Clinical Policy: Cell-free Fetal DNA Testing

Reference Number: CP.MP.84 Coding Implications
Date of Last Revision: 09/21 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Cell-free fetal DNA testing is a screening test of the woman's blood taken after 10 weeks of pregnancy. It measures the relative amount of free fetal DNA and indicates if the fetus is at increased risk of having Down syndrome (trisomy 21), Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13).

Policy/Criteria

I. It is the policy of health plans affiliated with Centene Corporation® that cell-free fetal DNA testing is **medically necessary** when meeting all of the following criteria:
- **A.** Underwent pretest counseling;
- **B.** No documentation that a chromosomal abnormality screening test has been performed in this pregnancy (i.e. sequential serum screening, quad screen, penta screen, and serum integrated, or contingent);
- **C.** No documentation of a prior abnormal nuchal translucency screening in this pregnancy;
- **D.** Current pregnancy is a singleton or twin gestation;
- **E.** At least 10 weeks gestation at the time the blood was drawn.

II. It is the policy of health plans affiliated with Centene Corporation that cell-free fetal DNA testing for any indication not listed above is considered **not medically necessary**.

III. It is the policy of health plans affiliated with Centene Corporation that cell-free fetal DNA testing for additional chromosomal abnormalities other than trisomy 21, 18 or 13, is considered **not medically necessary**, including, but not limited to, other trisomies, aneuploidies, or microdeletions. This testing has not be validated clinically and the screening accuracy with regard to detection and the false-positive rate is not established.

Background
Cell-free fetal DNA testing is a screening tool for fetal aneuploidy. Fragments of fetal DNA, known as cell-free fetal DNA, comprise approximately 3-13% of the total cell free maternal DNA. Since its discovery in 1997, techniques for identification and analysis of cell-free fetal DNA have rapidly advanced and the range of genetic traits identifiable using these process will continue to grow.

There are limitations of cell-free fetal DNA testing and they should be discussed during pre-test counseling. The decision for testing should be an active and informed choice of the mother. Patients should be counseled that cell-free DNA screening does not replace the precision obtained with diagnostic tests, such as chorionic villus sampling or amniocentesis and, therefore, is limited in its ability to identify all chromosome abnormalities. Cell-free DNA screening does not assess risk of fetal anomalies such as neural tube defects or ventral wall defects. Pre-test counseling should also include review of the family history and possible baseline ultrasound to

confirm viability, single gestation, gestational dating and review for anomalies. Also, the mother needs to be aware that a negative cell-free fetal DNA test result does not assure an unaffected pregnancy. Invasive prenatal testing and genetic counseling should be offered for any patient with a positive test result.

American College of Obstetricians and Gynecologists (ACOG)
In their 2020 practice bulletin on screening for fetal chromosomal abnormalities, ACOG states that cell-free fetal DNA testing is "the most sensitive and specific screening test for common fetal aneuploidies," and that cell-free DNA is among the tests that should "be offered to all pregnant women regardless of maternal age or risk of fetal aneuploidy."[1]

ACOG gave cell-free fetal DNA a "B" recommendation when used after an abnormal serum integrated screen for women who do not want diagnostic testing via amniocentesis. However, they note, "this approach may delay definitive diagnosis and will fail to identify some fetuses with chromosomal abnormalities."[1]

Twin Gestation
ACOG gives cell-free DNA testing a "B" recommendation for twin pregnancies, noting that evidence is encouraging for detection of fetuses affected by trisomy 21, but that the evidence is limited for detection of trisomy 18 and 13 due to its low incidence.[1] A 2020 retrospective analysis suggested that cell-free DNA testing is accurate for detection of aneuploidy when fetal fraction of cell-free DNA is determined for dizygotic twins.[2] An additional study published in 2019 with a total sample size of 2057 twin pregnancies, and 11 detected cases of chromosomal aneuploidy, found cell-free fetal DNA testing to be clinically valuable for the accurate detection of chromosomal aneuploidy in twin pregnancies.[3]

Coding Implications
This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

Codes that support medical necessity

CPT® Codes	Description
81420	Fetal chromosomal aneuploidy (e.g., 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.
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.

CPT® Codes	Description
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood
0168U	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma without fetal fraction cutoff, algorithm reported as a risk score for each trisomy.

Codes that do not support medical necessity

CPT® Codes	Description
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (e.g., DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood.
81479	Unlisted molecular pathology procedure.

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed, specialist reviewed	07/13	08/13
Added to criteria current pregnancy between 10 and 20 weeks gestation and only one per pregnancy	06/14	07/14
Updated coding implications	01/15	
Changed criteria to allow testing up to 22 weeks of pregnancy	03/15	03/15
Removed high-risk indication of ultrasound findings, updated background	07/15	07/15
Added CPT codes 81420 and 81479 as these are codes billed by providers for cell free fetal DNA testing	10/15	
Policy converted to new template. References reviewed and updated.	07/16	07/16
Added the statement that cell-free fetal DNA testing for any indication not listed above is considered **not medically necessary**.	03/17	
Added abnormal ultrasound findings as an indication. References reviewed and updated. Updated CPT codes.	05/17	06/17
Added III. "Cell-free fetal DNA testing for additional chromosomal abnormalities other than trisomy 21, 18 or 13 are considered not medically necessary, including, but not limited to, other trisomies, aneuploidies, or microdeletions. Background information updated.	04/18	04/18
References reviewed and updated.	03/19	03/19
Changed period in which authorizations can be requested from 5 days post-service to 10 days.	05/19	
Moved 81422 and 81479 to a table for codes that do not support medical necessity. Clarified that between "10 and 22 weeks gestation" is ≥ 10 weeks and < 23 weeks gestation.	08/19	
References reviewed and updated. Removed CPT-0009M as code deleted as of 1/1/2020. Specialist review.	02/20	03/20

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Replaced I.B. "A cell-free fetal DNA test has not been performed in this pregnancy" with "No documentation that a chromosomal abnormality screening test has been performed in this pregnancy," with examples noted. Removed requirement and criteria for high risk for aneuploidy. Added requirement of no documentation of a prior abnormal nuchal translucency screening in this pregnancy. Removed restriction that fetus is < 23 weeks gestation at the time of the blood draw. Added twin gestation as an option in addition to singleton. Background edited to reflect policy changes. Removed section on Authorization Protocols. Added quotation marks to B recommendations. Added CPT: 0168U as medically necessary. Replaced all instances of "members" with "members/enrollees." References reviewed and updated.	09/20	09/20
Annual review. Added to III for clarity, "This testing has not be validated clinically and the screening accuracy with regard to detection and the false-positive rate is not established." Revised first sentence in background, removing reference to "new test." Added CPT 0060U to table of codes that support medical necessity. Changed "review date" in the header to "date of last revision" and "date" in the revision log header to "revision date." References reviewed, reformatted and updated.	09/21	09/21

References

1. The American College of Obstetricians and Gynecologists Committee. Practice Bulletin: Screening for Fetal Chromosomal Abnormalities. No 226. Published October 2020. Accessed August 31, 2021.
2. Hedriana H, Martin K, Saltzman D, Billings P, Demko Z, Benn P. et al. Cell-free DNA fetal fraction in twin gestations in single-nucleotide polymorphism-based noninvasive prenatal screening. *Prenat Diagn*. 2020;40(2):179–184. doi:10.1002/pd.5609
3. Yin Y, Zhu H, Qian Y, Jin J, Mei J, Dong M. *Zhejiang Da Xue Bao Yi Xue Ban.* 2019;48(4):403-408.
4. Sayres LC, Allyse M, Norton ME, Cho MK. Cell-free fetal DNA testing: A pilot study of obstetric healthcare provider attitudes towards clinical implementation. *Prenat Diagn* 2011; 31(11):1070–1076. doi:10.1002/pd.2835
5. Palomaki GE, Messerlian GM, Halliday JV. Prenatal screening for common aneuploidies using cell-free DNA. UpToDate. www.uptodate.com. Published August 1, 2021. Accessed September 1, 2021.
6. The American College of Obstetricians and Gynecologists. Practice Advisory: Cell-free DNA to Screen for Single-Gene Disorders. Published February 21, 2019. Reaffirmed March 2020. Accessed August 31, 2021.
7. Clinical Utility Evaluation. Cell-Free DNA (CfDNA) [Formerly NIPS, NIPT] Screening For Fetal Trisomy 21, 18, And 13 In High-Risk Women. Published February 16, 2018. (annual review February 25, 2021) Accessed September 2, 2021.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note: For Medicaid members/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.