**03-59000-18**

**Original Effective Date: 03/15/13**

**Reviewed: 09/27/18**

**Revised: 10/15/18**

# Subject: Noninvasive Prenatal Screening for Fetal Aneuploidies and Microdeletions Using Cell-Free Fetal DNA





## DESCRIPTION:

National guidelines recommend that all pregnant women be offered screening for fetal chromosomal abnormalities, most of which are aneuploidies, an abnormal number of chromosomes. Trisomy syndromes are aneuploidies involving 3 copies of 1 chromosome. Trisomies 21 (T21), 18 (T18), and 13 (T13) are the most common forms of fetal aneuploidy. Fetuses with T18 and T13 generally do not survive to birth. There are numerous limitations to standard screening for these disorders using maternal serum and fetal ultrasound. Noninvasive prenatal screening (NIPS) analyzing cell-free fetal DNA in maternal serum is a potential complement or alternative to conventional serum screening. NIPS using cell-free fetal DNA has also been proposed to screen for microdeletions.

The technology for noninvasive, sequencing-based testing of maternal serum for fetal trisomy syndromes involves detection of cell-free fetal DNA fragments present in the plasma of pregnant women. As early as 8 to 10 weeks of gestation, these fetal DNA fragments comprise 6% to 10% or more of the total cell-free fetal DNA in a maternal plasma sample. The tests are unable to provide a result if the fetal fraction is too low (ie, <4%). Fetal fraction can be affected by maternal and fetal characteristics.

Microdeletions are chromosomal deletions that are too small to be detected by microscopy or conventional cytogenetic methods. Microdeletions are collectively known as copy number variants (CNVs). CNVs can lead to disease when the change in copy number of a dose-sensitive gene or genes disrupts the ability of the gene(s) to function and affects the amount of protein produced. Accurate

estimates of the prevalence of microdeletion syndromes during pregnancy or at birth are not available. The risk of a fetus with a microdeletion syndrome is independent of maternal age. Currently routine prenatal screening for microdeletion syndromes is not recommended by national organizations.

## POSITION STATEMENT:

**NOTE:** Coverage for genetic testing, screening, and counseling are applicable only under those contracts that include benefits for genetic testing, preventive health services, screening services, and medical counseling.

Nucleic acid sequencing-based testing of maternal plasma to screen for trisomy 21, 18, 13 **meets the definition of medical necessity** in women with singleton pregnancies.

Nucleic acid sequencing-based testing of maternal plasma for trisomy 13 and/or 18, other than in the situations specified above, is considered **experimental or investigational**. There is insufficient clinical evidence to permit conclusions on net health outcomes.

Nucleic acid sequencing–based testing of maternal plasma for trisomy 21 is considered **experimental or investigational** in women with twin or multiple pregnancies. The evidence is insufficient to determine the effects of the technology on health outcomes.

Nucleic acid sequencing-based testing of maternal plasma is considered **experimental or investigational** for the following indications:

- fetal sex chromosome aneuploidies
- microdeletions.

The evidence is insufficient to determine the effects of the technology on health outcomes.

## BILLING/CODING INFORMATION:

### CPT Coding:

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| 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 **(Investigational)** |
| 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 (Harmony™ Prenatal Test) |

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| 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 (VisibiliT™ Test) |
| 0060U | Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood (**Investigational**) |

CPT Code 88271 and unlisted codes 81599 and 81479 may also be used to report nucleic acid sequencing–based tests.

## ICD-10 Diagnosis Codes That Support Medical Necessity:

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| O09.511 | Supervision of elderly primigravida, first trimester |
| Z31.430-Z31.438 | Encounter for genetic testing of female for procreative management |
| Z36.0-Z36.9 | Encounter for antenatal screening of mother |

## REIMBURSEMENT INFORMATION:

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Advantage Products:**

No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline reviewed date

## DEFINITIONS:

No guideline specific definitions apply.

## RELATED GUIDELINES:

**Genetic Testing, 05-82000-28**

## OTHER:

Other names used to describe nucleic acid sequencing-based testing of maternal plasma:

**Note:** The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Harmony™ (tests for T21, T18, and T13)
InformaSeq℠ (tests for T21, T18, and T13 with optional testing for select sex chromosome abnormalities)
MaterniT21™ PLUS (test includes T21, T18, T13, fetal sex aneuploidies, & 7 microdeletions)
Panorama™ (test includes T21, T18, and T13; extended panel includes microdeletions)
QNatal™ (tests for T21, T18, and T13)
Verifi® tests for T21, T18, and T13)
VisibiliT™ (tests for T21 & T18)

## REFERENCES:


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5. ClinicalTrials.gov, Development of Non-invasive Prenatal Diagnostic Test for Microdeletion/Microduplication and Other Genetic Disorders Based on Fetal DNA Isolated From Maternal Blood, sponsored by Natera, Inc; accessed 08/10/18.
6. ClinicalTrials.gov, Development of Non-invasive Prenatal Diagnostic Test for Multiple Gestation Pregnancies Based on Fetal DNA Isolated From Maternal Blood, sponsored by Natera, Inc.; accessed 08/10/18.
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12. National Society of Genetic Counselors (NSGC), Noninvasive prenatal testing/ noninvasive prenatal diagnosis (NIPT/NIPD), accessed at nsgc.org 01/14/13.

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14. Society for Maternal-Fetal Medicine (SMFM) Publications Committee. SMFM Statement: clarification of recommendations regarding cell-free DNA aneuploidy screening. Am J Obstet Gynecol. Dec 2015;213(6):753-754.
15. Taylor-Phillips S, Freeman K, Geppert J, et al. Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis. BMJ Open. 2016;6(1):e010002.

## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy & Coverage Committee on 09/27/18.

## GUIDELINE UPDATE INFORMATION:

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| 03/15/13 | New Medical Coverage Guideline. |
| 07/01/13 | Quarterly HCPCS updates. Added code 0005M. Revised Program Exception section. |
| 10/15/13 | Revision; position statements and guideline title updated; formatting changes. |
| 01/01/14 | Annual HCPCS update. Added code 81507; deleted code 0005M. |
| 03/15/14 | Annual review; position statements maintained and references updated. |
| 01/01/15 | Annual HCPCS/CPT update. Added code 81420. |
| 04/15/15 | Annual review; position statements and references updated; formatting changes. |
| 09/15/15 | Revision; update position statement and references; formatting changes. |
| 11/15/15 | Revision; coding section updated. |
| 12/15/16 | Revision; title, description, position statements, and references updated; formatting changes. |
| 01/01/17 | Annual CPT/HCPCS update. Added 81422. |
| 07/01/18 | Quarterly CPT/HCPCS update. Added code 0060U. |

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| 08/01/18 | Revision; ICD10 codes added. |
| 10/15/18 | Revision; coverage statement, description, coding, and references updated. |