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Corporate Medical Policy

Prenatal Screening (Nongenetic) AHS – G2035

File Name: prenatal_screening_nongenetic
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Description of Procedure or Service

Prenatal screening encompasses any testing done to determine the health status of the pregnant individual and/or fetus. Biochemical prenatal screening encompasses screening for infectious diseases and conditions that may complicate the pregnancy. Screening refers to testing of asymptomatic or healthy individuals to search for a condition that may affect the pregnancy or individual, whereas diagnostic testing is used to either confirm or refute true abnormalities in an individual (Grant & Mohide, 1982; Lockwood & Magriples, 2023).

For guidance on thyroid screening in pregnant individuals, please see AHS-G2045-Thyroid Disease Testing.

For guidance on fetal aneuploidy screening, please see AHS-G2055-Prenatal Screening for Fetal Aneuploidy.

For guidance on screening for Zika virus infection in pregnant individuals, please see AHS-G2158-Testing for Vector-Borne Infections.

Related Policies:
Prenatal Screening (Genetic) AHS-M2179
ZIKA Virus Risk Assessment AHS-G2133
Thyroid Disease Testing AHS-G2045
Hepatis TestingAHS-G2036

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for prenatal screening when it is determined the medical criteria or reimbursement guidelines below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When prenatal screening is covered

1. Reimbursement is allowed for the following routine prenatal screening for all pregnant individuals:
   A. Screening for HIV infection.

B. Screening for Chlamydia trachomatis infection.
C. Screening for Neisseria gonorrhea infection.
D. Screening for hepatitis B.
E. Screening for syphilis.
F. Screening for hepatitis C.
G. Screening for type 2 diabetes at the first prenatal visit.
H. Screening for gestational diabetes during gestational weeks 24 – 28 and at the first prenatal visit if risk factors are present.
J. Determination of blood type, Rh(D) status, and antibody status during the first prenatal visit, and repeated Rh (D) antibody testing for all unsensitized Rh (D)-negative women at 24 to 28 weeks' gestation, unless the biological father is known to be Rh (D)-negative.
K. Screening for anemia with a CBC or hemoglobin and hematocrit with mean corpuscular volume.
L. Screening for Group B strep once recommended during gestational weeks 36 to 37 by American College of Obstetricians and Gynecologists (ACOG).
M. Urinalysis and urine culture.
N. Rubella antibody testing.
O. Testing for varicella immunity.
P. Screening for tuberculosis in pregnant individuals deemed to be at high risk for TB

2. Reimbursement is allowed for third trimester re-screening of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, syphilis, and or HIV infections for pregnant individuals who meet ANY one of the following high-risk criteria:
   A. For individuals under 25 years of age.
   B. For individuals with new or multiple sexual partners.
   C. For individuals with a history of sexually transmitted infections (bacterial vaginosis, chancroid, chlamydia, gonorrhea, genital herpes, hepatitis B, hepatitis C, HIV/AIDS, human papillomavirus, lymphogranuloma venereum, syphilis, trichomoniasis).
   D. For individuals with past or current injection drug use

3. Reimbursement is allowed for fetal Fibronectin (FFN) assays for pregnant individuals when **all** of the following criteria are met:
   A. Singleton or twin gestations;
   B. Intact membranes;
   C. Cervical dilation <3 cm,;
   D. The individual is experiencing symptoms suggestive of preterm labor between 24 and less than 35 weeks' gestation.

When prenatal screening is not covered

Reimbursement is not allowed for FFN assays for all other situations not described above.

Reimbursement is not allowed for serial monitoring of salivary estriol levels as a technique of risk assessment for preterm labor or delivery.

Reimbursement is not allowed for human chorionic gonadotropin (hCG) hormone testing for individuals with a normal pregnancy without complications.

Policy Guidelines

Prenatal screening is a part of overall prenatal care to promote optimal care of both mother and baby and allows for assessment and monitoring of the fetus for the presence of congenital defects or disease. Various professional medical organizations provide guidelines for prenatal screening. “Screening is an offer on the initiative of the health system or society, rather than a medical intervention in answer to a patient’s

complaint or health problem. Screening aims at obtaining population health gains through early detection that enables prevention or treatment" (de Jong et al., 2015).

Routine prenatal screening may include several laboratory tests, such as hematocrit or hemoglobin testing to check for anemia and possible thalassemia, pending further diagnostic testing. Blood typing and antibody screening can be performed to prevent possible alloimmunization or hemolytic diseases and glucose testing can screen for possible gestational diabetes mellitus. Screening for asymptomatic bacteriuria and proteinuria is recommended as well as screening for infectious disorders, such as HIV, syphilis, chlamydia, and gonorrhea (Lockwood & Magriples, 2023).

Red blood cell antigen discrepancy between a mother and fetus may also occur during pregnancy. This is known as hemolytic disease of the fetus and newborn (HDFN), and causes maternal antibodies to destroy the red blood cells of the neonate or fetus (Calhoun, 2023). Alloimmunization is the immune response which occurs in the mother due to foreign antigens after exposure to genetically foreign cells, occurring almost exclusively in mothers with type O blood. However, while ABO blood type incompatibility is identified in almost 15% of pregnancies, HDFN is only identified in approximately 4% of pregnancies (Calhoun, 2023). Another important inherited antigen sometimes found on the surface of red blood cells is known as the Rhesus (Rh)D antigen. During pregnancy and delivery, individuals who are RhD negative may be exposed to RhD positive fetal cells, which can lead to the development of anti-RhD antibodies. This exposure typically happens during delivery and affects subsequent pregnancies; infants with RhD incompatibility tend to experience a more severe form of HDFN than those with ABO incompatibility (Calhoun, 2023). The clinical presentation of HDFN may be mild (such as hyperbilirubinemia with mild to moderate anemia) to severe and life-threatening anemia (such as hydrops fetalis) (Calhoun, 2023). Less severely affected infants may develop hyperbilirubinemia within the first day of life; infants with RhD HDFN may also present with symptomatic anemia requiring a blood transfusion. In more severe cases, infants with severe life-threatening anemia, such as hydrops fetalis, may exhibit shock at delivery requiring an emergent blood transfusion (Calhoun, 2023).

The administration of anti-D immune globulin has been able to dramatically reduce, but not eliminate, the number of RhD alloimmunization cases. "Anti-D immune globulin is manufactured from pooled plasma selected for high titers of IgG antibodies to D-positive erythrocytes" (Moise Jr, 2022). Before the development of this anti-D immune globulin, it has been reported that 16% of pregnant RhD-negative individuals with two deliveries of RhD-positive ABO-compatible infants became alloimmunized. However, this rate falls to 1-2% with routine postpartum administration of a single dose of anti-D immune globulin. An additional administration in the third trimester of pregnancy further reduces the incidents of alloimmunization to 0.1-0.3% (Moise Jr, 2022).

Human chorionic gonadotropin (hCG) is a biomarker in the glycoprotein hormone family. Other hormones in this family include luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid stimulating hormone. hCG in pregnancy serves as an important biomarker for the detection of pregnancy-related disorders and hCG is also measured in some prenatal tests for Down syndrome. Low levels of hCG are associated with pregnancy loss and preeclampsia, while high levels can be associated with Down syndrome pregnancies (Richard Alan Harvey, 2023) A qualitative hCG test may be used to screen for pregnancy and gives a simple positive or negative result. A quantitative hCG measurement is used to assess pregnancy viability and screen for disorders. Quantitative hCG tests measures the exact amount of hCG in blood; for example, during 10-12 weeks of gestation, hCG levels are expected to approximately double every 24-48 hours, such that abnormal measurement results for hCG may indicate issues with the pregnancy (AACC, 2023).

Clinical Utility and Validity

Education and counseling are a key factor in prenatal screening and diagnostic tests. Yesilcinar and Guvenc (2021) found that a proactive intervention approach decreased anxiety and decisional conflict in the pregnant individual and increased attitudes towards the tests, having a positive effect on the pregnant

individual's knowledge level and decision satisfaction. This allowed the individual to make more informed decisions, such as opting to have screening and diagnostic testing performed. (Yesilcinar & Guvenc, 2021).

Implementation of prenatal screening tests can positively affect pregnancies and pregnancy outcomes. The Centers for Disease Control and Prevention (CDC) reports that implementation of the 1996 guidelines concerning Group B Streptococcus (GBS) had a profound effect. Prior to screening and widespread use of intrapartum antibiotics, invasive neonatal GBS occurred in 2 – 3 cases per 1,000 live births; however, after prenatal screening implementation, the rate declined to 0.5 cases per 1,000 live births in 1999 (Schrag et al., 2002). The CDC also reports from a multi-year study that screening for syphilis in all pregnant individuals at the first prenatal visit (and then rescreening in third trimester for individuals at risk) is very important in preventing congenital syphilis, which can cause spontaneous abortion, stillbirth, and early infant death. They show that 88.2% of cases of congenital syphilis was avoided when proper screening was applied; moreover, 30.9% of the cases of congenital syphilis that did occur happened when the mother did not receive proper prenatal care (≥45 days before delivery) (Slutsker et al., 2018).

Guidelines and Recommendations

American College of Obstetricians and Gynecologists (ACOG)

ACOG has several practice guidelines related to prenatal care as well as both pre-conception and prenatal testing. ACOG recommendations and guidelines include the following:

- **Vitamin D Screening:** Concerning vitamin D screening, "there is insufficient evidence to support a recommendation for screening all pregnant [individuals] for vitamin D deficiency. For pregnant [individuals] thought to be at increased risk of vitamin D deficiency, maternal serum 25-hydroxyvitamin D levels can be considered and should be interpreted in the context of the individual clinical circumstance" (ACOG, 2011). This was reaffirmed in 2021.
- **Lead Screening:** Concerning lead screening, ACOG recommends "evaluating risk factors for exposure as part of a comprehensive health risk assessment and perform blood lead testing if a single risk factor is identified. Assessment of lead exposure should take place at the earliest contact with the pregnant patient" (ACOG, 2012). This position was reaffirmed in 2023.
- **Depression and Anxiety:** "All obstetrician-gynecologists and other obstetric care providers screen patients at least once during the perinatal period for depression and anxiety symptoms using a standardized, validated tool. [They should] complete a full assessment of mood and emotional well-being (including screening for postpartum depression and anxiety with a validated instrument) during the comprehensive postpartum visit for each patient. If a patient is screened for depression and anxiety during pregnancy, additional screening should then occur during the comprehensive postpartum visit" (ACOG, 2018b).
- ***Listeria monocytogenes:*** Concerning testing for *Listeria monocytogenes*, "No testing, including blood and stool cultures, or treatment is indicated for an asymptomatic pregnant [individual] who reports consumption of a product that was recalled or implicated during an outbreak of listeria contamination. An asymptomatic patient should be instructed to return if she develops symptoms of listeriosis within 2 months of eating the recalled or implicated product" (ACOG, 2014). If an exposed pregnant individual shows signs and symptoms consistent with infection, then blood culture testing is the standard of care. Stool culture testing is not recommended since it has not been validated as a screening tool (ACOG, 2014). This position was reaffirmed in 2023.
- **HIV:** Concerning HIV, ACOG recommends that all individuals should be tested for HIV with the right to refuse testing. "Human immunodeficiency virus testing using the opt-out approach, which is currently permitted in every jurisdiction in the United States, should be a routine component of care for [individuals] during prepregnancy and as early in pregnancy as possible. Repeat HIV testing in the third trimester, preferably before 36 weeks of gestation, is recommended for pregnant [individuals] with initial negative HIV antibody tests who are known to be at high risk of acquiring HIV infection; who are receiving care in facilities that have an HIV incidence in pregnant [individuals] of at least 1 per 1,000 per year; who are incarcerated; who reside in jurisdictions with elevated HIV incidence; or who have signs and symptoms consistent with acute HIV infection (eg, fever, lymphadenopathy, skin rash, myalgias, arthralgias, headache, oral ulcers, leukopenia,

thrombocytopenia, or transaminase elevation). Rapid screening during labor and delivery or during the immediate postpartum period using the opt-out approach should be done for [individuals] who were not tested earlier in pregnancy or whose HIV status is otherwise unknown. Results should be available 24 hours a day and within 1 hour" (ACOG, 2018a).
    - For pregnant individuals who test positive for HIV, "Additional laboratory work, including $CD4^+$ count; HIV viral load; testing for antiretroviral resistance; hepatitis C virus antibody; hepatitis B surface antigen and viral load; and hepatitis A using antibody testing for immunoglobulin G for [individuals] who have hepatitis B virus infection and who have not already received the hepatitis A virus vaccine series; complete blood count with platelet count; and baseline chemistries with comprehensive metabolic testing, will be useful before prescribing antiretroviral therapy" (ACOG, 2018a).
- **Prevention of Rh D Alloimmunization:** Concerning the prevention of Rh D alloimmunization, ACOG has published the guidelines supporting the administration of anti-D immune globulin to individuals in various scenarios. However, these guidelines do not mention the use of cell-free fetal DNA for fetal RHD testing to determine if anti-D immune globulin is needed (ACOG, 2017).
- **Group B Streptococcal (GBS) Disease:** "all pregnant [individuals] should undergo antepartum screening for GBS at 36 0/7–37 6/7 weeks of gestation, unless intrapartum antibiotic prophylaxis for GBS is indicated because of GBS bacteriuria during the pregnancy or because of a history of a previous GBS-infected newborn. This new recommended timing for screening provides a 5-week window for valid culture results that includes births that occur up to a gestational age of at least 41 0/7 weeks" (ACOG, 2020).
- **Lab Tests:** ACOG lists the following lab tests to be performed early in pregnancy: complete blood count (CBC), blood type and Rh factor, urinalysis, urine culture, rubella, hepatitis B, hepatitis C, HIV, sexually transmitted infection (STI) testing, and tuberculosis (ACOG, 2021). ACOG lists the following lab tests to be performed later in pregnancy: glucose screening test and Group B streptococcus (GBS) screening (ACOG, 2021).

United States Preventive Services Task Force (USPSTF)

The United States Preventive Services Task Force (USPSTF) recommends the following testing for pregnant individuals:

- Screening for gestational diabetes in asymptomatic pregnant individuals at ≥24 weeks of gestation (Grade B) (Force, 2021).
- Screening for hepatitis B virus (HBV) infection at the first prenatal visit (Grade A) (Force, 2019c).
- Screening for asymptomatic bacteriuria with urine culture is recommended in pregnant persons (Grade B) (Force, 2019a).
- Screening for HIV is recommended in all pregnant persons, including those in labor or whose HIV status is unknown at delivery (Grade A) (Force, 2019d).
- Rh (D) blood typing and antibody testing for all pregnant individuals during their first visit for pregnancy-related care (Grade A) (USPSTF, 2005).
- Repeated Rh (D) antibody testing for all unsensitized Rh (D)-negative individuals at 24-28 weeks' gestation, unless the biological father is known to be Rh (D)-negative (Grade B) (USPSTF, 2005).
- Screening early for syphilis infection in all pregnant individuals (Grade A) (USPSTF, 2018).

Additional recommendations from the USPSTF that may be relevant during pregnancy include:

- Screening for chlamydia in sexually active individuals aged 24 years or younger and in older individuals who are at increased risk for infection (Grade B) (LeFevre & USPSTF, 2014).
- Screening for gonorrhea in sexually active individuals aged 24 years or younger and in older individuals who are at increased risk for infection (Grade B) (LeFevre & USPSTF, 2014).
- Screening for depression in general population, including pregnant and post-partum individuals (Grade B) (Siu & USPSTF, 2016).

Screening for hepatitis C virus (HCV) infection is recommended in all adults aged 18 to 79 years (Grade B) (Graham & Trooskin, 2020).

Concerning screening adults for drug use, Krist et al. (2020) state that "the USPSTF recommends screening by asking questions about unhealthy drug use in adults ages 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. (Screening refers to asking questions about unhealthy drug use, not testing biological specimens.)" The USPSTF also states that "this new evidence supports the current recommendation that primary care clinicians offer screening to adults 18 years or older, including those who are pregnant or postpartum, when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred" (Krist et al., 2020).

However, the USPSTF recommends against the following tests during pregnancy:

- Screening for bacterial vaginosis in pregnant individuals who are not at risk for preterm delivery (grade D); further, current evidence is insufficient for screening pregnant persons who are at increased risk for preterm delivery (Force, 2020).
- Serological screening for herpes simplex virus (HSV) in asymptomatic pregnant individuals (USPSTF, 2016).
- Screening for elevated blood lead levels in asymptomatic pregnant individuals has been given an I recommendation as current evidence is insufficient to determine if this testing is beneficial or not (Force, 2019b).
- "The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant [individuals] to prevent adverse maternal health and birth outcomes" (Siu, 2015).

American Diabetes Association (ADA)

The American Diabetes Association in the 2021 *Standards of Medical Care in Diabetes* make the following recommendations (American Diabetes, 2021a, 2021b):

- "Starting at puberty and continuing in all [individuals] with diabetes and reproductive potential, preconception counseling should be incorporated into routine diabetes care. [Grade] **A**
- Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications. [Grade] **B**
- [individuals] with preexisting diabetes who are planning a pregnancy should ideally be managed beginning in preconception in a multidisciplinary clinic including an endocrinologist, maternal-fetal medicine specialist, registered dietitian nutritionist, and diabetes care and education specialist, when available. [Grade] **B**
- [individuals] with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then patients should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care provider. [Grade] **B**
- Test for undiagnosed prediabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria. [Grade] **B**
- Test for gestational diabetes mellitus at 24–28 weeks of gestation in pregnant [individuals] not previously found to have diabetes. [Grade] **A**
- Screen [individuals] with a recent history of gestational diabetes mellitus at 4–12 weeks postpartum, using the 75-g oral glucose tolerance test and clinically appropriate nonpregnancy diagnostic criteria. [Grade] **B**
- [individuals] with a history of gestational diabetes mellitus should have lifelong screening for the development of type 2 diabetes or prediabetes every 1–3 years. [Grade] **B**
- [individuals] with a history of gestational diabetes mellitus found to have prediabetes should receive intensive lifestyle interventions and/or metformin to prevent diabetes. [Grade] **A**

- [individuals] with a history of gestational diabetes mellitus should seek preconception screening for diabetes and preconception care to identify and treat hyperglycemia and prevent congenital malformations. [Grade] **E**"

Centers for Disease Control and Prevention (CDC)

The Centers for Disease Control and Prevention (CDC) recommends:

Disease	First Prenatal Visit	Third Trimester	At Delivery
Syphilis	All pregnant individuals	Certain groups of pregnant individuals[5] at 28-32 weeks	Certain groups of pregnant individuals[5] at delivery
HIV	All pregnant individuals[1]	Rescreen individuals at high risk for acquiring HIV infection	Pregnant individuals not screened during pregnancy
Hepatitis B (HBV)	All pregnant individuals[2]	Test those not screened prenatally and whose who engage in behaviors that put them at a high risk[7] for infection	Pregnant individuals not screened during pregnancy[6], who are at high risk[7], or with signs or symptoms of hepatitis
Chlamydia	All pregnant individuals <25 years of age and older pregnant individuals at increased risk[3]	Pregnant individuals <25 years of age or continued high risk[3]	N/A
Gonorrhea	All pregnant individuals <25 years of age and older pregnant individuals at increased risk[4]	Pregnant individuals at continued high risk[4]	N/A
Hepatitis C (HCV)	All[8] pregnant individuals during each pregnancy	N/A	N/A

Endnotes:

1. To promote informed and timely therapeutic decisions, health care providers should test individuals for HIV as early as possible during each pregnancy.
2. All pregnant individuals should be tested for hepatitis B surface antigen (HbsAg) during an early prenatal visit (e.g., first trimester) in each pregnancy, even if they have been vaccinated or tested previously.
3. "Increased risk" means new or multiple sex partners, sex partner with concurrent partners, sex partners who have a sexually transmitted infection (STI).
4. "At increased risk" means living in a high-morbidity area, having a previous or coexisting STI, new or multiple sex partners, inconsistent condom use among persons not in mutually monogamous relationships, exchanging sex for money or drugs.
5. "Certain groups" includes individuals who are at high risk for syphilis during pregnancy, who live in areas with high numbers or syphilis cases, and/or who were not previously tested or had a positive test in the first trimester.
6. Individuals admitted for delivery at a health care facility without documentation of HbsAg test results should have blood drawn and tested as soon as possible after admission.
7. Having had more than one sex partner during the previous 6 months, an HbsAg-positive sex partner, evaluation or treatment for a STD, or injection-drug use (IDU).

8. All pregnant individuals except in a setting where the prevalence of HCV infection is (HCV RNA-positivity) <0.1%" (CDC, 2021a).

- "A second test during the third trimester, preferably at <36 weeks' gestation, should be considered and is recommended for [individuals] who are at high risk for acquiring HIV infection, [individuals] who receive health care in jurisdictions with high rates of HIV, and [individuals] examined in clinical settings in which HIV incidence is ≥1 per 1,000 [individuals] screened per year" (CDC, 2021f).
- "Regardless of whether they have been previously tested or vaccinated, all pregnant [individuals] should be tested for HBsAg at the first prenatal visit and again at delivery if at high risk for HBV infection (see STI Detection Among Special Populations). Pregnant [individuals] at risk for HBV infection and without documentation of a complete hepatitis B vaccine series should receive hepatitis B vaccination" (CDC, 2021d).
- "[individuals] aged <25 years and those at increased risk for chlamydia (i.e., those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI) should be screened at the first prenatal visit and rescreened during the third trimester to prevent maternal postnatal complications and chlamydial infection in the infant" (CDC, 2021b).
- "Annual screening for *N. gonorrhoeae* infection is recommended for all sexually active [individuals] aged <25 years and for older [individuals] at increased risk for infection (e.g., those aged ≥25 years who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI . . . [All individuals] who have been treated for gonorrhea should be retested 3 months after treatment regardless of whether they believe their sex partners were treated" (CDC, 2021c).
- "CDC recommends hepatitis C screening . . . all [individuals] during each pregnancy, except in settings where the prevalence of HCV infection is <0.1%" (CDC, 2021e).
- Zika virus testing for asymptomatic individuals is not currently recommended. For symptomatic pregnant individuals:
    - "For symptomatic pregnant [individuals] who had recent travel to areas with active dengue transmission and a risk of Zika, specimens should be collected as soon as possible after the onset of symptoms up to 12 weeks after symptom onset.
        - The following diagnostic testing should be performed at the same time:
            - Dengue and Zika virus NAAT testing on a serum specimen, and Zika virus NAAT on a urine specimen, and
            - IgM testing for dengue only.
        - Zika virus IgM testing is NOT recommended for symptomatic pregnant [individuals].
            - Zika IgM antibodies can persist for months to years following infection. Therefore, detecting Zika IgM antibodies might not indicate a recent infection.
            - There is notable cross-reactivity between dengue IgM and Zika IgM antibodies in serologic tests. Antibodies generated by a recent dengue virus infection can cause the Zika IgM to be falsely positive.
        - If the Zika NAAT is positive on a single specimen, the Zika NAAT should be repeated on newly extracted RNA from the same specimen to rule out false-positive NAAT results. If the dengue NAAT is positive, this provides adequate evidence of a dengue infection, and no further testing is indicated.
        - If the IgM antibody test for dengue is positive, this is adequate evidence of a dengue infection and no further testing is indicated" (CDC, 2019).
    - "Evidence does not support routine HSV-2 serologic testing among asymptomatic pregnant [individuals]" (CDC, 2021a).
    - "Evidence does not support routine screening for BV in asymptomatic pregnant [individuals] at high or low risk for preterm delivery" (CDC, 2021a).

To help circumvent prenatal transmission, the CDC also "recommends that all pregnant [individuals] get tested for HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), and syphilis during each pregnancy" as "screening is necessary to access medical services for HCV and treatment to prevent transmission of HIV, HBV, and syphilis to the infant" (CDC, 2020).

American College of Medical Genetics and Genomics (ACMG)

In 2014, the ACMG released guidelines concerning the diagnosis and management of phenylalanine hydroxylase (PAH) deficiency. They recommend PAH testing be part of newborn screening and that "quantitative blood amino acids testing should be performed for diagnostic testing following a positive newborn screen of PAH deficiency. Additional testing is needed to define the cause of elevated PHE and should include analysis of pterin metabolism; PAH genotypic is indicated for improved therapy planning" (Vockley et al., 2014).

World Health Organization (WHO)

In 2016, the WHO released their publication titled, *WHO recommendations on antenatal care for a positive pregnancy experience*, which had the following recommendations (WHO, 2016):

- Anemia (Context-specific recommendation)—"Full blood count testing is the recommended method for diagnosing anaemia in pregnancy."
- Asymptomatic bacteriuria (Context-specific recommendation)—"Midstream urine culture is the recommended method for diagnosing asymptomatic bacteriuria (ASB) in pregnancy. In settings where urine culture is not available, on-site midstream urine Gram-staining is recommended over the use of dipstick tests as the method for diagnosing ASB in pregnancy."
- Gestational diabetes mellitus (Recommended)—"Hyperglycaemia first detected at any time during pregnancy should be classified as either gestational diabetes mellitus (GDM) or diabetes mellitus in pregnancy, according to WHO criteria."
- HIV and syphilis (Recommended)—"In high-prevalence settings, provider-initiated HIV testing and counselling (PITC) for HIV should be considered a routine component of the package of care for pregnant [individuals] in all antenatal care settings. In low-prevalence settings, PITC can be considered for pregnant [individuals] in antenatal care settings as a key component of the effort to eliminate mother-to-child transmission of HIV, and to integrate HIV testing with syphilis, viral or other key tests, as relevant to the setting, and to strengthen the underlying maternal and child health systems."
- Tuberculosis (Context-specific recommendation)—"In settings where the tuberculosis (TB) prevalence in the general population is 100/100 000 population or higher, systematic screening for active TB should be considered for pregnant [individuals] as part of antenatal care" (WHO, 2016).

Department of Veterans Affairs/Department of Defense (VA/DoD)

In the 3rd edition of the VA/DoD *Clinical Practice Guideline for the Management of Pregnancy* (VA & DOD, 2018), they list the following lab tests as routine for all pregnancies in the first prenatal visit: HIV, CBC, ABO Rh blood typing, Antibody screen, anemia/hemoglobinopathies screen, rapid plasma reagin, gonorrhea, chlamydia, hepatitis B surface antigen test, rubella IgG, Urinalysis and culture, and varicella IgG (if status is unknown). They also list the following among their recommendations (VA & DOD, 2018):

- "We recommend screening for use of tobacco, alcohol, illicit drugs, and unauthorized use of prescription medication because their use is common and can result in adverse outcomes. For [individuals] who screen positive, we recommend additional evaluation and treatment." [Strong]
- "We recommend screening for depression using a standardized tool such as the Edinburgh Postnatal Depression Scale or the 9- item Patient Health Questionnaire periodically during pregnancy and postpartum." [Strong]
- "We suggest making prenatal diagnostic testing for aneuploidy available to all pregnant [individuals]." [Weak]
- "We recommend offering prenatal screening for aneuploidy and the most common clinically significant genetic disorders to all pregnant [individuals]. When aneuploidy screening is desired, cellfree fetal DNA screening should be considered; however, screening test selection should be individualized and take into account the patient's age, baseline aneuploidy risk, and test performance for a given condition." [Strong]

- "We suggest the two-step process (one-hour oral glucose challenge test followed by three-hour oral glucose tolerance test) to screen for gestational diabetes mellitus at 24-28 weeks gestation for all pregnant [individuals]." [Weak]
- "We suggest that pregnant [individuals] with an unexplained elevation of maternal serum alpha-fetoprotein be evaluated and counseled by a qualified obstetric provider due to increased risk for adverse perinatal outcomes." [Weak]
- "We recommend **against** routine screening for preterm delivery using the fetal fibronectin test in asymptomatic [individuals]." [Strong, against]
- "We recommend considering the use of fetal fibronectin testing as a part of the evaluation strategy in [individuals] between 24 and 34 6/7 weeks gestation with signs and symptoms of preterm labor, particularly in facilities where the result might affect management of delivery." [Strong]
- "We suggest that [individuals] who have undergone bariatric surgery should be evaluated for nutritional deficiencies and need for nutritional supplementation where indicated (e.g., vitamin B12, folate, iron, calcium)." [Weak]

Health Resources & Services Administration (HRSA)

The HRSA recommends the following:

- "Screening pregnant individuals for gestational diabetes mellitus after 24 weeks of gestation (preferably between 24 and 28 weeks of gestation)
- Individuals with risk factors for diabetes mellitus be screened for preexisting diabetes before 24 weeks of gestation—ideally at the first prenatal visit.
- Screening for HIV is recommended for all pregnant [individuals] upon initiation of prenatal care with retesting during pregnancy based on risk factors.
- Rapid HIV testing is recommended for pregnant [individuals] who present in active labor with an undocumented HIV status" HRSA (2022).

State and Federal Regulations, as applicable

The FDA has approved many tests for conditions that can be included in a prenatal screening, such as HSV, chlamydia, gonorrhea, syphilis, and diabetes. Additionally, many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 80081, 80055, 81001, 81002, 81003, 81007, 81015, 82677, 82731, 82947, 82950,82951, 82962,83020, 83021, 83036, 84702, 84703, 84704, 85004, 85007, 85009, 85014, 85018, 85025, 85027, 85032, 85041, 85048, 86480, 86580, 86592, 86593, 86631, 86632, 86701, 86702, 86703, 86704, 86706, 86762, 86787, 86780, 86803, 86804, 86850, 86900, 86901, 87077, 87081, 87086, 87088, 87110, 87270, 87320, 87340, 87341, 87490, 87491, 87590, 87591, 87592, 87653, 87800, 87802, 87810, 87850, G0306, G0307, G0432, G0433, G0435, G0472, 0176U, and S3652

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

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Specialty Matched Consultant Advisory Panel 04/2020

Medical Director review 04/2021

Medical Director review 04/2022

Medical Director review 7/2022

Medical Director Review 7/2023

Policy Implementation/Update Information

For policy titled: Prenatal Screening

1/1/19	New policy developed. BCBSNC will provide coverage for prenatal screening when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (an)
6/11/19	Reviewed by Avalon 1st quarter 2019 CAB. Updated Description section. Added Item 3.I to "When Covered" section: Next generation sequencing (NGS) panel testing of either Ashkenazi Jewish related disorders panel or panethnic carriers screening panel of 15 tests as long as a single appropriate AMA genetic sequencing procedure test code is submitted. Added codes 81507 and 0009M to Billing/Coding section. Medical Director review 5/2019. (an)
7/1/19	Correction to Billing/Coding section: code 81420 does not require PPA. (an)
12/31/19	Correction to Billing/Coding section: code 0009M deleted. Coding grid removed, and codes listed. No change to policy statement. (eel)
5/12/20	Reviewed by Avalon 1st quarter 2020 CAB. Medical Director review 4/2020. Specialty Matched Consultant Advisory Panel review 4/29/2020. Updated Description, Policy Guidelines, Coding and References. "Reimbursement is not allowed for carrier screening more than once per lifetime." added to When not covered section. Added Note 1 for clarity concerning proper carrier screening testing. Note 1 reads as follows: "Carrier testing should be performed using the most appropriate carrier test (e.g. dosage/deletion for SMN1 and NOT full gene sequencing; DMD del/dup testing and NOT full gene sequencing)." Changed Panel testing of carrier status for biological father from investigational to does not meet coverage criteria. Medical necessity language updated to reimbursement language. (eel)
10/1/20	Updated Coding section with new code 0222U effective 10/1/20. (eel)
11/10/20	Reviewed by Avalon 3rd quarter 2020 CAB. Updated Description, Policy Guidelines, and References. Clarified N. gonorrhea as Neisseria gonorrhoeae in when covered section. Removed high risk criteria from when covered section 1F. (eel)
3/31/21	Specialty Matched Consultant Advisory Panel 3/9/21. No change to policy statement. (bb)
5/4/2021	Reviewed by Avalon 1st quarter 2021 CAB. Description, Policy Guidelines, and Reference section updated. When covered items 1h, 1m, 3f, 3h updated for clarity. Code 81220 added to Billing/Coding section. (bb)

5/17/22 Reviewed by Avalon 1st quarter 2022 CAB. Description, Policy Guidelines, and Reference section updated. Changed woman/women to individual/individuals throughout coverage criteria. Eliminated ethnicity specific phrases in coverage criteria. Billing/Coding section updated. Medical Director Review 4/2022. (tt)

Policy Re-titled: Prenatal Screening (Nongenetic)

9/13/22 Reviewed by Avalon 2nd quarter 2022 CAB. Policy re-titled: Prenatal Screening (Nongenetic). Description, Related Policies, Policy Guidelines, and References updated. Coverage criteria updated to remove criteria related to genetic prenatal screening as this has been moved to new policy – Prenatal Screening (genetic). Billing/Coding section updated. Medical Director review 7/2022. **Notification given on 9/13/2022 for effective date 10/18/2022.** (tt)

8/15/23 Reviewed by Avalon 1st quarter 2023 CAB. Description, Policy Guidelines, and Reference section updated. Updated when covered section for clarity. Add the following to when not covered: "Reimbursement is not allowed for human chorionic gonadotropin (hCG) hormone testing for individuals with a normal pregnancy without complications." Added 84702, 84703, 84704, and 0167U to Billing/Coding section. Medical Director Review 4/2023. **Notification given 8/15/2023 for effective date 10/24/2023.** (tt)