Progesterone for Prevention of Preterm Birth

Intramuscular 17α-Hydroxyprogesterone

[Preauthorization Required]

Medical Policy: MP-ME-04-10
Original Effective Date: May 27, 2010
Reviewed: June 16, 2011

DESCRIPTION

Preterm birth is defined as a delivery that takes place between approximately 22 weeks gestation (the time of fetal viability) and 37 weeks gestation; birth before 22 weeks gestation is considered a miscarriage.

Hydroxyprogesterone caproate is a synthetic derivative of progesterone sharing the pharmacologic actions of all progestins. 17 α-hydroprogesterone (17-P) has minimal prostaglandin activity; however, the esterified form, hydroxyprogesterone caproate has significant progesterone effects and a prolonged duration of action, from 7 to 14 days. The drug also has reported androgenic, estrogenic, and glucocorticoid activity.

Hydroxyprogesterone caproate is used for the treatment of amenorrhea and for the treatment of dysfunctional uterine bleeding caused by fibroids or uterine cancer. The drug stimulates a proliferative endometrium into secretion as well as stimulates the growth of mammary alveolar tissues. Hydroxyprogesterone caproate’s mechanism of action in endometrial cancer is not understood; however, the drug has antineoplastic activity.

Although progestins have been used in the first trimester of pregnancy to prevent habitual abortion or threatened abortion, their use is not without risk and adverse effects. All progestins, including hydroxyprogesterone caproate have potential teratogenic effects.
Intravaginal progesterone suppositories have also been investigated, including female fetus masculinization. They have a pregnancy use category of D where studies have demonstrated fetal risk, but that use of the drug may outweigh potential risks.

More recent research studies use hydroxyprogesterone caproate to prevent preterm labor during second trimester when teratogenic risk is diminished. Preterm births occur in approximately one of every eight pregnancies and result in significant morbidity and mortality. The precise mechanism for hydroxyprogesterone caproate in prevention of preterm labor and delivery is unknown, although it is understood that progesterone has beneficial effects towards the maintenance of pregnancy.

In the past intramuscular injections of 17 alpha hydroxyporgesterone were used routinely to prevent premature labor. However, the drug was shown to have teratogenic (tending to produce abnormalities in the formative or developmental stage). Most recently there has been renewed research interest in intramuscular injection of 17-alpha-hydroxyprogesterone caproate (17P).

17P is a weak acting naturally occurring progesterone metabolite, which when coupled with Caproate dextram works as a long acting progestin when administered intramuscularly. 17P is not commercially available, but can be manufactured locally by compounding pharmacies. Intravaginal progesterone suppositories have also been investigated.

**COVERAGE**
Benefits may vary between groups and contracts. Please refer to the appropriate member certificate and subscriber agreement contract for applicable diagnostic imaging, DME, laboratory, machine tests, benefits and coverage.

**INDICATIONS**
MCS considers the administration of intramuscular 17 α-hydroxyprogesterone reasonable and medically necessary for the treatment of preterm labor, when all of the following criteria’s are met:

- History of spontaneous preterm birth (<37 wks)
- Singleton pregnancy
- When initiating treatment between 16 weeks, 0 days and 20 weeks, 6 days of gestation
- Treatment will be completed when the pregnancy reaches 37 weeks of gestation or birth; whichever comes first
Note: Initiation for late prenatal care, 17P may be initiated as late as 26 wks, 6 days gestation

HOME SERVICES

- Medical necessity for the administration of intramuscular 17α- hydroxyprogesterone at home services will be evaluated independently.
- MCS requires home visits be recorded in the progress notes and appointments must be recorded on a Patient Tracking Form.

EXCLUSION CRITERIA

- Known fetal anomaly
- Current or planned cervical cerclage
- Hypertension
- Seizure disorders

CONTRAINDICATIONS/LIMITATIONS

- Multi-fetal pregnancy
- Short cervix and no prior preterm birth
- Previous medically indicated preterm birth
- Current or past history of thrombophlebitis, thromboembolic disorders, or cerebral apoplexy or a history of these conditions
- Undiagnosed vaginal bleeding
- Missed abortion
- Known sensitivity to the drug or any ingredient in the formulation
- Known or suspected malignancy of breast or genital organs
- Markedly impaired liver function or liver disease
- Carcinoma of the breast
- Diabetic patients should be carefully observed while receiving such therapy
• Weekly intramuscular injection (suggested range of time in between injections is 5 to 9 days, progesterone stays in the body for approximately 7 days).

**NOTE:** Progesterone therapy as a technique to prevent preterm labor is considered **experimental/investigational** in pregnant women with other risk factors for preterm delivery, including but not limited to, multiple gestations, short cervical length, positive tests for cervicovaginal fetal fibronectin, and a prior cervical cerclage or a uterine anomaly.

**CODING INFORMATION**

**CPT® Codes**

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>DESCRIPTION</th>
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<tbody>
<tr>
<td>96372</td>
<td>Therapeutic, Prophylactic, or diagnostic injection (specify substance or drug); Subcutaneous or Intramuscular.</td>
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**HCPCS CODES**

<table>
<thead>
<tr>
<th>HCPCS® CODES</th>
<th>DESCRIPTION</th>
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<tr>
<td>S9208</td>
<td>Home management of Preterm labor, including administrative services, professional pharmacies services, care coordination, and all necessary supplies or equipment (drug and nursing visits coded separately), per diem (do not use this code with home infusion per diem code)</td>
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<tr>
<td>J3490</td>
<td>Unclassified Drug</td>
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*2011 HCPCS LEVEL II Professional Edition® (American Medical Association).*

*5 codes are excluded for Classicare LOB. 5 codes only apply to Commercial and HMO LOB.*
ICD-9 CM® Diagnosis Codes

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<thead>
<tr>
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<td>644.00</td>
<td>Threatened premature labor, unspecified as to episode of care</td>
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<tr>
<td>644.03</td>
<td>Threatened premature labor, ante partum condition or complication</td>
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<tr>
<td>644.20</td>
<td>Early onset of delivery, unspecified as to episode of care</td>
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<tr>
<td>V13.21</td>
<td>Personal History of pre-term labor</td>
</tr>
<tr>
<td>V23.41</td>
<td>Supervision of pregnancy with history of pre-term labor</td>
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REFERENCES


4. Drug Information Online. Progesterone INJECTION USP IN SESAME OIL FOR INTRAMUSCULAR USEONLY Rx only 695703790591*E1 Revised: December 2008. www.drugs.com


women at increased risk: a randomized placebo-controlled double-blind study. American Journal of Obstetrics and Gynecology 188, 419-24


POLICY HISTORY

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<thead>
<tr>
<th>DATE</th>
<th>ACTION</th>
<th>COMMENT</th>
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<tr>
<td>May 27, 2010</td>
<td>Origination of Policy</td>
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<tr>
<td>June 16, 2011</td>
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