Clinical Policy: Cell-free Fetal DNA Testing

Reference Number: LA.CP.MP.84 Coding Implications
Last Review Date: 08/2020 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 Louisiana Healthcare Connections that cell-free fetal DNA testing is medically necessary for members 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 that cell-free fetal DNA testing for any indication not listed above is considered not medically necessary.

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
Cell-free fetal DNA testing offers a new 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 that "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 (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.
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	Date	Approval Date
Converted corporate to local policy.	08/15/2020	

References

1. The American College of Obstetricians and Gynecologists Committee on Practice Bulletins-Obstetrics, Committee on Genetics, and Society for Maternal-Fetal Medicine. Practice Bulletin: Screening for Fetal Chromosomal Abnormalities. Number 226. August 2020.
2. Hedriana H, Martin K, Saltzman D, et al. ell-free DNA fetal fraction in twin gestations in single-nucleotide polymorphism-based noninvasive prenatal screening. Prenat Diagn. 2020 Jan; 40(2): 179–184.
3. Yin Y, Zhu H, Qian Y, et al. Noninvasive prenatal screening for twin pregnancy: an analysis of 2057 cases [published in Chinese]. Zhejiang Da Xue Bao Yi Xue Ban. 2019 Jun 25;48(4):403-408.
4. Sayres L, et al. Cell-free fetal DNA testing: A pilot study of obstetric healthcare provider attitudes towards clinical implementation. Prenat Diagn. 2011 November; 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. In: UpToDate, Wilkins-Haug L (Ed), UpToDate, Waltham, MA. Last updated June 2020. Accessed September 11, 2020.
6. The American College of Obstetricians and Gynecologists. Practice Advisory: Cell-free DNA to Screen for Single-Gene Disorders. Practice Advisory, February 21, 2019. Reaffirmed March 2020.
7. Hayes Clinical Utility Evaluation. Cell-Free DNA (CfDNA) [Formerly NIPS, NIPT] Screening For Fetal Trisomy 21, 18, And 13 In High-Risk Women. Feb 16, 2018. Reviewed Feb 3, 2020. Accessed Sep. 11, 2020.

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. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing

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