MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY:	Preterm Birth Prevention: Progesterone	**P&T DATE**	2/15/2017
CLASS:	Women's Health	**REVIEW HISTORY** (MONTH/YEAR)	2/2017
LOB:	Medi-Cal, SJHA		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Preterm birth (PTB), or birth at less than 37 gestational week, is the leading cause of neonatal mortality in the United States and is associated with long-term neurological disabilities such as developmental delays and cerebral palsy. Each year, preterm birth affects nearly 500,000 infants – or 1 in every 8 born in the United States[1]. Major risk factors for preterm birth include history of spontaneous preterm labor and a short cervix (< 25mm) in the mid-trimester.

The Society of Maternal-Fetal Medicine (SMFM) and American Congress of Obstetricians and Gynecologists (ACOG) publish guidelines and practice bulletins that address the major risk factors and role of progesterone and its synthetic derivative in prevention of preterm birth. Progesterone is a steroidal hormone essential for the maintenance of pregnancy.

Historically, progesterone oral capsules are administered as vaginal suppository. This route exhibits a substantially higher concentration of progesterone in the endometrial tissues, and is more effective than systemic administration for prevention of preterm labor. Newer formulations include Crinone (progesterone) vaginal gel, progesterone in oil injection, and Makena (hydroxyprogesterone caproate) injection. As of today, Makena is the only drug that is FDA-approved and indicated to reduce the risk of preterm birth.

Table 1: Available Preterm Birth Prevention Agents (Current as of 01/2017)

Therapeutic Class	Generic Name (Brand Name)	Strength & Dosage form	Formulary Limits	Average Cost per 30 days*	Notes/Restriction Language
Progesterone	**Progesterone (First-Progesterone Vgs)**	100mg suppository 200mg suppository	NF	N/A	Non-formulary. Formulary alternative = Micronized Progesterone Capsules.
	Micronized Progesterone Gel (Crinone)	4% vaginal gel 8% vaginal gel	NF	$425.93 $700.08	Non-Formulary Formulary alternative = Micronized Progesterone Capsules.
	Micronized Progesterone (Prometrium)	100mg capsules 200mg capsules	PA; QL	$44.09 $91.13	Limit 2 capsules per day. Reserved for women with history of preterm birth , short cervix (< 25 mm), or history of 2 miscarriages
	Progesterone in Oil	50mg/ml intramuscular oil	PA	$51.92	Reserved for women with history of 2 miscarriages
Progestin	**Hydroxyprogesterone caproate (Makena)**	1250mg/5mL vial 250mg/ml vial	PA; QL	$3,161.96 $2,985.36	Limit 5 mL per 35 days. Reserved for singleton pregnancy with history of preterm birth (less than 37 weeks). Therapy must be initiated between 16 and 23 weeks, 6 days.

PA = Prior Authorization; QL = Quantity Limit; NF = Non-formulary

*Cost/Rx based on HPSJ Medi-Cal utilization historical data from January 2016 to December 2016.

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HSPJ Medical Review Guidelines (UM06).

Progesterone
Micronized Progesterone, Progesterone in Oil

Micronized Progesterone (Prometrium)

- ❒ **Coverage Criteria:** Reserved for women with history of preterm birth , short cervix (< 25 mm), or history of 2 miscarriages
- ❒ **Limits:** Prometrium: 2 capsules per day.
- ❒ **Required Information for Approval:** Diagnosis of short cervical length (CL < 25mm) before 24 weeks and documentation of prior birth terms
- ❒ **Non-Formulary:** First-Progesterone Vgs, Endometrin, Prochieve, Crinone
- ❒ **Other Notes:** Therapy may be continue until 37 gestational weeks.

Progesterone in oil (50mg/mL)

- ❒ **Coverage Criteria:** Reserved for women with history of 2 miscarriages
- ❒ **Required Information for Approval:** Documentation of prior birth terms
- ❒ **Other Notes:** None

Progestin
Hydroxyprogesterone caproate (Makena)

Hydroxyprogesterone caproate (Makena®) 250mg/ml intramuscular oil

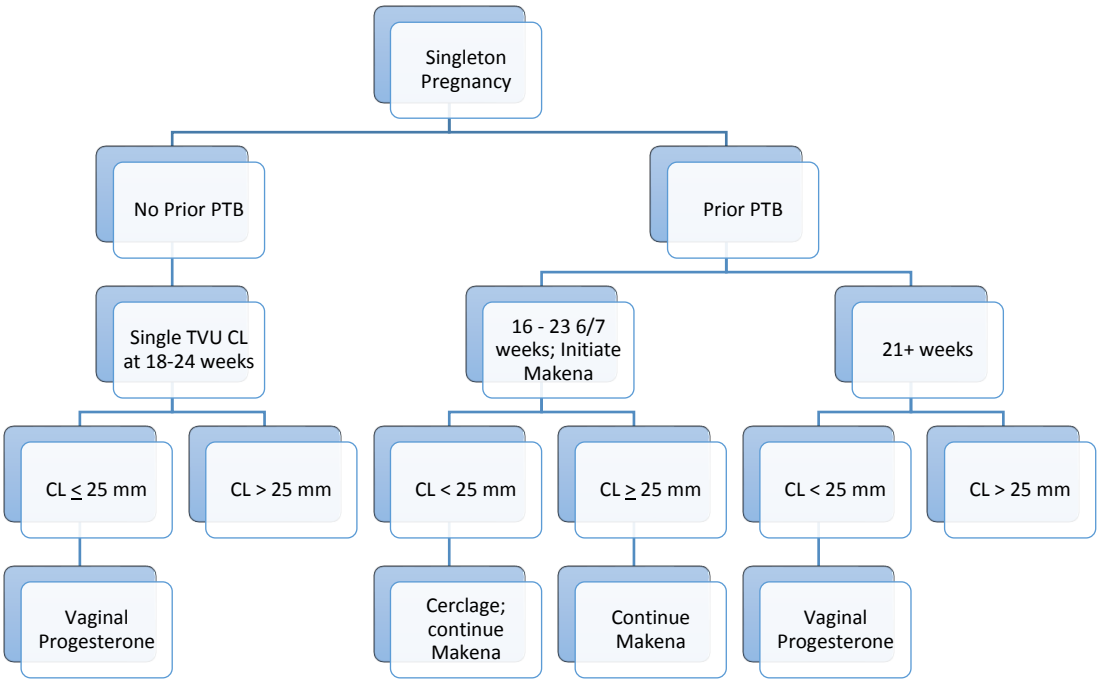
- ❒ **Coverage Criteria:** Singleton pregnancy with history of preterm birth (less than 37 weeks). Therapy must be initiated between 16 and 23 weeks, 6 days.
- ❒ **Limits:** 5 mL per 35 days.
- ❒ **Required Information for Approval:** Documented history of preterm birth with gestational age and current estimated due date (EDD)
- ❒ **Other Notes:** Therapy may be continue until 37 gestational weeks.

Clinical Justification:

Vaginal progesterone suppositories are recommended for women without a history of spontaneous preterm birth and develops a short cervix (< 25mm) during the mid-trimester. Prometrium, when administered as vaginal suppository, bypasses hepatic first pass effects to exhibit excellent bioavailability and is virtually without systemic side effects. Studies have used up to 400 mg of progesterone per day; thus, our quantity limit will be two capsules per day. Initiation as early as 16 gestational weeks has shown efficacy and safety in reducing the risk of preterm birth and prolonging gestation in high-risk pregnancies. First Progesterone VGS suppository-compounding kit is non-formulary because it is not FDA approved and not subject to the FDA's stringent Good Manufacturing Process (GMP). Guideline recommends either progesterone suppository or gel; thus, Crinone and Prochieve are non-formulary due to price differences.

Prior authorization for Makena (hydroxyprogesterone caproate) requires documented history of a singleton spontaneous preterm birth and current estimated due date (EDD) to ensure appropriate use. Unlike vaginal progesterone, Makena has not demonstrated efficacy in patients without history of preterm birth and cannot be used interchangeably. Therapy must be initiated between 16 weeks and 23 6/7 weeks.

Figure 1: HPSJ Algorithm for use of progesterone/progestin in prevention of preterm birth.



REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Endocrine: Preterm Birth Prevention	02/2017	Johnathan Yeh, PharmD