Blue Cross and Blue Shield of Minnesota medical policies do not imply that members should not receive specific services based on the recommendation of their provider. These policies govern coverage and not clinical practice. Providers are responsible for medical advice and treatment of patients. Members with specific health care needs should consult an appropriate health care professional.

**TESTING OF FETAL NUCLEIC ACIDS IN MATERNAL BLOOD FOR DETECTION OF FETAL ANEUPLOIDY**

*Description:* Current guidelines from the American College of Obstetricians and Gynecologists (ACOG) recommend that all pregnant women be offered screening for trisomy 21, 18, and 13 before 20 weeks of gestation, regardless of age. Standard screening tests given vary according to the needs of a particular patient after consultation with her provider. Tests may include fetal ultrasound biomarkers and/or serum biomarker testing. The most common ultrasound marker is nuchal translucency (NT). Other markers of trisomy that may be found on ultrasound include but are not limited to nasal bone abnormalities, tricuspid regurgitation and abnormal ductus venosus flow. The triple screen includes alpha-fetoprotein, human chorionic gonadotropin and unconjugated estriol. The quadruple screen includes the triple screen plus inhibin-A. Combined tests include NT with serum biomarkers to compute a pregnancy-specific risk for trisomy 21 (Down syndrome). If findings of screening tests confer a high level of suspicion for fetal trisomy, confirmation may be obtained by chorionic villus sampling (CVS) or amniocentesis. Both of these procedures are invasive and carry a risk of miscarriage.

Due to the invasive nature of these confirmatory tests, noninvasive tests that analyze fetal-specific DNA sequences in maternal plasma to detect fetal aneuploidy have been developed. These tests, which may be referred to as noninvasive prenatal testing (NIPT), use next generation DNA sequencing to identify increased representation of chromosomes 13, 18 and 21 in maternal blood. A greater proportion of sequence fragments from these chromosomes have been found in maternal blood of fetuses with aneuploidy. At the present time, the technology is such that while it may help to stratify pregnancies at risk for fetal trisomy, invasive amniocentesis or CVS is still required to confirm the findings.

Commercially available assays of fetal nucleic acid in maternal blood
include but are not limited to the following:

- Harmony™ Prenatal Test (Ariosa Diagnostics, Inc.)
- MaterniT21™ and MaterniT21™Plus (Sequenom Laboratories)
- Panorama™ Prenatal Test (Natera™)
- verifi® (Illumina; formerly Verinata Health)

These tests are regulated under the Clinical Laboratory Improvement Amendments (CLIA). Premarket approval by the U.S. Food and Drug Administration (FDA) is not required when the assay is performed in a laboratory that is licensed CLIA for high-complexity testing.

Definitions:

- **Aneuploidy**: an abnormal number of chromosomes in the cell. Except for red blood cells and the sperm and egg cells, every cell in the human body has 23 pairs of chromosomes (for a total of 46).

- **Translocation**: a translocation occurs when a segment of genetic material from one chromosome becomes linked to another chromosome:
  - A balanced translocation results in no excess or deficit in genetic material and causes no health difficulties.
  - An unbalanced translocation occurs when a child inherits a chromosome with an excess or deficit of genetic material from a parent with a balanced translocation.
  - Robertsonian translocations can occur in the five acrocentric chromosome pairs (numbers 13, 14, 15, 21, and 22). These are the chromosomes that have the centromere near the end, resulting in one chromosomal arm being much longer than the other. If a Robertsonian translocation occurs in one of these chromosomes, the chromosome breaks at the centromere and the long arms fuse to form a single chromosome with a single centromere. The short arms may also form a reciprocal product that usually contains nonessential genes and are usually lost within a few cell divisions. The child of someone with a balanced Robertsonian translocation may either be normal (carrying the fusion chromosome) or they may inherit an acrocentric chromosome with a missing or extra long arm. This results in multiple malformations including trisomy 13 (Patau syndrome) and trisomy 21 (Down syndrome).

- **Trisomy**: three copies of a chromosome are present instead of the usual pairs. Syndromes associated with trisomies include:
  - Down syndrome is caused by a trisomy of chromosome 21. Down syndrome is the most common single cause of birth defects, occurring in 1 in 800 live births. Down syndrome is associated with a variety of clinical abnormalities including mild-to-moderate mental retardation, cardiac defects, thyroid problems, seizures, hearing loss, and duodenal atresia (absence or closure of the first section of the small intestine).
  - Edwards syndrome is caused by a trisomy of chromosome 18, which causes major physical abnormalities and severe mental
retardation. Trisomy 18 occurs in approximately one in 5,000 live births.

- Patau syndrome is caused by a trisomy of chromosome 13. Trisomy 13 occurs in approximately one in 10,000 live births and causes neurological, heart and kidney defects.

**Policy:**

I. Testing of cell-free fetal nucleic acids in maternal blood may be considered **MEDICALLY NECESSARY** in pregnant women when **ALL** of the following criteria are met:

A. **Singleton pregnancy:**
   
   **AND**
   
   B. Member is at high risk of carrying a child with trisomy 13, 18, or 21 defined as one or more of the following:
      
      1. Maternal age 35 years or older at delivery
      2. History of prior pregnancy with a trisomy
      3. Parental balanced Robertsonian translocation with increased risk of fetal trisomy 13 or trisomy 21
      4. Fetal ultrasonographic findings indicating an increased risk of aneuploidy (e.g., nuchal translucency)
      5. Positive test results for aneuploidy (e.g., first trimester, sequential, or integrated screen, or a quadruple screen)

II. Testing of cell-free fetal nucleic acids in maternal blood is considered **INVESTIGATIVE** for all other indications including but not limited to:

A. Testing in women with one or more of the following:
   
   1. At average risk of carrying a child with Down syndrome or other trisomy; or
   2. Under age 35 at delivery; or
   3. With twin, triplet, or higher order pregnancy.

B. As part of a routine prenatal laboratory assessment

C. Testing for any indication other than trisomy 13, trisomy 18, or trisomy 21

**Coverage:**

Blue Cross and Blue Shield of Minnesota medical policies apply generally to all Blue Cross and Blue Plus plans and products. Benefit plans vary in coverage and some plans may not provide coverage for certain services addressed in the medical policies.

Medicaid products and some self-insured plans may have additional policies and prior authorization requirements. Receipt of benefits is subject to all terms and conditions of the member’s summary plan description (SPD). As applicable, review the provisions relating to a specific coverage determination, including exclusions and limitations. Blue Cross reserves the right to revise, update and/or add to its medical policies at any time without notice.

For Medicare NCD and/or Medicare LCD, please consult CMS or National Government Services websites.
Refer to the Pre-Certification/Pre-Authorization section of the Medical Behavioral Health Policy Manual for the full list of services, procedures, prescription drugs, and medical devices that require Pre-certification/Pre-Authorization. Note that services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial of claims may result if criteria are not met.

**Coding:**

The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

**CPT:**

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

**Deleted Code:** 0005M

**Policy History:**

Developed September 12, 2012

Most recent history:
Revised, September 11, 2013
Reviewed/Updated, no policy statement changes Sept. 10, 2014

**Cross Reference:**

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