Effective November 1, 2023, refer to CMS Manual 100-08, Chapter 3, Section 3.6.2.2- Reasonable and Necessary

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Fetal Fibronectin Enzyme Immunoassay

Policy #: 063
Latest Review Date: May 2023
Category: Laboratory
ARCHIVED 11/1/2023

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Blue Advantage will treat **FFN (fetal fibronectin enzyme) assays** as a **covered** benefit for use in women:

- With singleton or twin gestations; and
- With intact amniotic membranes; and
- Cervical dilation less than 3 cm; and
- Who are experiencing symptoms suggestive of preterm labor between 24 and less than 35 weeks gestation.

*This population represents women who are most likely to be hospitalized and treated in an attempt to prevent preterm birth.

Blue Advantage will treat **all other applications of the FFN (fetal fibronectin enzyme) assay** as a **non-covered benefit** and as **investigational**, including, but not limited to, the following:

- As part of routine pregnancy monitoring in asymptomatic women with singleton gestation and no risk factors for preterm birth;
- As part of clinical monitoring of asymptomatic women at high risk for preterm birth, including, but not limited to:
    - Those with multiple gestations;
    - History of preterm birth;
    - Uterine malformation;
    - Cervical incompetence;
    - History of two or more spontaneous second trimester abortions;
- As part of clinical monitoring in women with:
    - Triplet or higher-order gestations;
    - Intact amniotic membranes;
    - Cervical dilation less than 3 cm;
    - Who are experiencing symptoms suggestive of preterm labor;
- As a test to identify women at term being considered for induction that are likely to deliver within 24-48 hours and therefore, do not require induction.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Assessment of fetal fibronectin (FFN) is proposed for use in the diagnosis and management of preterm labor (PTL) and in the management of women at term being considered for induction. A rapid test is available that can provide results within 20 minutes. FFN testing has been considered for several categories of patients including women who are experiencing symptoms of preterm labor, asymptomatic women at increased risk of pre-term labor and asymptomatic women as part of routine pregnancy care.

Fetal fibronectin (FFN) is a high-molecular-weight glycoprotein that can be isolated from fetal connective tissue, placenta, and amniotic fluid. Fetal fibronectin can be measured in cervicovaginal secretions early in pregnancy (normally found in cervical secretion until 16-20 weeks of gestation) and at term, but is rarely detectable between 21 and 37 weeks' gestation in normal pregnancies that are delivered at term. However, in several studies FFN may also be detected between 21 and 37 weeks in association with preterm delivery. It has been hypothesized that 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 within a short period of time. Originally, immunoassays of FFN were available only at specialized reference laboratories performing the enzyme linked immunoabsorbent assay (ELISA), which produced semi-quantitative results. Because tests had to be sent to a reference lab, there was a minimum 24-hour delay between sampling and receipt of the results. A rapid fetal fibronectin test is now available permitting results within 20 minutes of testing. This assay produces qualitative results, reported as positive, negative, or indeterminate. Generally, a FFN level of 50 ng/mL or higher is considered a positive test.

The clinical importance of measurements of FFN relates to the diagnosis and management of preterm labor. Clinical symptoms of PTL are nonspecific and include vaginal spotting or bleeding, increased or changed vaginal discharge, intermittent abdominal cramping, backache, and inappropriate uterine contractions. Signs of PTL include cervical effacement and dilation, or a shortened cervix, as assessed by transvaginal ultrasound. When symptoms of PTL develop and the physical exam does not immediately confirm a diagnosis of progressive PTL, the patient is usually hospitalized for an initial period of observation to determine if the symptoms subside or progress. During this time, bed rest and possible treatment in the form of IV hydration, antibiotics, tocolytic drugs, or prostaglandin inhibitors depending upon the symptoms and results of the physical exam, are prescribed. All current tocolytic agents are considered superior to no treatment at delaying delivery for both 48 hours and seven days, however, prostaglandin inhibitors are considered superior to the other agents and may be considered the optimal first-line agent before 32 weeks of gestation to delay delivery. In many cases, the symptoms of PTL subside during the period of observation and prophylactic treatment. However, if the signs and symptoms of PTL are sufficiently advanced or suspicious, delivery within seven days may be highly likely. In these cases, particularly if gestation is 34 weeks or less, corticosteroid treatment for the induction of fetal lung maturity is indicated.

Accurate diagnosis of PTL is extremely difficult; current methods of assessing risk can result in overdiagnoses of PTL. FFN has been investigated as a method to more accurately diagnose PTL and thus eliminate unnecessary hospitalizations, tocolytic therapy, and corticosteroid treatment in

women who do not truly have PTL. The use of FFN has been studied in several different categories of patients:

- Women of average risk who are experiencing symptoms suggestive of preterm labor;
- Women with multiple gestations or other high-risk factors for preterm birth who are experiencing symptoms of preterm labor;
- Asymptomatic women with no risk factors for preterm birth; FFN is used in these patients as a screening test at certain intervals during pregnancy;
- Asymptomatic women with multiple gestations or other high-risk characteristics of preterm birth;
- Women at term being considered for induction who are likely to deliver within 24-48 hours and therefore do not require induction.

KEY POINTS:

Policy was updated with literature review performed on May 12, 2022.

Summary of Evidence

Systematic reviews have found a significant impact of FFN testing in women with singleton pregnancies and symptoms of preterm labor on reduced rates of preterm birth before 37 weeks' gestation and on hospitalization rates. There is insufficient evidence that FFN testing improves the net health outcome for asymptomatic women at average risk or at increased risk of preterm labor. No published evidence was identified on FFN assessment in women with triple or higher-order gestations or in women being considered for induction. Thus, FFN assessment may be considered medically necessary in women with singleton or twin gestations who have signs or symptoms of preterm labor, since the original premise has not been disproven. However, use of FFN assessment is considered investigational for all other applications.

Practice Guidelines and Position Statements

American Congress of Obstetricians and Gynecologists

The 2016 American Congress of Obstetricians and Gynecologists (ACOG) position statement is as follows: "The positive predictive value of a positive fetal fibronectin test redult or a short cervix alone is poor and should not be used exclusively to direct management in the setting of acute symptoms".

Society for Maternal Fetal Medicine

The Society for Maternal Fetal Medicine (SMFM) position statement is as follows: "FFN seems to be most helpful for women with a 'boarderline' transvaginal ultrasound cervical length of 20-29 mm."

U.S. Preventative Services Task Force

Not applicable.

KEY WORDS:
Fetal fibronectin enzyme immunoassay, fetal fibronectin, FFN, preterm labor testing, premature labor testing, cervicovaginal FFN, PTL

APPROVED BY GOVERNING BODIES:
In 1998, a rapid qualitative FFN test (Adeza Fetal Fibronectin Enzyme Immunoassay, Adeza Biomedical, Sunnyvale, CA) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process. The test is indicated:

- As an aid to rapidly assess the risk of preterm delivery in less than seven or less than 14 days from the time of sample collection in pregnant women with signs and symptoms of early preterm labor, intact amniotic membranes, and minimal cervical dilation (less than three cm) sampled between 24 weeks and less than 35 weeks' gestation;
- For use in conjunction with other clinical information to rapidly assess the risk of preterm delivery before 35 weeks in women with singleton pregnancies undergoing a routine prenatal examination between 22 weeks and less than 31 weeks.

BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:
CPT codes:

82731	Fetal fibronectin, cervicovaginal secretions, semiquantitative

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POLICY HISTORY:

Adopted for Blue Advantage, March 2005
Available for comment May 1-June 14, 2005
Medical Policy Group, August 2006
Medical Policy Group, August 2009
Medical Policy Group, October 2010: Active Policy but no longer scheduled for regular literature reviews and updates effective October 13, 2010.
Medical Policy Group, June 2019
Medical Policy Group, May 2021
Medical Policy Group, October 2021: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, May 2022: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, May 2023: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, November 2023: Archived effective 11/1/2023.
