Effective Date 11/1/2023
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Coverage Policy Number IP0091

Progesterone (Endometrin) for Individual and Family Plans

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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 of progesterone (Endometrin®) for Individual and Family Plans.

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

Progesterone (Endometrin) is considered medically necessary when ONE of the following is met (1 or 2):

1. **Infertility.** Individual meets the following criteria:
   A. Use is indicated as part of an Assisted Reproductive Technology (ART) treatment program.

2. **Prevention of pre-term birth.**

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.

Reauthorization Criteria

Not applicable for continuation beyond initial approval duration.

Authorization Duration

Initial approval duration is up to 6 months.
Reauthorization approval duration is not applicable.

Conditions Not Covered

Progesterone (Endometrin) is considered experimental, investigational or unproven for **ANY** other use.

Background

OVERVIEW
Progesterone gel is commercially available as Crinone (4% and 8% strengths).[1] Crinone 4% gel is indicated for the treatment of secondary amenorrhea and Crinone 8% gel is indicated for use in women who have failed to respond to treatment with the 4% progesterone gel. Crinone 8% is also indicated for progesterone supplementation or replacement as part of an Assisted Reproductive Technology (ART) treatment for infertile women with progesterone deficiency. Endometrin (vaginal insert[tablet]) and Milprosa (vaginal system [ring]) are indicated to support embryo implantation and early pregnancy by supplementation of corpus luteal function as part of an ART treatment program for infertile women.[2,3] Progesterone is also available as compounding kits (First-Progesterone VGS [100, and 200 mg]); these are *not* FDA-approved products.[4]

Progesterone is available in other dosage forms, including parenteral (e.g., progesterone in oil), oral capsules (Prometrium®), and powder; some of these formulations can be used to compound progesterone products.[5] Progesterone in oil formulations are approved for the treatment of amenorrhea and for abnormal uterine bleeding. The oral formulation of progesterone is indicated for the prevention of endometrial hyperplasia in non-hysterectomized postmenopausal women who are receiving conjugated estrogen tablets and for use in secondary amenorrhea. When administered vaginally, progesterone achieves high levels in the uterus.[6] In addition to infertility, there are many other uses for vaginally administered progesterone, including threatened abortion, prevention of recurrent miscarriage, and threatened preterm labor. Compounded progesterone products are used for oral, topical, sublingual, and vaginal administration as well as for injection.[7]

References

1. Crinone® 4%/Crinone® 8% vaginal gel [prescribing information]. Irvine, CA: Allergan; June 2017.
2. Endometrin® vaginal insert [prescribing information]. Parsippany, NJ: Ferring; January 2018.
3. Milprosa™ vaginal system [prescribing information]. Parsippany, NJ: Ferring; April 2020.
4. First™ – Progesterone VGS 100 & 200 [prescribing information]. Wilmington, MA: Azurity; March 2020.
5. Facts and Comparisons® Online. Wolters Kluwer Health; 2023. Available at: http://fco.factsandcomparisons.com/lco/action/home. Accessed on May 10, 2023. Search terms: progesterone.
6. Di Renzo GC, Mattei A, Gojnic M, Gerli S. Progesterone and pregnancy. Curr Opin Obstet Gynecol. 2005 Dec;17(6):598-600.
7. Report 4 of the Council on Science and Public Health (I-16). Hormone therapies – off-label uses and unapproved formulations. Resolution 512-A-15. Available at: https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/2016-interim-csaph-report-4.pdf. Accessed on May 10, 2023.