CLINICAL MEDICAL POLICY and PRIOR-AUTHORIZATION POLICY	
Policy Name:	Fetal Aneuploidy Testing Using Noninvasive Cell-Free Fetal DNA
Policy Number:	MP-003-MD-PA
Approved By:	Medical Management
Provider Notice Date:	5/3/16
Original Effective Date:	7/5/16
Annual Approval Date:	NA
Revision Date:	NA
Products:	Pennsylvania Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 5

Disclaimer

Gateway Health℠ (Gateway) medical payment and prior-authorization policy is intended to serve only as a general reference resource regarding payment and coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT:

Gateway Health Plan® provides coverage for laboratory benefit under the medical benefits of the Company's Medicaid products for medically necessary, noninvasive, circulating cell-free DNA prenatal testing of fetal aneuploidy as screening tools for trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) or trisomy 13 (Patau syndrome). Circulating cell free fetal DNA crosses the placenta and can be isolated in maternal plasma.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrants individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Commonwealth of Pennsylvania (PA) Department of Human Services (DHS) and all applicable state and federal regulations.

(Current applicable PA HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

DEFINITIONS:

Prior Authorization Review Panel (PARP) — A panel of representatives from within the PA Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

PROCEDURES

1) The following tests are commercially available:
   a) Harmony™ Prenatal Test
   b) MaterniT21™ Plus
   c) verifi® Prenatal Test
   d) Panorama
   e) informaSeq℠
2) These tests are considered eligible as advanced screening technology for pregnant women at high risk, as determined by the following medical necessity:
   a) Advanced maternal age (pregnant women age 35 years and older at expected time of delivery); and
   b) Testing is offered between 9 and 13 weeks gestational age in women with singleton gestation; or
   c) Fetal ultrasonography findings predictive of increased risk of fetal aneuploidy (i.e., absent or hypoplastic nasal bone, choroid plexus cyst, echogenic bowel, echogenic intracardiac focus, fetal pyelectasis, nuchal translucency, nuchal fold, ventriculomegaly, and shortened femur or humerus); or
   d) Positive screening test for an aneuploidy, including first trimester, sequential, or integrated screen, or a positive quadruple screen; or
   e) History of a prior maternal pregnancy with an aneuploidy; or
   f) Parental balanced Robertsonian translocation with increased risk for fetal trisomy 13 or trisomy 21.
   g) Use of noninvasive prenatal testing using the cell free DNA test for trisomies 21, 18 and 13 is to be used in pregnant women at increased risk in lieu of amniocentesis.
   h) Use of noninvasive prenatal testing using the cell free DNA test for the determination of fetal sex, fetal RHD genotyping is typically not medically necessary and will require case-by-case review.
   i) Women with positive cfDNA tests should be offered invasive prenatal diagnostic tests with amniocentesis or chorionic villus sampling.
   j) Genetic counseling is strongly recommended prior to this test in order to inform persons being tested about the advantages and limitations of the test as applied to a unique person.
3) Services for DNA-based noninvasive tests of fetal aneuploidy in pregnant women who do not meet the above criteria or women are pregnant with multiple gestations are unproven and will require case-by case review.

4) Post-payment Audit Statement
   a) The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway Health Plan® at any time pursuant to the terms of your provider agreement.

5) Place of Service for testing to be administered is outpatient.

6) Governing Bodies Approval
   a) The cell free DNA tests are laboratory developed tests that do not require premarket approval by the FDA. These types of tests are regulated by the Centers for Medicare & Medicaid as part of the Clinical Laboratory Improvement Amendments of 1988 (CLIA). The regulations of the CLIA Amendments do not include validation of specific tests but rather that there is procedural compliance.

b) Additional information is available online at:
   i) http://fda.gov/Medical Devices/DeviceRegulationsand Guidance/IVRegulatoryAssistance/ucm124105.htm.

AUTHORIZATION and CODING REQUIREMENTS:
Prior authorization is required for Maternal Genetic Testing performed as an outpatient.

REIMBURSEMENT
Participating providers will be reimbursed per their Gateway Health Plan® contract.

PROCEDURE AND DIAGNOSIS CODES
Procedure Codes

81420	81507

Diagnosis Codes

O09.511	O09.512	O09.513	O09.519	O09.52	O09.521
O09.522	O09.523	O09.529	O28.0	O28.1	O28.2
O28.3	O28.4	O28.5	O28.8	O28.9	
Z13.79	Z31.438				

Summary of Literature

In 2015, the American College of Obstetricians and Gynecologists (ACOG) reported that noninvasive prenatal testing using cell free fetal DNA from the plasma of pregnant women is an important screening tool for fetal aneuploidy. In addition, this society identified the following indications as appropriate for cell free DNA: maternal age 35 years or older at time of delivery; fetal ultra-sonographic findings predicting increased risk of fetal aneuploidy; history of prior pregnancy with aneuploidy; positive screening test for aneuploidy, including first trimester, sequential, or integrated screen, or a positive quadruple scree; parental balanced Robertsonian translocation with increased risk for fetal trisomy 13 or trisomy 21.

ACOG commented that cell free DNA testing should not be offered to low risk women, or women with multiple gestations or be part of routine prenatal laboratory testing because the test has not been evaluated in these groups.

In a nested case-controlled study, Bianchi et al (2012), reported on the use of massively parallel DNA sequencing to detect fetal aneuploidy with 2,882 high risk women. The study is termed the 'Maternal Blood is Source to Accurately' to diagnose fetal aneuploidy (MELISSA). These women were scheduled for amniocentesis or chorionic villus sampling at 60 different sites in the United States. The authors reported that 89 of 89 trisomy 18 cases were correctly identified (sensitivity 100%, 95% confidence interval 95.9 to 100), 35 of the 36 trisomy 18 were classified correctly, as were 11 of the 14 trisomy 13 cases and 15 of the 16 monosomy X cases. There were no false positive results for autosomal aneuploidies. However, it was noted that this was a nested case control study and did not represent true population prevalence. Further studies that included larger number of unaffected controls were recommended.

The Society for Maternal Fetal Medicine (2015) was found to state that the cell free DNA screening is largely recommended in patients at higher risk for aneuploidy and not the lower risk populations since there is limited studies on this population. The Society for Maternal Fetal Medicine (SMFM) does not consider cell free DNA screening as first line screening and that conventional seeing methods should be utilized in this group.

In the analysis performed by Norton and colleagues (2013), it was stated that the use of the cell free DNA in maternal plasma represents a tremendous advance in prenatal diagnosis. In this analysis it was noted that true cost-utility analysis is necessary to determine the actual clinical effectiveness of this screening in the general prenatal population.

Palomaki et al. (2011) noted that measurement of circulating cell-free DNA in maternal plasma resulted in a Down syndrome detection rate was 98.6% (209/212), the false-positive rate was 0.20% (3/1471), and the testing failed in 13 pregnancies (0.8%); all were euploid. Before unblinding, the primary testing laboratory also reported multiple alternative interpretations. Adjusting chromosome 21 counts for guanine cytosine base content had the largest impact on improving performance.

Langlois and colleagues (2013) provided an analysis of published studies on the use of cell free DNA in maternal plasma for the noninvasive diagnosis of Down syndrome, trisomy 18 and trisomy 13. They report that this testing should be an option available to women at increased risk in lieu of amniocentesis. Use of cell free fetal DNA testing in average risk pregnancies is not supported as a replacement for the current maternal screening approach using biochemical serum markers with or without fetal nuchal translucency ultrasound.

Norton et al. (2015) published a large study evaluating cell free DBA testing in a general population sample. The study included adult women with a singleton pregnancy undergoing routine first-trimester aneuploidy screening between 10.0 and 14.3 weeks of gestation. The patients underwent cell free DNA testing and standard screening with maternal serum markers and nuchal translucency. In addition, the authors conducted a preplanned sub-analysis in 'low risk' women defined as women younger than 35 years of age, and women who had a risk of T21 of less than 1 in 270 on standard screening.

There were a total of 15,841 participants and chromosomal anomalies were identified in 68 cases. There were 83 with T21, 10 with T18, 6 with T13 and the remainder of cases had less common aneuploidies. The Area Under the Curve (AUC) for T21 was 0.999 for cell free DNA testing and 0.958 for standard screening ($p = 0.001$).

In the sub-analysis of the low risk women, it was reported that cell free DNA testing correctly identified 19 cases of T21, with six false positives. When low risk was defined as a risk less than 1 in 270 on standard screening, cell free DNA testing identified all eight cases of T21 with six false positives.

Policy Sources

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