Subject: Genetic Testing for Non-Invasive Prenatal Testing (NIPT)

Medical Policy #: 20.15 **Original Effective Date:** 07/01/2015

Status: Reviewed **Last Review Date:** 03-22-2023

Disclaimer

Refer to the member's specific benefit plan and Schedule of Benefits to determine coverage. This may not be a benefit on all plans or the plan may have broader or more limited benefits than those listed in this Medical Policy.

Description

Genetic testing is the use of specific assays to determine the genetic status of individuals already suspected to be at high risk for a particular inherited condition. High risk means that the individual has a known family history or classic symptoms of the disorder. Genetic testing includes a variety of techniques that test for genetic diseases and analyzes genetic risk factors that may contribute to disease. Techniques involve the examination of a blood sample, or other body fluid, or tissue to indicate the presence, absence, or alteration (mutation) of genes linked to specific diseases or conditions.

Non-invasive prenatal testing (NIPT) employs genetic sequencing technology to magnify fetal cell-free DNA (cfDNA) obtained from maternal bloodstream. Through a variety of techniques, fetal DNA is prenatally identified early in a singleton pregnancy, as early 10 weeks.

Screening is performed for the presence of fetal aneuploidy, specifically trisomy 13 (Patau Syndrome), trisomy 18 (Edwards Syndrome) and trisomy 21 (Down Syndrome). It is estimated that 6% to 11% of stillbirths and neonatal deaths result from aneuploidy. The tests cannot diagnose or exclude the possibility of other chromosomal disorders.

The use of NIPT is offered in all singleton pregnancies as an alternative to invasive procedures such as amniocentesis and chorionic villus sampling (CVS), and the potential risks of infection, bleeding, fetal injury and pregnancy termination.

NIPT can produce a no-call test result in 4-5% of cases due to lack of sufficient quantity of cell-free fetal DNA in the sample.

False- positive rate is less than 1%. Each NIPT assay is different with respect to its exact methodology and algorithms for data analysis.

Coverage Determination

Prior Authorization is required except for 81420. Please use the Prior Authorization/Benefit Certification Guide to determine when a prior authorization/benefit certification is required: https://ds.phs.org/preslogin/index.jsp

General Requirements:

1. Pregnant woman (regardless of maternal age or risk of chromosomal abnormality) with a singleton pregnancy that is greater than 10 weeks:
2. NIPT test can only be ordered by those who regularly manage pregnancy.
3. No documentation that a chromosomal abnormality screening test has been performed **in this** pregnancy to include:
    a. Sequential serum Part 1 screening, CPT code 81508;
    b. Sequential serum Part 2 screening, CPT 81511;
    c. Quadruple screen, CPT code 81511;
    d. Penta screen, CPT code 81512;
    e. Serum integrated, or contingent.
4. Individual must have the capacity to make fully informed decisions and consent for treatment.
5. Individual must receive genetic counseling from a certified genetic counselor or a qualified healthcare professional and the test is ordered by individual who regularly manage pregnancy.
6. When screening for aneuploidy, only one screening approach should be used. Analyte screening and cell-free

DNA screening should not be sent concurrently as this strategy is not cost-effective and simultaneous, seemingly discordant results can be more distressing to patients than screen positive analyte results followed by reassuring cell-free DNA screening. The use of cell-free DNA screening as follow-up will be reviewed on a case-by-case basis, for patients with a screen positive serum analyte screening test result is an option for patients who want to avoid a diagnostic test (i.e amniocentesis or chorionic villus sampling).

Limitations:

No more than two NIPT testing in a rolling 12-month period. If it is repeated there needs to be documentation this is a new pregnancy

Regulatory Status:

No Food and Drug Administration regulatory information for NIPT. Genetic tests are regulated under the Clinical Laboratory Improvement Amendments (CLIA) certifications.

Exclusions:

Presbyterian Health Plan considers NIPT for all other indications to be experimental or investigational, including multiple-gestation pregnancies and the detection of microdeletions.

PHP follows, MCG A-0848 - Use of cell-free DNA (cfDNA) screening for fetal chromosomal copy number variants (**microdeletions**), (CPT Code 81422) have not been validated clinically and are not currently recommended (which includes both singleton or multiple gestation pregnancies). See Investigative List & New Technology Assessment (Non-Covered Services), MPM 36.0.

Definitions

Aneuploidy: any deviation from an exact multiple of the haploid number of chromosomes

Triple Screen: Alpha-fetoprotein (AFP) + Human Chorionic Gonadotropin (hCG) + Estriol

Quadruple Screen: Alpha-fetoprotein (AFP) + Human Chorionic Gonadotropin (hCG) + Estriol + Inhibin-A, Penta' screen: (AFP, uE3, total hCG, hyperglycosylated hCG, DIA), CPT code 81512.

Coding

The coding listed in this medical policy is for reference only. Covered and non-covered codes are within this list.

Current Procedural Terminology (CPT) Codes

CPT	Description
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
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
0252U	Fetal aneuploidy short tandem–repeat comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplications, mosaicism, and segmental aneuploidy
0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplications, mosaicism, and segmental aneuploidy, per embryo tested
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. **Effective July 01, 2022**
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 aneuploidy.

	(Effective 10/1/2022)

Only <u>one</u> screening approach is considered medically necessary. **NOTE: The following congenital abnormalities tests may not be covered, if screening for aneuploidy (81420 & 81507) has been performed, it is not medically necessary to test for other chromosomal abnormality screening test for the <u>same</u> pregnancy.**	
81508	Fetal congenital abnormalities, biochemical assays of two proteins (PAPP-A, HCG [any form]), utilizing maternal serum, algorithm reported as a risk score
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)
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

Reviewed by / Approval Signatures

Clinical Quality & Utilization Mgmt. Committee: <u>Gray Clarke MD</u>
Senior Medical Director: <u>David Yu MD</u>
Date Approved: 03-22-2023
Reviewed by: Sahar Chavez, MD, Medical Director and OB specialist

References

1. ACOG, Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin No. 226. American College of Obstetricians and Gynecologists. VOL. 00, NO. 00, MONTH 2020. [Cited 01/17/2023]
2. Hayes, Cell-Free DNA (cfDNA) [Formerly NIPS, NIPT] Screening for Fetal Trisomy 21, 18, and 13 in Low-Risk Women with Singleton Pregnancy, Annual review Oct 17, 2022. [Cited 01/17/2023]
3. MCG, Noninvasive Prenatal Testing (Cell-Free Fetal DNA) - Microdeletion Syndromes, (A-0848), 26th Edition. Cited 01/17/2023]

Publication History

07/01/2015	Original effective date
01/01/2016	Update
01/24/2018	Annual review. No change
03/27/2019	Annual review. Update CPT and ICD-10 codes also added additional information for fetal ultrasound findings on increased risk of fetal aneuploidy from article on Sonographic findings associated with fetal aneuploidy from UpToDate.
06/24/2019	Update to include the use of cell-free DNA technology for single gene disorder testing is not covered.
10/16/2019	Correction on effective date, should be 07/01/2015 not 05/22/2006.
07/22/2020	Annual review. Reviewed by PHP Medical Policy Committee on July 01, 2020. No change to criteria but stated genetic testing for Microdeletion (CPT-81422) is not covered per recommendation by MCG A-0848 and ACOG. Continue prior authorization for CPT codes 81420 and 81507. Title changed to add "Genetic Testing."
03/24/2021	Annual review. Reviewed by PHP Medical Policy Committee. Coverage for all singleton pregnancies after 10 weeks gestational age. CPT codes 81420 and 81507 continue PA. The policy has been updated with limitation language, that no more than two NIPT testing in a rolling 12-month period will be paid. When screening for aneuploidy (81420/81507), only one screening approach should be used no other chromosomal abnormality screening test (81508, 81511 & 81512) should be performed in the same pregnancy and NIPT test can only be ordered by those who regularly manage pregnancy. CPT code (81422) will be set as investigational, per ACOG and MCG.
06/29/2021	Language update only to say, "*a case-by-case*" review for when cell-free DNA screening is done as a follow-up for patients with a screen positive serum, (see #6) section.
03-23-2022	Annual review. Reviewed by PHP Medical Policy Committee on 03-02-2022. No change. Continue to use the homegrown policy. Continue requiring PA for NIPT codes 81420 and 81507 and for screening code 81512. Microdeletions with ctDNA (code 81422) will be removed from the PA grid; the test is considered investigational and will be listed in the Investigative List (non-Covered Services), MPM 36.0. Updated CPT codes only on 05-25-2022. The annual review date will remain as 03-23-2022. Reviewed by PHP Medical Policy Committee on 04-13-2022 for CPT code update only. Moved the fetal aneuploidy codes from

	Genetic and Genomic Testing, MPM 7.1 to this policy: 0252U and 0254U. New CPT code (0327U) announced by American Medical Association, Proprietary Laboratory Analyses (PLA) to be effective July 01, 2022. All three codes 0252U, 0254U and 0327U will be added to require PA. Update only on 09-28-2022. Annual review date will remain as 03-23-2022. Reviewed by PHP Medical Policy Committee on 08/24/2022, code 81420 will not require PA for all LOB, effective 10-01-2022. Update 01-25-2023: Committee approved on 11-11-22 to add code 0341U to policy and to also require PA.
03-22-2023	Annual review. Reviewed by PHP Medical Policy Committee on 01/18/2023. Language was added to include "regardless of maternal age or risk of chromosomal abnormality" and the overall criteria remains unchanged. Code 81420 will continue no PA requirement.

This Medical Policy is intended to represent clinical guidelines describing medical appropriateness and is developed to assist Presbyterian Health Plan and Presbyterian Insurance Company, Inc. (Presbyterian) Health Services staff and Presbyterian medical directors in determination of coverage. The Medical Policy is not a treatment guide and should not be used as such.

For those instances where a member does not meet the criteria described in these guidelines, additional information supporting medical necessity is welcome and may be utilized by the medical director in reviewing the case. Please note that all Presbyterian Medical Policies are available online at: ***Click here for Medical Policies***

Web links:

At any time during your visit to this policy and find the source material web links has been updated, retired or superseded, PHP is not responsible for the continued viability of websites listed in this policy.

When PHP follows a particular guideline such as LCDs, NCDs, MCG, NCCN etc., for the purposes of determining coverage; it is expected providers maintain or have access to appropriate documentation when requested to support coverage. See the References section to view the source materials used to develop this resource document.