PREFERRED SPECIALTY MANAGEMENT POLICY

POLICY: Chorionic Gonadotropins Preferred Specialty Management Policy

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

REVIEW DATE: 09/02/2020

OVERVIEW

Pregnyl, Novarel, and chorionic gonadotropin for injection are indicated for the following:

- **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:

- **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 (IM).[1-3] Ovidrel is a recombinant human chorionic gonadotropin (hCG) and is for subcutaneous (SQ) 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

Detail	Pregnyl, Novarel, chorionic gonadotropin	Ovidrel
Availability	**Pregnyl:** 10,000 USP units of hCG **Novarel Vial:** 5,000 USP units of hCG (10,000 USP unit vial no longer being manufactured) **Chorionic gonadotropin:** 10,000 USP units of hCG	**Prefilled single-dose syringe** contains 250 mcg/0.5 mL
Storage	**Pregnyl:** Store at room temperature. Reconstituted solution is stable for 60 days when refrigerated. **Novarel:** Store at room temperature. Reconstituted solution is stable for 30 days when refrigerated. **Chorionic gonadotropin:** Store at room temperature. Reconstituted solution is stable for 60 days when refrigerated.	**Prefilled syringe:** Store refrigerated prior to dispensing; patient may store at room temperature for up to 30 days or store refrigerated until expiration date.
Administration route	IM only	SQ only
Dosing	• **Prepubertal cryptorchidism dosing options*:** o 4,000 USP units TIW for 3 weeks; o 5,000 USP units every second day for 4 injections; o 15 injections of 500 to 1,000 USP units over a 6-week period; o 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*:** o 500 to 1,000 USP units TIW for 3 weeks, followed by the same dose twice a week for 3 weeks; o 4,000 USP units TIW for 6-9 months, then decreased to 2,000 USP units TIW for an additional 3 months. • **Induction of ovulation dosing*** is o 5,000 to 10,000 USP units one day following the last dose of menotropins (A dosage of 10,000 USP units is recommended in the labeling for menotropins.)	**Infertile women undergoing ART or ovulation induction:** Give 250 mcg one 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 – 3 times per week; ART – assisted reproductive technology.

POLICY STATEMENT

Currently, 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 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 approval 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 ESI Standard *Chorionic Gonadotropin Benefit Exclusion Overrides* criteria and requires the patient to try the preferred products, 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.

Automation: None

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

RECOMMENDED EXCEPTION CRITERIA

Non-Preferred Product	Exception Criteria
Chorionic Gonadotropin for injection, USP	**1.** If the patient has a diagnosis of cryptorchidism or hypogonadism, approve for 1 year if the patient has tried the preferred product Novarel. **2.** If the patient's benefit includes infertility coverage and the patient has a diagnosis related to infertility or induction of ovulation: approve for 1 year if the patient has tried one of the following preferred products: 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.** If the patient's benefit does NOT include infertility coverage and benefit exclusion overrides ARE utilized, approve for 1 year if the patient meets the following criteria (A and B): **A.** The patient meets the ESI Standard *Chorionic Gonadotropins Benefit Exclusion Overrides* criteria; AND **B.** The patient has tried the preferred product Novarel. **4.** If the patient's benefit does NOT include infertility coverage and benefit exclusion overrides are NOT utilized: not reviewable.
Pregnyl	**1.** If the patient has a diagnosis of cryptorchidism or hypogonadism, approve for 1 year if the patient has tried the preferred product Novarel. **2.** If the patient's benefit includes infertility coverage and the patient has a diagnosis related to infertility or induction of ovulation: approve for 1 year if the patient has tried one of the following preferred products: 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.** If the patient's benefit does NOT include infertility coverage and benefit exclusion overrides ARE utilized, approve for 1 year if the patient meets the following criteria (A and B): **A.** The patient meets the ESI Standard *Chorionic Gonadotropins Benefit Exclusion Overrides* criteria; AND **B.** The patient has tried the preferred product Novarel. **4.** If the patient's benefit does NOT include infertility coverage and benefit exclusion overrides are NOT utilized: not reviewable.

REFERENCES

1. Pregnyl® [prescribing information]. Roseland, NJ: Organon USA Inc.;January 2015.
2. Novarel® [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; May 2018.
3. Chorionic gonadotropin [prescribing information]. Lake Zurich, IL: Fresenius Kabi; February 2016.
4. Ovidrel ® [prescribing information]. Rockland, MA: EMD Serono, Inc.; June 2018.
5. Chorionic Gonadotropin Benefit Exclusion Overrides Policy. Express Scripts, Inc. Updated 09/02/2020.