PREFERRED STEP THERAPY POLICY

POLICY: Progesterone (Vaginal-Infertility) Preferred Step Therapy

APPROVAL DATE: 09/04/2019

DRUGS AFFECTED:

- Crinone® (progesterone 8% vaginal gel – Allergan USA, Inc.)
- Endometrin® (progesterone vaginal insert - Ferring Pharmaceuticals)

OVERVIEW

Progesterone gel is commercially available as Crinone 4% and 8% gel.[1] Crinone 8% is indicated for progesterone supplementation or replacement as part of an Assisted Reproductive Technology (ART) treatment for infertile women with progesterone deficiency. Endometrin is a vaginal insert which is indicated to support embryo implantation and early pregnancy by supplementation of corpus luteal function as part of an ART treatment program for infertile women.[2] Crinone 4% gel is indicated for the treatment of secondary amenorrhea and Crinone 8% gel is indicated for this use in women who have failed to respond to treatment with Crinone 4% gel. Crinone 4% gel is not part of this preferred step therapy program since it is not indicated for ART.

GUIDELINES

An education bulletin issued by the American Society for Reproductive Medicine (ASRM) on progesterone supplementation notes that available evidence supports using some form of luteal phase support when ART treatment includes any gonadotropin releasing hormone (GnRH) analogue (agonist or antagonist).[3] Progesterone supplementation can be achieved using oral, vaginal, or intramuscular (IM) progesterone formulations. However, of these available options, the ASRM bulletin notes that randomized controlled studies show that oral progesterone use appears to be associated with lower implantation and pregnancy rates, higher miscarriage rates, or both, as compared to use of IM or vaginal progesterone supplementation. In regards to the vaginal progesterone formulations, the ASRM bulletin notes that vaginal suppositories (only available in the US as compounded products) or vaginal tablets in doses ranging between 200 and 600 mg/day appear to have comparable treatment effects as vaginal progesterone 8% gel. However, the data are limited by relatively small study cohorts. In addition, the ASRM bulletin concludes that neither the optimal route of progesterone administration nor the optimal duration of supplemental progesterone therapy has been firmly established. A Practice Committee Opinion on luteal phase deficiency (2015) notes that the only well documented indication for supplemental vaginal or intramuscular (IM) progesterone is for the improvement of ART outcomes in GnRH agonist or antagonist stimulation cycles.[4] The committee opinion notes that IM progesterone is associated with the highest serum levels and vaginal progesterone increases endometrial tissue levels.

POLICY STATEMENT

A preferred step therapy program has been developed to encourage the use of a Step 1 product prior to the use of a Step 2 product. If the preferred step therapy rule is not met for a Step 2 agent at the point of service, coverage will be determined by the preferred step therapy criteria below. All approvals are provided for 1 year in duration.

Automation: Patients with a history of one Step 1 drug within the 130-day look-back period are excluded from the preferred step therapy.

Step 1: Crinone 8% gel
Step 2: Endometrin

CRITERIA

1. If the patient has tried a Step 1 product, then authorization for a Step 2 product may be given.

2. No other exceptions are recommended.

REFERENCES

1. Crinone® 4%/Crinone® 8% vaginal gel [prescribing information]. Irvine,, CA: Allergan USA, Inc.; June 2017.
2. Endometrin® vaginal insert [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; January 2018.
3. The Practice Committee of the American Society of Reproductive Medicine. Progesterone supplementation during the luteal phase and in early pregnancy in the treatment of infertility: an educational bulletin. *Fertil Steril.* 2008;89(4):789-792.
4. The Practice Committee of the American Society of Reproductive Medicine. Current clinical irrelevance of luteal phase deficiency: a committee opinion. Available at: https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/practice-guidelines/for-non-members/current_clinical_irrelevance_of_lpd_2015-noprint.pdf. Accessed on August 26, 2019.