PA.249.CC Noninvasive Genetic Testing During Pregnancy

Policy Number: PA.249.CC
Last Review Date: 03/04/2025
Effective Date: 04/01/2025

CLINICAL POLICY AND PROCEDURE MANUAL

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Summary:

ACOG estimates that 6-11% of stillbirths and neonatal deaths result from aneuploidies (fetus with missing or extra chromosomes). Most aneuploidies involve the presence of an extra chromosome, also referred to as trisomy.

Down syndrome, which is most commonly caused by trisomy 21 (T21), is routinely evaluated as the standard of care for the majority of the 4 million women who give birth each year in the United States. Conventional screening tests typically involve measurement of blood serum markers in conjunction with ultrasound followed by recommendation for diagnostic invasive procedures for abnormal results from screening.

First trimester combined screening (FTS) and integrated screening (INT) have the best screening performance, yet still only have T21 detection rates of 82-87% and 88-95%, respectively, at false positive rates of 5%. Invasive testing with amniocentesis or CVS is highly accurate but has up to a 3% risk of procedure related miscarriage. The reported complication rates have come down in the last 10 years, but there is still some procedure-related risk.

A prenatal test that evaluates cell-free DNA (cfDNA) in maternal blood has been shown to be highly accurate, with T21 detection rates >99%, 98% detection rate for fetal trisomy 18 and 99% detection rate for fetal trisomy 13 with a combined false positive rate of 0.13%.

cfDNA testing, can detect more T21 cases and at the same time reduce unnecessary invasive procedures and in turn fewer procedure related fetal losses. cfDNA testing, when used as a follow-up test for an abnormal result from the FTS or INT screening test can spare the vast majority of the 5% of women with false positive results from undergoing invasive diagnostic testing. Any woman with an abnormal result from cfDNA test should undergo diagnostic testing by amniocentesis or chorionic villus sampling.

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Clinical Criteria:

CountyCare considers cell-free fetal DNA-based prenatal screening for fetal aneuploidy (trisomy 13, 18, and 21) medically necessary as follows:

- For pregnant persons with a current single or twin gestation pregnancy
- Women who are aged 35 years or older at delivery and/or donor oocyte aged 35 years or older
- Fetal ultrasound findings indicate an increased risk of Aneuploidy
- History of a prior pregnancy with a trisomy due to translocation
- Positive first- or second-trimester screening test results for Aneuploidy
- Parental balanced Robertsonian translocation with an increased risk of fetal Trisomy 13 or Trisomy 21
- Screening after pre-test counseling from a board-certified genetic counselor
- Cell-free fetal DNA-based prenatal testing for fetal sex determination for singleton pregnancies at increased risk of a sex (X)-linked condition or congenital adrenal hyperplasia
- Serum screening high risk result earlier in the pregnancy and declining invasive diagnostic testing

CountyCare considers genomic sequence analysis of fetal chromosomal microdeletion using circulating cell-free fetal DNA (cffDNA) in maternal blood medically necessary when:

- There is a known family history of genetic disorders associated with chromosomal microdeletions
- Prenatal screening tests suggest a potential risk for chromosomal abnormalities
- Specific risk factors are identified during prenatal care, such as abnormal results from non-invasive prenatal testing (NIPT)

Limitations:

Cell-free fetal DNA-based prenatal screening for fetal aneuploidy (trisomy 13, 18, 21) is considered not medically necessary as follows:

- For individuals not meeting the criteria above, including pregnancies involving 3 or more fetuses; OR
- Cell-free fetal DNA-based prenatal screening for fetal aneuploidy (trisomy 13, 18, and 21) in twin pregnancies is considered not medically necessary when the current pregnancy is affected by fetal demise, vanishing twin, or one or more anomaly detected in one or both of the twins; OR
- Cell-free fetal DNA-based prenatal testing for fetal sex determination is

considered not medically necessary for pregnancies without an increased risk of a sex (X)-linked condition or congenital adrenal hyperplasia.
- Cell-free fetal DNA-based prenatal testing is considered not medically necessary for all other indications, including testing for microdeletion syndromes.

Cell-free fetal DNA-based screening for indications other than those listed in above clinical coverage criteria will not be covered.

Only one cell-free DNA testing will be covered per pregnancy.

In patients with a positive screen, providers should consider evaluation with a maternal fetal medicine specialist, genetic counseling, comprehensive ultrasound and diagnostic testing.

Fetal chromosomal microdeletion(s) genomic sequence analysis is considered not medically as follows:
- For routine screening of all pregnancies
- There are no indications of potential chromosomal issues
- When alternative testing methods are more suitable

Exclusions:

Due to insufficient evidence of efficacy, the following DNA-based noninvasive prenatal tests are unproven and not medically necessary:
- Genome-wide or exome-wide screening (e.g., MaterniT® Genome)
- Vanadis®
- Single gene disorders (e.g., Vistara™, PreSeek™)
- Tests that have not received approval from the Food and Drug Administration (FDA)

Applicable Codes:

CPT codes covered if selection criteria are met:	
Code	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
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
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

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6. Hayes GTE Report. Cell-Free DNA (cfDNA) [Formerly NIPS, NIPT] Screening for Fetal Trisomy 21, 18, and 13 in Low-Risk Women with Singleton Pregnancy. Annual Review Date: June 14, 2024.
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Revision History:

Revision	Date
Policy Created	April 2021
Approved	June 2021

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Renumbered Policy as it was originally assigned a duplicate number, removed code 81420 as it no longer requires prior auth	October 2022
Updated dates in Reference #s 3 through 7; Replaced the links in Reference #s 14 and 16; minor formatting update to Reference #15	November 2022
Updated Evolent Logo, changed Evolent Health to Evolent; formatting updates throughout the policy; format update to Reference #1; updated Annual Review Date in Reference #s 3 and 5; updated Last Updated Date in References #s 8, 9, 10, 11, 12, 13; format updates to Reference #s 14 and 15	November, 2023
Q4 2024 Review – Added additional information under Clinical Criteria; added Exclusions; updated Reference #2; updated Annual Review Date in Reference #s 3, 4, 5 and 6; format update to Reference #8; updated Reviewed Date in Reference #13; added date to Reference #16	November, 2024
Added Criteria and Limitations for fetal chromosomal microdeletion, updated exclusions, added procedure codes 81420 and 81422, added new References 17, 18 and 19	March, 2025

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