# Clinical Policy: Cell-free Fetal DNA Testing

Reference Number: PA.CP.MP.84
Effective Date: 06/18
Date Last Revision: 01/2022

Coding Implications
Revision Log

**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 PA Health & Wellness® (PHW) 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 PHW that cell-free fetal DNA testing for any indication not listed above is considered **not medically necessary**.

**III.** It is the policy of PA Health & Wellness® (PHW) 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 been validated clinically and the screening accuracy with regard to detection and the false-positive rate is not established..

**Authorization Protocols**
Requests for prior authorization will be accepted up to 10 business days after specimen collection and reviewed for medical necessity based on the above stated criteria.

**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**
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**Codes that support medical necessity**

| CPT® Codes | Description |
|---|---|
| 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 |
| 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. |

**Codes that do not support medical necessity**

| CPT® Codes | Description |
|---|---|
| 0060U | Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood. |
| 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 |
|---|---|---|
| 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 or microdeletions. Background information updated. | 05/18 | |
| Language updated in Policy/Criteria I. to reflect ACOG recommendation that all pregnant women be offered pre-natal screening for aneuploidy. | 12/18 | |
| References reviewed and updated. | 11/19 | |
| Changed period in which authorizations can be requested from 5 days post-service to 10 days. | 11/19 | |
| 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. | 11/19 | |
| Deleted E.1 Maternal age is no longer a criteria for testing | 7/20 | 2/9/2021 |
| Removed CPT-0009M as code deleted as of 1/1/2020. 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.<br>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." | 01/27/2022 | |

| Reviews, Revisions, and Approvals | Revision Date | Approval Date |
|---|---|---|
| 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. Removed deleted CPT 0168U. Moved code 0060U from the coding table supporting medical necessity to the table of codes that do not support medical necessity. | | |

**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.