MEDICAL POLICY

POLICY TITLE	NONINVASIVE PRENATAL SCREENING FOR FETAL ANEUPLOIDIES AND MICRODELETIONS USING CELL-FREE FETAL DNA
POLICY NUMBER	MP-2.256

Original Issue Date (Created):	**12/1/2013**
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I. POLICY

Nucleic acid sequencing-based testing of maternal plasma for trisomy 21, 18, and 13 may be considered **medically necessary** in women with singleton pregnancies.

Nucleic acid sequencing-based testing of maternal plasma for trisomy 21 is considered **investigational** in women with twin or multiple pregnancies. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure. Nucleic acid sequencing-based testing of maternal plasma for trisomy 13 and/or 18, other than in the situations specified above, is considered **investigational**. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Nucleic acid sequencing-based testing of maternal plasma for microdeletions is considered **investigational**. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Nucleic acid sequencing-based testing of maternal plasma for fetal sex chromosome aneuploidies is considered **investigational**. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Policy Guidelines

Karyotyping would be necessary to exclude the possibility of a false-positive, nucleic acid sequencing-based test. Before testing, women should be counseled about the risk of a false-positive test. In Committee Opinion No. 640, the American College of Obstetricians and Gynecologists (2015) recommended that all patients receive information on the risks and benefits of various methods of prenatal screening and diagnostic testing for fetal aneuploidies, including the option of no testing.

Studies published to date on noninvasive prenatal screening for fetal aneuploidies have reported rare but occasional false-positives. False-positive findings have been found to be associated with

factors including placental mosaicism, vanishing twins, and maternal malignancies. Diagnostic testing is necessary to confirm positive cell-free fetal DNA tests, and management decisions should not be based solely on the results of cell-free fetal DNA testing. The American College of Obstetricians and Gynecologists further recommended that patients with indeterminate or uninterpretable (i.e., "no call") cell-free fetal DNA test results be referred for genetic counseling and offered ultrasound evaluation and diagnostic testing because "no call" findings have been associated with an increased risk of aneuploidy.

Cell-free fetal DNA screening does not assess risk of neural tube defects. Patients should continue to be offered ultrasound or maternal serum -fetoprotein screening.

Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the HUman Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, and the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Diseased-Assoc.Variant	Disease-associated change in the DNA sequence.
	Variant	Change in DNA sequence
	Familial Variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives.

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely Pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease

Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

American College of Medical Genetics and Genomics; AMP: Association of Molecular Pathology.

Genetic Counseling
Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual's family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Cross-*reference:*
MP-2.242 Genetic Testing for Developmental Delay-Intellectual Disability, Autism Spectrum Disorder, and Congenital Anomalies
MP-2.258 Carrier Screening for Genetic Diseases
MP-2.278 Invasive Prenatal (Fetal) Diagnostic Testing

II. PRODUCT VARIATIONS TOP

This policy is only applicable to certain programs and products administered by Capital BlueCross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO-Refer to FEP Medical Policy Manual MP-4.01.21, Non-Invasive Prenatal Screening for Fetal Aneuploidies and Microdeletions Using Cell-Free Fetal DNA. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

III. DESCRIPTION/BACKGROUND TOP

FETAL ANEUPLOIDY
Fetal chromosomal abnormalities occur in approximately 1 in 160 live births. Most fetal chromosomal abnormalities are aneuploidies, defined as an abnormal number of chromosomes. The trisomy syndromes are aneuploidies involving 3 copies of 1 chromosome. The most important risk factor for trisomy syndromes is maternal age. The approximate risk of a trisomy

21 (T21; Down syndrome) –affected birth is 1 in 1100 at age 25 to 29. The risk of a fetus with T21 (at 16 weeks of gestation) is about 1 in 250 at age 35 and 1 in 75 at age 40.[1]

T21 is the most common chromosomal aneuploidy and provides the impetus for current maternal serum screening programs. Other trisomy syndromes include T18 (Edwards syndrome) and T13 (Patau syndrome), which are the next most common forms of fetal aneuploidy, although the percentage of cases surviving to birth is low and survival beyond birth is limited. The prevalence of these other aneuploidies is much lower than the prevalence of T21, and identifying them is not currently the main intent of prenatal screening programs. Also, the clinical implications of identifying T18 and 1T3 are unclear, because survival beyond birth is limited for both conditions.

Fetal Aneuploidy Screening

Standard aneuploidy screening involves combinations of maternal serum markers and fetal ultrasound done at various stages of pregnancy. The detection rate for various combinations of noninvasive testing ranges from 60% to 96% when the false-positive rate is set at 5%. When tests indicate a high risk of a trisomy syndrome, direct karyotyping of fetal tissue obtained by amniocentesis or chorionic villous sampling (CVS) is required to confirm that T21 or another trisomy is present. Both amniocentesis and CVS are invasive procedures and have procedure-associated risks of fetal injury, fetal loss, and infection. A new screening strategy that reduces unnecessary amniocentesis and CVS procedures or increases detection of T21, T18, and T13 could improve outcomes. Confirmation of positive noninvasive screening tests with amniocentesis or CVS is recommended; with more accurate tests, fewer women would receive positive screening results.

Commercial, noninvasive, sequencing-based testing of maternal serum for fetal trisomy syndromes is now available. The test technology 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 (i.e., <4%). Fetal fraction can be affected by maternal and fetal characteristics. For example, fetal fraction was found to be lower at higher maternal weights and higher with increasing fetal crown-rump length.

Cell-Free Fetal DNA Analysis Methods

Sequencing-based tests use one of two general approaches to analyzing cell-free fetal DNA. The first category of tests uses quantitative or counting methods. The most widely used technique to date uses massively parallel sequencing (MPS; also known as next-generation sequencing). DNA fragments are amplified by polymerase chain reaction; during the sequencing process, the amplified fragments are spatially segregated and sequenced simultaneously in a massively parallel fashion. Sequenced fragments can be mapped to the reference human genome to obtain numbers of fragment counts per chromosome. The sequencing-derived percent of fragments

from the chromosome of interest reflects the chromosomal representation of the maternal and fetal DNA fragments in the original maternal plasma sample. Another technique is direct DNA analysis, which analyzes specific cell-free fetal DNA fragments across samples and requires approximately a tenth the number of cell-free DNA fragments as MPS. The digital analysis of selected regions (DANSR™) is an assay that uses direct DNA analysis.

The second general approach is single-nucleotide variant–based methods. They use targeted amplification and analysis of approximately 20,000 single-nucleotide variants on selected chromosomes (e.g., 21, 18, 13) in a single reaction. A statistical algorithm is used to determine the number of each type of chromosome. At least some of the commercially available cell-free fetal DNA prenatal tests also test for other abnormalities including sex chromosome abnormalities and selected microdeletions.

COPY NUMBER VARIANTS AND CLINICAL DISORDERS

Microdeletions (also known as submicroscopic deletions) are chromosomal deletions that are too small to be detected by microscopy or conventional cytogenetic methods. They can be as small as 1 and 3 megabases (Mb) long. Along with microduplications, 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. A number of genomic disorders associated with microdeletion have been identified, which may be associated with serious clinical features, such as cardiac anomalies, immune deficiency, palatal defects, and developmental delay as in DiGeorge syndrome. Some of the syndromes (e.g., DiGeorge) have complete penetrance yet marked variability in clinical expressivity. A contributing factor is that the breakpoints of the microdeletions may vary, and there may be a correlation between the number of haplo-insufficient genes and phenotypic severity.

A proportion of microdeletions are inherited and some are de novo. 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. There are few population-based data and most studies published to date have based estimates on phenotypic presentation. The 22q11.2 (DiGeorge) microdeletion is the most common associated with a clinical syndrome. According to the GeneTests database, current estimates of prevalence range from 1 in 4000 to 1 in 6395 live births.[3] Prevalence estimates for other microdeletions are between 1 in 5000 and 1 in 10,000 live births for 1p36 deletion syndrome, between 1 in 10,000 and 1 in 30,000 for Prader-Willi syndrome, and between 1 in 12,000 and 1 in 24,000 for Angelman syndrome. The above figures likely underestimate the prevalence of these microdeletion syndromes in the prenatal population because the population of variant carriers includes phenotypically normal or very mildly affected individuals.

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Table 1. Recurrent Microdeletion Syndromes

Syndrome	Location	Estimated Prevalence
DiGeorge	22q11.2	1/2000
1p36 deletion	1p36-	1/5000
Prader-Willi and Angelman	Del 15q11.2	1/20,000
Wolf-Hirschhorn	4p-	1/50,000 to 1/20,000
Cri du chat	5p-	1/50,000
Miller-Dieker	Del 17p13.3	1/100,000

Adapted from Chitty et al (2018).[2]

Routine prenatal screening for microdeletion syndromes is not recommended by national organizations. Current practice is to offer invasive prenatal diagnostic testing in select cases to women when a prenatal ultrasound indicates anomalies (e.g., heart defects, cleft palate) that could be associated with a particular microdeletion syndrome. Samples are analyzed using fluorescence in situ hybridization, chromosomal microarray analysis, or karyotyping. Additionally, families at risk (e.g., those known to have the deletion or with a previously affected child) generally receive genetic counseling and those who conceive naturally may choose prenatal diagnostic testing. Most affected individuals, though, are identified postnatally based on clinical presentation and may be confirmed by genetic testing. Using 22q11.2 deletion syndrome as an example, although clinical characteristics vary, palatal abnormalities (e.g., cleft palate) occur in approximately 69% of individuals, congenital heart disease in 74%, and characteristic facial features are present in a majority of individuals of northern European heritage.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Act for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of noninvasive prenatal screening tests using cell-free fetal DNA. Commercially available tests include but are not limited to the following:

- VisibiliT™ (Sequenom Laboratories, now LabCorp) tests for T21 and T18, and tests for sex.
- MaterniT21™ PLUS (Sequenom Laboratories) core test includes T21, T18, and T13 and fetal sex aneuploidies. The enhanced sequencing series includes testing for T16 and T22 and 7 microdeletions: 22q deletion syndrome (DiGeorge syndrome), 5p (cri du chat syndrome), 15q (Prader-Willi and Angelman syndromes), 1p36 deletion syndrome, 4p (Wolf-Hirschhorn syndrome), 8q (Langer-Giedion syndrome), and 11q (Jacobsen syndrome). The test uses MPS and reports results as positive or negative. The enhanced sequencing series is offered on an opt-out basis.

- Harmony™ (Ariosa Diagnostics, now Roche) tests for T21, T18, and T13. The test uses directed DNA analysis and results are reported as a risk score.
- Panorama™ (Natera) is a prenatal test for detecting T21, T18, and T13, as well as select sex chromosome abnormalities. It uses single-nucleotide variant technology; results are reported as a risk score. An extended panel tests for 5 microdeletions: 22q deletion syndrome (DiGeorge syndrome), 5p (cri du chat syndrome), 15q11-13 (Prader-Willi and Angelman syndromes), and 1p36 deletion syndrome. Screening for 22q11.2 will be included in the panel unless the opt-out option is selected; screening for the remaining 4 microdeletions is offered on an opt-in basis.
- Verifi® (Verinata Health, now Illumina) is a prenatal test for T21, T18, and T13. The test uses MPS and calculates a normalized chromosomal value, reporting results as one of three categories: no aneuploidy detected, aneuploidy detected, or aneuploidy suspected.
- InformaSeq^{SM} (Integrated Genetics) is a prenatal test for detecting T21, T18, and T13, with optional additional testing for select sex chromosome abnormalities. It uses the Illumina platform and reports results in similar manner.
- QNatal Advanced™ (Quest Diagnostics) tests for T21, T18, and T13.

IV. RATIONALE

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SUMMARY OF EVIDENCE

For individuals who have a singleton pregnancy who receive NIPS for T21, T18, and T13 using cell-free fetal DNA, the evidence includes observational studies and systematic reviews. Relevant outcomes are test accuracy and validity, morbid events, and resource utilization. Published studies on available tests and meta-analyses of these studies have consistently demonstrated very high sensitivity and specificity for detecting Down syndrome (T21) in singleton pregnancies. Most studies included only women at high risk of T21, but several studies have reported similar levels of diagnostic accuracy in average-risk women. Compared with standard serum screening, both the sensitivity and specificity of cell-free fetal DNA screening are considerably higher. As a result, screening with cell-free fetal DNA for T21 will result in fewer missed cases of Down syndrome, fewer invasive procedures, and fewer cases of pregnancy loss following invasive procedures. Screening for T18 and T13 along with T21 may allow for preparation for fetal demise or termination of the pregnancy prior to fetal loss. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have a singleton pregnancy who receive NIPS for sex chromosome aneuploidies using cell-free fetal DNA, the evidence includes observational studies, mainly in high-risk pregnancies, and systematic reviews. Relevant outcomes are test accuracy and validity, morbid events, and resource utilization. Meta-analyses of available data have suggested high sensitivities and specificities, but the small number of cases makes definitive conclusions

difficult. In addition, the clinical utility of identifying sex chromosome aneuploidies during pregnancy is uncertain. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a twin or multiple pregnancy who receive NIPS for aneuploidies using cell-free fetal DNA, the evidence includes observational studies and a systematic review. Relevant outcomes are test accuracy and validity, morbid events, and resource utilization. The total number of cases of aneuploidy identified in these studies is small and is insufficient to draw conclusions about clinical validity. There is a lack of direct evidence of clinical utility, and a chain of evidence cannot be conducted due to the paucity of evidence on clinical validity. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals with pregnancy (ies) who receive NIPS for microdeletions using cell-free fetal DNA, the evidence includes several observational studies. Relevant outcomes are test accuracy and validity, morbid events, and resource utilization. The available studies on clinical validity have limitations (e.g., missing data on confirmatory testing, false-negatives), and the added benefit of NIPS compared with current approaches is unclear. Moreover, the clinical utility of NIPS for microdeletions remains unclear and has not been evaluated in published studies. The evidence is insufficient to determine the effects of the technology on health outcomes.

V. DEFINITIONS

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N/A

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital BlueCross. Members and providers should consult the member's health benefit plan for information or contact Capital BlueCross for benefit information.

VII. DISCLAIMER

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Capital BlueCross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy

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between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital BlueCross' Provider Services or Member Services. Capital BlueCross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational; therefore, not covered, testing of maternal plasma for microdeletions:

CPT Codes®								
81422								

Investigational; therefore, not covered, testing of maternal plasma for fetal sex chromosome aneuploidies:

CPT Codes®								
81479	81599							

Investigational, therefore not covered, women with twin or multiple pregnancies undergoing screening for trisomy 21 and/or women eligible for testing for trisomy 13 and/ or 18:

CPT Codes®								
81420	81507	0060U	0168U					

Covered when medically necessary, women with singleton pregnancies undergoing screening for trisomy 21 and/or women eligible for testing for trisomy 13 and/or 18:

CPT Codes®								
81420	81507	0168U						

ICD-10-CM Diagnosis Codes	Description
758.0	Down's syndrome
758.1	Patau's syndrome
758.2	Edwards' syndrome
Z13.79	Encounter for other screening for genetic and chromosomal anomalies

IX. REFERENCES

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1. *Hook EB, Cross PK, Schreinemachers DM. Chromosomal abnormality rates at amniocentesis and in live-born infants. JAMA. Apr 15 1983;249(15):2034-2038. PMID 6220164.*
2. *Chitty LS, Hudgins L, Norton ME. Current controversies in prenatal diagnosis 2: Cell-free DNA prenatal screening should be used to identify all chromosome abnormalities. Prenat Diagn. Feb 2018;38(3):160-165. PMID 29417608.*
3. *Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Sequencing-based tests to determine fetal down syndrome (trisomy 21) from maternal plasma DNA. TEC Assessment Program. 2013;Volume 27:Tab 10.*
4. *Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Noninvasive prenatal cell-free fetal DNA-based screening for aneuploidies other than trisomy 21. TEC Assessment Program. 2014;Volume 29:Tab 7.*
5. *Badeau M, Lindsay C, Blais J, et al. Genomics-based non-invasive prenatal testing for detection of fetal chromosomal aneuploidy in pregnant women. Cochrane Database Syst Rev. Nov 10 2017;11:CD011767. PMID 29125628.*
6. *Ohno M, Caughey A. The role of noninvasive prenatal testing as a diagnostic versus a screening tool--a cost- effectiveness analysis. Prenat Diagn. Jul 2013;33(7):630-635. PMID 23674316.*
7. *Liao H, Liu S, Wang H. Performance of non-invasive prenatal screening for fetal aneuploidy in twin pregnancies: a meta-analysis. Prenat Diagn. Sep 2017;37(9):874-882. PMID 28728213.*
8. *Gil, MM, Galeva, SS, Jani, JJ, Konstantinidou, LL, Akolekar, RR, Plana, MM, Nicolaides, KK. Screening for trisomies by cfDNA testing of maternal blood in twin pregnancy: update of The Fetal Medicine Foundation results and meta-analysis. Ultrasound Obstet Gynecol, 2019 Jun 6;53(6). PMID 31165549.*
9. *Gross SJ, Stosic M, McDonald-McGinn DM, et al. Clinical experience with single-nucleotide polymorphism-based non-invasive prenatal screening for 22q11.2 deletion syndrome. Ultrasound Obstet Gynecol. Feb 2016;47(2):177-183. PMID 26396068.*
10. *Helgeson J, Wardrop J, Boomer T, et al. Clinical outcome of subchromosomal events detected by whole-genome noninvasive prenatal testing. Prenat Diagn. Oct 2015;35(10):999-1004. PMID 26088833.*
11. *Petersen AK, Cheung SW, Smith JL, et al. Positive predictive value estimates for cell-free noninvasive prenatal screening from data of a large referral genetic diagnostic laboratory. Am J Obstet Gynecol. Dec 2017;217(6):691 e691-691 e696. PMID 29032050.*
12. *Practice Bulletin No. 163 Summary: Screening for Fetal Aneuploidy. Obstet Gynecol. May 2016;127(5):979-981. PMID 27101120.*

13. *Gregg AR, Skotko BG, Benkendorf JL, et al. Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics. Genet Med. Oct 2016;18(10):1056-1065. PMID 27467454.*

14. *Benn P, Borrell A, Chiu RW, et al. Position statement from the Chromosome Abnormality Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. Prenat Diagn. Aug 2015;35(8):725- 734. PMID 25970088.*

15. *Benn P, Borell A, Chiu R, et al. Position statement from the Aneuploidy Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. Prenat Diagn. Jul 2013;33(7):622-629. PMID 23616385.*

17. *Blue Cross Blue Shield Association Medical Policy Reference Manual. 4.01.21 Noninvasive Prenatal Screening for Fetal Aneuploidies. January 29, 2020.*

Other Sources:

Benacerraf, BR. Sonographic findings associated with fetal aneuploidy. In: UpToDate Online Journal [serial online]. Waltham, MA: UpToDate; updated May 2, 2018... [Website]: www.uptodate.com. Accessed January 29, 2020.

X. POLICY HISTORY

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MP-2.256	**CAC 7/30/13** New policy Adopting BCBSA. Medically necessary with criteria. Policy coded.
	12/19/2013- New 2014 Code updates made.
	CAC 5/20/14 Consensus review. No change to the policy statements. References and rationale updated. Codes reviewed.
	1/2015-New 2015 CPT code added to policy
	CAC 6/2/15 Minor revision. Policy title changed to "Non-Invasive Prenatal Testing for Fetal Aneuploidies Using Cell-Free Fetal DNA". Statement Added that concurrent nucleic acid sequencing-based testing of maternal plasma for trisomy 13 and/or 18 may be considered medically necessary in women who are eligible for and are undergoing nucleic acid sequencing-based testing of maternal plasma for trisomy 21. In addition, 2 investigational statements were added, 1 for nucleic acid sequencing based testing of maternal plasma for trisomy 13 and/or 18, other than in the situations specified in the medically necessary statement and the other for fetal sex chromosome aneuploidies. References and rationale updated. Policy coding reviewed.
	CAC 11/24/15 Minor revision. "High-risk" removed from the medically necessary statement for singleton pregnancies. Not medically necessary

	statement on average-risk women removed. In the title "testing" changed to "screening". Statement added that nucleic acid sequencing-based testing of maternal plasma for microdeletions is considered investigational. "And Microdeletions" also added to title. Policy guidelines revised. Reference and rationale update. Coding updated.
	CAC 11/29/2016 Consensus review. No change to the policy statements. References and rationale updated. Codes reviewed. Revised diagnosis code descriptions updated effective 10/1/16. Added new code 81422; effective 1/1/17. Variation section reformatted.
	Admin update 10/1/17: Added new ICD 10 codes effective from 10/1/17 and deleted old ICD 10 codes.
	12/29/17 Consensus review. Policy statements unchanged. Cross-Reference, Description/Background, Rationale and Reference sections updated.
	Admin Update 7/6/18: New code 0060U added with an effective date of 7/1/2018. Update rationale to include Summary of Evidence only.
	Admin updated 10/12/18: Coding reviewed and updated. Appendix removed.
	1/15/19 Consensus review. The first policy statement was revised to include testing for trisomy 18 and 13 which had been addressed in the second policy statement. The second policy statement which addressed testing for trisomies 18 and 13 has been deleted. Background, guidelines, references, and rationale updated.
	01/29/2020 Consensus review. No changes to policy statements, coding reviewed and references updated. Added new April 2020 code 0168U as medically necessary for singleton pregnancy. Effective 4/1/2020.

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