Noninvasive Prenatal Testing

Humana®

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Medical Coverage Policy

Table of Contents

Related Medical/Pharmacy Coverage Policies

Genetic and Coagulation Testing for Noncancer Blood Disorders
Genetic Testing
Genetic Testing for Carrier Screening

Description

First trimester noninvasive prenatal testing (NIPT) is usually done between 11 to 14 gestational weeks to check for chromosomal abnormalities and can be completed in a single combined test or in a multistep process. A blood sample, taken from a pregnant woman, is analyzed for free ß-human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein A (PAPP-A) levels. In addition, an ultrasound may be performed to measure nuchal translucency (thickness of the space between the back of the fetal neck and overlying skin). The results of these tests (and consideration of maternal age) are used to calculate specific risk for fetal chromosomal disorders. If these results demonstrate a significant probability of a fetal abnormality, invasive testing such as amniocentesis or chorionic villus sampling (CVS), may be performed.

Second trimester NIPT may include maternal serum testing for alpha-fetoprotein (AFP) levels to check for neural tube defects. This test is generally performed between 16 to 18 weeks of pregnancy. Multiple marker screening (also referred to as triple screen or quad screen) may be performed during the second

trimester and includes testing maternal serum levels of AFP, hCG, unconjugated estriol (uE3) and/or inhibin-A to combine screening for chromosome abnormalities and neural tube defects. This panel is usually done around 15 to 20 gestational weeks when abnormal levels could indicate that further evaluation may be needed with invasive testing.

For **NIPT for Zika virus**, please refer to the Centers for Disease Control and Prevention (CDC) for the current guidelines.

Prenatal cell-free deoxyribonucleic acid (cfDNA) noninvasive screening tests are laboratory studies that examine changes in human DNA, chromosomes, genes or gene products (such as proteins) of cfDNA that are isolated in the maternal plasma during pregnancy. Examples include:

- Genome testing (eg, MateriniT Genome, PreSeek, Resura, UNITY Fetal Risk [0489U], VERAgene, Vistara) analyzes fetal chromosomes for extra or missing parts of chromosomes or other whole chromosome changes. **(Refer to Coverage Limitations section)**

- Trisomy tests for fetal aneuploidy detect chromosome abnormalities. These advanced screening tests are used to detect one or more of the following:

    - Aneuploidies involving chromosomes 13, 18 and 21
    - Aneuploidies involving sex chromosomes **(Refer to Coverage Limitations section)**
    - Microdeletions/microduplications **(Refer to Coverage Limitations section)**
    - Screening for single gene variants **(Refer to Coverage Limitations section)**
    - Screening for twin zygosity **(Refer to Coverage Limitations section)**

cfDNA NIPT that isolates fetal DNA from rare fetal trophoblast cells, circulating in maternal blood, has also been proposed for prenatal screening and diagnosis. This method of testing is purported to detect fetal chromosomal aneuploidy and chromosomal deletions/duplications commonly linked to genetic conditions, as early as 8 weeks gestation. **(Refer to Coverage Limitations section)**

Alloimmunization (formation of antibodies against blood type antigens) of red blood cells (RBCs) may occur in pregnancy when the pregnant individual and their fetus have different blood types. Both the ABO and the Rh blood groups are encoded by genes (*ABO, RHD* and *RHCE*) that are inherited by the fetus and have the potential to be different (heterozygous) from either parent. ABO blood type incompatibility occurs when the mother lacks an A or B antigen on their RBCs, while the fetal blood cells have that specific antigen due to paternal inheritance. The maternal antibodies (IgM) formed during pregnancy from an ABO blood group incompatibility do not cross the placental barrier and therefore, do not cause harm to the fetus.

In the Rh blood group, the D antigen (RhD) is the most likely to produce an immune response of the known Rh blood group antigens. Incompatibility most commonly occurs when the mother is Rh negative (Rh-) and the fetus is Rh positive (Rh+). When an Rh- mother is exposed to an Rh+ baby during a delivery, the mother's immune system will develop antibodies. These existing maternal antibodies (IgG) can cross the placenta in subsequent pregnancies and attack an Rh- fetuses' RBCs, causing hemolytic disease of the fetus and newborn (HDFN). Fetal antigen genotyping is recommended when the paternal genotype is heterozygous or unknown.[7] Historically, amniocentesis with testing of amniotic fluid has been the gold

standard to assess for RhD alloimmunization in at-risk pregnancies. However, cfDNA testing has been developed as an alternative to assess for fetal RhD gene compatibility in pregnant individuals that are known to be RhD negative.

Pre-eclampsia is a disorder of pregnancy characterized by the onset of high blood pressure and protein in the urine which typically begins after the twentieth week of pregnancy. Monitoring of maternal blood pressure is routinely used as a screening tool to evaluate for pre-eclampsia during prenatal visits. Available tests include, but not may not be limited to:

- BRAHMS PlGF plus KRYPTOR (an automated immunofluorescent assay for quantitative placental growth factor [PlGF] in plasma) is to be used in conjunction with the BRAHMS sFlt-1 KRYPTOR (an automated immunofluorescent assay for quantitative soluble fms-like tyrosine kinase-1 [sFlt-1], also known as VEGF receptor-1) along with other laboratory tests and clinical assessments to assess pregnant women (singleton pregnancies 23 to 35 weeks gestation) who have been hospitalized for hypertensive disorders of pregnancy (preeclampsia, chronic hypertension with or without superimposed preeclampsia or gestational hypertension) to purportedly aid in the risk for progression to preeclampsia with severe features. **(Refer to Coverage Limitations section)**

- Mirvie RNA platform uses RNA analyses and machine-learning to identify pre-eclampsia risk before the clinical presentation of symptoms[35] **(Refer to Coverage Limitations section)**

- PlGF 1-2-3 Assay is a biochemical assay of PlGF, time-resolved fluorescence immunoassay, maternal serum and predictive algorithm that is used as a risk score for preeclampsia **(Refer to Coverage Limitations section)**

- PEPredictDx evaluates a serum specimen for three biomarkers (kinase insert domain receptor, endoglin and retinol-binding protein 4) using immunoassay technique that reports a risk score for preeclampsia PE as early as 11 weeks in pregnancy **(Refer to Coverage Limitations section)**

- Preeclampsia sFlt-1/PlGF (soluble fms-Like Tyrosine Kinase 1/ Placental Growth Factor) ratio, serum assay (0482U) **(Refer to Coverage Limitations section)**

Preterm birth (delivery prior to 37 weeks gestation) occurs in approximately 10% of pregnancies in the United States. The PreTRM test is purported to predict spontaneous preterm birth as early as 19 weeks of gestation in asymptomatic, singleton pregnancies by analyzing multiple maternal serum proteins and other clinical data.[38] **(Refer to Coverage Limitations section)**

Three-dimensional (3D) ultrasound uses special probes and software to acquire a 2D static display of 3D data. Although the indications for its use have not been well-defined, 3D technology can purportedly reduce scanning time and better demonstrate abnormalities previously detected with 2D sonography including facial abnormalities and neural tube defects. Four-dimensional (4D) ultrasound (also called dynamic 3D sonography) refers to 3D images that can be viewed in real-time. Five-dimensional (5D) ultrasound (also known as high-definition live) includes a software package on the ultrasound unit that purportedly enhances facial skin tone and depth perception through lighting techniques which results in high-resolution images. **(Refer to Coverage Limitations section)**

Fetal magnetocardiography is a noninvasive technique for recording magnetic fields generated by the electrical activity of the fetal heart. It is a passive recording technique utilizing high sensitivity Superconducting Quantum Interference Device (SQUID) sensors. These sensors amplify signals that are naturally occurring, yet weak. **(Refer to Coverage Limitations section)**

Coverage Determination

Any state mandates for noninvasive prenatal screening take precedence over this medical coverage policy.

Humana members may be eligible under the Plan for **NIPT for chromosomal abnormalities** using **ONE** of the following:

- Multiple marker screening (inhibin-A, free or total hCG, PAPP-A and/or uE3 levels) with or without 2D ultrasonography***** (measurement of nuchal translucency); **OR**

- cfDNA tests in **single or twin gestation pregnancies**, using cfDNA to screen for fetal trisomy aneuploidy 13, 18 and 21 (81420, 81507, 0327U)

Humana members may be eligible under the Plan for **NIPT using cfDNA for fetal RhD genotyping (0494U)** in alloimmunized pregnancies that are known to be RhD negative and decline amniocentesis.

Humana members may be eligible under the Plan for **NIPT for neural tube defects** performed in the second trimester using 2D ultrasonography***** (eg, screening for fetal anomalies) with or without maternal serum AFP.

*****2D ultrasonography may be performed up to the terms and conditions of the member's individual certificate.

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for the following **NIPT** for any indication:

- 3D, 4D or 5D ultrasonography
- Fetal magnetocardiography
- First trimester ultrasound assessment of the nasal bone

These are considered experimental/investigational as they are not identified as widely used and generally accepted for the proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the Plan for **cfDNA prenatal screening for fetal trisomy aneuploidy (13, 18 and 21) (eg, 81420, 81507, 0327U)** for any indications other than those listed above in the coverage determination section including, but may not be limited to, the following:

- Duplicative or repeat (during the same pregnancy) testing for low fetal fraction or test failure); **OR**
- Duplicative or repeat NIPT testing for chromosomal abnormalities (eg, multiple marker screening with or without 2D ultrasound for nuchal translucency) has been performed during the current pregnancy; **OR**
- Expanded testing of microdeletion/microduplication analysis (eg, DiGeorge syndrome, Prader-Willi syndrome) (81422); **OR**
- Screening for monogenic disorders (eg, beta thalassemia, hemophilia, sickle cell anemia); **OR**
- Screening for sex chromosome aneuploidies; **OR**
- Screening for single gene variants (eg, known familial variant); **OR**
- Screening for trisomies other than 13, 18 and 21; **OR**
- Screening for twin zygosity (0060U); **OR**
- Testing prior to 10 weeks gestation; **OR**
- Triplet or higher gestation pregnancies

These are considered experimental/investigational as it is not identified as widely used and generally accepted for any other proposed use as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the Plan for the following **NIPT** for any indication:

- BRAHMS SFlt-1/ PlGF KRYPTOR Test System; **OR**
- cfDNA genotyping for non-RhD alloimmunization (0488U); **OR**
- Luna Prenatal Test (0341U); **OR**
- MaterniT GENOME; **OR**
- Mirvie RNA platform; **OR**
- PEPredictDx (0390U); **OR**
- PlGF 1-2-3 assay (0243U); **OR**
- Preeclampsia sFlt-1/PlGF assay (0482U); **OR**
- PreSeek; **OR**
- PreTRM (0247U); **OR**
- Resura; **OR**
- UNITY Fetal Risk (0489U); **OR**
- VERAgene; **OR**
- Vistara

These are considered experimental/investigational as they are not identified as widely used and generally accepted for the proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the Plan for **NIPT** for any indications other than those listed above, including the detection of genetic susceptibility to adult-onset/late-onset disorders. This is considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition.

Fetal sex testing is considered integral to the panel of standard blood tests and is not separately reimbursable.

Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (81508, 81509, 81510, 81511, 81512) are not separately reimbursable.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
76376	3D rendering with interpretation and reporting of computed tomography, magnetic resonance imaging, ultrasound, or other tomographic modality with image postprocessing under concurrent supervision; not requiring image postprocessing on an independent workstation	**Not covered if used to report routine pregnancy ultrasound**
76377	3D rendering with interpretation and reporting of computed tomography, magnetic resonance imaging, ultrasound, or other tomographic modality with image postprocessing under concurrent supervision; requiring image postprocessing on an independent workstation	**Not covered if used to report routine pregnancy ultrasound**
76801	Ultrasound, pregnant uterus, real time with image documentation, fetal and maternal evaluation, first trimester (< 14 weeks 0 days), transabdominal approach; single or first gestation	
76802	Ultrasound, pregnant uterus, real time with image documentation, fetal and maternal evaluation, first trimester (< 14 weeks 0 days), transabdominal approach; each additional gestation (List separately in addition to code for primary procedure)	

76811	Ultrasound, pregnant uterus, real time with image documentation, fetal and maternal evaluation plus detailed fetal anatomic examination, transabdominal approach; single or first gestation	**Not covered if used to report first trimester ultrasound assessment of the nasal bone**
76812	Ultrasound, pregnant uterus, real time with image documentation, fetal and maternal evaluation plus detailed fetal anatomic examination, transabdominal approach; each additional gestation (List separately in addition to code for primary procedure)	**Not covered if used to report first trimester ultrasound assessment of the nasal bone**
76813	Ultrasound, pregnant uterus, real time with image documentation, first trimester fetal nuchal translucency measurement, transabdominal or transvaginal approach; single or first gestation	
76814	Ultrasound, pregnant uterus, real time with image documentation, first trimester fetal nuchal translucency measurement, transabdominal or transvaginal approach; each additional gestation (List separately in addition to code for primary procedure)	
76815	Ultrasound, pregnant uterus, real time with image documentation, limited (eg, fetal heart beat, placental location, fetal position and/or qualitative amniotic fluid volume), 1 or more fetuses	
76816	Ultrasound, pregnant uterus, real time with image documentation, follow-up (eg, re-evaluation of fetal size by measuring standard growth parameters and amniotic fluid volume, re-evaluation of organ system(s) suspected or confirmed to be abnormal on a previous scan), transabdominal approach, per fetus	
76999	Unlisted ultrasound procedure (eg, diagnostic, interventional)	**Not covered if used to report routine pregnancy ultrasound outlined in Coverage Limitations section**
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	**Not Covered if used to report any test outlined in Coverage Limitations section**
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood	**Not Covered**

81479	Unlisted molecular pathology procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
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	
81508	Fetal congenital abnormalities, biochemical assays of two proteins (PAPP-A, hCG [any form]), utilizing maternal serum, algorithm reported as a risk score	**Individual serum levels reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies are not separately reimbursable**
81509	Fetal congenital abnormalities, biochemical assays of three proteins (PAPP-A, hCG [any form], DIA), utilizing maternal serum, algorithm reported as a risk score	**Individual serum levels reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies are not separately reimbursable**
81510	Fetal congenital abnormalities, biochemical assays of three analytes (AFP, uE3, hCG [any form]), utilizing maternal serum, algorithm reported as a risk score	**Individual serum levels reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies are not separately reimbursable**
81511	Fetal congenital abnormalities, biochemical assays of four analytes (AFP, uE3, hCG [any form], DIA) utilizing maternal serum, algorithm reported as a risk score (may include additional results from previous biochemical testing)	**Individual serum levels reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies are not separately reimbursable**

81512	Fetal congenital abnormalities, biochemical assays of five analytes (AFP, uE3, total hCG, hyperglycosylated hCG, DIA) utilizing maternal serum, algorithm reported as a risk score	**Individual serum levels reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies are not separately reimbursable**
81599	Unlisted multianalyte assay with algorithmic analysis	**Fetal gender testing is considered integral to the panel of standard blood tests that are taken when assessing for sex chromosome aneuploidies and not separately reimbursable**
82105	Alpha-fetoprotein (AFP); serum	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**
82106	Alpha-fetoprotein (AFP); amniotic fluid	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**

82677	Estriol	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**
84163	Pregnancy-associated plasma protein-A (PAPP-A)	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**
84702	Gonadotropin, chorionic (hCG); quantitative	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**
84703	Gonadotropin, chorionic (hCG); qualitative	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**

84704	Gonadotropin, chorionic (hCG); free beta chain	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**
84999	Unlisted chemistry procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
86336	Inhibin A	**Individual serum levels (eg, AFP, hCG [duplicate form], inhibin-A, PAPP-A, uE3) reported with multianalyte assays with algorithmic analysis (MAAA) for fetal congenital anomalies (eg, 81508, 81509, 81510, 81511, 81512) are not separately reimbursable**
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood	**Not Covered**
0243U	Obstetrics (preeclampsia), biochemical assay of placental-growth factor, time-resolved fluorescence immunoassay, maternal serum, predictive algorithm reported as a risk score for preeclampsia	**Not Covered**
0247U	Obstetrics (preterm birth), insulin-like growth factor–binding protein 4 (IBP4), sex hormone– binding globulin (SHBG), quantitative measurement by LC-MS/MS, utilizing maternal serum, combined with clinical data, reported as predictive-risk stratification for spontaneous preterm birth	**Not Covered**
0327U	Fetal aneuploidy (trisomy 13, 18, and 21), DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy, includes sex reporting, if performed	

0341U	Fetal aneuploidy DNA sequencing comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploid	**Not Covered**
0390U	Obstetrics (preeclampsia), kinase insert domain receptor (KDR), Endoglin (ENG), and retinol-binding protein 4 (RBP4), by immunoassay, serum, algorithm reported as a risk score	**Not Covered** **New Code Effective 07/01/2023**
0482U	Obstetrics (preeclampsia), biochemical assay of soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF), serum, ratio reported for sFlt-1/PlGF, with risk of progression for preeclampsia with severe features within 2 weeks	**Not Covered** **New Code Effective Date 10/01/2024**
0488U	Obstetrics (fetal antigen noninvasive prenatal test), cell-free DNA sequence analysis for detection of fetal presence or absence of 1 or more of the Rh, C, c, D, E, Duffy (Fya), or Kell (K) antigen in alloimmunized pregnancies, reported as selected antigen(s) detected or not detected	**Not Covered** **New Code Effective Date 10/01/2024**
0489U	Obstetrics (single-gene noninvasive prenatal test), cell-free DNA sequence analysis of 1 or more targets (eg, CFTR, SMN1, HBB, HBA1, HBA2) to identify paternally inherited pathogenic variants, and relative mutation-dosage analysis based on molecular counts to determine fetal inheritance of maternal mutation, algorithm reported as a fetal risk score for the condition (eg, cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemia)	**Not Covered** **New Code Effective Date 10/01/2024**
0494U	Red blood cell antigen (fetal RhD gene analysis), next-generation sequencing of circulating cell-free DNA (cfDNA) of blood in pregnant individuals known to be RhD negative, reported as positive or negative	**New Code Effective Date 10/01/2024**
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

References

1. American College of Cardiology (ACC). New insights into fetal atrioventricular block using fetal magnetocardiography. https://www.acc.org. Published 2008.

2. American College of Medical Genetics and Genomics (ACMG). Laboratory screening and diagnosis of open neural tube defects, 2019 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). https://www.acmg.net. Published November 2019.

3. American College of Medical Genetics and Genomics (ACMG). Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics. https://www.acmg.net. Published October 2016.

4. American College of Medical Genetics and Genomics (ACMG). 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). https://www.acmg.net. Published December 2022.

5. American College of Medical Genetics and Genomics (ACMG). Systematic evidence-based review: the application of noninvasive prenatal screening using cell-free DNA in general-risk pregnancies. https://www.acmg.net. Published May 2022.

6. American College of Obstetricians and Gynecologists (ACOG). Clinical Practice Update. Biomarker prediction of preeclampsia with severe features. https://www.acog.org. Published June 2024.

7. American College of Obstetricians and Gynecologists (ACOG). Clinical Practice Update. Paternal and fetal genotyping in the management of alloimmunization in pregnancy. https://www.acog.org. Published August 2024.

8. American College of Obstetricians and Gynecologists (ACOG). Practice Advisory. Cell-free DNA to screen for single-gene disorders. https://www.acog.org. Published February 2019. Updated October 2022.

9. American College of Obstetricians and Gynecologists (ACOG). Practice Advisory. Rho(D) immune globulin shortages. https://www.acog.org. Published March 2024.

10. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin. Antepartum fetal surveillance. https://www.acog.org. Published June 2021.

11. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin. Neural tube defects. https://www.acog.org. Published December 2017. Updated 2021.

12. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin. Screening for fetal chromosomal abnormalities. https://www.acog.org. Published October 2020.

13. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin. Ultrasound in pregnancy. https://www.acog.org. Published December 2016. Updated 2020.

14. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD). Cytogenetic studies (190.3). https://www.cms.gov. Published July 16, 1998.

15. ClinicalKey. Strausburger JF, Cheulkar B, Wakai R. Magnetocardiography for fetal arrhythmias. *Heart Rhythm.* 2008;5(7):1073-1076. https://www.clinicalkey.com.

16. ECRI Institute. ECRIgene Evidence Report. Harmony Cell-free fetal DNA test (Ariosa Diagnostics, Inc.) for prenatal screening. https://www.ecri.org. Published October 2017.

17. ECRI Institute. ECRIgene Evidence Report. MaterniT 21 Plus, MaterniT genome, and VisibiliT tests (Sequenom, Inc.) for prenatal screening. https://www.ecri.org. Published June 26, 2018.

18. ECRI Institute. ECRIgene Evidence Report. Panorama cell-free fetal DNA test (Natera, Inc.) for prenatal screening. https://www.ecri.org. Published May 2017.

19. ECRI Institute. ECRIgene Evidence Report. Verifi cell-free fetal DNA test (Illumina, Inc.) for prenatal screening. https://www.ecri.org. Published March 30, 2018.

20. ECRI Institute. Genetic Test Assessment. Cell-free DNA tests for prenatal screening in twin pregnancies. https://www.ecri.org. Published September 9, 2022.

21. ECRI Institute. Hotline Response (ARCHIVED). Prenatal ultrasound for monitoring routine pregnancy. https://www.ecri.org. Published April 17, 2017.

22. Hayes, Inc. Clinical Utility Evaluation. Cell-free DNA (cfDNA) [formerly NIPS, NIPT] screening for fetal chromosomal copy number variants. https://evidence.hayesinc.com. Published February 23, 2022. Updated March 15, 2024.

23. Hayes, Inc. Clinical Utility Evaluation. Cell-free DNA (cfDNA) [formerly NIPS, NIPT] screening for fetal rare autosomal trisomies. https://evidence.hayesinc.com. Published December 21, 2021. Updated December 1, 2023.

24. Hayes, Inc. Clinical Utility Evaluation. Cell-free DNA (cfDNA) [formerly NIPS, NIPT] screening for fetal sex chromosome aneuploidy. https://evidence.hayesinc.com. Published September 23, 2021. Updated September 26, 2023.

25. Hayes, Inc. Clinical Utility Evaluation. Cell-free DNA (cfDNA) [formerly NIPS, NIPT] screening for fetal trisomy 21, 18, and 13 in high-risk women. https://evidence.hayesinc.com. Published February 16, 2018. Updated February 11, 2022.

26. Hayes, Inc. Clinical Utility Evaluation. Cell-free DNA (cfDNA) [formerly NIPS, NIPT] screening for fetal trisomy 21, 18, and 13 in low-risk women with singleton pregnancy. https://evidence.hayesinc.com. Published April 19, 2021. Updated June 14, 2024.

27. Hayes, Inc. Clinical Utility Evaluation. Cell-free DNA (cfDNA) [formerly NIPS, NIPT] screening for fetal trisomy 21, 18, and 13 in women with twin pregnancies. https://evidence.hayesinc.com. Published July 7, 2021. Updated August 25, 2023.

28. Hayes, Inc. Evidence Analysis Research Brief. Four-dimensional and five-dimensional ultrasound for diagnosis of fetal cardiovascular abnormalities. https://evidence.hayesinc.com. Published January 11, 2024.

29. Hayes, Inc. Evidence Analysis Research Brief. Four-dimensional and five-dimensional ultrasound for diagnosis of fetal noncardiac abnormalities. https://evidence.hayesinc.com. Published December 29, 2023.

30. Hayes, Inc. Medical Technology Directory. Routine ultrasound examination in low-risk pregnancy. https://evidence.hayesinc.com. Published December 6, 2010. Updated January 15, 2014.

31. Hayes, Inc. Medical Technology Directory. Three-dimensional and four-dimensional ultrasound for high-risk pregnancies and routine screening. https://evidence.hayesinc.com. Published November 9, 2005. Updated November 17, 2009.

32. Hayes, Inc. Precision Medicine Research Brief. Pre-eclampsia Screening for Prediction and Prevention (PerkinElmer Inc.). https://evidence.hayesinc.com. Published April 21, 2021.

33. Hayes, Inc. Precision Medicine Research Brief. PreTRM (Sera Prognostics). https://evidence.hayesinc.com. Published July 21, 2022.

34. Hayes, Inc. Precision Medicine Research Brief. Fetal RhD noninvasive prenatal testing. https://evidence.hayesinc.com. Published July 3, 2024.

35. Mirvie. Mirvie RNA platform. https://www.mirvie.com. Published 2024.

36. National Society of Genetic Counselors (NSGC). Position Statement. Prenatal cell-free DNA screening. https://www.nscg.org. Published April 23, 2021.

37. National Society of Genetic Counselors (NSGC). Position Statement. Prenatal testing for adult-onset conditions. https://www.nscg.org. Published June 26, 2019.

~~Perkin Elmer. Preeclampsia screening with PGIF 1-2-3 assay. https://www.perkinelmer.com. Published 2020.~~

38. Sera Prognositcs. PreTRM test for risk management. https://www.seraprognostics.com. Published 2024.

39. UpToDate, Inc. Approach to prenatal diagnosis of life-limiting skeletal dysplasias. https://www.uptodate.com. Updated July 2024.

40. UpToDate, Inc. Biophysical profile test for antepartum fetal assessment. https://www.uptodate.com. Updated July 2024.

41. UpToDate, Inc. Cell-free DNA screening for fetal conditions other than the common aneuploidies. https://www.uptodate.com. Updated July 2024.

42. UpToDate, Inc. Chromosomal translocations, deletions, and inversions. https://www.uptodate.com. Updated July 2024.

43. UpToDate, Inc. Congenital cytogenetic abnormalities. https://www.uptodate.com. Updated July 2024.

44. UpToDate, Inc. D alloimmunization in pregnancy: management. https://www.uptodate.com. Updated July 2024.

45. UpToDate, Inc. Down syndrome: overview of prenatal screening. https://www.uptodate.com. Updated July 2024.

46. UpToDate, Inc. Fetal arrhythmias. https://www.uptodate.com. Updated July 2024.

47. UpToDate, Inc. Fetal echogenic bowel. https://www.uptodate.com. Updated July 2024.

48. UpToDate, Inc. First trimester combined test and integrated tests for screening for Down syndrome and trisomy 18. https://www.uptodate.com. Updated July 2024.

49. UpToDate, Inc. Management of non-RhD red blood cell alloantibodies during pregnancy. https://www.uptodate.com. Updated July 2024.

50. UpToDate, Inc. Management of non-RhD red blood cell alloantibodies during pregnancy. https://www.uptodate.com. Updated July 2024.

51. UpToDate, Inc. Maternal serum marker screening for Down syndrome: levels and laboratory issues. https://www.uptodate.com. Updated July 2024.

52. UpToDate, Inc. Microdeletion syndromes (chromosomes 1 to 11). https://www.uptodate.com. Updated July 2024.

53. UpToDate, Inc. Microdeletion syndromes (chromosomes 12 to 22). https://www.uptodate.com. Updated July 2024.

54. UpToDate, Inc. Microduplication syndromes. https://www.uptodate.com. Updated July 2024.

55. UpToDate, Inc. Neural tube defects: overview of prenatal screening, evaluation, and pregnancy management. https://www.uptodate.com. Updated July 2024.

56. UpToDate, Inc. Neural tube defects: prenatal sonographic diagnosis. https://www.uptodate.com. Updated July 2024.

57. UpToDate, Inc. Overview of antepartum fetal surveillance. https://www.uptodate.com. Updated July 2024.

58. UpToDate, Inc. Prediction of preeclampsia in asymptomatic pregnant patients. https://www.uptodate.com. Updated July 2024.

59. UpToDate, Inc. Preeclampsia: clinical features and diagnosis. https://www.uptodate.com. Updated July 2024.

60. UpToDate, Inc. Prenatal care: initial assessment. https://www.uptodate.com. Updated July 2024.

61. UpToDate, Inc. Prenatal care: second and third trimesters. https://www.uptodate.com. Updated July 2024.

62. UpToDate, Inc. Prenatal genetic evaluation of the fetus with anomalies or soft markers. https://www.uptodate.com. Updated July 2024.

63. UpToDate, Inc. Prenatal screening for common fetal aneuploidies: cell-free DNA test. https://www.uptodate.com. Updated July 2024.

64. UpToDate, Inc. RhD alloimmunization in pregnancy: management. https://www.uptodate.com. Updated July 2024.

65. UpToDate, Inc. RhD alloimmunization in pregnancy: overview. https://www.uptodate.com. Updated July 2024.

66. UpToDate, Inc. RhD alloimmunization: prevention in pregnant and postpartum patients. https://www.uptodate.com. Updated July 2024.

67. UpToDate, Inc. Spontaneous preterm birth: overview of risk factors and prognosis. https://www.uptodate.com. Updated July 2024.

68. UpToDate, Inc. Sex chromosome abnormalities. https://www.uptodate.com. Updated July 2024.

69. UpToDate, Inc. Sonographic findings associated with fetal aneuploidy. https://www.uptodate.com. Updated July 2024.

70. UpToDate, Inc. Twin pregnancy: overview. https://www.uptodate.com. Updated July 2024.

71. US Preventive Services Task Force (USPSTF). Recommendation Statement. Hypertensive disorders of pregnancy: screening. https://www.uspreventiveservicestaskforce.org. Published September 2023.

Change Summary

- 08/29/2024 Annual Review, Coverage Change.