Progesterone Therapy as a Technique to Reduce Preterm Birth in High-Risk Pregnancies

Policy Number: MM.03.005
Line(s) of Business: HMO; PPO; QUEST
Section: OB/GYN & Reproduction
Place(s) of Service: Outpatient

I. Description

Preterm birth is the leading cause of neonatal morbidity and mortality, and effective primary preventive interventions have remained elusive. In recent years, there has been renewed interest in the use of progesterone (injectable and intravaginal formulations) to prevent preterm birth.

Preterm labor and delivery are major determinants of neonatal morbidity and mortality. In the U.S., the rate of preterm birth is 12%. A variety of diagnostic and prophylactic measures have been investigated including home uterine activity monitoring, subcutaneous terbutaline tocolytic therapy, and routine culture and antibiotic treatment of subclinical bacterial vaginosis. To date, none of these had made a significant demonstrable impact on the incidence of preterm delivery. In the past, intramuscular injections of hydroxyprogesterone caproate (i.e., Delalutin) were used routinely to prevent premature labor. However, the drug was shown to have teratogenic properties, and the U.S. Food and Drug Administration (FDA) labeled the drug as Category D (i.e., studies have demonstrated fetal risk, but use of the drug may outweigh the potential risk). Delalutin is no longer marketed.

In recent years, there has been renewed research interest in intramuscular injection of 17 alpha-hydroxyprogesterone caproate (17P). 17P is a weakly acting, naturally occurring progesterone metabolite, which when coupled with caproate dextran works as a long-acting progestin when administered intramuscularly. 17P has been manufactured locally by compounding pharmacies. After an extended application process, Makena®, another injectable form of 17P was approved by the FDA in February 2011. Intravaginal progesterone gel and suppositories have also been used.

On February 3, 2011, an injectable formulation containing 17-alpha-hydroxyprogesterone caproate was approved by the FDA through the premarket approval process. The product is called Makena...
and will be marketed by KV Pharmaceuticals. It is indicated to reduce preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. Makena is not intended for use in women with multiple gestations or in women with other risk factors for preterm birth.

II. **Criteria/Guidelines**

Progesterone therapy is covered as follows (subject to Limitations/Exclusions and Administrative Guidelines):

A. Weekly injections of 17 alpha-hydroxyprogesterone caproate, performed in the office setting, initiated between 16 and 20 weeks of gestation and continued until 36 weeks 6 days are covered for women with a prior history of spontaneous preterm birth* before 37 weeks’ gestation.

B. Daily vaginal progesterone between 24 and 34 weeks of gestation is covered for women with a prior history of spontaneous preterm birth* before 37 weeks’ gestation.

C. Daily vaginal progesterone initiated between 20 and 23 weeks 6 days of gestation and continued until 36 weeks 6 days is covered for women with a short cervix (less than 20 mm).

*Spontaneous preterm birth is defined as birth due to spontaneous preterm labor or preterm premature rupture of the fetal membranes. Preterm birth due to infection, uterine anomaly, multiple gestation, polyhydramnios, abruption placenta, placenta previa or trauma do not meet the definition of spontaneous preterm birth for the use of 17P.

Note: It should be noted that appropriate training of certified ultrasonographers with ongoing quality assurance programs are considered critical to the accurate measurement of cervical length in the second trimester.

III. **Limitations/Exclusions**

Progesterone therapy as a technique to prevent preterm delivery does not meet payment determination criteria in pregnant women with other risk factors for preterm delivery, including but not limited to multiple gestations, or positive tests for cervicovaginal fetal fibronectin, cervical cerclage, or a uterine anomaly.

IV. **Administrative Guidelines**

A. Precertification is required for Makena. To precertify, please complete HMSA's [Precertification Request](#) and mail or fax the form as indicated.

B. Precertification is not required for other forms of 17P. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.

C. QUEST members must obtain the drug through a participating pharmacy.

D. Applicable codes
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<thead>
<tr>
<th>CPT</th>
<th>Description</th>
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<tr>
<td>96372</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular</td>
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<tr>
<th>HCPCS</th>
<th>Description</th>
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<tr>
<td>J1725</td>
<td>Injection, hydroxyprogesterone caproate, 1 mg (new code effective 1/1/12)</td>
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V. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VI. References


21. Blue Cross Blue Shield Association. Progesterone Therapy as a Technique to Reduce Preterm Birth in High-Risk Pregnancies. 4.01.16; September 2012.