BSC_CON_2.08	Genetic Testing: Prenatal Cell-Free DNA Testing		
Original Policy Date:	January 1, 2023	**Effective Date:**	February 1, 2025
Section:	2.0 Medicine	**Page:**	Page 1 of 12

Example Test Table

The tests, associated laboratories, CPT codes, and ICD codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the Concert Platform for a comprehensive list of registered tests.

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies	Vasistera (Natera)	0327U
	Panorama Prenatal Panel (with or without twin zygosity testing) (Natera)	81420, 0060U (twin zygosity only)
	Harmony Prenatal Test (BioReference Laboratories)	81507
Prenatal Cell-free DNA Testing for Microdeletions	Panorama Extended Panel (Natera)	81422
	MaterniT21 Plus Core + ESS (LabCorp)	
	Prequel Prenatal Screen: Microdeletions (Myriad Genetics)	
Prenatal Cell-free DNA Testing for Single-gene Disorders	Vistara - Single-Gene NIPT (Natera)	81302, 81404, 81405, 81406, 81407, 81408, 81442
	PreSeek Non-invasive Prenatal Gene Sequencing Screen (Baylor Genetics, LLC)	
	UNITY Fetal Antigen NIPT	0488U
	UNITY Fetal Risk Screen	0489U
Maternal Serum Screening (MSS)	First Trimester Maternal Screen, Serum (Mayo Clinic Laboratories)	81508
	Quad Screen (Quest Diagnostics)	81509, 81510, 81511, 81512
	Serum Integrated Screen, Part 2 (Quest Diagnostics)	
	Penta Screen (Quest Diagnostics)	81512

Policy Statement

Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies

I. Prenatal cell-free DNA testing for 13, 18, 21, X and Y aneuploidy (0327U, 81420, 81507) may be considered **medically necessary** when:
   A. The member has a singleton or twin pregnancy, **AND**
   B. The member has NOT previously had cell-free DNA screening in the current pregnancy.

II. Prenatal cell-free DNA testing to predict twin zygosity (0060U) is considered **investigational**.

III. Prenatal cell-free DNA testing is considered **investigational** for all other indications, including the following:
   A. For all other aneuploidies (other than trisomy 13, 18, and 21)
   B. For multiple gestation pregnancies (triplets or higher)
   C. Prenatal cell-free DNA performed simultaneously with maternal serum screening

D. Use on a singleton pregnancy with a known vanishing twin
E. For the sole purpose of fetal sex determination.

Prenatal Cell-free DNA Testing for Microdeletions

IV. Prenatal cell-free DNA testing for microdeletions and microduplications (81422) is considered **investigational**.

Prenatal Cell-free DNA Testing for Single-gene Disorders

V. Prenatal cell-free DNA testing for mutations associated with single gene disorders (81302, 81404, 81405, 81406, 81407, 81408, 81442) is considered **investigational.**

Maternal Serum Screening (MSS)

VI. Maternal serum screening for aneuploidy using no more than one of the following one time per pregnancy may be considered **medically necessary**:
   A. First trimester screening (free or total beta-HCG and PAPP-A) (81508)
   B. Second trimester screening (hCG, msAFP, uE3, and DIA) (81509, 81510, 81511, 81512)
   C. Integrated, stepwise sequential, or contingent sequential screening (81508, 81509, 81510, 81511, 81512)
   D. Penta screen (hCG, msAFP, uE3, DIA, ITA) (81512).

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Other common names for this test include: Non-invasive Prenatal Testing (NIPT), Cell-free DNA Testing (cfDNA), Cell-free Fetal DNA Testing (cffDNA)

DEFINITIONS

1. **Prenatal Cell-free DNA Testing** is a screening test that is used to determine the risk of specific genetic disorders by analyzing traces of cell-free DNA (cfDNA) in a pregnant woman's blood.
2. **Sequencing tests** use 1 of 2 general approaches to analyze cell-free DNA. The most widely used technique to date uses massively parallel sequencing (MPS; also known as next-generation or "next gen" sequencing). The second general approach uses the single nucleotide polymorphism (SNP) method.
3. **Singleton pregnancy** is a pregnancy with one fetus.
4. **Twin zygosity** testing is used to predict the degree of genetic similarity within each pair (i.e., monozygotic versus dizygotic). Monozygotic (genetically identical twins) are at a higher risk for pregnancy complications, such as twin-twin transfusion syndrome (TTTS).

Coding

See the Codes table for details.

Description

Prenatal cell-free DNA testing (prenatal cfDNA) is a sequencing test performed on placental cell-free DNA found in maternal serum and is most commonly used to screen for fetal aneuploidy (trisomy 21, trisomy 13, and trisomy 18). Sex chromosomes are also screened for fetal sex determination and sex chromosome aneuploidy. Prenatal cfDNA is a screening test and does not provide definitive diagnosis for a fetus. When prenatal cfDNA is positive, or high risk, for a genetic abnormality, the fetus is at increased risk for that condition. Further testing via karyotype, fluorescent in situ hybridization (FISH), or chromosomal microarray (CMA) would be necessary to exclude the possibility of a false-positive.

Before testing, guidelines recommend that pregnant people be counseled about the risk of a false-positive result. False-positive findings have been associated with several factors, including placental mosaicism, vanishing twin, or a confounding factor within the pregnant person (such as a genetic condition or malignancy).

Prenatal cfDNA testing has expanded to include microdeletion and microduplication syndromes, as well as single-gene disorders, although this is an area of ongoing research. Prenatal cfDNA has also expanded to predict twin zygosity (i.e., monozygotic versus dizygotic twins). Monozygotic twins have a higher risk for certain complications, such as twin-twin transfusion syndrome (TTTS).

Prenatal screening can also be performed via maternal serum screening (MSS), which examines levels of various analytes produced by the fetus and placenta and provides risks for certain genetic conditions and birth defects.

Related Policies

This policy document provides coverage criteria for Prenatal Cell-free DNA Testing. Please refer to:

- ***Oncology: Circulating Tumor DNA and Circulating Tumor Cells (Liquid Biopsy)*** for criteria related to circulating tumor DNA (ctDNA) or circulating tumor cell testing performed on peripheral blood for cancer diagnosis, management and surveillance.
- ***Genetic Testing: Prenatal Diagnosis (via amniocentesis, CVS, or PUBS) and Pregnancy Loss*** for coverage related to prenatal and pregnancy loss diagnostic genetic testing.
- ***Genetic Testing: Prenatal and Preconception Carrier Screening*** for coverage criteria related to carrier screening for genetic disorders.
- ***Genetic Testing: Preimplantation Genetic Testing*** for coverage criteria related to genetic testing of embryos prior to in vitro fertilization.
- ***Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay*** for coverage criteria related to diagnostic genetic testing in the postnatal period.
- ***Genetic Testing: General Approach to Genetic and Molecular Testing*** for coverage criteria related to non-invasive prenatal screening that is not specifically discussed in this or other non-general policies, including known familial variant testing.

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

California Prenatal Screening Program
The previous California Prenatal Screening Program (using serum analyte testing and ultrasound) was offered to all pregnant women who reside in California prior to 9/19/2022 . NIPT is considered an equivalent or better test and had been offered to Blue Shield of California patients as an alternative.

However, both should not be done during the same pregnancy. As of 9/19/2022, California will only be offering NIPT and AFP screening going forward. It will be offered to all pregnant individuals in CA. The old program is no longer being offered as an alternative.

The new CA state program covers the usual aneuploidies (21, 18, 13) but will also allow for determining the sex of the baby and testing with twin pregnancies. It will not, however, report other abnormalities. When a member elects the state program, the tests are sent to one of the contracted labs and the state bills the plan when the individual has insurance. If additional testing is requested by the individual or their provider, the state does not cover that testing and it then falls to the coverage of the individual's health plan. The individual also has the option of paying for additional testing. Generally, 81420 (aneuploidy testing) will be covered by plans but add on tests will be reviewed for coverage by the health plans when requested. If a member elects NIPT screening outside of the state program, the provider will order testing from their lab of choice directly.

Rationale

Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal-Fetal Medicine (SMFM)

ACOG and SMFM (2020) released a joint practice bulletin (No. 226) with the following recommendations for screening for fetal chromosomal abnormalities:

"The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

- Cell-free DNA is the most sensitive and specific screening test for the common fetal aneuploidies. Nevertheless, it has the potential for false-positive and false-negative results. Furthermore, cell-free DNA testing is not equivalent to diagnostic testing." (p. e63)

"The following recommendations and conclusions are based on limited and inconsistent scientific evidence (Level B)":

- "Cell-free DNA screening can be performed in twin pregnancies. Overall, performance of screening for trisomy 21 by cell-free DNA in twin pregnancies is encouraging, but the total number of reported affected cases is small. Given the small number of affected cases it is difficult to determine an accurate detection rate for trisomy 18 and 13. (p. e64)

Regarding prenatal screening for multiple gestation pregnancies of triplets or higher, Practice Bulletin No. 226 also states: "…there are no data available for serum screening for higher-order multiple gestations such as triplets and quadruplets." (p. e59)

Regarding screening a pregnancy with a vanishing twin: "In a patient with both a vanishing twin and a viable intrauterine pregnancy, cell-free DNA screening is not advised because of the high risk for aneuploidy in the nonviable sac or embryo, which can lead to false-positive results." (p. e53)

The Practice Bulletin No. 226 also notes that "[i]f screening is accepted, patients should have one prenatal screening approach, and should not have multiple screening tests performed simultaneously." (p. e49)

American College of Medical Genetics and Genomics (ACMG)

ACMG (2016) published a position statement on noninvasive prenatal screening (NIPS) for fetal aneuploidy.

ACMG recommends:

- Informing all pregnant women that NIPS is the most sensitive screening option for traditionally screened aneuploidies (i.e., T13, T18, and T21). (p. 1059)

- Referring patients to a trained genetics professional when an increased risk of aneuploidy is reported after NIPS. (p. 1059)
- Providers should make efforts to deter patients from selecting sex chromosome aneuploidy screening for the sole purpose of biologic sex identification in the absence of a clinical indication for this information (p. 1060)

Current ACMG practice guidelines (2022) "strongly recommends NIPS over traditional screening for all pregnant patients with singleton and twin gestations for fetal trisomies 21, 18, and 13 and strongly recommends NIPS be offered to patients to screen for fetal sex chromosome aneuploidy." (p. 1 and p. 5)

National Society for Genetic Counselors (NSGC)
The National Society for Genetic Counselors adopted the following statement updated in 2021 supporting prenatal cell-free DNA (cfDNA) screening as an option for pregnant patients:
The National Society of Genetic Counselors believes that all pregnant patients, regardless of aneuploidy risk, should have access to prenatal aneuploidy screening using cell-free DNA (cfDNA)*. Healthcare providers should present cfDNA screening for aneuploidy within the context of other available prenatal screening and diagnostic testing options. Included in this discussion should be the option of pursuing diagnostic testing as a first line approach or declining all screening/testing. Pretest counseling should also include a discussion of the individual patient's values, preferences, and needs, as well as the benefits and limitations of cfDNA screening. Many factors influence cfDNA screening performance; therefore, it may not be appropriate for every clinical scenario. Additionally, some laboratories offer screening for conditions beyond common aneuploidies, so it is essential to consider the test's positive predictive value, particularly when the prevalence of the disorder is low. Patients who receive increased risk or inconclusive/atypical results should receive post-test genetic counseling with a knowledgeable healthcare provider, such as a genetic counselor. In such cases, confirmatory diagnostic testing may be indicated, and patients should be counseled that no irreversible actions should be taken based on the cfDNA screening alone.

Wojas, et al
In a 2022 study of 59,471 twin pregnancies, the authors stated: "Further research should determine the impact of the addition of first trimester zygosity assignment for twin pregnancies upon the accuracy of chorionicity assignment, and the differences in healthcare costs for pregnancies assigned either MZ [monozygotic] or DZ [dizygotic] genetic origin. Finally, there is limited information on the impact of zygosity (corrected for chorionicity) upon pregnancy outcome. Our study lays a foundation for such research, to better determine the degree to which these two factors contribute independently to complicated and normal outcomes." (p. 1239)

Prenatal Cell-free DNA Testing for Microdeletions

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal-Fetal Medicine (SMFM)
ACOG and SMFM (2020) released a joint practice bulletin (No. 226) with the following recommendations for screening for fetal chromosomal abnormalities:
Screening for a limited number of microdeletions with cell-free DNA is available; however, this testing has not been validated clinically and is not recommended. Although microdeletions are relatively common when considered in aggregate, cell-free DNA panels only include a few specific clinically significant microdeletions and these are very rare. Therefore, the PPV for these disorders is much lower than for common trisomies. (p. e53)

American College of Medical Genetics (ACMG)
The ACMG 2022 practice guideline, Noninvasive prenatal screening (NIPS) for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG), includes a conditional recommendation, suggesting 22q11.2 deletion syndrome be offered to all patients. The guideline defines a conditional

recommendation as follows: "most patients would request this testing and most clinicians would offer NIPS for this purpose, after a discussion about the benefits and limitations of screening and in the context of shared-decision making." (p. 5)

Concert Note
Overall, studies attempting to validate the clinical utility of microdeletion analysis via NIPS have overall shown low positive predictive values and higher false positive rates, likely because of the low prevalence of the individual targeted microdeletion syndromes in the general population.
At the present time, testing for microdeletions, including 22q11.2, via cell-free DNA testing has insufficient evidence in peer-reviewed publications to effectively result in improved health outcomes compared to the current standard of care.

Prenatal Cell-free DNA Testing for Single-gene Disorders
The American College of Obstetricians and Gynecologists (ACOG)
ACOG issued a practice advisory for the use of cell-free DNA to screen for single-gene disorders (February 2019, reaffirmed October 2022 and September 2023), which states the following:
The continued innovation in cell-free technology combined with the desire for a maternal blood test to predict the risk for fetal genetic disorders during a pregnancy has broadened the application of cell-free DNA screening beyond aneuploidy to single-gene disorders. Examples of single-gene disorders include various skeletal dysplasias, sickle cell disease and cystic fibrosis. Although this technology is available clinically and marketed as a single-gene disorder prenatal screening option for obstetric care providers to consider in their practice, often in presence of advanced paternal age, there has not been sufficient data to provide information regarding accuracy and positive and negative predictive value in the general population. For this reason, single-gene cell-free DNA screening is not currently recommended in pregnancy.

Maternal Serum Screening (MSS)
The American College of Obstetricians and Gynecologists (ACOG)
ACOG provided an updated position statement (number 226) regarding Screening for Fetal Chromosomal Abnormalities.

Specifically, these guidelines state: "Prenatal genetic screening (serum screening with or without nuchal translucency [NT] ultrasound or cell-free DNA screening) and diagnostic testing (chorionic villus sampling [CVS] or amniocentesis] options should be discussed and offered to all pregnant women regardless of maternal age or risk of chromosomal abnormality." (p. 862)
The use of multiple screening approaches performed independently (e.g., a first-trimester screening test followed by a quad screen as an unlinked test) is not recommended because it will result in an unacceptably high positive screening rate and could deliver contradictory results. (p. 865)

References

1. 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*. 2016;18(10):1056-1065. doi:10.1038/gim.2016.97
2. "Prenatal Cell-Free DNA Screening." Position Statement from National Society of Genetic Counselors. https://www.nsgc.org/Policy-Research-and-Publications/Position-Statements/Position-Statements/Post/prenatal-cell-free-dna-screening-1. Released October 11, 2016. Revised April 2021.
3. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. *Obstet Gynecol*. 2020;136(4):859-867. doi:10.1097/AOG.0000000000004084

4. "Cell-free DNA to Screen for Single-Gene Disorders". Practice Advisory from The American College of Obstetricians and Gynecologists. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2019/02/cell-free-dna-to-screen-for-single-gene-disorders Published February 2019. Reaffirmed October 2022 and September 2023
5. Dungan JS, Klugman S, Darilek S, et al. Noninvasive prenatal screening (NIPS) for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2023;25(2):100336. doi:10.1016/j.gim.2022.11.004
6. Wojas A, Martin KA, Koyen Malashevich A, Hashimoto K, Parmar S, White R, Demko Z, Billings P, Jelsema R, Rebarber A. Clinician-reported chorionicity and zygosity assignment using single-nucleotide polymorphism-based cell-free DNA: Lessons learned from 55,344 twin pregnancies. Prenat Diagn. 2022 Sep;42(10):1235-1241. doi: 10.1002/pd.6218. Epub 2022 Sep 7. PMID: 35997139; PMCID: PMC9541063.

Documentation for Clinical Review

Please provide the following documentation:

- Name of the test being requested or the Concert Genetics GTU identifier. The Concert Genetics GTU can be found at https://app.concertgenetics.com
- CPT codes to be billed for the particular genetic test (GTU required for unlisted codes)
- History and physical and/or consultation notes including:
  - Clinical findings:
    - Signs/symptoms leading to a suspicion of genetic condition
    - Family history if applicable
  - Prior evaluation/treatment:
    - Previous test results (i.e., imagining, lab work, etc.) related to reason for genetic testing
    - Family member's genetic test result, if applicable
  - Rationale
    - Reason for performing test
    - How test result will impact clinical decision making

Post Service (in addition to the above, please include the following):

- Results/reports of tests performed

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood

Type	Code	Description
	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
	0488U	Obstetrics (fetal antigen noninvasive prenatal test), cell-free DNA sequence analysis for detection of fetal presence or absence of 1 or more of the Rh, C, c, D, E, Duffy (Fya), or Kell (K) antigen in alloimmunized pregnancies, reported as selected antigen(s) detected or not detected ***(Code effective 10/1/2024)***
	0489U	Obstetrics (single-gene noninvasive prenatal test), cell-free DNA sequence analysis of 1 or more targets (e.g., CFTR, SMN1, HBB, HBA1, HBA2) to identify paternally inherited pathogenic variants, and relative mutation-dosage analysis based on molecular counts to determine fetal inheritance of maternal mutation, algorithm reported as a fetal risk score for the condition (e.g., cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemia) ***(Code effective 10/1/2024)***
	0494U	Red blood cell antigen (fetal RhD gene analysis), next-generation sequencing of circulating cell-free DNA (cfDNA) of blood in pregnant individuals known to be RhD negative, reported as positive or negative ***(Code effective 10/1/2024)***
	81302	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis
	81404	Molecular Pathology Procedure Level 5
	81405	Molecular Pathology Procedure Level 6
	81406	Molecular Pathology Procedure Level 7
	81407	Molecular Pathology Procedure Level 8
	81408	Molecular Pathology Procedure Level 9
	81420	Fetal chromosomal aneuploidy (e.g., 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 (e.g., DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
	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
	81508	Fetal congenital abnormalities, biochemical assays of two proteins (PAPP-A, hCG [any form]), utilizing maternal serum, algorithm reported as a risk score
	81509	Fetal congenital abnormalities, biochemical assays of three proteins (PAPP-A, hCG [any form], DIA), utilizing maternal serum, algorithm reported as a risk score
	81510	Fetal congenital abnormalities, biochemical assays of three analytes (AFP, uE3, 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

Type	Code	Description
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
01/01/2023	New policy.
01/01/2024	Annual review. Policy statement, guidelines and literature updated.
01/01/2025	Annual review. Policy statement, guidelines and literature updated. Policy title changed from Genetic Testing: Non-Invasive Prenatal Screening (NIPS)/ Non-Invasive Prenatal Testing (NIPT) to current one.
02/01/2025	Coding update.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue

Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Genetic Testing: Prenatal Cell-Free DNA Testing BSC_CON_2.08 **Policy Statement:** **Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies** I. Prenatal cell-free DNA testing for 13, 18, 21, X and Y aneuploidy (0327U, 81420, 81507) may be considered **medically necessary** when: A. The member has a singleton or twin pregnancy, **AND** B. The member has NOT previously had cell-free DNA screening in the current pregnancy. II. Prenatal cell-free DNA testing to predict twin zygosity (0060U) is considered **investigational**. III. Prenatal cell-free DNA testing is considered **investigational** for all other indications, including the following: A. For all other aneuploidies (other than trisomy 13, 18, and 21) B. For multiple gestation pregnancies (triplets or higher) C. Prenatal cell-free DNA performed simultaneously with maternal serum screening D. Use on a singleton pregnancy with a known vanishing twin E. For the sole purpose of fetal sex determination. **Prenatal Cell-free DNA Testing for Microdeletions** IV. Prenatal cell-free DNA testing for microdeletions and microduplications (81422) is considered **investigational**. **Prenatal Cell-free DNA Testing for Single-gene Disorders** V. Prenatal cell-free DNA testing for mutations associated with single gene disorders (81302, 81404, 81405, 81406, 81407, 81408, 81442) is considered **investigational.** **Maternal Serum Screening (MSS)**	**Genetic Testing: Prenatal Cell-Free DNA Testing BSC_CON_2.08** **Policy Statement:** **Prenatal Cell-free DNA Testing for Chromosome 13, 18, 21, X and Y Aneuploidies** I. Prenatal cell-free DNA testing for 13, 18, 21, X and Y aneuploidy (0327U, 81420, 81507) may be considered **medically necessary** when: A. The member has a singleton or twin pregnancy, **AND** B. The member has NOT previously had cell-free DNA screening in the current pregnancy. II. Prenatal cell-free DNA testing to predict twin zygosity (0060U) is considered **investigational**. III. Prenatal cell-free DNA testing is considered **investigational** for all other indications, including the following: A. For all other aneuploidies (other than trisomy 13, 18, and 21) B. For multiple gestation pregnancies (triplets or higher) C. Prenatal cell-free DNA performed simultaneously with maternal serum screening D. Use on a singleton pregnancy with a known vanishing twin E. For the sole purpose of fetal sex determination. **Prenatal Cell-free DNA Testing for Microdeletions** IV. Prenatal cell-free DNA testing for microdeletions and microduplications (81422) is considered **investigational**. **Prenatal Cell-free DNA Testing for Single-gene Disorders** V. Prenatal cell-free DNA testing for mutations associated with single gene disorders (81302, 81404, 81405, 81406, 81407, 81408, 81442) is considered **investigational.** **Maternal Serum Screening (MSS)**

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
VI. Maternal serum screening for aneuploidy using no more than one of the following one time per pregnancy may be considered **medically necessary**: A. First trimester screening (free or total beta-HCG and PAPP-A) (81508) B. Second trimester screening (hCG, msAFP, uE3, and DIA) (81509, 81510, 81511, 81512) C. Integrated, stepwise sequential, or contingent sequential screening (81508, 81509, 81510, 81511, 81512) D. Penta screen (hCG, msAFP, uE3, DIA, ITA) (81512).	VI. Maternal serum screening for aneuploidy using no more than one of the following one time per pregnancy may be considered **medically necessary**: A. First trimester screening (free or total beta-HCG and PAPP-A) (81508) B. Second trimester screening (hCG, msAFP, uE3, and DIA) (81509, 81510, 81511, 81512) C. Integrated, stepwise sequential, or contingent sequential screening (81508, 81509, 81510, 81511, 81512) D. Penta screen (hCG, msAFP, uE3, DIA, ITA) (81512).