PREFERRED SPECIALTY MANAGEMENT POLICY

POLICY: Chorionic Gonadotropins Preferred Specialty Management Policy

- Pregnyl® (chorionic gonadotropin intramuscular injection [urine-derived] – Organon)
- Novarel® (chorionic gonadotropin intramuscular injection [urine-derived] – Ferring)
- Chorionic gonadotropin intramuscular injection (urine-derived) – Fresenius Kabi, others
- Ovidrel® (choriogonadotropin alfa subcutaneous injection [recombinant] – EMD Serono)

REVIEW DATE: 04/30/2025; selected revision 5/7/2025 (Effective Date: 07/01/2025)

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.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Pregnyl, Novarel, and chorionic gonadotropin for injection are indicated for the following uses:[1-3]

- **Prepubertal cryptorchidism** not due to anatomical obstruction.
- Selected cases of **hypogonadotropic hypogonadism** (hypogonadism secondary to a pituitary deficiency) in males.

- **Induction of ovulation and pregnancy** in the anovulatory, infertile women in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins.

Ovidrel is indicated for the following uses:[4]

- **Induction of final follicular maturation and early luteinization** in infertile women who have undergone pituitary desensitization and who have been appropriately pretreated with follicle stimulating hormones as part of an Assisted Reproductive Technology (ART) program such as *in vitro* fertilization and embryo transfer.
- **Induction of ovulation and pregnancy** in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure.

Pregnyl, Novarel, and chorionic gonadotropin for injection are highly purified preparations obtained from the urine of pregnant females and are administered intramuscularly.[1-3] Ovidrel is a recombinant human chorionic gonadotropin (hCG) and is for subcutaneous use only.[4] The physicochemical, immunological, and biological activities of recombinant hCG are comparable to those of placental and human pregnancy-urine derived hCG.

The action of hCG is very similar to the pituitary luteinizing hormone (LH), although hCG possesses slight follicle-stimulating hormone (FSH) activity.[1-3] hCG also stimulates production of gonadal steroid hormones by stimulating the interstitial cells of the testis to produce androgens and the corpus luteum of the ovary to produce progesterone.

In males, androgen stimulation by hCG results in the development of secondary sex characteristics that may lead to testicular descent when no anatomical obstruction is present.[1-3] When hCG is discontinued, the descent is usually reversible. During the normal menstrual cycle, LH acts with FSH in the maturation and development of the normal ovarian follicle and the mid-cycle LH surge causes ovulation; hCG can replace LH in this capacity. When pregnancy occurs, hCG produced by the placenta maintains the corpus luteum after LH secretion decreases, supporting continued secretion of estrogen and progesterone and preventing menstruation.

Table 1. Chorionic Gonadotropin Product Descriptions/Dosing Regimens.[1-4]

Detail	Pregnyl, Novarel, chorionic gonadotropin	Ovidrel
Formulation type	Urine-derived	Recombinant
Availability	**Pregnyl:** 10,000 USP units of hCG. **Novarel Vial:** 5,000 USP and 10,000 USP units of hCG. **Chorionic gonadotropin:** 10,000 USP units of hCG.	**Prefilled single-dose syringe** contains 250 mcg/0.5 mL.
Administration route	IM only	SC only
Dosing	• **Prepubertal cryptorchidism dosing options*:**	**Infertile women undergoing ART or ovulation induction:**

Detail	Pregnyl, Novarel, chorionic gonadotropin	Ovidrel
	○ 4,000 USP units TIW for 3 weeks. ○ 5,000 USP units every second day for 4 injections. ○ 15 injections of 500 to 1,000 USP units over a 6-week period. ○ 500 USP units TIW for 4 to 6 weeks. If unsuccessful, then another series starting 1 month later is given, using 1,000 USP units per injection. • **Selected cases of hypogonadotropic hypogonadism in males dosing options*:** ○ 500 to 1,000 USP units TIW for 3 weeks, followed by the same dose twice a week for 3 weeks. ○ 4,000 USP units TIW for 6 to 9 months, then decreased to 2,000 USP units TIW for an additional 3 months. • **Induction of ovulation dosing***: ○ 5,000 to 10,000 USP units 1 day following the last dose of menotropins. A dosage of 10,000 USP units is Non-Preferred Product in the labeling for menotropins.	250 mcg 1 day following the last dose of follicle stimulating agent. Administer only if there is adequate follicular development as indicated by serum estradiol and vaginal ultrasonography. Withhold dose if there is an excessive ovarian response (clinically significant ovarian enlargement or excessive estradiol production).

hCG – Human chorionic gonadotropin; IM – intramuscularly; SC – subcutaneously; * The dosage regimen used in any particular patient will depend upon the indication for the use, the age and weight of the patient, and the physician's preference. The regimens listed have been advocated by various authorities; TIW – Three times per week; ART – Assisted reproductive technology.

POLICY STATEMENT

Utilization of these products is not managed by a Prior Authorization Policy, but rather based on whether a patient's benefit includes infertility coverage. If the patient's benefit includes infertility coverage, this Preferred Specialty Management Program has been developed to encourage the use of Preferred Products. The program also directs the patient to try one Preferred Product prior to the approval of a Non-Preferred Product. Requests for the Non-Preferred Products will also be reviewed using the exception criteria (below). All approvals are provided for the duration noted below.

If the patient's benefit does not include infertility coverage, benefit exclusion overrides may be in place. This Preferred Specialty Management program requires the patient to meet standard *Chorionic Gonadotropin Benefit Exclusion Overrides Policy* criteria and requires the patient to try a Preferred Product, when clinically appropriate, prior to the approval of Non-Preferred Products.

If the patient's benefit does not include infertility coverage and benefit exclusion overrides are not utilized, coverage will be denied.

National Preferred Formulary and High Performance Formulary

Preferred Products: Ovidrel, Pregnyl
Non-Preferred Products: Chorionic Gonadotropin for injection, Novarel

Basic Formulary
Preferred Products: Novarel, Ovidrel
Non-Preferred Products: Chorionic Gonadotropin for injection, Pregnyl

Chorionic Gonadotropins Preferred Specialty Management Policy non-preferred product(s) is(are) covered as medically necessary when the following non-preferred product exception criteria is(are) met. Any other exception is considered not medically necessary.

NON-PREFERRED PRODUCT EXCEPTION CRITERIA

Non-Preferred Product	Exception Criteria
Chorionic Gonadotropin for injection	**National Preferred, High Performance.** Approve if the patient meets ONE of the following (1, 2, 3, or 4): **1.** Cryptorchidism or hypogonadism: Approve for 1 year if the patient has tried Pregnyl. **2.** Infertility or induction of ovulation AND the patient's benefit includes infertility coverage: Approve for 1 year if the patient has tried ONE of the following: Pregnyl or Ovidrel. Note: If the patient has a diagnosis related to infertility or induction of ovulation, a one-time approval may be given if the patient is at risk of missing the optimal administration timeframe window of the product (in order to avoid disruption of the current fertility medication cycle). **3.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are utilized: Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the standard *Chorionic Gonadotropins Benefit Exclusion Overrides Policy* criteria; AND **B)** Patient has tried Pregnyl. **4.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are NOT utilized: Not reviewable. **Basic Formulary.** Approve if the patient meets ONE of the following (1, 2, 3, or 4): **1.** Cryptorchidism or hypogonadism: Approve for 1 year if the patient has tried Novarel. **2.** Infertility or induction of ovulation AND the patient's benefit includes infertility coverage: Approve for 1 year if the patient has tried ONE of the following: Novarel or Ovidrel. Note: If the patient has a diagnosis related to infertility or induction of ovulation, a one-time approval may be given if the patient is at risk of missing the optimal administration

	timeframe window of the product (in order to avoid disruption of the current fertility medication cycle). **3.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are utilized: Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the standard *Chorionic Gonadotropins Benefit Exclusion Overrides Policy* criteria; AND **B)** Patient has tried Novarel. **4.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are NOT utilized: Not reviewable.
Novarel	**National Preferred and High Performance Formulary.** Approve if the patient meets ONE of the following (1, 2, 3, or 4): **1.** Cryptorchidism or hypogonadism: Approve for 1 year if the patient has tried Pregnyl. **2.** Infertility or induction of ovulation AND the patient's benefit includes infertility coverage: Approve for 1 year if the patient has tried one of the following: Pregnyl or Ovidrel. Note: If the patient had a diagnosis related to infertility or induction of ovulation, a one-time approval may be given if the patient is at risk of missing the optimal administration timeframe window of the product (in order to avoid disruption of the current fertility medication cycle). **3.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are utilized: Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the standard Chorionic Gonadotropins Benefit Exclusion Overrides Policy criteria; AND **B)** Patient has tried Pregnyl. **4.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are NOT utilized: Not reviewable. **Basic Formulary.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are utilized: Approve for 1 year if the patient mees the standard *Chorionic Gonadotropins Benefit Exclusion Overrides Policy* criteria.
Pregnyl	**National Preferred and High Performance Formulary.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are utilized: Approve for 1 year if the patient mees the standard *Chorionic Gonadotropins Benefit Exclusion Overrides Policy* criteria. **Basic Formulary.** Approve if the patient meets ONE of the following (1, 2, 3, or 4): **1.** Cryptorchidism or hypogonadism: Approve for 1 year if the patient has tried Novarel.

	2. Infertility or induction of ovulation AND the patient's benefit includes infertility coverage: Approve for 1 year if the patient has tried ONE of the following: Novarel or Ovidrel. Note: If the patient has a diagnosis related to infertility or induction of ovulation, a one-time approval may be given if the patient is at risk of missing the optimal administration timeframe window of the product (in order to avoid disruption of the current fertility medication cycle). **3.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are utilized: Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the standard *Chorionic Gonadotropins Benefit Exclusion Overrides Policy* criteria; AND **B)** Patient has tried Novarel. **4.** Patient's benefit does NOT include infertility coverage AND benefit exclusion overrides are NOT utilized: Not reviewable.

REFERENCES

1. Pregnyl® intramuscular injection [prescribing information]. Jersey City, NJ: Organon; June 2024.
2. Novarel® intramuscular injection [prescribing information]. Parsippany, NJ: Ferring; May 2023.
3. Chorionic gonadotropin intramuscular injection [prescribing information]. Lake Zurich, IL: Fresenius Kabi; February 2025.
4. Ovidrel® subcutaneous injection [prescribing information]. Rockland, MA: EMD Serono; June 2018.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Changes effective for 1/1/2024. Chorionic Gonadotropin (Fresenious) moved from a Preferred product to a Non-Preferred product. Chorionic Gonadotropin (Fresenious) was removed from criteria as an alternative.	11/01/2023
Annual Revision	No criteria changes.	10/30/2024
Early Annual Revision	Changes effective for 07/01/2025. Created criteria for National Preferred Formulary, High Performance Formulary, and Basic Formulary. National Preferred Formulary and High Performance Formulary: Ovidrel and Pregnyl were updated as Preferred products. Chorionic Gonadotropin and Novarel were updated as Non-Preferred products. Basic Formulary: Novarel and Ovidrel were updated as Preferred products. Chorionic Gonadotropin and Pregnyl were updated as Non-Preferred products. Added clinical criteria for Novarel.	04/230/2025
Selected Revision	Changes effective for 07/01/2025. Chorionic Gonadotropin: For National Preferred Formulary and High Performance Formulary, updated to a trial of Novarel to Pregnyl.	05/07/2025