Pharmacy Medical Necessity Guidelines: Makena® (hydroxyprogesterone caproate)

Effective: January 1, 2018

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<tr>
<th>Prior Authorization Required</th>
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<th>Type of Review – Care Management</th>
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<td>Type of Review – Clinical Review √</td>
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<td>Pharmacy (RX) or Medical (MED) Benefit</td>
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This Pharmacy Medical Necessity Guideline applies to the following:

**Tufts Health Plan Commercial Plans**
- Tufts Health Plan Commercial Plans – large group plans
- Tufts Health Plan Commercial Plans – small group and individual plans

**Tufts Health Public Plans**
- Tufts Health Direct – Health Connector
- Tufts Health Together – A MassHealth Plan
- Tufts Health RITogether – A Rite Care + Rhody Health Partners Plan

**Tufts Health Freedom Plan products**
- Tufts Health Freedom Plan – large group plans
- Tufts Health Freedom Plan – small group plans

**Fax Numbers:**
- All plans except Tufts Health Public Plans: PRECERT: 617.972.9409
- Tufts Health Public Plans only: MM: 888.415.9055

**Note:** For Tufts Health Plan Medicare Preferred Members, please refer to the Tufts Medicare Preferred Prior Authorization Criteria. Background, applicable product and disclaimer information can be found on the last page.

**OVERVIEW**

**FDA-APPROVED INDICATIONS**
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.

Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

Preterm birth is defined as a live birth before 37 completed weeks of gestation. Additional classifications include late preterm (34 to 36 weeks), moderately preterm (32 to 36 weeks) and very preterm (< 32 weeks). In the U.S., preterm birth affects approximately 12%, or 480,000 births, and about 13 million births globally. Preterm birth has increased 27% over the last decade in the U.S., accounting for 85% of all perinatal morbidity and mortality.

Risk factors for preterm delivery include a history of preterm delivery, maternal weight less than 50 kg, African American race, bleeding, sexually transmitted infection during the pregnancy, and multiple gestation. Preterm labor is considered to be a multifactorial process and varies according to gestational age, genetic, and environmental factors. There are several commonly recognized pathways and etiologies leading to spontaneous preterm birth. Although these pathways may cause preterm birth at any point in gestation, certain pathways are more predominant at a specific gestational age.

Few interventions have moderate- to high-quality evidence for reducing preterm birth. Two interventions, progesterone and smoking cessation, are supported by high quality of evidence and are strongly recommended to prevent preterm births, especially in low- and middle-income countries. For more than forty years, 17-alpha hydroxyprogesterone caproate has been used for prevention of preterm labor, although it was never FDA-approved for this indication. In normal pregnancy, progesterone may suppress immunity to prevent rejection of fetal cells and may induce myometrial quiescence. The ACOG and the Society for Maternal Fetal Medicine acknowledge the benefits of progesterone for preterm birth, although the ideal progesterone formulation is unknown. Makena (hydroxyprogesterone caproate) is the only FDA-approved therapy for the prevention of recurrent preterm labor.

On March 30, 2011, the FDA released a statement saying that they do not intend to take enforcement action against pharmacies that compound hydroxyprogesterone caproate based on a valid prescription...
for an individually identified patient unless the compounded products are unsafe, of substandard quality, or are not being compounded in accordance with appropriate standards for compounding sterile products.

**COVERAGE GUIDELINES**
The plan may authorize coverage of Makena (hydroxyprogesterone caproate) for Members when all of the following criteria are met:

1. The Member has a documented history of a singleton spontaneous preterm birth (prior to 37 weeks gestation)

   AND

2. The Member is pregnant with a single fetus

   AND

3. The prescribing physician is an OB-GYN specialist.

**LIMITATIONS**
1. Treatment should begin between 16 weeks, 0 days and 20 weeks, 6 days of gestation. Treatment must end before week 37 (through 36 weeks, 6 days).
2. Coverage is limited to one dose every 7 days and a maximum total of 20 doses (16 weeks gestation to 36 weeks gestation).
3. Makena (hydroxyprogesterone caproate) will not be approved for the following indications as it is considered experimental and investigational and of unproven medical efficacy:
   a) Prevention of spontaneous preterm birth in women with:
      • Short cervix with or without cerclage and no prior preterm birth
      • Current multi-fetal pregnancy (twins or greater)
      • Previous medically indicated preterm birth
   b) Initiation of Makena (hydroxyprogesterone caproate) after 26 weeks, 6 days of gestation.

**CODES**
The following HCPCS/CPT code(s) are:

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<thead>
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<th>Code</th>
<th>Description</th>
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<tr>
<td>J1726</td>
<td>Injection, hydroxyprogesterone caproate, (Makena), 10 mg</td>
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**REFERENCES**
Pharmacy Medical Necessity Guidelines: Makena® (hydroxyprogesterone caproate)


13. Makena (hydroxyprogesterone caproate) [prescribing information]. Chesterfield, MO: Lumara Health; December 2015.


APPROVAL HISTORY

September 13, 2011: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
- September 11, 2012: Administrative update: Removed HCPCS code Q2042
- August 6, 2013: No changes
- August 12, 2014: No changes
- August 11, 2015: No changes
- January 1, 2016: Administrative change to rebranded template.
- May 10, 2016: Effective July 1, 2016, coverage is limited to one dose every 7 days.
- June 13, 2017: No changes

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They are used in conjunction with a Member’s benefit document and in coordination with the Member’s physician(s). The plan makes coverage decisions on a case-by-case basis considering the individual Member’s health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan Members or to certain delegated service arrangements. Unless otherwise noted in the Member’s benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity Guidelines do not apply to CareLinkSM Members. For self-insured plans, drug coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. Applicable state or federal mandates will take precedence.

For Tufts Health Plan Medicare Preferred, please refer to Tufts Health Plan Medicare Preferred Prior Authorization Criteria.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to Member eligibility and benefits on the date of service,
coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.