MetroPlus Health

Policy and Procedure

Title: Cell-free Fetal DNA Testing	Division: Medical Management Department: Utilization Management
Approval Date:	LOB: Medicaid, HIV SNP, CHP, MetroPlus Gold, Goldcare I&II, Market Plus, Essential, HARP
Effective Date: 3/28/22	Policy Number: UM-MP332
Review Date: 3/25/2024	Cross Reference Number:
Retired Date:	Page 1 of 7

1. **POLICY 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).

   For the Medicare and UltraCare lines of business, MetroPlusHealth determines medical necessity based on applicable Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD).
   https://www.cms.gov/medicare-coverage-database/search.aspx

2. **RESPONSIBLE PARTIES:**
   Medical Management Administration, Utilization Management, Integrated Care Management, Pharmacy, Claim Department, Providers Contracting.

3. **DEFINITIONS:**
   Aneuploidy: A normal human cell has 23 pairs of chromosomes. The gain or loss of chromosomes is called Aneuploidy (Genetics Home Reference, 2018d).

   Cell Free Fetal DNA (cffDNA or cfDNA): Small fragments of fetal DNA that cross the placenta and enter the maternal blood. Fragments can be measured using different DNA testing techniques in the first trimester (Allyse and Wick, 2018).

   Non-Invasive Prenatal Testing/Screening (NIPT/NIPS): A common term used to describe different types of analysis of cellfree fetal DNA (cffDNA) (Allyse and Wick, 2018).

   Trisomy 13 (Patau Syndrome): A chromosomal condition with an extra chromosome 13. It is associated with multiple congenital anomalies and significant developmental delay. Most infants die in the first month after birth, with only 5-10% surviving past the first year. The risk of having a child with trisomy 13 increases with a mother's age (Genetics Home Reference, October 2018c).

   Trisomy 18 (Edwards Syndrome): A chromosomal condition with an extra chromosome 18. It is associated with multiple congenital anomalies and developmental delay. Most infants die in the first year of life, with only 5-10% surviving past the first year. The risk of having a child with trisomy 18 increases with a mother's age (Genetics Home Reference, October 2018b).

Trisomy 21 (Down Syndrome): A chromosomal condition with an extra chromosome 21. It is associated with intellectual disability, a characteristic facial appearance and poor muscle tone (hypotonia) in infancy. The degree of intellectual disability varies, but it is usually mild to moderate. Individuals with Down syndrome may be born with a variety of birth defects, including heart defects and digestive abnormalities. The risk of having a child with trisomy 21 increases with a mother's age (Genetics Home Reference, 2018a).

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.

4. POLICY:

It is the policy of MetroPlus Health plan that cell-free fetal DNA testing is medically necessary when meeting all of the following criteria:

i. Underwent pretest counseling;
ii. 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);
iii. No documentation of a prior abnormal nuchal translucency screening in this pregnancy;
iv. Current pregnancy is a singleton or twin gestation;
v. At least 10 weeks gestation at the time the blood was drawn.

It is the policy of MetroPlus Health plan 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 been validated clinically and the screening accuracy with regard to detection and the false-positive rate is not established.

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."

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."

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. 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. 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.

5. LIMITATIONS/ EXCLUSIONS:

It is the policy of MetroPlus Health plan that cell-free fetal DNA testing for any indication **not listed** above in Section 4 is considered **not medically necessary.**

6. APPLICABLE PROCEDURE CODES:

Codes that support medical necessity.
Only one allowed per pregnancy.

CPT	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	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 (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
*81479	Unlisted molecular pathology procedure

*When reporting CPT code 81479, the specific gene being tested must be reported on the claim. Failure to include this information on the claim will result in claims being denied. In addition, medical records may be requested when 81479 is billed. The medical record must clearly identify the unique molecular pathology procedure performed, its analytic validity and clinical utility, and why CPT code 81479 was billed.

When the documentation does not meet the criteria for the service rendered or the documentation does not establish the medical necessity for the services, such services will be denied as not reasonable and necessary.

7. REFERENCES:

New York State Medicaid Update - April 2022 Volume 38 - Number 4. Section: New York State Medicaid Non-Invasive Prenatal Screening for Trisomy 21, 18, and 13 Policy. https://health.ny.gov/health_care/medicaid/program/update/2022/no04_2022-04.htm#prenatalscreening

New York State Medicaid Update - August 2021 Volume 37 - Number 10. Section: New York State Medicaid Expansion of Non-Invasive Prenatal Trisomy Screening Policy.

https://health.ny.gov/health_care/medicaid/program/update/2021/no10_2021-08.htm#trisomy

New York State Medicaid Update - October 2014 Volume 30 - Number 9. Section: NYS Medicaid Now Covers Non-invasive Prenatal Testing for Trisomy 21, 18 and 13. https://health.ny.gov/health_care/medicaid/program/update/2014/2014-10.htm#nys

Genetic Non-Invasive Prenatal Screening Tests May Have False Results: FDA Safety Communication. https://www.fda.gov/medical-devices/safety-communications/genetic-non-invasive-prenatal-screening-tests-may-have-false-results-fda-safety-communication

The American College of Obstetricians and Gynecologists Committee. Practice Bulletin: Screening for Fetal Chromosomal Abnormalities. No 226. Published October 2020.

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

Yin Y, Zhu H, Qian Y, Jin J, Mei J, Dong M. Zhejiang Da Xue Bao Yi Xue Ban. 2019;48(4):403-408.

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

Palomaki GE, Messerlian GM, Halliday JV. Prenatal screening for common aneuploidies using cell-free DNA. UpToDate. www.uptodate.com. Published August 1, 2021. Updated November 23, 2021.

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.

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). www.hayesinc.com

Clinical Utility Evaluation. Cell-Free DNA (cfDNA) [Formerly NIPS, NIPT] Screening for Fetal Trisomy 21, 18, and 13 in Women with Twin Pregnancies. Published July 7, 2021. www.hayesinc.com

REVISION LOG:

REVISIONS	DATE
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Annual review	3/25/24

Approved:

David Ackman — Digitally signed by David Ackman Date: 2024.08.29 12:33:06 -04'00'

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Sanjiv Shah, MD
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Medical Guideline Disclaimer:

 The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, MetroPlus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan

established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and or paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members.

All coding and website links are accurate at time of publication.

MetroPlus Health Plan has adopted the herein policy in providing management, administrative and other services to our members, related to health benefit plans offered by our organization.