Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 06/08/2023
Retired

Makena® (hydroxyprogesterone caproate)

HCPCS: J1726/J1729

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Administered by a healthcare professional
   c. Ultrasound confirmed gestational age between 16w0d and 20w6d at treatment initiation
   d. Singleton pregnancy
   e. Previous history of spontaneous preterm delivery (<37 weeks gestation) in singleton pregnancy
   f. No known fetal anomalies incompatible with life
   g. Patient does not have any other risk factors for pre-term delivery
   h. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSM/BCN utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Maximum of 21 weeks starting at 16 weeks 0 days gestational age ending at 36 weeks 6 days gestational age
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Makena is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered < 37 weeks of gestation. There are no controlled trials demonstrating a direct

clinical benefit, such as improvement in neonatal mortality and morbidity. A limitation of use listed as part of the indication is Makena is not intended for use in women with multiple gestations or other risk factors for preterm birth.

- Makena's prescribing information recommends the following:
    - Administration by a healthcare provider
    - Use is not indicated in women under 16 years of age as the safety and effectiveness have not been established as these patients were not included in the clinical trials
    - Treatment beings between 16 weeks, 0 days and 20 weeks, 6 days of gestation and continues until week 37 (through 36 weeks, 6 days) of gestation or delivery, whatever occurs first. This reflects the population that was included the key clinical trials that led to approval of Makena
- Fetal anomalies incompatible with life were excluded from the study and therefore efficacy and safety has not been established.
- Other risk factors for preterm delivery include alcohol or substance abuse, certain medications, low weight gain, poor nutrition, inadequate vitamin intake, infections (e.g.: rubella, certain STDs, vaginal infections, UTIs), hormone imbalance, placenta previa, maternal chronic conditions (HTN, heart disease, liver disease, DM, kidney disease), abnormal shaped uterus, polyhydramnios, chorioamnionitis.
- The American College of Obstetrics and Gynecology recommends Makena as standard of care for patients with previous preterm birth and at risk of another.

References:

1. Makena [package insert]. St. Louis, MO: Ther-Rx Corporation; November 2020.
2. Meis, JP, et al. "Prevention of Recurrent Preterm Delivery by 17 Alpha-Hydroxyprogesterone Caproate". NEJM 2003; 348 (24): 2379-85.
3. Progesterone and preterm birth prevention: translating clinical trials data into clinical practice. Am J Obstet Gynecol. 2012 May;206(5):376-86.
4. Robinson JN & Norwitz ER. (2020). Preterm birth: Risk factors and interventions for risk reduction. In CJ Lockwood & VA Barss (Eds.), UptoDate. Available at: http://www.uptodate.com/contents/preterm-birth-risk-factors-and-interventions-for-risk-reduction
5. Society for Maternal-Fetal Medicine (SMFM) Publications Committee. SMFM Statement: Use of 17-alpha Hydroxyprogesterone Caproate for Prevention of Recurrent Preterm Birth (2020, Apr 8). Am J Obstet Gynecol; S0002-9878(20):30425-30427.
6. American College of Obstetricians and Gynecologists (ACOG), Committee on Obstetric Practice. Use of progesterone to reduce preterm birth. ACOG Committee Opinion No. 419. Washington, DC: ACOG; October 2008.
7. American College of Obstetricians and Gynecologists (ACOG), Committee on Practice Bulletins - Obstetrics. Prediction and prevention of preterm birth. ACOG Practice Bulletin No. 130. Washington, DC: ACOG; October 2013 (Reaffirmed 2014).
8. American College of Obstetricians and Gynecologists (ACOG). Progesterone treatment decreases preterm birth rate. ACOG News Release. Washington, DC: ACOG; January 31, 2005.
9. Prediction and Prevention of Spontaneous Preterm Birth. Obstetrics & Gynecology. 2021; 138 (2): e65-e90.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.2</td><td>Effective Date: 06/08/2023</td><td>Policy retired. Approval for Makena was withdrawn by the FDA effective 4/6/2023 citing lack of favorable post-market benefit-risk assessment.</td></tr>
<tr><td>2.1</td><td>Effective Date: 08/04/2022</td><td>Annual review performed, no changes to criteria</td></tr>
<tr><td>2.0</td><td>Effective Date: 08/12/2021</td><td>Annual review performed, no changes to criteria</td></tr>
<tr><td>1.9</td><td>Effective Date: 08/13/2020</td><td>Annual review performed, no changes to criteria</td></tr>
<tr><td>1.8</td><td>Effective Date: 08/15/2019</td><td>Updated t/f of preferred products statement</td></tr>
<tr><td>1.7</td><td>Effective Date: 02/14/2019</td><td>Added trial of a generic product</td></tr>
<tr><td>1.6</td><td>Effective Date: 08/09/2018</td><td>Added subcutaneous product</td></tr>
<tr><td>1.5</td><td>Effective Date: 08/10/2017</td><td>Removed incompetent cervix/cerclage as an exclusion</td></tr>
<tr><td>1.4</td><td>Effective Date: 11/10/2016</td><td>Updated to new template
Revised coverage criteria (Risk factors)</td></tr>
<tr><td>1.3</td><td>Effective Date: 05/08/2014</td><td>Deletion of compound</td></tr>
<tr><td>1.2</td><td>Effective Date: 01/22/2013</td><td>UM medical management system update for BCBS and BCN
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>No</td></tr>
<tr><td>BCNA</td><td>No</td></tr>
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<tr><td>1.1</td><td>Effective Date: 08/09/2012</td><td>Considerations Updates</td></tr>
<tr><td>1.0</td><td>Effective Date: 06/2010</td><td>New Policy</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*