Drug Coverage Policy

Effective Date……8/1/2026
Coverage Policy Number……BEO003
Policy Title…..Progesterone (Vaginal)
Benefit Exclusion Overrides Policy

Progesterone (Vaginal) Benefit Exclusion Overrides Policy for Employer Plans

- Endometrin® (progesterone vaginal insert – Ferring, generics)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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

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. Progesterone vaginal insert (tablet) [Endometrin, generics) 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] Milprosa is not currently available. 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] The parenteral form is 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]

Coverage Policy

POLICY STATEMENT

This Benefit Exclusion Overrides policy has been developed to authorize coverage of the targeted drugs for all medical conditions, except infertility. **This Benefit Exclusion Overrides policy is not applicable if clients have infertility as a covered benefit.** All approvals are provided for the duration noted below.

Infertility treatment services may be excluded under many benefit plans. Please refer to the applicable benefit plan document to determine benefit availability and the terms and conditions of coverage (0089 Infertility Services).

Progesterone vaginal insert (Endometrin, generics) is considered medically necessary when the following are met (1):

1. **Indications other than infertility treatments**. Approve for 1 year.
   Note: Progesterone requested *only* for use as an infertility treatment (e.g., in vitro fertilization [IVF], in utero fertilization [IUI]) prior to a pregnancy would NOT be an approvable condition.

Conditions Not Covered

Coverage of Endometrin for the treatment of infertility is not medically necessary:

1. **Treatment of Infertility.** The purpose of this Benefit Exclusion Overrides policy is to exclude use of the targeted agent when used for the treatment of infertility.

References

1. Crinone® 4%/Crinone® 8% vaginal gel [prescribing information]. North Chicago, IL: AbbVie; May 2024.
2. Progesterone vaginal inserts [prescribing information]. Elmwood Park, NJ: Glenmark; March 2026.
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; 2026. Available at: Home - MICROMEDEX. Accessed on May 15, 2026. 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 15, 2026.

Revision Details

Summary of Changes	Review Date	Effective Date
New policy.	5/14/2026	7/15/2026
Added generic Endometrin vaginal inserts to the policy. No criteria changes.	6/4/2026	8/1/2026

The policy effective date is in force until updated or retired.