PREDICTORS OF PRETERM LABOR
OB401.013

COVERAGE:

**Fetal Fibronectin (fFN)**

Fetal Fibronectin Rapid System (Rapid fFN) testing may be eligible for coverage for use in women with a single fetus gestation and the following criteria:

- Amniotic membranes are intact;
- Cervical dilatation is minimal (less than 3 centimeters);
- Cervicovaginal swab (method to collect and test cervicovaginal secretions) is performed no earlier than 24 weeks, 0 days of gestation and no later than 34 weeks, 6 days of gestation; and,
- Symptoms of preterm labor are suggestive of an increased risk for preterm delivery of less than 34 weeks gestation, warranting consideration of admission for monitoring, inhibiting uterine contractions, and/or treating with corticosteroids.

The patient may remain in an outpatient setting during the minimum one hour delay in receiving the results, but may be released to daily activities promptly if the fFN test is negative and symptoms have resolved. Negative test results indicate the patient is not experiencing preterm labor.

Fetal Fibronectin Rapid System testing is not eligible for coverage as it is considered investigational for all other situations including, but is not limited to:

- routine pregnancy monitoring in women with single fetus gestations, with no risk factors for preterm delivery, and without symptoms of preterm labor;
- high risk clinical monitoring in women with multiple fetus gestations or other high risk characteristics for preterm delivery (such as previous history of preterm delivery, uterine malformation, cervical incompetence, history of two or more spontaneous second trimester abortions) and without symptoms of preterm labor;
- women at term (greater than 37 weeks gestation) being considered for induction (the process of causing labor and delivery to occur) and who are likely to deliver within 24 - 48 hours; and
- women with multiple fetus gestations or other high-risk characteristics for preterm delivery, and who are experiencing symptoms suggestive of preterm labor.

Fetal Fibronectin Immunoabsorbent Assay is not eligible for coverage as it has been replaced by the newer Rapid fFN testing to assess
patients at risk for preterm delivery.

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Salivary Estriol (SE)

Serial monitoring of salivary estriol levels, using the Salivary Estriol (SE) SalEst system, is not eligible for coverage as a technique of risk assessment for spontaneous preterm labor or delivery.

DESCRIPTION:

Predictors of Preterm Labor are used to assess the risk of subsequent early delivery. In addition to risk factors, history, symptoms, and physical examination, which includes assessment by sonography of cervical length, several diagnostic tests have been developed for the purpose of diagnosing preterm labor (PTL). Fetal fibronectin (fFN) and salivary estriol (SE) have been helpful in predicting labor and/or preventing preterm delivery.

Fetal Fibronectin (fFN)

Fetal Fibronectin (fFN) is a high molecular weight glycoprotein that can be isolated from fetal connective tissue, placenta and amniotic fluid. fFN can be measured with an immunoassay of monoclonal antibody in cervicovaginal secretions early in pregnancy, and at term. fFN is rarely detectable between 21 and 37 weeks gestation in normal pregnancies that are subsequently delivered at term (greater than 37 weeks). The studies indicate that the elevation of fFN signals the separation of the placental uterine junction, and thus fFN may be a useful marker in predicting which women will achieve spontaneous labor usually within a 7 day period of time.

In January 1997, the FDA had approved the fFN enzyme immunoassay or immunoabsorbent assay kit as an aid in assessing the risk of preterm delivery. Results are provided within 24 to 36 hours from the manufacturer's clinical laboratory. In August 1998, the FDA had approved the fFN Rapid System, also, as an aid in assessing risk of preterm delivery. Results are provided within 60 minutes from the hospital's laboratory. Their primary value is in ruling out PTL in women who are experiencing signs and symptoms of PTL, but whose signs and symptoms subside during an initial period of observation. If fFN testing is to be used, specific criteria (listed earlier in this policy) should be followed.

The test is not recommended for routine screening of the general obstetrical population. According to the American College of Obstetrics and Gynecology, widespread use of the test in asymptomatic low-risk patients has the potential to add significant cost to prenatal care without any proven benefit.

Salivary Estriol (SE)

Salivary Estriol (SE) (SalEst) is an estrogenic hormone that can be isolated in saliva. SalEst is intended to detect and measure, by enzyme-linked immunoabsorbent assay (ELISA) technology, the level of salivary estriol in pregnant women. The studies indicate a surge in estriol concentrations consistently occur approximately three weeks
before the onset of labor in both women delivering at term and those delivering preterm. Salivary estriol has only been implicated as a possible predictor of spontaneous PTL.

In April 1998, the FDA approved SalEst (registered) device and recommends "the test should be used as an aid in assessing the risk of preterm labor." The manufacturer reports that SE testing is more accurate in predicting risk than the traditional scoring methods. SalEst is sent from the physician's office or the patient's home or work to the manufacturer's lab for processing. The results are returned to the physician's office.

RATIONALE:

**Fetal Fibronectin (fFN)**

Studies have concluded that a negative fFN result can be used immediately to prompt discontinuation or avoidance of hospitalization and elimination further treatment, since the consistently high negative predictive value of this test within a 2-week interval provides evidence that only 1% of these women will deliver preterm. Because of the relatively low positive predictive value of the test, positive results may support the need for hospitalization and preventive measures. It should be noted that the target patient population in any of these scenarios MAY/MAY NOT be hospitalized, whether positive or negative results are used to direct treatment.

A recent TEC assessment concluded that there was inadequate data to support the other proposed applications of fFN testing. Specifically, in asymptomatic patients both with and without additional risk factors for preterm birth, the assessment concluded that the positive predictive value was inadequate to identify women who require preventive treatment based upon the fFN result alone. There were no studies addressing the use of fFN in symptomatic patients with additional high-risk factors for preterm birth; these high-risk patients are presumably already undergoing standard aggressive management of symptoms and there is no data to suggest that the results of fFN would alter management. Finally, the assessment concluded that there is insufficient evidence to support the use of fFN testing to identify women at term being considered for induction who are likely to deliver within 24-48 hours and therefore do not require induction.

**Salivary Estriol (SE)**

The convenience of measuring estriol in the saliva creates the opportunity of routine monitoring of pregnant women to identify women at risk of preterm labor. The scientific rationale for this approach is based on the observation that a rise in estriol typically rises prior to delivery at term, as well as prior to preterm delivery. The manufacturers of the SalEst recommend the following clinical applications of the test:

- monitoring of SE should be used as a component of the clinician's assessment or risk for preterm labor and delivery.

- in the event of an initial positive test, further monitoring for other risk factors for preterm birth, INCLUDING REPEATED SALIVARY
ESTRIOL TEST, should be performed. If the rescan test is also positive, high-risk case should be maintained.

- a negative test predicts the likelihood of not delivering within the ensuing two weeks.

Despite the above recommendations, there are no clinical studies available that demonstrate that treatment decisions made based on either the positive or negative predictive value of SE result in beneficial outcomes. There is no evidence that compares the birth outcomes of a group of patients undergoing SE testing compared with a group of patients without SE testing. Improved outcomes of patients undergoing testing would result if physicians make better management decisions based on the test results. Prediction of an outcome does not imply that prevention is possible. When compared to fFN, the assays are done only at the time the patient becomes symptomatic (one time only). Whereas monitoring SE, it is recommended that the patient undergo testing every 1 to 2 weeks from 24 weeks on. If the patient becomes symptomatic, a new test can be done and compared to the previous test to determine if there has been an increase of estriol levels.

DISCLAIMER:

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, takes precedence over Medical Policy and must be considered first in determining coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Any benefits are subject to the payment of premiums for the date on which services are rendered. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically. HMO Blue Texas physicians who are contracted/affiliated with a capitated IPA/medical group must contact the IPA/medical group for information regarding HMO claims/reimbursement information and other general polices and procedures.

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