Title

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

Related Policies:
Home Uterine Activity Monitoring, #043
Acute and Maintenance Tocolysis, #518

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.

Background

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.

Regulatory Status

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.

When services are considered medically necessary (covered) for all commercial products and for Medicare HMO Blue and Medicare PPO Blue

For women with a singleton pregnancy and prior history of spontaneous preterm birth before 37 weeks’ gestation, the following may be considered medically necessary (covered):

- 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
- Daily vaginal progesterone between 24 and 34 weeks of gestation.

**For women with a singleton pregnancy and a short cervix (less than 20 mm),** the following may be considered medically necessary (covered):
- Daily vaginal progesterone initiated between 20 and 23 weeks 6 days of gestation and continued until 36 weeks 6 days.

**When services are investigational (not covered) for all commercial products and for Medicare HMO Blue and Medicare PPO Blue**

**Progesterone therapy as a technique to prevent preterm delivery** is considered investigational (not covered) 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.

**Individual consideration (Clinical Exceptions)**

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual’s unique clinical circumstances may be considered in light of current scientific literature. For consideration of an individual patient, physicians may send relevant clinical information to:

Blue Cross Blue Shield of Massachusetts  
Clinical Pharmacy Department  
25 Technology Place  
Hingham, MA 02043  
Tel: 1-800-366-7778  
Fax for retail pharmacy authorizations: 1-800-583-6289  
Fax for home infusion and outpatient office administration: 1-888-641-5355

**Authorization Information**

**For Managed Care members:**
- **No authorization is required for this service;** see **Managed Care Guidelines** for additional requirements.

**For Indemnity and PPO members:**
- **No authorization is required for this service;** see **Indemnity and PPO Guidelines** for additional requirements.

**Managed Care Guidelines**

All authorization requirements are determined by the individual’s subscriber certificate, explanation of coverage, or summary plan description; however,

**For Medicare HMO Blue members:**
- The service must meet the criteria for coverage noted in this policy, be medically necessary, prescribed by a plan physician and provided by a network provider.
- Referrals are required for all visits to a specialist.

**For all other Managed Care plans:**
- Any specialist visit requires a referral, except for visits performed by OB/GYN specialists.
- Authorization is required for an inpatient admission.
Indemnity and PPO Guidelines

All authorization requirements are determined by the individual’s subscriber certificate, explanation of coverage, or summary plan description, however;

- Authorization is required for an inpatient admission.
- Authorizations are not required for most outpatient services as determined by the individual’s subscriber certificate.
- Referrals to a specialist are not required.

Other information

For our Medical Technology Assessment Guidelines, see document #350.

Coding information

Procedure codes are from current CPT, HCPCS Level II, Revenue Code, and/or ICD-9-CM manuals, as recommended by the American Medical Association, Centers for Medicare and Medicaid Services and American Hospital Associations. Blue Cross Blue Shield Association national codes may be developed when appropriate.

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

CPT codes
96372: Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
99506: Home visit for intramuscular injections

HCPCS codes
Q2042: Injection, hydroxyprogesterone caproate, 1 mg (new code effective 7/1/11)
S9208: Home management of preterm labor, including administrative services, professional pharmacy services, care coordination, and all necessary supplies or equipment (drugs and nursing visits coded separately), per diem (Do not use this code with any home infusion per diem code)

Policy update history

New policy describing ongoing coverage and non-coverage, effective 5/1/2012. Updated 12/2013 to add new references from BCBSA National medical policy.

References

References for footnote 1:


Footnotes

1 Based on BCBSA national policy # 4.01.16, Progesterone Therapy as a Technique to Reduce Preterm Birth in High-Risk Pregnancies, September 2013.