Hydroxyprogesterone caproate injection (Makena®, generics) *While Makena and generic hydroxyprogesterone are commercially manufactured drugs, hydroxyprogesterone caproate may be compounded for injection through one of the pharmacies listed in Section 5.*	**Place of Service** **Home Infusion Administration** **Office Administration** **Outpatient Facility Administration*** [***Prior authorization required – see section (1)]** **Specialty Pharmacy** **Self-Administration -** *May be covered under pharmacy benefit* [Makena (brand)] **HCPCS:** **Makena** (brand)**: J1726** per 10 mg **Hydroxyprogesterone caproate, not otherwise specified** (generic)**: J1729** per 10 mg **Hydroxyprogesterone caproate, Compounded version: J3490** Use code **S9560** for 17-P services provided by **Alere** Women's and Children's Health only (formerly Matria Healthcare)

Condition(s) listed in policy (*see criteria for details*)

- Abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology (e.g., submucous fibroids or uterine cancer) *(generic or compound)*
- Advanced adenocarcinoma of the uterine corpus (Stage III or IV) *(generic or compound)*
- Amenorrhea (primary and secondary) *(generic or compound)*
- Prevention of preterm labor in women who are at high risk *(Makena, generic or compound)*
- Production of secretory endometrium and desquamation *(generic or compound)*
- Test for endogenous estrogen production *(generic or compound)*

AHFS therapeutic class: Progestins

Mechanism of action: Hydroxyprogesterone caproate, also known as 17-P, is an esterified derivative of the naturally occurring 17α-hydroxyprogesterone which has substantial progestational activity and prolonged duration of action.

(1) Special Instructions and Pertinent Information

Makena:

- **If member has a Prescription Benefit, Makena may be covered** under the Pharmacy Services with a prior authorization.
- **Covered under the Medical Benefit,** please submit clinical information for prior authorization review via fax.

Generic hydroxyprogesterone caproate injection:

1. **Covered under the Medical Benefit,** please submit clinical information for prior authorization review via fax.

Makena and hydroxyprogesterone caproate may be obtained and billed by a specialty pharmacy.

**** CRITERIA FOR HOSPITAL OUTPATIENT FACILITY ADMINISTRATION****

AAAAI Guidelines 2011, MCG™ Care Guidelines, 19th edition, 2015, Makena PI, 4/16

Members with the following plans: **PPO, Direct Contract HMO, and when applicable, ASO, Shared Advantage, HMO (non-direct contract)** may be required to have their medication administered at a preferred site of service, including the home, a physician's office, or an independent infusion center not associated with a hospital.

For members that cannot receive infusions in the preferred home or ambulatory setting AND meet one of the following criteria points, drug administration may be performed at a hospital outpatient facility infusion center.

ADMINISTRATION OF HYDROXYPROGESTERONE CAPROATE INJECTIONS IN THE HOSPITAL OUTPATIENT FACILITY SITE OF CARE REQUIRES ONE OF THE FOLLOWING: (*Supporting Documentation must be submitted to support the need for additional clinical monitoring)*

1. **Patient is receiving their first dose or is being re-initiated after at least 6 months off therapy.** *Subsequent doses will require medical necessity for continued use in the hospital outpatient facility site of care.*

OR

Additional clinical monitoring is required during administration as evidenced by one of the following:

2. **Patient has experienced a previous severe adverse event on the medication based on documentation submitted.**
3. **Patient continues to experience moderate to severe adverse events on the medication based on documentation submitted, despite receiving premedication such as acetaminophen, steroids, diphenhydramine, fluids, etc.**
4. **Patient is clinically unstable based on documentation submitted.**
5. **Patient is physically or cognitively unstable based on documentation submitted.**

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for hydroxyprogesterone caproate injection NOT LISTED in section 3 must be sent for clinical review and receive authorization prior to drug administration or claim payment

Abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology (e.g. submucous fibroids or uterine cancer) – *Only for generic hydroxyprogesterone caproate injection (J1729) / Compounded version (J3490)*

1. Patient has had an inadequate response, intolerance or contraindication to an oral progestin

Covered Doses
375 mg IM x1
For cyclic therapy with estradiol valerate injection: 250mg IM on day 15 of 28-day cycles for up to 4 cycles

Coverage Period
One time dose as monotherapy
For cyclic therapy with estradiol valerate injection: up to four 28-day cycles

ICD-10:
N93.8

Advanced adenocarcinoma of the uterine corpus (Stage III or IV) – *Only for generic hydroxyprogesterone caproate injection (J1729) / Compounded version (J3490)*

1. Patient has had an inadequate response, intolerance or contraindication to medroxyprogesterone (NCCN category 2A-recommended treatment)

Covered Doses
1000 mg (or more) at once; repeat with up to 7 grams per week

Coverage Period
Indefinite (if patient had clinical benefit)

ICD-10:
C54.1-C54.3, C54.9

Amenorrhea (primary and secondary) – *Only for generic hydroxyprogesterone caproate injection (J1729) / Compounded version (J3490)*

1. Patient has had an inadequate response, intolerance or contraindication to an oral progestin

Covered Doses
375 mg IM x1
For cyclic therapy with estradiol valerate injection: 250 mg IM on day 15 of 28-day cycles for up to 4 cycles

Coverage Period
One time dose as monotherapy
For cyclic therapy with estradiol valerate injection: up to four 28-day cycles

ICD-10:
N91.0, N91.1, N91.2

Prevention of preterm labor in women who are at high risk (i.e. prior history of preterm labor) – *Makena or generic hydroxyprogesterone caproate injection*

1. Must be a singleton pregnancy, **AND**
2. Treatment with hydroxyprogesterone caproate is being initiated within 16 weeks, 0 days and 24 weeks, 6 days of gestation,**AND**
3. Patient has a history of a prior spontaneous preterm singleton delivery that occurred during a timeframe between 20 weeks, 0 days and 36 weeks, 6 days of gestation

Covered Doses
Makena vial: Up to 250 mg IM once weekly
Makena auto-injector: Up to 275 mg SC once weekly

Coverage Period
Cover for up to 36 weeks, 6 days gestation

ICD-10:
O09.212, O09.213, O09.219

(3) The following condition(s) DO NOT require Prior Authorization/Preservice
All requests for hydroxyprogesterone caproate injection NOT LISTED in section 3 must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Production of secretory endometrium and desquamation – (J1729 only) *generic hydroxyprogesterone caproate injection*

Covered Doses
375 mg x1
For cyclic therapy with estradiol valerate injection: 250mg on day 15 of 28-day cycles for up to six months

ICD-10:
N85.8

Test for endogenous estrogen production – (J1729 only) *generic hydroxyprogesterone caproate injection*

Covered Doses
250 mg x 2 IM injections; separated by 4 weeks

ICD-10:
Includes but is not limited to E22.8

(4) This Medication is NOT medically necessary for the following condition(s)

Blue Shield's research indicates there is inadequate clinical evidence to support off-label use of this drug for the following conditions (Health and Safety Code 1367.21):

- Prevention of preterm labor in women pregnant with multiple gestations
- Prevention of preterm labor in pregnant women with a short cervical length and no prior history of preterm birth

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information

How supplied:
Makena vial:
250 mg (single dose)
1,250 mg (multi-dose)

Makena auto-injector:
275 mg/1.1 mL (single-use)

Hydroxyprogesterone caproate (generic):
1,250 mg (multi-dose vial)

The chemical name for Makena and hydroxyprogesterone caproate is pregn-4-ene-3,20-dione, 17[(1-oxohexyl) oxy], and is also known as 17 alpha-hydroxyprogesterone caproate or 17P.

Hydroxyprogesterone is commercially available but may also be prepared by specialty pharmacies. Below is a list of some specialty pharmacies which may be supplying this product:

- Alere Women's and Children's Health (formerly Matria Healthcare)
- Wedgewood Pharmacy
- Vitality
- Freedom Pharmacy

(6) References

- AHFS®. Available by subscription at http://www.lexi.com
- American College of Obstetricians and Gynecologists. Prediction and Prevention of Preterm Birth. Practice Bulletin Number 130, October 2012.
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
- Hydroxyprogesterone caproate injection [Prescribing information]. Shirley, NY: American Regent, Inc., 1/2019.
- Makena® (hydroxyprogesterone caproate injection) [Prescribing information]. Waltham, MA: AMAG pharmaceuticals; 2/2018.

- Meis PJ, et al. Prevention of recurrent preterm delivery by 17 alpha hydroxyprogesterone caproate. N Engl J Med 2003; 348: 2379-2385.
- Northern A, et al. Follow-up of children exposed in utero to 17-hydroxyprogesterone caproate compared with placebo. American College of Obstetricians and Gynecologists. Vol 110, No 4, October 2007.
- Rouse DJ, et al. A trial of 17 alpha-hydroxyprogesterone caproate to prevent prematurity in twins. N Eng J Med 2007; 357: 454-461.
- Society for Maternal-Fetal Medicine Publications Committee, Berghella V. Progesterone and preterm birth prevention: translating clinical trials data into clinical practice. Am J Obstet Gynecol 2012;206(5):376-86.
- Use of Progesterone to Reduce Preterm Birth. The American College of Obstetricians and Gynecologists. Volume 112. no. 4 October 2008.
- William A. Grobman et al. use of 17-p to Reduce Preterm Birth in Women with Short Cervix. American Journal of Obstetrics and Gynecology Nov 2012.

(7) Policy Update

Date of last review: 3Q2021
Date of next review: 3Q2022
Changes from previous policy version:

- No clinical change to policy following routine annual review.