Medica Coverage Policy

Policy Name:	**Hydroxyprogesterone Caproate**
Effective Date:	**12/1/2021**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica plans. Please refer to the member's plan document for specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

Coverage Policy

Use of hydroxyprogesterone caproate, including but not limited to Makena® for the FDA-approved indication (to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of a singleton spontaneous preterm birth) is COVERED.

Non-FDA approved indications are investigative and therefore NOT COVERED. Examples include, but are not limited to: the prevention of preterm labor in patients with other high-risk obstetric factors, such as multiple gestations, short cervical length, or positive test results for cervicovaginal fetal fibronectin.

Note: Claims received for hydroxyprogesterone caproate, including but not limited to Makena®, for NOT COVERED indications will be denied as the financial responsibility of the servicing provider.

Description

Preterm labor and delivery is a major determinant of neonatal morbidity and mortality; in the United States the rate of preterm birth is 12%. Preterm birth is defined as delivery prior to 37 weeks' completed gestation. Why preterm labor occurs in most patients is unknown, but the risk is increased in situations where hemorrhage, cervical incompetence, uterine distortion, cervical inflammation, infection, maternal inflammation/fever, hormonal changes, or uteroplacental insufficiency occur, as well as with multiple gestations. Risk factors for the development of preterm labor include previous preterm birth, short cervix, nonwhite race, extremes of maternal age (younger than 17 years or older than 35 years), low socioeconomic status, low pre-pregnancy weight, and stressful life situations. An infant who is born preterm is more likely to die during the neonatal period (with the risk being inversely related to gestational age) and be prone to respiratory distress syndrome, chronic lung disease, and long-term handicaps (e.g., cerebral palsy).

The use of progesterone and progesterone derivatives can increase the duration of the high-risk pregnancy and decrease serious neonatal morbidity. The American College of Obstetricians and Gynecologists Committee of Obstetric Practice and the Society of Obstetricians and Gynecologists of Canada advised in 2008 that progesterone use be limited to women with a documented history of a previous spontaneous birth at less than 37 weeks' gestation. These committees advocate further research to evaluate the use of progesterone in patients with other high-risk obstetric factors, such as multiple gestations, short cervical length, or positive test results from cervicovaginal fetal fibronectin. In the past, intramuscular injections of 17 alpha hydroxyprogesterone (17P), (i.e., Delalutin®) were used routinely to prevent premature labor. However, the drug was shown to have teratogenic properties, and the FDA labeled the drug as Category D, (i.e., studies have demonstrated fetal risk, but that the use of the drug may outweigh

the potential risk). Delalutin® is no longer marketed. Most recently, there has been renewed research interest in intramuscular injections of 17 alpha-hydroxyprogesterone caproate during the second trimester when the teratogenic risk is minimized. 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 is not commercially available, but can be manufactured locally by compounding pharmacies. After an extended application process, Makena®, another injectable form of 17P was approved by the FDA in February 2011. On 11/6/2019, an FDA panel recommended market withdrawal of Makena stating that the PROLONG confirmatory trial failed to demonstrate clinical benefit. In October 2020, ACOG released a statement supporting the FDA's recommendation that obstetric health care professionals discuss Makena's benefits, risks and uncertainties with their patients to decide whether to use Makena while the FDA finalizes its decisions. At this time the ACOG recommendations outlined in the October 2019 practice advisory remain unchanged.

The costs of treatment with Makena® has created concern amongst prescribing obstetricians as well as third party payers. On March 30, 2011, in order to support continued access to compounded versions of 17P, the FDA stated that it will not prevent compounding pharmacies from continuing to produce valid prescriptions for 17P. The March 2011 statement was super seceded by a June 2012 statement released by the FDA that recommended using the FDA approved product such as Makena® instead of compounding the drug unless there is a specific medical need that cannot be met by the approved product. In a statement issued on April 28, 2011 the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine stated that "there is no evidence that Makena® is more effective or safer than the currently used compounded versions." Furthermore, the evidence used to obtain FDA approval for Makena® relied primarily on data obtained using the compounded product. However, in 2012, the Society for Maternal-Fetal Medicine revised its recommendations stating "In singleton gestations with prior spontaneous PTB 20-36 6/7 weeks, 17P 250 mg IM weekly preferably starting at 16-20 weeks of gestation until 36 weeks of gestation is recommended.

FDA Approval
Hydroxyprogesterone caproate is indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of a singleton spontaneous preterm birth. The effectiveness of hydroxyprogesterone caproate 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.

Limitations of use: While there are many risk factors for preterm birth, hydroxyprogesterone caproate (Makena®) is FDA approved for 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.

Prior Authorization
Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

Coding Considerations
Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

ICD-10 codes:

O09.212 - Supervision of pregnancy with history of pre-term labor, second trimester
O09.213 - Supervision of pregnancy with history of pre-term labor, third trimester

CPT code

96372 - Therapeutic, prophylactic, or diagnostic injection; subcutaneous or intramuscular injection

HCPCS code:

J1726 - Injection, hydroxyprogesterone caproate, (Makena), 10 mg
J1729 - Injection, hydroxyprogesterone caproate, not otherwise specified, 10 mg

Original Effective Date:	6/16/2011
Re-Review Date(s):	4/11/2012 9/11/2017 3/1/2018, 11/5/2021