17-alpha-hydroxyprogesterone caproate (Makena™ and 17P)

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Table of Contents **Page**

Related Medical or Drug Policies:
Preterm Labor: Identification and Treatment

Related Coverage Determination Guidelines:
None

INSTRUCTIONS FOR USE
This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee's document (e.g., Certificate of Coverage (COC) or Summary Plan Description (SPD)) may differ greatly. In the event of a conflict, the enrollee's specific benefit document supersedes this Drug Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

COVERAGE RATIONALE

17-alpha-hydroxyprogesterone caproate, commonly called 17P, may also be referred to as 17-OHP, 17-OHPC, 17Pc, Makena™, 17-alpha hydroxyprogesterone, hydroxyprogesterone, hydroxy-progesterone, and hydroxy progesterone. Hereafter, it will be referred to as 17P.

Note: Oral and intravaginal formulations of progesterone are not addressed in this policy.

Intramuscular injection of 17P is **proven** for prevention of spontaneous preterm birth when **all** of the following criteria are met:

A. Current singleton pregnancy
AND
B. History of a prior spontaneous preterm birth of a singleton pregnancy
AND

C. Treatment is initiated between 16 weeks, 0 days of gestation and 26 weeks, 6 days of gestation.
AND
D. Administration is to continue weekly until 36 weeks, 6 days of gestation or delivery, whichever occurs first

Additional information to support medical necessity review where applicable:
The above indication and criteria also apply to medical necessity review

Intramuscular injection of 17P is **unproven** and not medically necessary for:
1. Prevention of spontaneous preterm birth in women with **any** of the following:
   A. Short cervix with or without cerclage and no prior preterm birth
   B. Current mutli-fetal pregnancy (twins or greater)
   C. Previous medically indicated preterm birth
2. Initiation of 17P after 26 weeks, 6 days of gestation

Although there are ongoing clinical trials to broaden the indications for the use of 17P, at this time uses as indicated above are considered unproven.

***Additional Information regarding compounded 17P:**
The active ingredient in the compounded 17P and Makena is hydroxyprogesterone caproate. Both have castor oil as an inactive ingredient. The compounded version can be made with an alternate oil base in the event of patient hypersensitivity to castor oil. Makena has the additional inactive ingredients of benzyl benzoate and benzyl alcohol (a preservative). Based on the active ingredient, compounded preservative-free 17P is considered clinically interchangeable with Makena.

Compounding pharmacies must comply with United States Pharmacopeia (USP) Chapter 797, which sets standards for the compounding, transportation, and storage of compounded sterile products (CSP).[1] The Pharmacy Compounding Accreditation Board will verify that the pharmacy is adhering to these standards.[2]

*Note: The FDA has stated that approved drug products provide a greater assurance of safety and effectiveness than do compounded products. Please refer to the U.S. Food and Drug Administration (FDA) section of this policy for additional information.

Centers for Medicare and Medicaid Services (CMS):
Medicare does not have a National Coverage Determination (NCD) for the identification or treatment of preterm labor; including the use of the drug Makena (17-hydroxyprogesterone). Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, section 50 Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf.

(Accessed March 20, 2014)

BENEFIT CONSIDERATIONS

The UnitedHealthcare standard Certificate of Coverage excludes coverage for non-injectable medications administered in a physician's office.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Where such mandates apply, they supersede language in the benefit

document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. See the Policy and Procedure addressing the treatment of serious rare diseases.

Oral and intravaginal progesterone formulations are administered as a pharmacy benefit.

BACKGROUND

Preterm birth is defined as the birth of an infant between 20 weeks 0 days and 36 weeks 6 days of gestation. Deliveries that are early by five weeks or more are the leading cause of infant morbidity and mortality in the United States. Progesterone is known to have an inhibitory effect on uterine contractility and is thought to play a key role in the maintenance of pregnancy until term. Progesterone is administered during pregnancy either vaginally (suppository) or intramuscularly (injection) beginning in the second trimester of pregnancy in asymptomatic women at high risk of spontaneous preterm delivery. Asymptomatic women can be considered high risk due to various risk factors, including previous preterm delivery, preterm labor, multiple pregnancy, or short cervix. The objective of progesterone administration is to prevent preterm birth, prolong gestation, and avoid associated infant mortality and morbidity.[3]

CLINICAL EVIDENCE

Singleton Pregnancy

Intramuscular administration

Berghella et al. (2010) evaluated intramuscular 17P for the prevention of preterm birth (PTB) in women with prior spontaneous preterm birth (SPTB) and shortened cervical length (CL) (<25 mm).[4] The authors conducted a secondary analysis of a randomized trial evaluating cerclage for PTB prevention in women with singleton pregnancies, prior SPTB and shortened cervical length. Women were stratified at randomization to intent to use or not use 17P. The effect of 17P was analyzed separately for cerclage and no-cerclage groups. Primary outcome was PTB <35 weeks. In 300 women, 17P had no effect on PTB <35 weeks in either cerclage or no-cerclage groups. Only PTB <24 weeks and perinatal death were significantly lower for those with 17-P in the no-cerclage group. The authors concluded that 17P had no additional benefit for prevention of PTB in women who had prior SPTB and had cerclage for a shortened cervix. In women who did not get cerclage, 17P reduced previable birth and perinatal mortality.

Gonzalez-Quintero et al. (2010) examined whether the efficacy of 17P is dependent upon the earliest gestational age (GA) at prior SPTB.[5] Enrollee data were divided into 3 groups according to earliest GA of prior SPTB (20-27.9, 28-33.9, and 34-36.9 weeks). GA at delivery of current pregnancy and incidence of recurrent SPTB were compared between women enrolled in outpatient 17P administration program (n=2978) and women receiving other outpatient services without 17P (n=1260). Rates of recurrent SPTB for those with and without 17P prophylaxis, respectively, according to GA at earliest SPTB were: 20-27.9 weeks at earliest SPTB, 32.2% vs 40.7%, p=0.025; 28-33.9 weeks at earliest SPTB, 34.1% vs 45.5%, p<0.001; and 34-36.9 weeks at earliest SPTB, 29.3% vs 38.8%, p<0.001. The authors concluded that 17P given to prevent recurrent SPTB is effective regardless of GA at earliest SPTB.

How et al. (2010) performed a retrospective analysis to study whether GA at initiation of treatment would change outcome.[6] Women with singleton gestations with ≥1 PTB treated with 17P prophylaxis for recurrent PTB before 27 weeks were identified from a data base. Data were stratified by GA at 17P initiation (16-20.9 [n=599] weeks and 21-26.9 [n=307] weeks) and number of PTB (1, 2, >2). Outcome variables were PTB at <37, <35, and <32 weeks. No significant differences were found among groups. No significant differences in GA at delivery or rates of recurrent PTB <37, <35, and <32 weeks were identified between those women initiating 17P at 16-20.9 weeks or 21-26.9 weeks, or when stratified by number of prior preterm deliveries.

Gonzalez-Quintero et al. (2007) compared rates of recurrent preterm birth between women starting treatment with 17a-hydroxyprogesterone caproate (17P) at 16–20.9 weeks of gestation versus 21–26.9 weeks. [7] Their retrospective analysis included women enrolled in an outpatient program of education, nursing assessment, and weekly 17P injections beginning at 16–26.9 weeks. Included were patients with singleton pregnancies having a history of preterm delivery (PTD) and who were without symptoms of preterm labor. Pregnancy outcome was compared between women starting 17P at 16–20.9 weeks (n=156) and those starting 17P at 21–26.9 weeks (n=119), with $p<0.05$ considered significant. Mean gestational age at delivery (36.8±3.0 vs. 36.7±2.5) and rates of PTD at <37 weeks (40.4% vs. 48.7%), <35 weeks (16.7% vs. 16.8%), and <32 weeks (5.1% vs. 5.0%) were similar between the groups (all $p<0.05$). Because the greatest difference in pregnancy outcome was found in the incidence of spontaneous preterm labor and delivery less than 37 weeks (26.3% of the 16–20 weeks group vs. 37.0% of the 21–26 weeks group ($p<0.065$), the authors concluded that further study using a larger sample size is warranted.

Mason et al. (2007) retrospectively evaluated whether providing 17P to high-risk pregnant women who have a history of preterm delivery (PTD) in a Medicaid managed care population reduces the rate of recurrent PTD and neonatal intensive care unit (NICU) admissions.[8] A longitudinal (2004-2009) review of birth outcomes in singleton pregnant women with a history of spontaneous PTD and who received 17P (n=193) was conducted versus a control group (n=60) of members with the same characteristics who did not receive 17P. Members for this study were identified by claims review and obstetrical case managers in the health plans. Deliveries with a GA of <35 weeks decreased from 41.67% in the control group to 26.42% in the 17P group when 17P was initiated by 28 weeks of gestation ($p=0.024$). The NICU admission rate decreased from 45% in the control group to 33.68% in the 17P group ($p=0.095$).

Rebarber et al. (2007) conducted a retrospective analysis of data of women with previous PTD and current singleton pregnancy who received outpatient weekly 17P injections (250 mg intramuscularly) beginning at 16-20.9 weeks of gestation.[9] The study group was comprised of patients who were electively terminating 17P at <32.0 weeks and who delivered >10 days from the last injection. The control group consisted of patients who received weekly 17P injections until PTD or 36.9 weeks of gestation. The authors found that study group patients were significantly more likely to have spontaneous recurrent PTD at <37 weeks of gestation (48.1% vs 33.3%; $p=0.011$), at <35 weeks of gestation (30.9% vs 14.0%; $p<0.001$), and at <32 weeks of gestation (16.0% vs 7.0%; $p=0.020$). Early cessation of 17P treatment is associated with an increased risk for spontaneous recurrent PTD.

Meis et al. (2003) conducted an NICHD-sponsored, multicenter, double-blind, placebo-controlled trial involving pregnant women with a documented history of spontaneous PTD.[10] Women were randomly assigned, in a 2:1 ratio, to receive either weekly injections of 250 mg of 17P (n=310) or weekly injections of a placebo (n=153). Treatment with 17P significantly reduced the risk of delivery at <37 weeks of gestation (incidence, 36.3% in the progesterone group vs. 54.9% in the placebo group; RR (RR), 0.66 [95% CI, 0.54 to 0.81]), delivery at <35 weeks of gestation (incidence, 20.6% vs. 30.7%; RR, 0.67 [95% CI, 0.48 to 0.93]), and delivery at <32 weeks of gestation (11.4% vs. 19.6%; RR, 0.58 [95% CI, 0.37 to 0.91]). A four-year follow-up study found no adverse health outcomes of surviving children (Northen 2007).[11]

A secondary analysis of the Meis et al. study group was conducted by Spong et al. (2005) to evaluate the effectiveness of 17P for pregnancy prolongation based on GA at earliest previous delivery according to clinically relevant groupings (20-27.9, 28-33.9, and 34-36.9 weeks).[12] Women with earliest delivery at 20 to 27.9 weeks and at 28 to 33.9 weeks delivered at significantly more advanced GA if treated with 17P than with placebo (median 37.3 vs 35.4 weeks, $p=0.046$ and 38.0 vs 36.7 weeks, $p=0.004$, respectively) and were less likely to deliver <37 weeks (42% vs 63%, $p=0.026$ and 34% vs 56%, $p=0.005$, respectively). Those with earliest delivery at 34 to 36.9 weeks were not significantly different between 17P and control. 17P therapy

given to prevent recurrent PTB was associated with a prolongation of pregnancy overall, and especially for women with a previous spontaneous PTB at <34 weeks.

Review articles and meta-analyses (containing information related to all routes of progesterone administration)

In a Cochrane review, Su et al. (2010) performed a meta-analysis to assess the efficacy of progestational agents in the treatment of threatened or established preterm labor.[13] Randomized controlled trials comparing progestational agents, given either alone or in combination with other tocolytics, with a control group receiving another tocolytic, placebo or no treatment, for the treatment of preterm labor were included in the analysis. There are some data suggesting that the use of progestational agents resulted in a reduction of PTD at <37 weeks of gestation. The use of progestational agents may also attenuate the shortening of cervical length and reduce the frequency of uterine contractions. However, the analysis was limited by the small number of available studies (four studies were included in this analysis). Because the number of participants in each of the included studies ranged from 35 to 60, the overall power of the meta-analysis is limited. The authors concluded that there is insufficient evidence to advocate progestational agents as tocolytic agents for women presenting with preterm labor.

Rode et al. (2009) conducted a meta-analysis of 6 randomized trials including singleton pregnancies with previous PTB.[14] The data showed that in women with a singleton pregnancy and previous PTD, progesterone reduced the rates of PTD before 32 weeks, perinatal death, as well as respiratory distress syndrome and necrotizing enterocolitis in the newborn. Women with a short cervix or preterm labor may also benefit from progesterone, but further evidence is needed to support such a recommendation.

Tita and Rouse (2009) systematically reviewed emerging data on the use of progesterone to prevent PTB.[15] Seventeen relevant reports (8 RCTs, 6 meta-analyses and 3 national guidelines) were identified. Individual trials and meta-analyses support that synthetic intramuscular 17P effectively reduces the incidence of recurrent PTB in women with a history of SPTB. One trial found that vaginally administered natural progesterone reduced the risk of early PTB in women with a shortened cervix. The data are suggestive but inconclusive about the benefits of progesterone in the setting of arrested preterm labor and whether progesterone lowers perinatal morbidity or mortality. Further study is required to identify appropriate candidates and optimal formulations.

A 2006 Cochrane Review (Dodd, 2006a) reported that for all women administered progesterone, there was a reduction in the risk of PTB <37 weeks [six studies, 988 participants, RR 0.65, 95% CI 0.54 to 0.79)] and PTB <34 weeks (one study, 142 participants, RR 0.15, 95% CI 0.04 to 0.64).[16] Infants born to mothers administered progesterone were less likely to have birthweight <2500 grams (four studies, 763 infants, RR 0.63, 95% CI 0.49 to 0.81) or intraventricular hemorrhage (one study, 458 infants, RR 0.25, 95% CI 0.08 to 0.82). There was no difference in perinatal death between women administered progesterone and those administered placebo (five studies, 921 participants, RR 0.66, 95% CI 0.37 to 1.19). Intramuscular progesterone is associated with a reduction in the risk of PTB <37 weeks gestation, and infant birthweight <2500 grams. However, other important maternal and infant outcomes have been poorly reported to date, with most outcomes reported from a single trial only (Meis, 2003). It is unclear if the prolongation of gestation translates into improved maternal and longer-term infant health outcomes. Similarly, information regarding the potential harms of progesterone therapy to prevent PTB is limited. Further information is required about the use of vaginal progesterone in the prevention of PTB.

Ina systematic review and meta-analysis that included three trials, Mackenzie et al. (2006) concluded that progestational agents, initiated in the second trimester of pregnancy, may reduce the risk of delivery <37 weeks gestation, among women at increased risk of spontaneous PTB,

but the effect on neonatal outcome is uncertain.[17] Larger randomized controlled trials are required to determine whether this treatment reduces perinatal mortality or serious neonatal morbidity.

Sanchez-Ramos et al. (2005) performed a systematic review with meta-analysis and reported that compared with women allocated to receive placebo, those who received progestational agents had lower rates of PTD (26.2% versus 35.9%; OR 0.45, 95% CI 0.25-0.80).[18] Similar results were noted when comparing patients who were specifically treated with 17P (29.3% versus 40.9%; OR 0.45, 95% CI 0.22-0.93). Additionally, subjects allocated to receive 17P had lower rates of birth weights <2,500 g (OR 0.50, 95% CI 0.36-0.71). The team concluded that the use of progestational agents and 17P reduced the incidence of PTB and low birth weight newborns.

Multiple Gestations

Intramuscular administration

Combs et al. (2011) conducted a randomized, double-blind, placebo-controlled trial to study the effect of 17P during twin pregnancy on neonatal morbidity and prolongation of pregnancy.[19] Mothers carrying dichorionic-diamniotic twins were randomly assigned to weekly injections of 250 mg of 17P (n=160) or placebo (n=80), starting at 16-24 weeks and continued until 34 weeks. Prophylactic treatment with 17P did not prolong gestation or reduce neonatal morbidity in twin pregnancy.

In a multicenter, double-blind, placebo-controlled trial, Combs et al. (2010) tested whether 17P would reduce neonatal morbidity by increasing GA at delivery in triplet pregnancies.[20] Mothers carrying trichorionic-triamniotic triplets were randomly assigned to weekly injections of 250 mg of 17P (n=56) or placebo (n=25), starting at 16-22 weeks and continued until 34 weeks. In triplet pregnancy, prophylactic treatment with 17P did not reduce neonatal morbidity or prolong gestation but was associated with increased midtrimester fetal loss.

Caritis et al. (2009) conducted a randomized, double-blind, placebo-controlled trial in 14 centers.[21] Healthy women with triplets were randomly assigned to weekly intramuscular injections of either 250 mg of 17P (n=71) or placebo (n=63), starting at 16-20 weeks and ending at delivery or 35 weeks of gestation. Treatment with 17P did not reduce the rate of PTB in women with triplet gestations.

Rouse et al. (2007) performed a multicenter, randomized, double-blind, placebo-controlled trial (n=661) of healthy women pregnant with twins and found that treatment with 17P injections did not reduce the rate of PTB in women with twin gestations.[22]

Durnwald et al. (2010) performed a secondary analysis of the Rouse et al. study group (n=661) to compare rates of PTB based on cervical length measurement at 16-20 weeks.[23] Intramuscular administration of 17P did not reduce PTB before 35 weeks among those with either a short or a long cervix (64.3 vs. 45.8%, p=0.18 and 38.1 vs. 35.5%, p= 0.85, respectively).

Technology Assessments

Hayes has compiled a Medical Technology Directory on the use of progesterone for the prevention of PTB, dated August 9, 2011.[3] An updated search summary was performed on August 22, 2012 and again on September 6, 2013, resulting in no changes to the Hayes Rating(s) included in the original report. Based on available data, the following Hayes Ratings are assigned for the use of intramuscular progesterone for preventing preterm birth:

Asymptomatic pregnancy:

C – For intramuscular (IM) 17 alpha-hydroxyprogesterone caproate (17α-HPC), when used in women with a singleton pregnancy and prior preterm birth or history of preterm labor in a prior pregnancy.
D – For IM 17α-HPC, progesterone vaginal suppository capsules, or progesterone vaginal gel, when used in women with multiple gestations. This rating reflects the lack of benefit demonstrated for these progesterone protocols in the reviewed RCTs.

Symptomatic pregnancy:
D – For IM 17α-HPC when used in women with a singleton pregnancy characterized by premature rupture of membranes (PROM).
D – For any progesterone protocol, when used in women with risk factors other than prior preterm birth, a history of preterm labor, a short or incompetent cervix, or preterm labor or PROM in the current pregnancy.

The Hayes Rating system reflects the strength and direction of the evidence regarding a medical technology, including safety and efficacy, impact on health outcomes and patient management, indications for use, and patient selection criteria compared with the standard treatment/testing. Hayes Ratings are scaled A through D and are defined as follows:
A – Established benefit.
B – Some proven benefit.
C – Potential but unproven benefit.
D – No proven benefit and/or not safe.

Professional Societies

American College of Obstetricians and Gynecologists
A 2012 Practice Bulletin makes the following recommendations based upon good and consistent scientific evidence (Level A):[24]

- A woman with a singleton gestation and a prior spontaneous preterm singleton birth should be offered progesterone supplementation starting at 16-24 weeks of gestation, regardless of transvaginal ultrasound cervical length, to reduce the risk of recurrent spontaneous preterm birth.
- Progesterone treatment does not reduce the indicence of preterm birth in women with twin or triplet gestationsand, therefore, is not recommened as an interventionto prevent preterm birth in women with multiple gestations.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

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.[25]

Treatment is indicated to begin 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.[25]

The FDA issued a statement dated March 30, 2011 regarding the availability of a compounded version of Makena. The FDA states that it 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.[26]

In a statement dated November 8, 2011, the FDA reported that it was conducting an ongoing sampling and analysis of compounded hydroxyprogesterone caproate products and the bulk active pharmaceutical ingredients (APIs) used to make them. Physicians and patients were reminded that before approving the Makena new drug application, the FDA reviewed manufacturing information, such as the source of the API used by its manufacturer, proposed manufacturing processes, and the firm's adherence to current good manufacturing practice. Therefore, as with other approved drugs, greater assurance of safety and effectiveness is generally provided by the approved product than by a compounded product.[27]

On June 15, 2012, the FDA issued an update regarding compounded versions of hydroxyprogesterone caproate. Although their analysis of a limited sample of compounded hydroxyprogesterone caproate products and APIs did not identify any major safety problems, the FDA stated that approved drug products provide a greater assurance of safety and effectiveness than do compounded products. Therefore, when an FDA-approved drug is commercially available, the FDA recommends that practitioners prescribe the FDA-approved drug rather than a compounded drug unless the prescribing practitioner has determined that a compounded product is necessary for the particular patient and would provide a significant difference for the patient as compared to the FDA-approved commercially available drug product. The FDA emphasized that it is applying its normal enforcement policies for compounded drugs to compounded hydroxyprogesterone caproate. The compounding of any drug, including hydroxyprogesterone caproate, should not exceed the scope of traditional pharmacy compounding. As the Agency has previously explained, the FDA generally prioritizes enforcement actions related to compounded drugs using a risk-based approach, giving the highest enforcement priority to pharmacies that compound products that are causing harm or that amount to health fraud.[28]

APPLICABLE CODES

The [Current Procedural Terminology (CPT), HCPCS and/or ICD-9] codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. Coverage is determined by the benefit document.

HCPCS Code	Description
J1725	Injection, hydroxyprogesterone caproate, 1 mg
J2675	Injection, progesterone, per 50 mg

ICD-9 Code	Description
640.00	Threatened abortion, unspecified as to episode of care
640.01	Threatened abortion, delivered
640.80	Other specified hemorrhage in early pregnancy, unspecified as to episode of care
640.81	Other specified hemorrhage in early pregnancy, delivered
640.83	Other specified hemorrhage in early pregnancy, antepartum
640.90	Unspecified hemorrhage in early pregnancy, unspecified as to episode of care
640.91	Unspecified hemorrhage in early pregnancy, delivered
640.93	Unspecified hemorrhage in early pregnancy, antepartum
644.00	Threatened premature labor, unspecified as to episode of care
644.03	Threatened premature labor, antepartum
644.10	Other threatened labor, unspecified as to episode of care
644.13	Other threatened labor, antepartum
644.20	Early onset of delivery, unspecified as to episode of care

644.21	Early onset of delivery, delivered, with or without mention of antepartum condition
V13.21	Personal history of pre-term labor
V23.41	Supervision of pregnancy with history of pre-term labor

ICD-10 Codes (Preview Draft)
In preparation for the transition from ICD-9 to ICD-10 medical coding on **October 1, 2015***, a sample listing of the ICD-10 CM and/or ICD-10 PCS codes associated with this policy has been provided below for your reference. This list of codes may not be all inclusive and will be updated to reflect any applicable revisions to the ICD-10 code set and/or clinical guidelines outlined in this policy. **The effective date for ICD-10 code set implementation is subject to change.*

ICD-10 Diagnosis Code (Effective 10/01/15)	Description
O09.211	Supervision of pregnancy with history of pre-term labor, first trimester
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
O09.219	Supervision of pregnancy with history of pre-term labor, unspecified trimester
O20.0	Threatened abortion
O20.8	Other hemorrhage in early pregnancy
O20.9	Hemorrhage in early pregnancy, unspecified
O47.00	False labor before 37 completed weeks of gestation, unspecified trimester
O47.02	False labor before 37 completed weeks of gestation, second trimester
O47.03	False labor before 37 completed weeks of gestation, third trimester
O47.1	False labor at or after 37 completed weeks of gestation
O47.9	False labor, unspecified
O60.00	Preterm labor without delivery, unspecified trimester
O60.02	Preterm labor without delivery, second trimester
O60.03	Preterm labor without delivery, third trimester
O60.10X0	Preterm labor with preterm delivery, unspecified trimester, not applicable or unspecified
O60.12X0	Preterm labor second trimester with preterm delivery second trimester, not applicable or unspecified
O60.13X0	Preterm labor second trimester with preterm delivery third trimester, not applicable or unspecified
O60.14X0	Preterm labor third trimester with preterm delivery third trimester, not applicable or unspecified
O60.20X0	Term delivery with preterm labor, unspecified trimester, not applicable or unspecified
O60.22X0	Term delivery with preterm labor, second trimester, not applicable or unspecified
O60.23X0	Term delivery with preterm labor, third trimester, not applicable or unspecified
Z3A.16	16 weeks gestation of pregnancy
Z3A.17	17 weeks gestation of pregnancy
Z3A.18	18 weeks gestation of pregnancy
Z3A.19	19 weeks gestation of pregnancy
Z3A.20	20 weeks gestation of pregnancy
Z3A.21	21 weeks gestation of pregnancy
Z3A.22	22 weeks gestation of pregnancy
Z3A.23	23 weeks gestation of pregnancy

Z3A.24	24 weeks gestation of pregnancy
Z3A.25	25 weeks gestation of pregnancy
Z3A.26	26 weeks gestation of pregnancy
Z3A.27	27 weeks gestation of pregnancy
Z3A.28	28 weeks gestation of pregnancy
Z3A.29	29 weeks gestation of pregnancy
Z3A.30	30 weeks gestation of pregnancy
Z3A.31	31 weeks gestation of pregnancy
Z3A.32	32 weeks gestation of pregnancy
Z3A.33	33 weeks gestation of pregnancy
Z3A.34	34 weeks gestation of pregnancy
Z3A.35	35 weeks gestation of pregnancy
Z3A.36	36 weeks gestation of pregnancy
Z87.51	Personal history of pre-term labor

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
8/1/2014	Annual policy review. Removed medical necessity heading such that criteria applies to all requests for 17P. Clinical evidence and references updated. Added ICD-10 codes. Approved by the National Pharmacy & Therapeutics Committee on 5/21/2014. Policy 2013D0040E archived.
7/1/2103	Annual policy review. Added medical necessity criteria. Clinical evidence and references updated. Updated ICD-10 codes. Approved by the National Pharmacy & Therapeutics Committee on 5/21/2013. Policy 2013D0040D archived.
1/1/2013	Policy updated. Parenthetical reference in policy title changed from "(17P and Makena)" to "(Makena and 17P)." Added Updated FDA Statements on Makena and Compounded Versions of Hydroxyprogesterone Caproate. Approved by the National Pharmacy & Therapeutics Committee on 11/13/2012. Policy 2012D0040C archived.
9/1/2012	Added list of applicable ICD-10 codes (preview draft) in preparation for the transition from ICD-9 to ICD-10 medical coding on 10/01/14.
7/1/2012	Annual policy review. Removed clinical evidence regarding intravaginal and oral administration of progesterone. Updated Hayes Technology Directory added. Approved by the National Pharmacy & Therapeutics Committee on 5/15/2012. Policy 2012D0040B archived.
1/1/2012	Removed Q2042 which becomes inactive on 1/1/2012. Added J1725 which becomes effective on 1/1/2012. Policy 2011D0040A archived.
10/1/2011	New policy 2011D0040A. Approved by the National Pharmacy & Therapeutics Committee on 5/10/2011.