VENTURA COUNTY HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

PROGESTERONE (Crinone, Endometrin)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 10/30/19, 2/18/20

Progesterone is a natural steroid hormone that induces secretory changes in the endometrium, promotes mammary gland development, relaxes uterine smooth muscle, blocks follicular maturation and ovulation, and maintains pregnancy. When used as part of an ART program in the luteal phase, progesterone supports embryo implantation.

Pre-Authorization Criteria:
Note: This guideline addressed the use of progesterone for infertility, not for other medical uses such as amenorrhea, functional uterine bleeding or endometrial hyperplasia prevention.

Progesterone is used as part of assisted reproductive technology (ART) for infertile women with progesterone deficiency. If pregnancy occurs, progesterone may be continued for 10-12 weeks.

VCHCP requires that Progesterone, for this indication, be prescribed by an infertility specialist.

Dosing: Adult:
Females:
ART in patients who require progesterone supplementation:
Intravaginal gel: 90 mg (8% gel) once daily. If pregnancy occurs, may continue treatment for 10-12 weeks.
Intravaginal tablet: 100 mg 2-3 times daily starting at oocyte retrieval and continuing for up to 10 weeks.
ART in patients with partial or complete ovarian failure:
Intravaginal gel: 90 mg (8% gel) twice daily. If pregnancy occurs, continue treatment for 10-12 weeks.
Intramuscular Progesterone oil: 50 ml vial, 10 ml IM daily. This is used in conjunction with the intravaginal tablet. It is used every three (3) days if pregnancy is achieved for 10-12 weeks.

Dosing: Geriatric:
Refer to adult dosing.

Dosing: Renal Impairment:
Intravaginal gel, insert: No dosage adjustment provided in manufacturer's labeling .

Dosing: Hepatic Impairment:
Use is contraindicated in liver dysfunction or disease.

Dosage Forms: U.S.:

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Gel, Vaginal:
Crinone: 4% (1.45 g); 8% (1.45 g)
Insert, Vaginal:
Endometrin: 100 mg (21 ea)
Suppository, Vaginal:
First-Progesterone VGS 25: 25 mg (30 ea)
First-Progesterone VGS 50: 50 mg (30 ea)
First-Progesterone VGS 100: 100 mg (30 ea)
First-Progesterone VGS 200: 200 mg (30 ea)
First-Progesterone VGS 400: 400 mg (30 ea)

Generic Equivalent Available: U.S.-May be product dependent

Administration:
Intravaginal:
Vaginal gel: (A small amount of gel will remain in the applicator following insertion): Administer into the vagina directly from sealed applicator. Remove applicator from wrapper; holding applicator by thickest end, shake down to move contents to thin end; while holding applicator by flat section of thick end, twist off tab; gently insert into vagina and squeeze thick end of applicator.
For use at altitudes above 2500 feet: Remove applicator from wrapper; hold applicator on both sides of bubble in the thick end; using a lancet, make a single puncture in the bubble to relieve air pressure; holding applicator by thickest end, shake down to move contents to thin end; while holding applicator by flat section of thick end, twist off tab; gently insert into vagina and squeeze thick end of applicator.
Vaginal tablet: Insert tablet in vagina using disposable applicator provided.

Hazardous agent; use appropriate precautions for handling and disposal (NIOSH, 2012).

Exclusions:
Progesterone is not covered for reducing the risk of recurrent spontaneous preterm birth as this is an unlabeled use. See the VCHCP policy on Coverage of Prescription Medicaion for Off-Label Use.
Progesterone use is contraindicated in liver dysfunction or disease.

Adverse Reactions:
>10%: Somnolence, headache, nervousness, depression, breast enlargement, breast pain, libido decreased, constipation, nausea, cramps, abdominal pain, perineal pain, nocturia.
Other Serious Less Common Adverse Reactions: thromboembolism, ovarian hyperstimulation syndrome, breast cancer

Contraindications:
Hypersensitivity to progesterone or any component of the formulation; undiagnosed abnormal vaginal bleeding; history of or current thrombophlebitis or venous thromboembolic disorders (including DVT, PE); active or history of arterial thromboembolic disease (eg, stroke, MI); history of or known or suspected carcinoma of the breast or genital organs; hepatic dysfunction or disease; missed abortion or ectopic pregnancy; diagnostic test for pregnancy; capsules are also contraindicated for use during pregnancy

References:

1. American College of Obstetricians and Gynecologists (ACOG), Practice Bulletin No. 130, "Prediction and Prevention of Preterm Birth," *Obstet Gynecol*, 2012, 120(4):964-73. [PubMed 22996126]
2. Doody K, Shamma N, Paulson R, et al. "Endometrin® for Luteal Phase Support in a Randomized, Controlled, Open-Label, Prospective IVF Clinical Trial Using a Combination of Menopur® and Bravelle®," *Fertil Steril*, 2007, 87(4 Suppl 2):24. [PubMed 17081533]
3. National Institute for Occupational Safety and Health (NIOSH), "NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2012." Available at http://www.cdc.gov/niosh/docs/2012-150/pdfs/2012-150.pdf. Accessed January 21, 2013.
4. Ng EH, Chan CC, Tang OS, et al, "A Randomized Comparison of Side Effects and Patient Convenience Between Cyclogest® Suppositories and Endometrin® Tablets Used for Luteal Phase Support in IVF Treatment," *Eur J Obstet Gynecol Reprod Biol*, 2007, 131(2):182-8. [PubMed 16920249]
5. www.uptodate.com: Progesterone: Drug Information
6. www.epocrates.com: Crinone: Drug information

Revision History:

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Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review

10/30/19	Yes	Howard Taekman, MD; Robert Sterling, MD	Added *Intramuscular Progesterone oil*: 50 ml vial, 10 ml IM daily. This is used in conjunction with the intravaginal tablet. It is used every 3 days if pregnancy is achieved for 10-12 weeks.
2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review