Medical Coverage Policy | Progesterone Therapy to Reduce Preterm Birth in High Risk Pregnancies

EFFECTIVE DATE: XXXX
POLICY LAST UPDATED: XXXX

OVERVIEW

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. This policy addresses treatment with the use of progesterone (injectable) to prevent preterm birth. This policy is applicable to Blue CHip for Medicare and Commercial products.

Note: Intravaginal formulations are covered as part of the members pharmacy benefit.

MEDICAL CRITERIA

Makena is medically necessary when all of the following criteria has been met:

1. Patient is between 16 and 36 weeks gestation AND
2. Patient has a history of live spontaneous preterm singleton delivery before 37 weeks gestation AND
3.. Patient has no preterm labor in the current pregnancy AND
4. Patient has no allergies to components of Makena AND
5. Patient does not have any of the following exclusions (other risk factors for preterm delivery):
    a. twin or multiple gestation;
    b. prior episode of preterm labor in current pregnancy (ie, progesterone therapy in conjunction with tocolysis or following successful tocolysis);
    c. positive test for cervicovaginal fetal fibronectin;
    d. cervical cerclage; and/or
    e. uterine anomaly
    f. fetal anomaly

PRIOR AUTHORIZATION

Prior authorization is required for BlueCHiP for Medicare and recommended for Commerical Products for Makena only

POLICY STATEMENT

Progesterone therapy is medically necessary for women with a singleton pregnancy and prior history of spontaneous preterm birth before 37 weeks of gestation or for women with a singleton pregnancy and a short cervix (<20 mm). All other indications are not medically necessary that there is not any peer reviewed scientific evidence to support its efficacy.

Compounded 17P

- Compounded 17P is available from participating compounding pharmacies to commercial members with BCBSRI pharmacy benefit for their non-preferred brand tier cost-share.

- Compounded 17P is available to buy and bill under medical coverage for members ***without*** mandatory specialty benefits. There is no prior authorization required, and providers should submit the unclassified J-code with the NDC.

Makena

If it is necessary for a patient to take the brand Makena rather than the compounded version 17P, Makena is medically necessary if the medical criteria is met and it is administered in the physician office.

- Makena is available from Walgreens Specialty Pharmacy to commercial members with BCBSRI pharmacy benefits for their specialty tier cost-share with a prior authorization from Catamaran.
    - Prescribers should request prior authorizations from Catamaran, (800) 391-1164, fax (866) 391-7222 (Commercial). Forms and guidelines are available on BCBSRI.com.
    - Walgreens Specialty Pharmacy, (888) 782-8443, is BCBSRI's exclusive partner for members with mandatory specialty benefits.
- Makena administered in an office setting is available under medical coverage for members ***without*** mandatory specialty benefits.
    - Prescribers should request a medical preauthorization from BCBSRI's Health Services Management Department at (401) 272-5670, extension 3012, or fax your request to (401) 272-8885. Please see the full text of this policy at BCBSRI.com.
    - Prescribers should obtain Makena from Walgreens Specialty Pharmacy (888) 782-8443, who will submit a claim for the drug.
    - Providers may submit a claim for administration of the drug.


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COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Evidence of Coverage, Subscriber Agreement for applicable physician administered drug or specialty pharmacy benefits/coverage.

BACKGROUND

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.
There is sufficient evidence from randomized controlled trials (RCTs) and meta-analyses of RCTs that injectable and vaginal progesterone are associated with improved health outcomes in women with singleton pregnancies who have a history of prior preterm birth. In addition, there is sufficient evidence that progesterone improves health outcomes in women with singleton pregnancies and short cervical length. Thus, progesterone therapy may be considered medically necessary in these situations for selected women who meet clinical criteria.

Preterm labor and delivery are major determinants of neonatal morbidity and mortality. In the United States, 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 have made a significant demonstrable impact on the incidence of preterm delivery. In the past, intramuscular (IM) injections of hydroxyprogesterone caproate (ie, Delalutin) were used routinely to prevent premature labor. However, the drug was shown to have teratogenic properties, and FDA labeled the drug as Category D (ie, studies have demonstrated fetal risk, but use of the drug may outweigh the potential risk). Delalutin was voluntarily withdrawn from the market in 1999.
In recent years, there has been renewed research interest in IM injection of 17□ -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 FDA in February 2011. Intravaginal progesterone gel and suppositories have also been used.

The FDA reviewed the potency and purity data on the compounded versions of 17P, findings that all samples tested passed the USP tests for potency and total purity and stating that the compounded versions "do not raise safety concerns" and released a statement permitting the continued compounding of 17P despite the availability of Makena.

Although Makena and 17P contain the same active ingredient in the same concentration, with castor oil as an inactive ingredient, only Makena contains preservatives (benzyl benzoate and benzyl alcohol). Based on the active ingredient, compounded 17P is considered clinically interchangeable with Makena. The ACOG and the Society for Maternal Fetal Medicine (SMFM) released a joint statement: "[While] there are clear benefits to having an FDA-approved version of 17P, there is no evidence that Makena is more effective or safer than the currently used compounded version."

Progesterone is used for the following indications:
For women with a singleton pregnancy and prior history of spontaneous preterm birth before 37 weeks of gestation, the following may be considered **medically necessary**:

- Weekly injections of 17□ -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
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For women with a singleton pregnancy and a short cervix (<20 mm), the following may be considered **medically necessary**:

- Daily vaginal progesterone initiated between 20 and 23 weeks 6 days of gestation and continued until 36 weeks 6 days

Progesterone therapy as a technique to prevent preterm delivery is considered **investigational** in pregnant women with other risk factors for preterm delivery, including but not limited to:

- twin or multiple gestation;
- prior episode of preterm labor in current pregnancy (ie, progesterone therapy in conjunction with tocolysis or following successful tocolysis);
- positive test for cervicovaginal fetal fibronectin;
- cervical cerclage; and/or
- uterine anomaly.

There is sufficient evidence from randomized controlled trials (RCTs) and meta-analyses of RCTs that injectable and vaginal progesterone are associated with improved health outcomes in women with singleton pregnancies who have a history of prior preterm birth. In addition, there is sufficient evidence that progesterone improves health outcomes in women with singleton pregnancies and short cervical length. Thus, progesterone therapy may be considered medically necessary in the above situations for selected women who meet clinical criteria.

The evidence is insufficient that progesterone is effective for reducing preterm delivery in other situations such as women with twin or multiple gestations, women with preterm rupture of the membranes, or women with a prior episode of preterm labor in the current pregnancy (in conjunction with or following tocolysis) and thus these indications are considered investigational.

CODING

Compound Formula

Claims must be submitted with the unlisted J code and the applicable NDC

The following HCPCS is not medically necessary as this is used for the brand name drug
J1725 - Injection, hydroxyprogesterone caproate, 1 mg (new code effective 01/01/12)

RELATED POLICIES
None

PUBLISHED
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