOG.0000000000003714. PMID: 32080053.

Prenatal Cell-Free DNA Screening

Prenatal cell-free DNA screening (cfDNA) for trisomy 21, trisomy 18, trisomy 13, plus or minus sex chromosome aneuploidies is medically necessary for singleton or twin pregnancies.

Targeted prenatal cell-free DNA (cfDNA) screening for fetal red blood cell antigen detection is medically necessary when all of the following are met:

- A maternal antibody has been identified
- Paternal status for the corresponding antigen is unknown, unavailable, or heterozygous
- The patient has declined amniocentesis
- The test is targeted to the antigen(s) corresponding to the known maternal antibody(ies)

Prenatal cell-free DNA screening is never medically necessary for the following indications:

- copy number variants (microdeletions or microduplications)
- autosomal trisomies other than 13, 18, and 21
- single gene conditions
- high-order multiple gestations (i.e., triplets or higher)
- multiple gestation pregnancies with fetal demise or vanishing twin
- miscarriage (including recurrent pregnancy loss) or fetal demise

Criteria listed above are based primarily on the following resources. Publications issued after this guideline's effective date will be evaluated on an individual basis until criteria are incorporated in the next iteration of this guideline.

- American College of Obstetricians and Gynecologists; Clinical Practice Update: Paternal and Fetal Genotyping in the Management of Alloimmunization in Pregnancy. *Obstetrics & Gynecology* 144(2):p e47-e49, August 2024. | DOI: 10.1097/AOG.0000000000005630.
- American College of Obstetricians and Gynecologists Committee on Genetics; Hoskovec J, Russo M. Practice Advisory: Cell-free DNA to Screen for Single-Gene Disorders. 2019 Feb [reaffirmed 2024 Sept]. Available from: <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2019/02/cell-free-dna-to-screen-for-single-gene-disorders>

- c. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. *Obstet Gynecol.* 2020 Oct;136(4):e48-e69. doi: 10.1097/AOG.0000000000004084. PMID: 32804883.
- d. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics, Society for Maternal-Fetal Medicine. Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies: ACOG Practice Bulletin, Number 231. *Obstet Gynecol.* 2021 Jun 1 [reaffirmed 2024];137(6):e145-e162. doi: 10.1097/AOG.0000000000004397. PMID: 34011891.
- e. American College of Obstetricians and Gynecologists Practice Bulletin No. 181: Prevention of Rh D Alloimmunization. *Obstet Gynecol.* 2017 Aug;130(2):e57-e70. doi: 10.1097/AOG.0000000000002232. PMID: 28742673.
- f. American College of Obstetricians and Gynecologists; Practice Advisory: Rho(D) Immune Globulin Shortages. March 2024 [Updated July 2024]. Available at <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2024/03/rhod-immune-globulin-shortages>.
- g. Dungan JS, Klugman S, Darilek S, et al. Noninvasive prenatal screening (NIPS) for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2023 Feb;25(2):100336. doi: 10.1016/j.gim.2022.11.004. Epub 2022 Dec 16. Erratum in: *Genet Med.* 2023 Aug;25(8):100874. doi: 10.1016/j.gim.2023.100874. PMID: 36524989.
- h. Hui L, Ellis K, Mayen D, et al. Position statement from the International Society for Prenatal Diagnosis on the use of non-invasive prenatal testing for the detection of fetal chromosomal conditions in singleton pregnancies. *Prenat Diagn.* 2023 Jun;43(7):814-828. doi: 10.1002/pd.6357. Epub 2023 May 16. PMID: 37076973.
- i. Mari G, Norton ME, Stone J, et al. Society for Maternal-Fetal Medicine (SMFM) Clinical Guideline #8: the fetus at risk for anemia—diagnosis and management. *Am J Obstet Gynecol.* 2015 Jun;212(6):697-710. doi: 10.1016/j.ajog.2015.01.059. Epub 2015 Mar 27. PMID: 25824811.
- j. Palomaki GE, Chiu RWK, Pertile MD, et al. International Society for Prenatal Diagnosis Position Statement: cell free (cf)DNA screening for Down syndrome in multiple pregnancies. *Prenat Diagn.* 2021 Sep;41(10):1222-1232. doi: 10.1002/pd.5832. Epub 2020 Nov 15. PMID: 33016373.

Prenatal Molecular Testing of a Fetus

Prenatal molecular testing of a fetus (i.e., single gene or multi-gene testing) is medically necessary when the results of the genetic test will impact clinical decision-making and the requested method is scientifically valid for the suspected condition.

Chromosomal microarray/genome wide copy number variant analysis (81228, 81229, 81349) is medically necessary when invasive prenatal diagnostic testing is being performed.

Prenatal molecular testing in a fetus for familial variants of uncertain significance is never medically necessary.

Molecular analysis of intact fetal cells, i.e., fetal trophoblast(s) in a maternal sample, is never medically necessary.

Criteria listed above are based primarily on the following resources. Publications issued after this guideline's effective date will be evaluated on an individual basis until criteria are incorporated in the next iteration of this guideline.

- a. Committee on Genetics and the Society for Maternal-Fetal Medicine. Committee Opinion No.682: Microarrays and Next-Generation Sequencing Technology: The Use of Advanced Genetic Diagnostic Tools in Obstetrics and Gynecology. *Obstet Gynecol.* 2016 Dec;128(6):e262-e268. [Reaffirmed 2023] doi: 10.1097/AOG.0000000000001817. PMID: 27875474.
- b. Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. *Obstet Gynecol.* 2016 May;127(5):e108-e122. doi: 10.1097/AOG.0000000000001405. PMID: 26938573.

Key Terms and Definitions

Aneuploidy is characterized by an extra or missing chromosome, as seen in conditions such as Down syndrome (trisomy 21), trisomy 13, or trisomy 18.

Autosomal dominant conditions are genetic disorders caused by one copy of a pathogenic or likely pathogenic variant in a gene.

Autosomal recessive conditions are genetic disorders caused by two copies of a pathogenic or likely pathogenic variant in a gene.

Chromosomes carry DNA; humans typically have 23 pairs of chromosomes.

Chromosomal microarray analysis is a genetic test that analyzes the entire genome for small deletions or duplications, known as copy number variants, in the DNA.

Chromosomal rearrangements are genetic alterations that involve the rearrangement of chromosome segments.

Copy number variants are small deletions or duplications in the DNA.

Deoxyribonucleic acid (DNA) is a molecule that contains the genetic instructions for all living organisms and plays a crucial role in the development and susceptibility to diseases.

Fetal trophoblasts are specialized cells that ultimately give rise to the placenta and can be found circulating in the maternal bloodstream.

Genes are segments of DNA with instructions for specific traits, characteristics, or functions within an organism.

Genetic (molecular) testing examines a person's DNA or RNA to identify variations that can aid in the diagnosis of disease and/or provide valuable information about a person's risk of developing certain diseases.

Genome refers to an individual's entire set of genetic material (DNA).

Genome-wide copy number variant analysis is a genetic testing technique used to examine the entire genome to detect regions where there are abnormal gains or losses of DNA segments that can have significant implications for an individual's health.

Microdeletions refer to the loss of a small segment of DNA from one of the chromosomes.

Microduplications refer to the gain of a small segment of DNA from one of the chromosomes.

Monogenic disease is a genetic disorder caused by pathogenic variant(s) in a single gene.

Multifactorial conditions are health conditions that result from a combination of genetic and environmental factors, e.g. cancer, heart disease, and hypertension.

Multi-gene panels simultaneously analyze multiple genes associated with a particular condition or a group of related conditions.

Non-disclosure testing is a type of preimplantation genetic testing (PGT) that can be performed when an individual is at risk for a late-onset genetic disorder and does not want to know their own status but wants to prevent inheritance of the specific familial pathogenic variant.

Pathogenic/likely pathogenic variant(s) describe specific genetic changes that are known or highly likely to cause a particular genetic disorder, which can aid in diagnosis and/or guide treatment and management strategies.

Polygenic risk scores are numerical scores that estimate a person's risk for developing a particular trait or disease based on information from multiple genetic variants, each with small effects on the trait or disease in question.

Preimplantation genetic testing (PGT) is a genetic test used to screen embryos created during in vitro fertilization (IVF) for specific genetic disorders or chromosomal abnormalities.

Prenatal cell-free DNA screening (cfDNA) is a type of genetic test used during pregnancy to screen for certain chromosomal abnormalities in the fetus by examining DNA in the mother's bloodstream.

Sex chromosome aneuploidies are genetic disorders caused by an abnormal number of sex chromosomes; typically, either two X chromosomes (XX) or one X and one Y chromosome (XY) are present.

Structural rearrangements are genetic alterations that involve the rearrangement of chromosome segments.

Twin zygosity is the genetic similarity between twins, i.e., monozygotic (identical) or dizygotic (fraternal) twins.

X-linked disorder is a genetic disorder caused by a pathogenic variant in a gene located on the X chromosome.

Variants of uncertain significance (VUS) are genetic changes detected during genetic testing that cannot be definitively classified as benign (harmless) or pathogenic (disease-causing). Their impact on a person's health is not well understood based on scientific evidence available at the time of testing.

CPT[®] Codes

Medical necessity review of claims may include evaluation of the submitted codes. Laboratories must accurately represent their services using the most applicable and specific CPT code(s). Tier 1 molecular pathology procedure codes or Proprietary Laboratory Analyses (PLA) codes should be used when available for the specific test. Tier 2 molecular pathology procedure codes should only be used if the American Medical Association (AMA) has specifically assigned the performed test to such a code. Genomic sequencing procedures (GSP) codes (e.g., CPT codes 81410-81471) were developed by the AMA to represent multi-gene panels utilizing DNA or RNA analysis for specific clinical scenarios (e.g., carrier screening, tumor testing, etc.) and should be utilized when applicable.

Coding guidelines can be found in the AMA's CPT manual as well as the Centers for Medicare and Medicaid Services (CMS) National Correct Coding Initiative (NCCI) policy manuals. NCCI General Correct Coding Policy states that procedures should be reported with the most comprehensive CPT code describing the services performed and that the services described by

a CPT code cannot be unbundled into multiple less specific codes. Additionally, GSP codes should be utilized when appropriate for the described test and should not be submitted along with other CPT codes that represent components of the GSP code.

Claims may not be approved if the submitted codes are not the most appropriate for the described procedure (i.e., as accurate and specific as available).

The following code(s) are medically necessary when coverage criteria are met. This list is not all inclusive.

Code	Full Description
81105	Human Platelet Antigen 1 genotyping (HPA-1), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-1a/b (L33P)
81106	Human Platelet Antigen 2 genotyping (HPA-2), GP1BA (glycoprotein Ib [platelet], alpha polypeptide [GPIba]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-2a/b (T145M)
81107	Human Platelet Antigen 3 genotyping (HPA-3), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex], antigen CD41 [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3a/b (I843S)
81108	Human Platelet Antigen 4 genotyping (HPA-4), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-4a/b (R143Q)
81109	Human Platelet Antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (eg, HPA-5a/b (K505E))
81110	Human Platelet Antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-6a/b (R489Q)
81111	Human Platelet Antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41] [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9a/b (V837M)
81112	Human Platelet Antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-15a/b (S682Y)
81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants, comparative genomic hybridization (CGH) microarray analysis
81265	Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (eg, pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [eg, buccal swab or other germline tissue sample])
81266	Comparative analysis using Short Tandem Repeat (STR) markers; each additional specimen (eg, additional cord blood donor, additional fetal samples from different cultures, or additional zygosity in multiple birth pregnancies) (List separately in addition to code for primary procedure)
81349	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and loss-of-heterozygosity variants, low-pass sequencing analysis

81420	Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21
81442	Noonan spectrum disorders (eg, Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic sequence analysis panel, must include sequencing of at least 12 genes, including BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1
81507	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy
0327U	Fetal aneuploidy (trisomy 13, 18, and 21), DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy, includes sex reporting, if performed
0488U	Obstetrics (fetal antigen noninvasive prenatal test), cell free DNA sequence analysis for detection of fetal presence or absence of 1 or more of the Rh, C, c, D, E, Duffy (Fya), or Kell (K) antigen in alloimmunized pregnancies, reported as selected antigen(s) detected or not detected
0494U	Red blood cell antigen (fetal RhD gene analysis), next-generation sequencing of circulating cell-free DNA (cfDNA) of blood in pregnant individuals known to be RhD negative, reported as positive or negative
0536U	Red blood cell antigen (fetal RhD), PCR analysis of exon 4 of RHD gene and housekeeping control gene GAPDH from whole blood in pregnant individuals at 10+ weeks gestation known to be RhD negative, reported as fetal RhD status
0552U	Reproductive medicine (preimplantation genetic assessment), analysis for known genetic disorders from trophoctoderm biopsy, linkage analysis of disease-causing locus, and when possible, targeted mutation analysis for known familial variant, reported as low-risk or high-risk for familial genetic disorder

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The following code(s) are considered never medically necessary. This list is not all inclusive.

Code	Full Description
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood
0253U	Reproductive medicine (endometrial receptivity analysis), RNA gene expression profile, 238 genes by next-generation sequencing, endometrial tissue, predictive algorithm reported as endometrial window of implantation (eg, pre-receptive, receptive, post-receptive)
0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplications, mosaicism, and segmental aneuploidy, per embryo tested
0489U	Obstetrics (single-gene noninvasive prenatal test), cell free DNA sequence analysis of 1 or more targets (eg, CFTR, SMN1, HBB, HBA1, HBA2) to identify paternally inherited pathogenic variants, and relative mutation-dosage analysis based on molecular counts to determine fetal inheritance of maternal mutation, algorithm reported as a fetal risk score for the condition (eg, cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemia)

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Change Summary

Version	Review Date	Effective Date	Summary of Revisions
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Created	CSC: 8/11/2022 PAB: 9/12/2022	November 2022	Not applicable
v1.2023	COOC: 2/15/2023 PAB: 3/16/2023	April 1, 2023	Semi-annual review. No criteria changes.
v2.2023	COOC: 8/16/2023 PAB: 9/25/2023	October 1, 2023	Semi-annual review. Criteria were reformatted with no impact on coverage.
v1.2024	COOC: 2/14/2024 PAB: 3/25/2024	April 1, 2024	Semi-annual review. No criteria changes. Clarifications were made to the scope and CPT code section with no impact on coverage except 0449U was removed from the NMN CPT code table. References were updated.
v2.2024	COOC: 08/19/2024 PAB: 09/20/2024	October 1, 2024	Semi-annual review. No criteria changes. CPT codes and references were updated.
v1.2025	COOC: 02/17/2025 PAB: 03/24/2025	July 3, 2025	Semi-annual review. No criteria changes. CPT codes and references were updated.
v1.2026	COOC: 8/5/2025 PAB: 09/16/2025	January 9, 2026	Semi-annual review. General testing criteria, HLA testing criteria, and fetal antigen testing criteria were added. CPT codes were updated. Key references were added as rationale under each criteria section replacing the formal reference section.