Effective Date 11/1/2023
Next Review Date… 11/1/2024
Coverage Policy Number IP0548

Progesterone – Employer Group Plans

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for formulary exceptions to the following Vaginal Progesterone non-covered products:

- **Crinone**® (progesterone 4% gel)

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

Fertility medications are specifically excluded under most benefit plans. Please refer to the applicable benefit plan document to determine benefit availability and the terms and conditions of coverage.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Coverage criteria are listed for products **in below table:**

Non-Covered Product	Criteria
Crinone 4% (progesterone 4% gel)	Documentation of failure, contraindication, or intolerance to **ONE** of the following: 1. medroxyprogesterone 2. megestrol acetate 3. norethindrone tablets 4. progesterone capsules

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Crinone, Endometrin, and Milprosa are currently the only FDA-approved vaginal progesterone products available.[1-3] Note that as of March 2022, the anticipated availability of Milprosa is still unknown.
Crinone 8%, Endometrin, and Milprosa are indicated for use as part of an Assisted Reproductive Technology (ART) regimen for infertile women. Crinone 8% is also indicated for use in women who have failed to respond to treatment of secondary amenorrhea with Crinone 4%.

In women, progesterone, a sex steroid, is primarily produced by the corpus luteum after maturation of the dominant ovarian follicle during the reproductive years.[4] Progesterone can also be produced by the adrenal cortex and by the placenta during pregnancy.[5,6] Progesterone and the other sex steroids (estradiol and androgens) are important for the normal functioning of many organs, such as the bones, brain, skin, and reproductive and urogenital tracts.[4,5]

In premenopausal women, progesterone plays a key role in the preparation of the endometrium for implantation, successful gestation, and the normal development of the fetus.[6] Progesterone levels vary depending upon the phase of the menstrual cycle.[5,7] In the follicular phase of the menstrual cycle, progesterone levels are low. Levels slowly increase in the luteal phase after ovulation when the corpus luteum is formed and produces progesterone. Progesterone levels peak in the mid-luteal phase of the menstrual cycle and decline if there is no fertilization of the egg or are maintained by the corpus luteum if fertilization occurs.[7] The corpus luteum continues to produce progesterone to maintain the pregnancy until the placenta is able to take over the production of progesterone, typically around 6 to 8 weeks of gestation.[6,7]

After menopause, the ovaries are no longer the primary source of estradiol and progesterone production.[4] Women who experience menopausal symptoms such as vasomotor symptoms or vulvar or vaginal atrophy may decide to manage these symptoms with hormone replacement therapy (HRT), principally by using exogenous estrogens. In a postmenopausal woman with an intact uterus, administration of a progestin (a natural or synthetic progestational substance) concomitantly with an exogenous estrogen is highly recommended to protect the endometrium from hyperplastic changes and thus decrease the risk of endometrial adenocarcinoma (cancer).

There are other uses for exogenous progestins: contraception (with or without an estrogen), management of secondary amenorrhea and dysfunctional uterine bleeding, prevention and/or treatment of threatened or recurrent miscarriage or premature birth/labor, and prevention of endometrial hyperplasia in postmenopausal women receiving HRT.[5,6]

References

1. Crinone® 4%/Crinone® 8% vaginal gel [prescribing information]. Irvine, CA: Allergan; June 2017.
2. Endometrin® vaginal insert [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals; January 2018.
3. Milprosa™ vaginal system [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals; April 2020.
4. Kalantaridou SN, Davis SR, Calis KA. Hormone therapy in women. In: DiPiro JT, Talbert RL, Yee GC, et al., (Eds). *Pharmacotherapy – A Pathophysiologic Approach*. 7th ed. New York, NY: McGraw-Hill. 2008; 1351-1368.
5. Goletiani NV, Keith DR, Gorsky SJ. Progesterone: review of safety for clinical studies. *Exp Clin Psychopharmacol.* 2007; 15(5):427-444.
6. Fitzpatrick LA, Good A. Micronized progesterone: clinical indications and comparison with current treatments. *Fertil Steril.* 1999; 72(3):389-397.