



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Hydroxyprogesterone caproate injection (Makena™)

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Coverage Position Number..... 1108

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Hyperlink to Related Coverage Positions

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers hydroxyprogesterone caproate injection (Makena™) as medically necessary to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth.

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to hydroxyprogesterone caproate injection (Makena™) therapy.

Note: Coverage of Compounded 17 Progesterone

CIGNA continues to provide coverage under an individual's benefit plan for both compounded 17 Progesterone, as well as the brand medication Makena, in accordance with the physician's prescription. Coverage of both drugs is consistent with the recent U.S. Food and Drug Administration statement in which the agency said, in part: "In order to support access to this important drug, at this time and under this unique situation, FDA does 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." Following is a link to the complete statement: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm249025.htm>

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. 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.

FDA Recommended Dosing

Administer intramuscularly at a dose of 250 mg (1 mL) once weekly (every 7 days) by a healthcare provider. • Begin treatment between 16 weeks, 0 days and 20 weeks, 6 days of gestation. Continue administration once weekly until week 37 (through 36 weeks, 6 days) of gestation or delivery, whichever occurs first.

Drug Availability

Makena is supplied as 5 mL of a sterile solution in a multidose glass vial. Each 5 mL vial contains hydroxyprogesterone caproate USP, 250 mg/mL (25% w/v), in castor oil USP (28.6% v/v) and benzyl benzoate USP (46% v/v) with the preservative benzyl alcohol NF (2% v/v). Single unit carton: Contains one 5 mL multidose vial of Makena (250 mg/mL containing 1250 mg of hydroxyprogesterone caproate).

General Background

Pharmacology

Hydroxyprogesterone caproate is a synthetic progestin. The mechanism by which hydroxyprogesterone caproate reduces the risk of recurrent preterm birth is not known.

Clinical Efficacy

In a multicenter, randomized, double-blind, vehicle (placebo)-controlled clinical trial, the safety and effectiveness of Makena for the reduction of the risk of spontaneous preterm birth was studied in women with a singleton pregnancy (age 16 to 43 years) who had a documented history of singleton spontaneous preterm birth (defined as delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes). At the time of randomization (between 16 weeks, 0 days and 20 weeks, 6 days of gestation), an ultrasound examination had confirmed gestational age and no known fetal anomaly. Women were excluded for prior progesterone treatment or heparin therapy during the current pregnancy, a history of thromboembolic disease, or maternal/obstetrical complications (such as current or planned cerclage, hypertension requiring medication, or a seizure disorder). A total of 463 pregnant women were randomized to receive either Makena (N=310) or vehicle (N=153) at a dose of 250 mg administered weekly by intramuscular injection starting between 16 weeks, 0 days and 20 weeks, 6 days of gestation, and continuing until 37 weeks of gestation or delivery. In this main study, about 37 of 100 women who received Makena gave birth preterm (before 37 weeks of pregnancy), compared to about 55 of 100 women who did not receive Makena. Another study of Makena is going on to see whether Makena reduces the number of babies who have serious problems shortly after birth or who die. It is not known whether Makena is safe and effective in women who have other risk factors for preterm birth. It is not known whether Makena is safe and effective in women less than 16 years old. Makena is not intended for use to stop active preterm labor.

Adverse Reactions

Most common adverse reactions reported in > 2% of subjects and at a higher rate in the Makena group than in the control group are injection site reactions (pain, swelling, pruritus, nodule), urticaria, pruritus, nausea, and diarrhea.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary when used to report hydroxyprogesterone caproate injection (Makena™) in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth:

HCPCS Codes	Description
J3490	Unclassified drugs

ICD-9-CM Diagnosis Codes	Description
V23.41	Supervision of high risk pregnancy with history of pre-term labor

References

1. Baxter Pharmaceutical Solutions, LLC. Makena™ (hydroxyprogesterone caproate injection) for intramuscular use prescribing information. Bloomington, IN: Baxter Pharmaceutical Solutions, LLC. Feb 2011
2. McEvoy GK, ed. AHFS 2010 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2010.

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