Medica Central Coverage Policy

Policy Name:	**Genetic Testing - Reproductive Testing: Prenatal Screening**
Effective Date:	**July 01, 2025**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

OVERVIEW

Other common names for these tests include: Non-invasive Prenatal Testing (NIPT), Cell-free Fetal DNA Testing (cffDNA)

This policy addresses the use of tests for fetal screening of genetic disorders during pregnancy. These include prenatal cell-free DNA testing for chromosome 13, 18, 21, X, and Y aneuploidies, microdeletions, and single-gene disorders, as well as maternal serum screening (MSS).

Before testing, guidelines recommend that pregnant people be counseled about the risk of a false-positive result. Pre-test and post-test genetic counseling that facilitates informed decision-making, addresses the possibility of secondary or incidental findings, and a plan for returning results before testing occurs is strongly advised.
For additional information see the Rationale section.

The tests, CPT codes, and ICD codes referenced in this policy are not comprehensive, and their inclusion does not represent a guarantee of coverage or non-coverage.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
Prenatal Cell-Free DNA Testing			
Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies	Panorama Prenatal Panel (with or without twin zygosity testing - 0060U) (Natera)	81420, 81507, 0060U, 0327U, O09, O28, O30, O35, Q90-Q99, Z34, Z36.0	1, 2, 3, 5, 6
	Harmony Prenatal Test - 81507 (ACL Laboratories)		
	Vasistera - 0327U (Natera)		
Prenatal Cell-free DNA Testing for Microdeletions	Panorama Extended Panel (Natera)	81422, O09, O28, O35, Q90-Q99, Z34, Z36.0	3, 5
	MaterniT21 Plus Core + ESS (LabCorp)		
	Prequel Prenatal Screen: Microdeletions (Myriad Genetics)		
Prenatal Cell-free DNA Testing for Single-gene Disorders	Vistara - Single-Gene NIPT (Natera)	81302, 81404, 81405, 81406, 81407, 81408, 81442, 0489U, O09, O28, O30, O35, Q90-Q99, Z34, Z36.04	4
	PreSeek Non-invasive Prenatal Gene Sequencing Screen (Baylor Genetics, LLC)		
	UNITY Fetal Risk Screen - 0489U (Billion to One)		
Prenatal Cell-free DNA Testing for Fetal RhD Genotyping			
	Fetal RhD NIPT (add-On) - 0494U (Natera)	0488U, 0494U, 81403	7, 8, 9
	UNITY Fetal RhD NIPT (add on) (Billion to One)		
UNITY Fetal Antigen NIPT (add on) - 0488U (Billion to One)			

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
Maternal Serum Screening			
Maternal Serum Screening (MSS)	First Trimester Maternal Screen, Serum (Mayo Clinic Laboratories)	81508, 81509, 81510, 81511, 81512, O09, O28, O30, O35, Q90-Q99, Z34, Z36.0	3
	Quad Screen (Quest Diagnostics)		
	Serum Integrated Screen, Part 2 (Quest Diagnostics)		

RELATED POLICIES

This policy document provides coverage criteria for cell-free prenatal screening. Please refer to:

- ***Oncology Testing: Solid Tumor Molecular Diagnostics*** for coverage criteria related to molecular profiling of a known or suspected cancer (e.g. broad molecular profiling, including Minimal Residual Disease (MRD) Testing, Tumor Mutational Burden (TMB), and cytogenetic / fusion testing).
- ***Reproductive Testing: Carrier Screening*** for coverage criteria related to parental carrier screening for genetic disorders before or during pregnancy.
- ***Reproductive Testing: Fertility*** for coverage criteria related to preimplantation diagnosis.
- ***Reproductive Testing: Prenatal Diagnosis*** for coverage criteria related to fetal diagnostic testing for genetic disorders during pregnancy and following a pregnancy loss.
- ***Specialty Testing: Multisystem Genetic Conditions*** for coverage criteria related to diagnostic tests for genetic disorders that affect multiple organ systems (e.g. whole exome and genome sequencing, chromosomal microarray, and multigene panels for broad phenotypes).
- ***General Approach to Laboratory Testing*** for coverage criteria related to reproductive testing, including known familial variant testing, that is not specifically discussed in this or another non-general policy.

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COVERAGE CRITERIA

PRENATAL CELL-FREE DNA TESTING

Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies

I. Prenatal cell-free DNA testing for 13, 18, 21, X and Y aneuploidy may be considered **medically necessary** when:

   A. The member has a singleton or twin pregnancy, **AND**

B. The member has NOT previously had cell-free DNA screening in the current pregnancy.

II. Prenatal cell-free DNA testing to predict twin zygosity is considered **investigational**.

III. Prenatal cell-free DNA testing is considered **investigational** for all other indications, including the following:

A. For all other aneuploidies (other than trisomy 13, 18, 21, X, and Y)

B. For multiple gestation pregnancies (triplets or higher)

C. Prenatal cell-free DNA performed simultaneously with maternal serum screening

D. Use on a singleton pregnancy with a known vanishing twin

E. For the sole purpose of fetal sex determination.

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Prenatal Cell-free DNA Testing for Microdeletions

I. Prenatal cell-free DNA testing for microdeletions is considered **investigational** for all indications.

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Prenatal Cell-free DNA Testing for Single-gene Disorders

I. Prenatal cell-free DNA testing for mutations associated with single gene disorders is considered **investigational** for all indications**.**

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Prenatal Cell-free DNA Testing for Fetal RhD Genotyping

I. Prenatal cell-free DNA testing for fetal RhD genotyping is considered **medically necessary** when:

A. The member is pregnant, **AND**

B. The member is confirmed to be RhD negative, **AND**

C. The member is not planning to undergo amniocentesis, **AND**

D. One of the following:

1. The member's practice setting is experiencing Rho(D) immune globulin (RhIG) shortages, **OR**

2. There is documentation of an unknown or heterozygous RhD genotype in the biological father of the fetus.

II. Prenatal cell-free DNA testing for fetal RhD genotyping is **investigational** for all other indications.

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MATERNAL SERUM SCREENING

Maternal Serum Screening (MSS)

I. Maternal serum screening for aneuploidy using no more than one of the following one time per pregnancy is considered **medically necessary**:

   A. First trimester screening (free or total beta-HCG and PAPP-A)

   B. Second trimester screening (hCG, msAFP, uE3, and DIA)

   C. Integrated, stepwise sequential, or contingent sequential screening

   D. Penta screen (hCG, msAFP, uE3, DIA, ITA).

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PRIOR AUTHORIZATION

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

RATIONALE

Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal-Fetal Medicine (SMFM)

ACOG and SMFM (2020, reaffirmed 2024) released a joint practice bulletin (No. 226) with the following recommendations for screening for fetal chromosomal abnormalities:

“The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

- Cell-free DNA is the most sensitive and specific screening test for the common fetal aneuploidies. Nevertheless, it has the potential for false-positive and false-negative results. Furthermore, cell-free DNA testing is not equivalent to diagnostic testing” (p. e63).

“The following recommendations and conclusions are based on limited and inconsistent scientific evidence (Level B)”:

- “Cell-free DNA screening can be performed in twin pregnancies. Overall, performance of screening for trisomy 21 by cell-free DNA in twin pregnancies is encouraging, but the total number of reported affected cases is small. Given the small number of affected cases it is difficult to determine an accurate detection rate for trisomy 18 and 13 (p. e64).

Regarding prenatal screening for multiple gestation pregnancies of triplets or higher, Practice Bulletin No. 226 also states: “...there are no data available for serum screening for higher-order

multiple gestations such as triplets and quadruplets" (p. e59).

Regarding screening a pregnancy with a vanishing twin: "In a patient with both a vanishing twin and a viable intrauterine pregnancy, cell-free DNA screening is not advised because of the high risk for aneuploidy in the nonviable sac or embryo, which can lead to false-positive results" (p. e53).

The Practice Bulletin No. 226 also notes that "[i]f screening is accepted, patients should have one prenatal screening approach, and should not have multiple screening tests performed simultaneously" (p. e49).

American College of Medical Genetics and Genomics (ACMG)

ACMG (2016) published a position statement on noninvasive prenatal screening (also called prenatal cell-free screening) for fetal aneuploidy.

ACMG recommends:

- Informing all pregnant women that prenatal cell-free screening is the most sensitive screening option for traditionally screened aneuploidies (i.e., T13, T18, and T21) (p. 1059).
- Referring patients to a trained genetics professional when an increased risk of aneuploidy is reported after prenatal cell-free screening (p. 1059).
- Providers should make efforts to deter patients from selecting sex chromosome aneuploidy screening for the sole purpose of biologic sex identification in the absence of a clinical indication for this information (p. 1060).

Current ACMG practice guidelines (2022) "strongly recommends prenatal cell-free screening over traditional screening for all pregnant patients with singleton and twin gestations for fetal trisomies 21, 18, and 13 and strongly recommends prenatal cell-free screening be offered to patients to screen for fetal sex chromosome aneuploidy" (p. 1 and p. 5).

National Society for Genetic Counselors (NSGC)

The National Society for Genetic Counselors adopted the following statement updated in 2021 supporting prenatal cell-free DNA (cfDNA) screening as an option for pregnant patients:

> "The National Society of Genetic Counselors believes that all pregnant patients, regardless of aneuploidy risk,
> should have access to prenatal aneuploidy screening using cell-free DNA (cfDNA)."

Wojas, et al

In a 2022 study of 59,471 twin pregnancies, the authors stated: "Further research should determine the impact of the addition of first trimester zygosity assignment for twin pregnancies upon the accuracy of chorionicity assignment, and the differences in healthcare costs for pregnancies assigned either MZ [monozygotic] or DZ [dizygotic] genetic origin. Finally, there is limited information on the impact of zygosity (corrected for chorionicity) upon pregnancy outcome. Our study lays a foundation for such research, to better determine the degree to which these two factors contribute independently to complicated and normal outcomes" (p. 1239).

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Prenatal Cell-free DNA Testing for Microdeletions

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal-Fetal Medicine (SMFM)

ACOG and SMFM (2020, reaffirmed 2024) released a joint practice bulletin (No. 226) with the following recommendations for screening for fetal chromosomal abnormalities:

> "Screening for a limited number of microdeletions with cell-free DNA is available; however, this testing has not been validated clinically and is not recommended. Although microdeletions are relatively common when considered in aggregate, cell-free DNA panels only include a few specific clinically significant microdeletions and these are very rare. Therefore, the PPV for these disorders is much lower than for common trisomies (p. e53)."

American College of Medical Genetics (ACMG)

The ACMG evidence-based clinical practice guideline (2022) on prenatal cell-free DNA screening includes a conditional recommendation, suggesting 22q11.2 deletion syndrome be offered to all patients. The guideline defines a conditional recommendation as follows: "most patients would request this testing and most clinicians would offer prenatal cell-free DNA screening for this purpose, after a discussion about the benefits and limitations of screening and in the context of shared-decision making" (p. 5).

Concert Note

Overall, studies attempting to validate the clinical utility of microdeletion analysis via prenatal cell-free DNA screening have shown low positive predictive values and higher false positive rates, likely because of the low prevalence of the individual targeted microdeletion syndromes in the general population.
At the present time, testing for microdeletions (including 22q11.2) via cell-free DNA testing has insufficient evidence in peer-reviewed publications to effectively result in improved health outcomes compared to the current standard of care.

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Prenatal Cell-free DNA Testing for Single-gene Disorders

The American College of Obstetricians and Gynecologists (ACOG)

ACOG issued a practice advisory for the use of cell-free DNA to screen for single-gene disorders (February 2019, reaffirmed October 2022 and September 2023). In the advisory, they include various skeletal dysplasias, sickle cell disease, and cystic fibrosis as examples of single-gene disorders, and state that at this time, there is insufficient evidence regarding the accuracy of cell-free testing for these and other single gene conditions during pregnancy.

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Prenatal Cell-free DNA Testing for Fetal RhD Genotyping

American College of Obstetrics and Gynecology (ACOG)

ACOG issued a practice advisory in March 2024 due to an FDA announcement regarding a shortage of Rho(D) immune globulin (RhId) shortages. The advisory acknowledges that ACOG guidelines currently do not recommend routine use of prenatal cell-free DNA testing for Rh(D) status due to "cost-effectiveness analyses". However, the committee states that the use of cfDNA

testing “is a reasonable consideration” in a practice that is experiencing shortages, and that if a cfDNA test confirms an Rh(D)-negative fetus, they do not recommend further RhIg treatments.

Additionally, ACOG issued a clinical practice update in August 2024 providing new recommendations for noninvasive cfDNA in alloimmunized patients for fetal RhD genotyping. Their updated clinical recommendation includes fetal antigen genotyping in the setting of heterozygous or unknown paternal Rh(D) genotype. They recommend consideration of fetal cell-free RHD testing as an alternative test in alloimmunized individuals who have declined invasive diagnostic procedures (p. e.1 and e.2).

Rego, et al.

A 2024 prospective, multisite, blinded study titled “Cell-Free DNA Analysis for the Determination of Fetal Red Blood Cell Antigen Genotype in Individuals With Alloimmunized Pregnancies” demonstrated that cf-DNA testing for fetal antigen genotype, including Rh(D), was highly sensitive and specific as early as 10 weeks gestation (p. 437). Per the discussion, “Concordance between fetal antigen genotype as determined by cell-free DNA analysis and neonatal antigen genotype as determined by an outside laboratory was 100% for all 190 calls on antigens to which the pregnant person was alloimmunized. Concordance was also 100% when the antigen calls were expanded to include all 465 antigens for which the pregnant person was genotype negative, resulting in a calculated assay sensitivity and specificity of 100%” (p. 439).

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Maternal Serum Screening (MSS)

The American College of Obstetricians and Gynecologists (ACOG)

ACOG provided an updated position statement (number 226) (2020, reaffirmed 2024) regarding Screening for Fetal Chromosomal Abnormalities. Specifically, these guidelines state: “Prenatal genetic screening (serum screening with or without nuchal translucency [NT] ultrasound or cell-free DNA screening) and diagnostic testing (chorionic villus sampling [CVS] or amniocentesis] options should be discussed and offered to all pregnant women regardless of maternal age or risk of chromosomal abnormality” (p. 862).

The use of multiple screening approaches performed independently (e.g., a first-trimester screening test followed by a quad screen as an unlinked test) is not recommended because it will result in an unacceptably high positive screening rate and could deliver contradictory results (p. 865).

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DEFINITIONS

1. **Prenatal Cell-free DNA Testing** is a screening test that is used to determine the risk of specific genetic disorders by analyzing traces of cell-free DNA (cfDNA) in a pregnant woman’s blood.

2. **Singleton pregnancy** is a pregnancy with one fetus.

3. **Twin zygosity** testing is used to predict the degree of genetic similarity within each pair (i.e.,

monozygotic versus dizygotic). Monozygotic (genetically identical twins) are at a higher risk for pregnancy complications, such as twin-twin transfusion syndrome (TTTS).

4. **Rho(D) immune globulin (RhIG)** is a medication that is used to help manage and treat Rh-negative pregnancies

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REFERENCES

1. Gregg AR, Skotko BG, Benkendorf JL, et al. Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics. *Genet Med*. 2016;18(10):1056-1065. doi:10.1038/gim.2016.97
2. "Prenatal Cell-Free DNA Screening." Position Statement from National Society of Genetic Counselors. https://www.nsgc.org/Policy-Research-and-Publications/Position-Statements/Position-Statements/Post/prenatal-cell-free-dna-screening-1. Released October 11, 2016. Revised April 2021.
3. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. *Obstet Gynecol*. 2020, reaffirmed 2024;136(4):859-867. doi:10.1097/AOG.0000000000004084
4. "Cell-free DNA to Screen for Single-Gene Disorders". Practice Advisory from The American College of Obstetricians and Gynecologists. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2019/02/cell-free-dna-to-screen-for-single-gene-disorders Published February 2019. Reaffirmed October 2022 and September 2023
5. Dungan JS, Klugman S, Darilek S, et al. Noninvasive prenatal screening (NIPS) for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2023;25(2):100336. doi:10.1016/j.gim.2022.11.004
6. Wojas A, Martin KA, Koyen Malashevich A, Hashimoto K, Parmar S, White R, Demko Z, Billings P, Jelsema R, Rebarber A. Clinician-reported chorionicity and zygosity assignment using single-nucleotide polymorphism-based cell-free DNA: Lessons learned from 55,344 twin pregnancies. Prenat Diagn. 2022 Sep;42(10):1235-1241. doi: 10.1002/pd.6218. Epub 2022 Sep 7. PMID: 35997139; PMCID: PMC9541063.
7. "Rho(D) Immune Globulin Shortages". Practice Advisory from The American College of Obstetricians and Gynecologists. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2024/03/rhod-immune-globulin-shortages. Published March 2024, Updated July 9th, 2024.
8. "Paternal and Fetal Genotyping in the Management of Alloimmunization in Pregnancy". Clinical Practice Update from The American College of Obstetricians and Gynecologists (ACOG). https://journals.lww.com/greenjournal/abstract/2024/08000/acog_clinical_practice_update__paternal_and_fetal.34.aspx. Published August 2024.
9. Rego S, Ashimi Balogun O, Emanuel K, et al. Cell-Free DNA Analysis for the Determination of Fetal Red Blood Cell Antigen Genotype in Individuals With Alloimmunized Pregnancies. Obstet Gynecol. 2024;144(4):436-443. doi:10.1097/AOG.0000000000005692

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Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

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