Medica Central Coverage Policy

Policy Name:	**Genetic Testing - Reproductive Testing: Prenatal Screening**
Effective Date:	**01/01/2026**

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 and References 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	SUPPORT
Prenatal Cell-Free DNA Testing			

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
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	Rationale/ References
	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	Rationale/ References
	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	Rationale/ References
	PreSeek Non-invasive Prenatal Gene Sequencing Screen (Baylor Genetics, LLC)		
	UNITY Fetal Risk Screen - 0489U (BillionToOne, Inc.)		
Prenatal Cell-free DNA Testing for Fetal RhD Genotyping	Fetal RhD NIPT (add-On) - 0494U (Natera)	81403, 0488U, 0494U	Rationale/ References
	UNITY Fetal RhD NIPT (add on) (BillionToOne, Inc.)		
	UNITY Fetal Antigen NIPT (add on) - 0488U (BillionToOne, Inc.)		
Prenatal Cell-free DNA Testing for Fetal Blood Group Genotyping	PreciseType HEA Test - 0001U (Immucor, Inc.)	0001U, 0246U, 0488U, 0494U, 0536U	Rationale/ References
	PrecisionBlood - 0246U (San Diego Blood Bank)		
	Unity Fetal Antigen NIPT - 0488U (BillionToOne, Inc.)		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Rh Test - 0494U (Natera)		
	Prenatal Detect RhD - 0536U (Devyser Genomic Laboratories)		
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	Rationale/ References
	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.

back to top

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 is 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.

view rationale
back to top

Prenatal Cell-free DNA Testing for Microdeletions

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

view rationale
back to top

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**.**

view rationale
back to top

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 considered **investigational** for all other indications.

view rationale
back to top

Prenatal Cell-free DNA Testing for Fetal Blood Group Genotyping

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

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

B. The member is confirmed to have a positive antibody screen (ABSC) for an antibody or antibodies identified to be a clinically significant blood group antigen associated with hemolytic disease of the fetus and newborn[1], **AND**

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

D. There is documentation of an unknown or heterozygous genotype in the biological father of the fetus for the antigen to which the mother has been alloimmunized.

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

[1]**Clinically significant blood group antigen associated with hemolytic disease of the fetus and newborn** include those that have at least a moderate risk of disease and/or moderate severity. This includes antigens C, c, D, E, e, Fy^a, Fy^b, Jk^a, Jk^b, K, k, Kp^a, Kp^b, Js^a, Js^b and/or M. The remaining blood group antigens are thought to be low or no risk with mild severity.

view rationale
back to top

MATERNAL SERUM SCREENING

Maternal Serum Screening (MSS)

I. Maternal serum screening for aneuploidy is considered **medically necessary** a maximum of once per pregnancy for any of the following:

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).

II. Maternal serum screening for aneuploidy is considered **investigational** for all other indications.

view rationale
back to top

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 AND REFERENCES

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 joint practice bulletin no. 226 recommending that prenatal screening for genetic conditions be offered to all pregnant women regardless of age or other risk factors. Cell-free DNA screening is included in the list of options that can be discussed and offered to all women (p. e63).

Additionally, they state that cell-free DNA screening can be performed in twin pregnancies (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 multi-fetal 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).

Practice bulletin no. 226 also notes that only one screening approach should be performed and a patient should not have multiple screening tests (p. e64).

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

American College of Medical Genetics and Genomics (ACMG)

ACMG published a position statement in 2016 on prenatal cell-free screening for fetal aneuploidy, where they recommended offering prenatal cell-free DNA as it is the most sensitive screening method for aneuploidies (T13, T18 and T21) (p. 1059).

The guideline also states that 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).

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

Current ACMG practice guidelines (2022) "strongly recommend" 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, 4 and 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

National Society for Genetic Counselors (NSGC)

The National Society for Genetic Counselors adopted the following statement, which was revised in 2021 and reaffirmed in 2025, 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)".

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 and Reaffirmed 2025

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).

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. Epub 2022 Sep 7. PMID: 35997139; PMCID: PMC9541063. doi:10.1002/pd.6218.

back to top

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 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 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

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).

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

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.

back to top

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, September 2023, and September 2024). 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.

American College of Obstetricians and Gynecologists (ACOG). ACOG Practice Advisory: cell-free DNA to screen for single-gene disorders. Published February 2019. Reaffirmed October 2022, September 2023 and September 2024. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2019/02/cell-free-dna-to-screen-for-single-gene-disorders

back to top

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 (Rhlg). 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 Rhlg treatments.

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.

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).

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.

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 cfDNA 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).

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

back to top

Prenatal Cell-free DNA Testing for Fetal Blood Group Genotyping

Rego, et al.

In the 2024 publication “Cell-free DNA Analysis for the Determination of Fetal Red Blood Cell Antigen Genotype in Individuals With Alloimmunized Pregnancies,” the authors support the use of cell-free fetal DNA testing for fetal red blood cell antigens and state the test is highly specific and sensitive in samples from alloimmunized pregnancies as early as 10 weeks of gestation citing their study of validation of next-generation sequencing based analysis of cell-free DNA. The validation showed a 100% specificity and sensitivity for the assay on 1,601 preclinical samples and 1,683 clinical samples with a specificity of 99.9%. 53 total clinical samples were compared to neonatal antigen typing performed by an independent laboratory with a 100% concordance between the results. The authors then extended the study to strengthen the support, including an additional 156 participants and their neonates in the US from 37 states with varied race and ethnic backgrounds and including four sets of twins. Again, the results were 100% concordance with neonatal results in comparison to the cell-free fetal antigen testing (p. 436-439).

The authors also mention the risks associated with the traditional method of approach to alloimmunized pregnancies, stating amniocentesis is the current standard. However, amniocentesis can lead to fetal loss or further strengthening of alloimmunization, putting the fetus at a greater risk which leads to the choice to not have the testing. In many cases, the fetal antigen status remains unknown whether by choice due to fear of fetal demise or poor uptake of the amniocentesis, exposing the fetus to further harm. Performing cell-free fetal DNA analysis provides a noninvasive alternative that is highly specific, sensitive, and mitigates the potentially unnecessary monitoring and invasive procedures, such as cordocentesis or intrauterine transfusions, that may follow. The authors also cited an average of $8,000 cost of care reduction by having cell-free fetal DNA testing (p. 440-442).

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

Haimila K

In the 2023 publication “Overview of Non-invasive Fetal Blood Group Genotyping,” the author describes the cause of hemolytic disease of the fetus and newborn (HDFN) as being caused by maternal IgG antibodies crossing the placenta and binding to and attacking the fetal red blood cells. The antibodies that are specifically associated with this are anti-D as well as other Rh antibodies (anti-C, anti-c, anti-E, anti-e), Kell (anti-K, anti-k), anti-Fy^a (a Duffy antibody) and anti-Jk^a (a Kidd antibody). Anti-A and Anti-B from the ABO blood group are also capable of causing HDFN but pose their risk after birth.

When the mother has a clinically significant antibody (or antibodies) associated with HDFN and the father is heterozygous for the same blood group allele or father’s status is unknown, diagnostic fetal blood group genotyping is needed to determine the fetal risk involved. False negatives are a concern due to complicated blood group genetics and the abundance of maternal DNA inherent to the specimen, however advancements have been made and systems put in place to combat this providing highly accurate results. The use of special cfDNA preservative tubes and processing within a certain time frame are among the pre-analytical steps taken to improve accuracy and outcomes of testing. The fetal DNA fraction of the sample is relatively small already but reliability has been indicated as early as 9 to 12 weeks gestation. In the case of a negative in early pregnancy, repeat testing may be performed in a couple of weeks. The use of genetic blood group typing has taken the place of invasive procedures in pregnancies in which there are maternal antibodies associated with HDFN and has increased the health and wellbeing of both the mother and fetus (p. 1-4, 8).

Katri Haimila. Overview of non-invasive fetal blood group genotyping. Ann Blood. 2023;8(5). doi:10.21037/aob-21-41

Mustafa, et al.

The 2024 publication titled “Monitoring and Management of Hemolytic Disease of the Fetus and Newborn Based on an International Expert Delphi Consensus” includes advice from an international panel of experts spanning 25 countries and 6 continents who practice in fetal medicine, neonatology, and hematology. The consensus agreed that cfDNA should be used to determine fetal antigen status, particularly for the clinically significant antigens associated with hemolytic disease of the fetus and newborn such as the RhD, Kell, and Rhc antigens (p. 280).

Anti-M alloimmunization monitoring and workup of the fetus and newborn for the M antigen to include RBC phenotyping/molecular genotyping were included as necessary despite a consensus not being reached due to its role in hemolytic disease of the fetus and newborn. The authors noted it was vital for accurate diagnosis and management (p. 284).

Mustafa HJ, Sambatur EV, Shamshirsaz AA, et al. Monitoring and management of hemolytic disease of the fetus and newborn based on an international expert Delphi consensus. Am J Obstet Gynecol. 2025;232(3):280-300. doi:10.1016/j.ajog.2024.11.003

de Haas, et al.

In the 2015 review “Haemolytic Disease of the Fetus and Newborn,” the authors describe the pathophysiology of hemolytic disease of the newborn (HDFN) in which a mother is alloimmunized, creating antibodies against the corresponding antigen(s) carried on the fetal or newborn red blood cells. Only the IgG alloantibodies are actively transported across the placenta where they cause destruction of the fetal red blood cells when they bind to the corresponding antigen (p. 99-100).

Severity and risk of HDFN depends on multiple factors including immunoglobulin class, specificity of the maternal alloantibody, and intensity of antigen expression on the fetal red cells (occasionally present on other tissues as well). Based upon these factors, a majority of the over 400 blood group antigens are inappropriate candidates as causes of HDFN narrowing the antigens and alloantibodies of concern to a handful of blood groups including the following antigens: C, c, D, E, e, Fy^a, Fy^b, Jk^a,

Jk^{b}, K, k, Kp^{a}, Kp^{b}, Js^{a}, Js^{b} and/or M. M is a special case as anti-M is commonly found in pregnant women, and while anti-M is typically an immunoglobulin M (IgM) antibody, it can manifest as an immunoglobulin G (IgG) antibody and produce a severe case of HDFN. The rest of the blood group antigens are low or no risk with mild severity and pose a much lower threat for the fetus and newborn. Noninvasive fetal genotyping can be a reliable method to identify these fetal antigens and monitor those at risk for the development of severe HDFN (p. 102-103).

de Haas M, Thurik FF, Koelewijn JM, et al. Haemolytic disease of the fetus and newborn. Vox Sang. 2015;109(2):99-113. doi:10.1111/vox.12265

back to top

Maternal Serum Screening (MSS)

American College of Obstetricians and Gynecologists (ACOG)

ACOG issued practice bulletin no. 226 (2020, reaffirmed 2024) regarding “Screening for Fetal Chromosomal Abnormalities.” These guidelines state that serum screening, either with or without nuchal translucency (NT), should be offered to all pregnant individuals regardless of maternal age or a prior risk for aneuploidy (p. 862).

ACOG also recommends against the use of multiple screening approaches (e.g., a first trimester screening test followed by a second trimester screening test). This has been shown to result in discordant results as well as an “unacceptably high positive screening rate” (p. 865).

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

American College of Medical Genetics (ACMG)

ACMG issued a practice guideline in 2009 titled “Screening for fetal aneuploidy and neural tube defects (NTDs).” In the guideline, ACMG recommends offering screening for aneuploidy and NTDs to all pregnant individuals prior to 20 weeks gestation regardless of maternal age. Effective screening strategies include first or second trimester, serum integrated, or sequential screening (p. 820).

Driscoll DA, Gross SJ; Professional Practice Guidelines Committee (American College of Medical Genetics and Genomics). Screening for fetal aneuploidy and neural tube defects. Genet Med. 2009;11(11):818-821. doi:10.1097/GIM.0b013e3181bb267b

back to top

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

back to top

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.

	Committee/Source	Date(s)
Document Created:	Medical Policy Committee/Health Services Division	October 19, 2022
Revised:	Medical Policy Committee/Health Services Division	November 16, 2022
	Medical Policy Committee/Health Services Division	February 15, 2023
	Medical Policy Committee/Health Services Division	March 15, 2023
	Medical Policy Committee/Health Services Division	August 16, 2023
	Medical Policy Committee/Health Services Division	March 20, 2024
Reviewed:	Medical Policy Committee/Health Services Division	November 16, 2022
	Medical Policy Committee/Health Services Division	February 15, 2023
	Medical Policy Committee/Health Services Division	March 15, 2023
	Medical Policy Committee/Health Services Division	August 16, 2023
	Medical Policy Committee/Health Services Division	March 20, 2024

Original Effective Date:	11/01/2022
Re-Review Date(s):	12/19/2024- Concert Genetics Effective Date: January 01, 2025 (V.1.2025)
	06/18/2025 - Concert Genetics Effective Date: July 01, 2025 (V.2.2025)
	12/18/2025 - Concert Genetics Effective Date: January 01, 2026 (V.1.2026)
Administrative Update:	

© 2026 Medica