Oscar Clinical Guideline: Prenatal Testing (CG043, Ver. 11)

Prenatal Testing

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

The Plan members who are pregnant may be eligible for prenatal testing to provide information about the health of both the mother and the baby. Prenatal testing can be performed invasively or noninvasively to look for a variety of birth defects and genetic conditions. Invasive testing includes several more involved procedures such as directly sampling the fluid or tissue surrounding the baby. Non-invasive testing is performed with simple blood tests. Medical necessity for expanded carrier screenings may be limited to risk-based conditions.

These tests can be performed at different stages of the pregnancy depending on the conditions being tested. Screening or diagnostic testing for fetal genetic disorders may be appropriate, regardless of maternal age. Additionally, high risk women, such as those over 35 years of age or with certain medical conditions, are eligible for more advanced testing. Testing must be performed by an in-network provider when available.

This guideline provides medical necessity criteria for prenatal tests and procedures. For a list of tests that includes, but not limited to services considered experimental or investigational, please refer to the Plan Clinical Guideline: Experimental or Investigational (Unproven) Services, Products, Drugs, and Biologicals (CG012).

Definitions

"Aneuploidy" is a broad term used to define the presence of an abnormal number of chromosomes. This can include trisomy syndromes, or conditions such as Turner's syndrome where there is a missing chromosome (sex-chromosome aneuploidy)

"Analytic validity" refers to the extent to which a test accurately and reliably measures the specific genomic variation, biomarker, or analyte of interest. It is determined by the test's precision (repeatability and reproducibility) and accuracy (closeness to the true value).

"Carrier Screening" refers to the genetic testing of certain rare, inheritable conditions such as cystic fibrosis or spinal muscular atrophy. These conditions are usually inherited in an autosomal recessive fashion, meaning, both parents need to have the mutation in order for the baby to be at risk of having the condition.

"Clinical utility" refers to a test's ability to improve health outcomes by considering its benefits, harms, efficacy, and effectiveness, while guiding decision-making.

"Clinical validity" refers to the strength of association between the test result and the presence or absence of a specific genomic variation, biomarker, trait, or condition. It is assessed by measures such as sensitivity (the ability to correctly identify individuals with the condition), specificity (the ability to correctly identify individuals without the condition), positive predictive value (the probability that a positive test result indicates the presence of the condition), and negative predictive value (the probability that a negative test result indicates the absence of the condition).

"Expanded Carrier Screening" refers to genetic screening for multiple disorders instead of screening targeted for at-risk disorders.

"Invasive Prenatal Testing" includes procedures such as amniocentesis and chorionic villus sampling, where the tissue or fluid surrounding the baby is directly sampled.

"Noninvasive Prenatal Testing (NIPT) or Noninvasive Prenatal Screening (NIPS) " is a test where a small amount of the mother's blood is drawn to look for fragments of fetal genetic material called cell-free DNA. These small fragments can be used to look for fetal trisomy syndromes and determine the sex of the baby. NIPT can be performed as early as the first trimester (e.g.,10 weeks of gestation). NIPT may be used to a screen for trisomy syndromes (trisomy 13, 18, and 21), but an abnormal result should be followed by a diagnostic test (e.g., chorionic villus sampling or amniocentesis) when making decisions to continue or terminate a pregnancy.

"Nuchal Translucency" is a procedure where ultrasound is used to determine the fluid in the neck of the growing baby to determine risk of various conditions such as trisomy 21 or cardiac problems.

"Trisomy" is the genetic condition of having an extra chromosome. Where the normal human genome has 23 pairs of chromosomes, errors in reproductive division to create the egg or sperm can result in an extra chromosome being included. The most common trisomy conditions are trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome).

Clinical Indications

General Indications

The Plan considers genetic testing medically necessary to establish a molecular diagnosis of an inheritable disease or genetic disorder when ALL of the following are met:

1. The test is FDA-approved/cleared and the requested use is consistent with FDA labeling or evidence-based guidelines or consensus recommendations (e.g., ACOG, ACMG, published health technology assessments, (e.g., Hayes), UpToDate). In scenarios without FDA approval or clearance, the test reflects analytic validity, clinical validity, and clinical utility; *and*
2. The member (mother or fetus) displays clinical features or is at direct risk of inheriting the mutation in question (pre-symptomatic). However, for requested screening tests listed under Condition-Specific Indications, average-risk members (no prior history or risk factors) may meet medical necessity when criteria is met under the subsections below such as Non-Invasive Prenatal Cell-Free DNA testing, Standard CFTR, Spinal Muscular Atrophy Testing (SMN1 and SMN2), or Down Syndrome testing; *and*
3. The result of the test will directly impact the treatment being delivered to the member; *and*
4. After history, physical examination, pedigree analysis, genetic counseling, and completion of conventional diagnostic studies, a definitive diagnosis remains uncertain; *and*
5. Testing is accompanied by genetic counseling and documented by a licensed genetic counselor, obstetrician, or maternal-fetal medicine specialist.

(Please note: In April 2022, the FDA issued a Safety Communication for patients and providers that genetic non-invasive prenatal screening tests may have false results and most laboratory developed tests are offered on market without FDA review. Therefore, members should discuss the risks and benefits with providers and receive genetic counseling.)

State Law Conflicts

For any provision of this policy that directly conflicts with or is prohibited by state law, the provisions of the state law will apply instead of the provisions of this policy. This means that in instances where state regulations diverge from or directly oppose the Prenatal Testing (CG043) Medical Necessity Criteria for Authorization or requirements, the policy's criteria will not apply.

Condition-Specific Indications

Non-Invasive Prenatal Cell-Free DNA testing

The Plan considers non-invasive prenatal cell-free DNA testing medically necessary when the above general criteria above are met AND ALL of the following criteria are met:

1. The test is used to screen for fetal sex chromosome aneuploidy, trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) or trisomy 13 (Patau syndrome); *and*
2. The member has a confirmed single or twin pregnancy; *and*
3. The member has not previously had NIPT for this pregnancy*; and*
4. The NIPT test is being performed at ≥ 10 weeks gestation.

Standard CFTR (cystic fibrosis transmembrane conductance regulator) Mutation Panel

The Plan considers carrier screening for cystic fibrosis with the ACMG (American College of Medical Genetics) standard CFTR (cystic fibrosis transmembrane conductance regulator) mutation panel medically necessity when the above general criteria are met AND ANY of the following criteria are met:

1. Couples seeking prenatal care; *or*
2. Couples planning a pregnancy; *or*
3. Members with a family history of cystic fibrosis; *or*
4. Members with a 1st degree relative identified as a cystic fibrosis carrier; *or*
5. Members with a partner who has cystic fibrosis or is a cystic fibrosis carrier; *or*
6. When the newborn screen is positive for CF *and* the sweat chloride test is inconclusive, intermediate or cannot be performed.

Factor V Leiden Testing

The Plan considers Factor V Leiden genetic testing in pregnant members or those planning pregnancy medically necessary when the above general criteria AND ALL of the following criteria are met:

1. Abnormal activated protein C (APC) resistance assay test (unless member is receiving anticoagulation); *and*
2. One of the following situations are met:
    a. Venous thromboembolism (VTE) during the current or past pregnancy, or in the 6 weeks following a prior pregnancy; *or*
    b. First-degree blood relative with history of high-risk thrombophilia (e.g., antithrombin deficiency, Factor V Leiden mutation, or prothrombin G20210A mutation); *or*
    c. First-degree blood relative with history of venous thromboembolism prior the age of 50 years old; *or*
    d. Personal history of unprovoked VTE; *or*
    e. Personal history of VTE associated with use of oral contraceptives or hormone therapy

Prothrombin G20210A Thrombophilia (F2 Gene) Testing

The Plan considers prothrombin G20210A thrombophilia (F2 Gene) testing in pregnant members or those planning pregnancy medically necessary when the above general criteria AND ONE of the following criteria are met:

1. Venous thromboembolism (VTE) during the current or past pregnancy, or in the 6 weeks following a prior pregnancy; *or*

2. First-degree blood relative with history of high-risk thrombophilia (e.g. antithrombin deficiency, Factor V Leiden mutation, or prothrombin G20210A mutation); *or*
3. First-degree blood relative with history of venous thromboembolism prior the age of 50 years old; *or*
4. Personal history of unprovoked VTE; *or*
5. Personal history of VTE associated with use of oral contraceptives or hormone therapy

Hemoglobinopathy and Thalassemia Testing

The Plan considers genetic testing for hemoglobinopathies and thalassemias (includes, but not limited to: Sickle Cell Anemia [HBB Gene], Alpha Thalassemia [HBA1/HBA2 Genes] and Beta Thalassemia [HBB Gene]) for couples planning pregnancy or seeking prenatal care medically necessary when the above general criteria AND ONE of the following criteria are met:

1. Family history of a hemoglobinopathy; *or*
2. Family member who is affected or is a carrier with a known mutation; or
3. Suspected hemoglobinopathy based on results of a complete blood count (CBC) and hemoglobin analysis, such as low mean corpuscular hemoglobin or mean corpuscular volume; *or*
4. African, Mediterranean, Middle Eastern, Southeast Asian, or West Indian descent

Spinal Muscular Atrophy Testing (SMN1 and SMN2)

The Plan considers spinal muscular atrophy genetic testing (SMN1 and SMN2) medically necessary when the above general criteria AND ONE of the following criteria is met:

1. Carrier screening for couples seeking prenatal care or planning pregnancy; *or*
2. In the fetus or as a pre-implantation test when both parents are known carriers of the mutation

Fragile X Testing (FMRI gene)

The Plan considers fragile X testing (FMRI gene) in pregnant members or those planning pregnancy medically necessary when the above general criteria AND ONE of the following criteria are met:

1. A family history of fragile X syndrome, *or*
2. A family history of unexplained developmental delay/intellectual disability, autism or primary ovarian insufficiency (POI); *or*
3. Fetuses of known carrier mothers

Tay-Sachs Disease Testing (HEXA gene)

The Plan considers Tay-Sachs disease testing (HEXA gene) in pregnant members or those planning pregnancy medically necessary when the above general criteria AND ONE of the following criteria are met:

1. The member has an abnormal or inconclusive beta-hexosaminidase A enzyme activity; *or*
2. The member has an affected or carrier family member in whom a mutation has been identified; *or*

3. The member or member's partner is of Ashkenazi Jewish, French Canadian, or Cajun descent; *or*
4. The member or member's partner is affected with or carrier of Tay-Sachs disease

Down Syndrome Testing

The Plan considers the following non-invasive testing options for Down syndrome in pregnant women wishing to undergo testing that have been adequately counseled medically necessary when the above general criteria are met and ANY of the following:

- First trimester combined test, consisting of the following tests, to be used when earlier identification of aneuploidy is desired:
    - Nuchal translucency; *and*
    - PAPP-A and beta-HCG.
- Other first trimester tests: Non-Invasive Prenatal Cell-Free DNA testing to support decision-making. Not to be used concurrently with the first trimester combined test, unless high risk.
- When nuchal translucency is not available or the results are indeterminate, serum analyte combined test consisting of the following is warranted:
    - First trimester PAPP-A and beta-HCG; *and*
    - Second trimester quadruple screen.
- Second trimester quadruple screen, consisting of the following biomarkers:
    - Dimeric inhibin A; *and*
    - Human chorionic gonadotropin (hCG); *and*
    - Maternal serum alpha-fetoprotein (MSAFP); *and*
    - Unconjugated estriol.
- Full integrated testing, as defined by combination of the following:
    - First trimester combined test; *and*
    - Second trimester quadruple screen.
- Stepwise sequential testing, as defined by:
    - Initial first trimester combined test, followed by risk stratification, and if necessary, second trimester quadruple screen.

In addition to the above carrier screens and genetic tests, the Plan considers genetic testing of the diseases listed in Table 1 medically necessary when general criteria and ANY of the following criteria are met:

1. Genetic testing for a known familial variant mutation when it has been identified in the member, the member's partner, or a blood relative; *or*
2. Targeted mutation analysis when ONE of the following criteria is met:
    a. The member or reproductive partner is a known carrier of a disease-causing recessively inherited mutation; *or*
    b. A disease-causing recessively inherited mutation has been identified in a blood relative and the relative has not had testing or is unavailable for genetic testing; *or*

3. Gene sequencing and/or gene duplication/deletion analysis when ONE of the following criteria is met:
    a. The member meets criteria for target mutation analysis above; *or*
    b. Targeted mutation analysis is not available or was previously negative

Table 1: Genetic diseases

Nuclear mitochondrial genes	Muscular dystrophies	Alpha and beta thalassemia
Long QT syndrome	DFNB1 non-syndromic hearing loss and deafness	21-hydroxylase deficiency
Retinoblastoma		Niemann-Pick disease
Gaucher disease	Rett syndrome	Von Hippel-Lindau disease
PTEN-related disorders	Canavan disease	Huntington disease

Expanded Carrier Screening Panels

Expanded carrier screening may be considered medically necessary when general criteria are met and the indication and testing performed are consistent with the criteria set forth by the American Congress of Obstetricians and Gynecologists Committee on Genetics:

- The carrier frequency is greater than 1 in 100; *and*
- The phenotype is well-defined; *and*
- The condition will have a detrimental effect on quality of life; *and*
- The condition will cause cognitive and/or physical impairment; *and*
- The condition may require medical or surgical intervention; *and*
- The condition can be diagnosed prenatally; *and*
- The condition may be amenable to antenatal intervention to improve perinatal outcomes and may change delivery management; *and*
- The condition is associated with early onset in life and not adult onset.

Chorionic Villus Sampling or Amniocentesis

For women with a major fetal structural abnormality detected on ultrasound examination and when MCG criteria are met, chorionic villus sampling or amniocentesis with chromosomal microassay are medically necessary.

Experimental or Investigational / Not Medically Necessary

In addition to the below, please check Oscar Clinical Guideline: Experimental or Investigational Services, Products, Drugs, and Biologicals (CG012) for codes considered experimental, investigational, or unproven.

- Non-Invasive Prenatal Cell-Free DNA testing is considered experimental, investigational, or unproven for the following:
- Multiple gestation pregnancies with ≥ 3 fetuses.
    - *Rationale:* The use of NIPT cell-free DNA testing in multiple gestations more than twins is not endorsed by the ACOG, ACMG, SMFM, or other professional societies due to lack of testing in this population and concerns over a higher rate of false negatives given the potential for variable amounts of cell-free DNA from each fetus. As per Galeva, et al. (2019), the analysis of the risks and benefits of screening or diagnostic testing in patients carrying multiple fetuses is complex, given the lower effectiveness of screening and how the prenatal identification of a single aneuploid fetus might affect the pregnancy management.
- Vanishing twin syndrome or demised twin
    - *Rationale:* There are increased rates of false positives in cases of vanishing or demised twin in cases where the twin was aneuploid. As per Curnow, et al. (2015), 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.
- Screening for trisomy of chromosome: 7, 9, 16, or 22
    - *Rationale:* Evaluation for rare trisomies has not been fully explored in the literature, therefore the diagnostic utility of cell-free DNA testing in this setting has not yet been adopted by expert consensus guidelines. As per Norton, et al. (2015), the accuracy of screening for fetal trisomy 7,9, 16 or 22 with cfDNA in regard to detection and the false-positive rate is not established.
- Screening for microdeletions
    - cfDNA screening tests for microdeletions have not been validated clinically and are not recommended at this time (ACOG, 2020). Kagan et al. (2022) confirms the lack of clinical validity of microdeletion testing with cfDNA. This confirms that microdeletion testing by cfDNA is not validated clinically and is not recommended at this time.
- Whole genome NIPT
    - *Rationale:* The outcomes and clinical utility of whole genome sequencing have not been validated in the scientific literature. Further research is required prior to guide clinical use. As per Zhang et al. (2024), the data on cfDNA screening with whole genome sequencing in regard to detection and the false-positive rate has not been established according to the most current review.
- When used to determine the etiology of recurrent miscarriage
    - *Rationale:* The outcomes and clinical utility of cell-free DNA testing have not been validated in the scientific literature for evaluation of recurrent miscarriage. Further research is required prior to guiding clinical use.
- When used to determine fetal sex
    - *Rationale:* While NIPT has demonstrated the potential for determining fetal sex, the clinical outcomes and medical necessity of this indication have not been validated in the

literature and using NIPT to determine fetal sex has not received formal guidance from the expert societies.

- Fetal rhesus D (RhD) genotyping
    - *Rationale:* NIPT has seen some adoption across Europe in prenatal determination of rhesus D (RhD) genotyping, however, has not yet demonstrated improvement in clinical outcomes across large, validated studies. The ACOG and SMFM currently do not recommend routine use of fetal rhesus D genotyping as an indication for NIPT cfDNA testing. However, as per 2024 ACOG practice advisory (expert opinion based) for Rho(D) Immune Globulin Shortages, in the event of a shortage of Rho(D) immune globulin (RhIg) then the testing Rh(D) status in cell-free DNA (cfDNA) from maternal plasma may help triage to administer RhIg.
- Cystic hygroma
    - *Rationale:* Cystic hygroma is considered a high-risk condition for fetal aneuploidy and thus direct consideration for invasive testing should be the next step. ACOG guidelines for cell-free DNA testing state, "If a fetal structural anomaly is identified on ultrasound examination, diagnostic testing should be offered rather than cell-free DNA screening".

Non-Invasive Down Syndrome Screening

The following tests and biomarkers for the non-invasive screening for Down syndrome and other prenatal conditions are considered experimental, investigational, or unproven and thus not medically necessary unless performed as

- Second trimester screening with:
    - Beta subunit of hCG
    - Human placental lactogen
    - Pregnancy-associated plasma protein A (PAPP-A)
    - Urinary beta-core
    - *Rationale:* The clinical efficacy of diagnosing trisomy syndromes with these biomarkers has been evaluated primarily for first trimester pregnancies and has not been established for use in the second trimester and may be inferior to first trimester use.
- A Disintegrin Metalloprotease 12 (ADAM12)
    - *Rationale:* Laigaard et al (2007) looked at the use of ADAM12 as a first trimester screen for Down syndrome and found reduced levels of the biomarker, however stated that further research was needed to define its role in the screening process. A second study by Christiansen et al (2007) came to the same conclusions for ADAM12 use in the second trimester. ACOG and other societies do not currently mention the use of this biomarker.
- Placental protein 13 (PP13)
    - *Rationale:* Koster et al (2009) looked at the use of PP13 as a first trimester screen for Down syndrome and other common trisomies. They found non-significant differences in Down syndrome and variable decreases of the biomarker in other trisomies, and concluded that PP13 was NOT a good marker for Down Syndrome screening.

- First-trimester NT measurement alone (without first-trimester serum analyte testing) in the absence of fetal cystic hygroma in singleton pregnancies
    - *Rationale:* Nuchal translucency testing alone is not recommended by any of the expert consensus guidelines from ACOG or other speciality-specific societies. Research has shown that adding biomarker testing to the ultrasound decreases the rate of fetal karyotyping required and improves the predictive value.
- First-trimester serum analyte testing (hCG* and PAPP-A) alone without NT measurement
    - *Rationale:* First trimester biomarker testing alone is not recommended by any of the expert consensus guidelines from ACOG or other speciality-specific societies. The FASTER and SURUSS studies have shown that combining first trimester screening with nuchal translucency or with second trimester quadruple screen increases the detection rate and decreases false positives.
- First-trimester ultrasound assessment of the nasal bone
    - *Rationale:* A large study of 1027 patients by Orlandi et al (2003) looked at ultrasound of the nasal bone as a marker for Down syndrome. While they noted that its inclusion in first trimester screening might have some utility, they concluded that "Large datasets are needed to confirm whether the measurement of nasal bone length provides additional benefits beyond the assessment of the presence or absence of the nasal bone."
- Any other biomarker not defined above, including but not limited to the following, is considered investigational, experimental, and/or not medically necessary for use in prenatal screening:
    - First-trimester maternal serum anti-Mullerian hormone level
    - First-trimester maternal serum placental growth factor level
    - Maternal plasma microRNA
    - First-trimester maternal plasma levels of follistatin-related gene protein
- Ultrasound evaluation of the right subclavian artery (RSA)
    - *Rationale:* A 2008 study by Zalel et al. looked at the utility of aberrant subclavian artery with ultrasound as a marker of Down syndrome. They found that 37.5% of fetuses with Down Syndrome had an aberrant right subclavian artery, and 1.4% without Down syndrome. However, they concluded that "Larger prospective studies are needed to examine the significance of ARSA as an isolated finding and the potential of ARSA as a marker in Down syndrome screening.

Prenatal Lead Level Testing

Prenatal lead level testing is considered not medically necessary in women without risk factors for lead exposure.

- *Rationale:* The Centers for Disease Control and Prevention (CDC) and the American College of Obstetricians and Gynecologists (ACOG) do not recommend blood lead testing of all pregnant women unless at least one risk factor is present for elevated lead levels.

Applicable Billing Codes (HCPCS/CPT Codes)

Table 1	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
0236U	SMN1 (survival of motor neuron 1, telomeric) and SMN2 (survival of motor neuron 2, centromeric) (eg, spinal muscular atrophy) full gene analysis, including small sequence changes in exonic and intronic regions, duplications, deletions, and mobile element insertions (Genomic Unity® SMN1/2 Analysis, Variantyx Inc, Variantyx Inc)
59015	Chorionic villus sampling, any method
76813	Ultrasound, pregnant uterus, real time with image documentation, first trimester fetal nuchal translucency measurement, transabdominal or transvaginal approach; single or first gestation
76814	Ultrasound, pregnant uterus, real time with image documentation, first trimester fetal nuchal translucency measurement, transabdominal or transvaginal approach; each additional gestation (List separately in addition to code for primary procedure)
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities
81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	F5 (coagulation factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant

81243	FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81244	FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and methylation status)
81255	HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (eg, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring)
81258	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants
81329	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)
81361	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)
81362	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)
81363	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)

81364	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence
81412	Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1
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
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)
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
82105	Alpha-fetoprotein (AFP); serum

82677	Estriol
84163	Pregnancy-associated plasma protein-A (PAPP-A)
86336	Inhibin A
88235	Tissue culture for non-neoplastic disorders; amniotic fluid or chorionic villus cells
88271	Molecular cytogenetics; DNA probe, each (eg, FISH)
88291	Cytogenetics and molecular cytogenetics, interpretation and report
84704	Gonadotropin, chorionic (hCG); free beta chain
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
O09.00 - O09.03	Supervision of pregnancy with history of infertility
O09.10 - O09.13	Supervision of pregnancy with history of ectopic pregnancy
O09.A0 - 009.A3	Supervision of pregnancy with history of molar pregnancy
O09.20 - O09.23	Supervision of pregnancy with other poor reproductive or obstetric history
O09.30 - O09.33	Supervision of pregnancy with insufficient antenatal care
O09.40 - O09.43	Supervision of pregnancy with grand multiparity
O09.511 - O09.519	Supervision of elderly primigravida and multigravida
O09.521 - O09.529	Supervision of elderly multigravida
O09.611 - O09.619	Supervision of young primigravida and multigravida
O09.70 - O09.73	Supervision of high risk pregnancy due to social problems
O09.811 - O09.899	Supervision of other high risk pregnancies
O28.1	Abnormal biochemical finding on antenatal screening of mother

O28.5	Abnormal chromosomal and genetic finding on antenatal screening of mother
O30.001 - O30.099	Twin pregnancy
Z14.1	Cystic fibrosis carrier
Z14.01 - Z14.02	Hemophilia A carrier
Z14.8	Genetic carrier of other disease
Z31.430	Encounter of female for testing for genetic disease carrier status for procreative management
Z31.440	Encounter of male for testing for genetic disease carrier status for procreative management
Z31.5	Encounter for procreative genetic counseling
Z34.00 - Z34.93	Encounter for supervision of normal pregnancy
Z36.0 - Z36.9	Encounter for antenatal screening of mother
Z84.81	Family history of carrier of genetic disease
Additional ICD-10 codes considered medically necessary if criteria are met for prothrombin G20210A thrombophilia (F2 Gene) or V leiden genetic testing	
Code	*Description*
O22.30 - O22.33	Deep phlebothrombosis in pregnancy
Z86.718	Personal history of other venous thrombosis and embolism
ICD-10 codes *not* considered medically necessary for Table 1:	
Code	*Description*
O30.101 - O30.199	Triplet pregnancy or greater
O30.201 - O30.299	Quadruplet pregnancy
O30.801 - O30.899	Other specified multiple gestation

O30.90 - O30.93	Multiple gestation, unspecified
O31.00x0 - O31.8x99	Complications specific to multiple gestation
Q93.88	Other microdeletions

Table 2	
CPT/HCPCS Codes for Genetic Counseling required for prenatal testing to be considered medically necessary:	
96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family
S0265	Genetic counseling, under physician supervision, each 15 minutes

Table 3	
CPT/HCPCS codes *not* considered medically necessary for indications listed in this guideline:	
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
76815	Ultrasound, pregnant uterus, real time with image documentation, limited (e.g., fetal heart beat, placental location, fetal position and/or qualitative amniotic fluid volume), 1 or more fetuses [when used for ultrasound assessment of nasal bone translucency]
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence [when requested for routine carrier screening]

81508	Fetal congenital abnormalities, biochemical assays of two proteins (PAPP-A, hCG [any form]), utilizing maternal serum, algorithm reported as a risk score [in second trimester]
81509	Fetal congenital abnormalities, biochemical assays of three proteins (PAPP-A, hCG [any form], DIA), utilizing maternal serum, algorithm reported as a risk score [in second trimester]
82397	Chemiluminescent assay [when used for anti-Mullerian hormone level]
83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method [not medically necessary for prenatal genetic testing]
83520	Immunoassay, analyte, quantitative; not otherwise specified [not medically necessary for prenatal genetic testing]
83632	Lactogen, human placental (HPL) human chorionic somatomammotropin [in second trimester]

Table 4	
CPT/HCPCS codes considered experimental or investigational for prenatal screening:	
Code	*Description*
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood
0252U	Fetal aneuploidy short tandem-repeat comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy (POC (Products of Conception), Igenomix®, Igenomix® USA)
0341U	Fetal aneuploidy DNA sequencing comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploid (Single Cell Prenatal Diagnosis (SCPD) Test, Luna Genetics, Inc, Luna Genetics, Inc)
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (e.g., DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood

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