Non-Invasive Prenatal Screening (NIPS)2/ Cell-Free DNA Screening for Fetal Aneuploidy

Policy Number: PG0287
Last Review: 12/18/2020

PARAMOUNT

ADVANTAGE | ELITE | HMO
INDIVIDUAL MARKETPLACE |
PROMEDICA MEDICARE
PLAN | PPO

GUIDELINES

This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder contract. Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards. This guideline is solely for explaining correct procedure reporting and does not imply coverage and reimbursement.

SCOPE

X Professional
X Facility

DESCRIPTION

Humans have 23 pairs of chromosomes. Aneuploidy is an abnormal number of chromosomes. Trisomy is a type of aneuploidy in which there are three copies of a chromosome instead of two.

Trisomy 21, also called Down syndrome, is a chromosomal condition that is associated with intellectual disability, a characteristic facial appearance and poor muscle tone in infancy. The degree of intellectual disability varies, but it is usually mild to moderate. Individuals with Down syndrome may be born with a variety of birth defects including heart defects and digestive abnormalities. The risk of having a child with trisomy 21 increases with a mother's age. Down syndrome can also be caused by translocation, which occurs when a part of chromosome 21 breaks away and becomes attached to another chromosome. In a balanced translocation, pieces of chromosomes are rearranged but no genetic material is gained or lost in the cell. In these cases, the parent's health is not affected.

Trisomy 18, also called Edwards syndrome, is a chromosomal condition associated with slow growth before birth and a low birth weight. Affected individuals may have heart defects and abnormalities of other organs that develop before birth. Other features of trisomy 18 include a small, abnormally shaped head; a small jaw and mouth; and clenched fists with overlapping fingers. The risk of having a child with trisomy 18 increases with a mother's age.

Trisomy 13, also called Patau syndrome, is a chromosomal condition associated with severe intellectual disability and physical abnormalities in many parts of the body. Individuals with trisomy 13 often have heart defects, brain or spinal cord abnormalities, very small or poorly developed eyes, extra fingers and/or toes, a cleft lip with or without a cleft palate and weak muscle tone. The risk of having a child with trisomy 13 increases with a mother's age. Patau syndrome can also be caused by translocation.

Routine screening tests for trisomies 13, 18 and 21 include maternal serum screening and ultrasound evaluation in the first and second trimester. These tests may identify women with an increased risk of having a child with trisomy 13, 18 or 21, but they cannot diagnose, confirm or exclude the possibility of a chromosomal disorder. Conventional prenatal diagnosis (i.e., chorionic villus sampling (CVS) or amniocentesis) can definitively diagnose fetal trisomies, although these invasive procedures are associated with a risk of miscarriage.

Non-invasive prenatal screening tests, also known as cell-free DNA screening, can detect fetal trisomies, by analyzing cell-free DNA (cfDNA) fragments in maternal blood. During pregnancy, there are cfDNA fragments from both the mother and fetus in maternal circulation. The tests detect an increased amount of chromosomal material in maternal blood and can be offered as early as 10 weeks of pregnancy. Available tests use different methodologies and algorithms for data analysis. Depending on the test, the methodology may involve massively parallel sequencing (MPS), targeted sequencing of specific chromosomal segments or directed sequence analysis of single

nucleotide polymorphisms. Cell-free DNA tests, also known as Non-invasive prenatal screening (NIPS) for pregnant women include:

- MaterniT21® PLUS
- Harmony®
- Panorama®
- InformaSeq®
- VisibiliT™
- QNatal Advanced™
- Verifi™ Prenatal Test
- Myriad Prequel™ Prenatal Screen

Non-invasive prenatal screening (NIPS) using cell-free DNA is being researched as a tool to screen for microdeletions. Microdeletions (also referred to as submicroscopic deletions) are chromosomal deletions that are too small to be detected by conventional cytogenetic methods or microscopy. Microdeletions, in conjunction with microduplications, are collectively known as copy number variations (CNVs). CNVs can lead to disease development when the change in copy number of a dose-sensitive gene or genes disturbs the ability of the gene(s) to function and effects the volume of protein produced.

Several genomic disorders associated with microdeletion have been identified. Microdeletion syndromes have distinctive and, in many cases, serious clinical features, including cardiac anomalies, immune deficiency, palatal defects, and cognitive delay. While some microdeletions are inherited, other occur de novo. Microdeletion syndromes include, but are not limited to the following:

- DiGeorge syndrome (22q deletion);
- Shprintzen syndrome (22q11 deletion syndrome);
- Prader-Willi/Angelman syndromes (15q11.2 deletion);
- Cri-du-chat syndrome (5p deletion);
- Wolf-Hirschhorn syndrome (4p deletion); and
- 1p36 deletion syndrome.

The clinical implications of prenatal testing for microdeletions are not clearly defined. It has not yet been determined whether prenatal diagnosis is appropriate given the inherent complexity of accurately predicting the phenotype for the numerous of microdeletion syndromes.

POLICY

HMO, PPO, Individual Marketplace, Elite/ProMedica Medicare Plan, Advantage
Non-invasive prenatal screening (81420) (e.g., MaterniT21®, Harmony®, Panorama®, InformaSeq®, VisibiliT™, QNatal Advanced™, Verifi™ Prenatal test, and Myriad Prequel™ Prenatal Screen) requires prior authorization for all product lines.

HMO, PPO, Individual Marketplace, Elite/ProMedica Medicare Plan
Codes 81422 and 81507 are non-covered

Advantage
Codes 81422 and 81507 require prior authorization for Advantage.

COVERAGE CRITERIA

HMO, PPO, Individual Marketplace, Elite/ProMedica Medicare Plan, Advantage

Pre-test genetic counseling documentation is required for coverage of non-invasive prenatal screening (NIPS). Pre-test genetic counseling should address the following components (ACMG, 2013):

- A brief explanation of the purpose of NIPS.
- Advantages of NIPS when compared to maternal serum analyte screening.
    - Based upon current data, detection rates appear to be higher.
    - There is a high negative predictive value for Down syndrome; this may be important to patients seeking to avoid the inherent risks of invasive testing.

    - NIPS has a lower false-positive rate; it necessitates fewer invasive procedures.
    - Risk assessment is less dependent on gestational age.
- Considerations for follow-up invasive testing if NIPS indicates an increased risk for aneuploidy.
- Limitations of NIPS.

Post-test genetic counseling for "screen-negative" results should involve a conversation regarding residual risk.

Post-test genetic counseling for "screen-positive" results should include the following components (ACMG, 2013):

- There is possibility of false-positive screening results for reasons such as confined placental mosaicism or theoretically a "vanishing twin."
- NIPS is not diagnostic; confirmatory testing (CVS or amniocentesis) is recommended, and risks of those procedures should be reviewed.
- If the patient declines invasive testing, effort should be made to obtain a sample of cord blood for postnatal confirmation by karyotype or cytogenomic microarray analysis.
- Accurate up-to-date and balanced information about Down syndrome (or other tested conditions) should be provided.

Post-test genetic counseling for a "screen-uninformative" results should include the offer of invasive diagnostic testing (ACMG, 2013).

If obstetric care providers are uncomfortable providing genetic counseling related to NIPS, referral to a certified genetics professional (such as a genetic counselor) is warranted.

Paramount considers cell-free DNA testing (81420) (e.g., MaterniT21®, Harmony®, Panorama®, InformaSeq®, VisibiliT™, QNatal Advanced™, Verifi™ Prenatal test, and Myriad Prequel™ Prenatal Screen) medically necessary as screening tools for trisomy 13 (Patau syndrome), or trisomy 18 (Edwards syndrome), or trisomy 21 (Down syndrome) in pregnant women with single gestations who are ≥10 weeks gestation who meet one of the following criteria:

- Maternal age of 35 years or older at delivery
- Fetal ultrasound findings indicating an increased risk of aneuploidy
- History of a prior pregnancy with a trisomy
- Positive test results for aneuploidy, including first trimester , sequential, or integrate screen, or a quadruple screen
- Parental balanced Robertsonian translocation with an increased risk of fetal trisomy 13 or trisomy 21

Cell-free DNA testing for any indication other than those listed above is non-covered, including, but not limited to, women with a current multiple gestation pregnancy.

Chromosomal microdeletion analysis and determining fetal sex using a cell-free DNA test is considered experimental/investigational, as it is not identified as widely used and generally accepted for the proposed use as reported in published nationally recognized peer-reviewed medical literature. Although using cell-free DNA testing to screen for fetal chromosomal microdeletions is considered experimental/investigational by Paramount Health Care, it is a covered benefit per Ohio Medicaid; therefore, CPT code 81422 may be covered for Advantage members with prior authorization.

NOTE: CPT code 88271 (Molecular cytogenetic testing, DNA probe, each) should not be billed for cell-free DNA testing.

CODING/BILLING INFORMATION

The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

CPT CODES	
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
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
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
0009M	Fetal aneuploidy (trisomy 21, and 18) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy

REVISION HISTORY EXPLANATION

ORIGINAL EFFECTIVE DATE: 02/01/2010

07/01/11: No changes

09/09/14: Removed deleted codes effective 12/31/13 S3625 & S3626. Changed name of policy from Prenatal Fetal Screening Services to Cell-Free DNA Tests For Fetal Aneuploidy. Deleted codes 76813, 76814, 82105, 82106, 82677, 84702, 84703, 84704, 84163, & 86336. Added code 81507. Policy reviewed and updated to reflect most current clinical evidence per Medical Policy Steering Committee.

12/17/15: Added effective 7/1/15 new code 0009M. Added code 81420. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

03/25/16: Codes 81507 and 0009M are now non-covered for all product lines per CMS and ODM guidelines. Policy reviewed and updated to reflect most current clinical evidence per TAWG.

08/26/16: Policy reviewed and updated to reflect most current clinical evidence per TAWG.

03/24/17: Added effective 01/01/17 new code 81422 as non-covered for HMO, PPO, Individual Marketplace, & Elite and covered for Advantage with prior authorization per ODM guidelines. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

12/15/17: Clarified criteria to state that physicians may perform genetic counseling and should bill evaluation and management codes. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

01/25/18: Added documentation requirements. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

07/09/2019: Policy reviewed and updated to reflect most current clinical evidence. Added required genetic counseling components to the policy. Eliminated requirement of 2nd trimester results to be reviewed.

09/10/2020: Updated the medical policy to indicate the coverage and prior authorization for procedures 81422 and 81507 for the Advantage product, per ODM guidelines. Removed procedure code 0009M, as this is a deleted code, as of 1/1/2020.

12/18/2020: Medical policy placed on the new Paramount Medical Policy Format

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services
Ohio Department of Medicaid
American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services
Industry Standard Review
Hayes, Inc.
The American College of Obstetricians and Gynecologists (ACOG) & Society for Maternal Fetal Medicine, Practice Bulletin Number 163, May 2016, Screening for Fetal Aneuploidy
European Journal of Human Genetics (EJHG), 2015, Policy: Non-Invasive Prenatal Testing for Aneuploidy and Beyond: Challenges of Responsible Innovation in Prenatal Screening
American College of Medical Genetics and Genomics (ACMG), ACMG Statement on Noninvasive Prenatal

Screening for Fetal Aneuploidy
Genetics Home Reference, National Institute of Health, U.S. National Library of Medicine, Down syndrome
Genetics Home Reference, National Institute of Health, U.S. National Library of Medicine, Trisomy 13
Genetics Home Reference, National Institute of Health, U.S. National Library of Medicine, Trisomy 18