HCG Powder, Novarel, Pregnyl, Ovidrel

Description

HCG Powder (human chorionic gonadotropin); Novarel, Pregnyl (chorionic gonadotropin); Ovidrel (choriogonadotropin alfa)

Background

Human chorionic gonadotropin (HCG), a polypeptide hormone produced by the human placenta, is composed of an alpha and a beta sub-unit. The alpha sub-unit is essentially identical to the alpha sub-units of the human pituitary gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), as well as to the alpha sub-unit of human thyroid-stimulating hormone (TSH). The beta sub-units of these hormones differ in amino acid sequence. The action of HCG is virtually identical to that of pituitary LH, although HCG appears to have a small degree of FSH activity as well. It stimulates production of gonadal steroid hormones by stimulating the interstitial cells (Leydig cells) of the testes to produce androgens and the corpus luteum of the ovary to produce progesterone. Androgen stimulation in the male leads to the development of secondary sex characteristics and may stimulate testicular descent when no anatomical impediment to descent is present. During the normal menstrual cycle, LH participates with FSH in the development and maturation of the normal ovarian follicle, and the mid-cycle LH surge triggers ovulation. During a normal pregnancy, HCG secreted by the placenta maintains the corpus luteum after LH secretion decreases, supporting continued secretion of estrogen and progesterone and preventing menstruation (1-3).

HCG may be used as a pharmacologic intervention in the treatment of undescended testes, and the induction of ovulation in both coital reproduction and for controlled ovarian hyperstimulation (COH) with assisted reproductive technologies (ART). Off-label and alternative uses of HCG such as enhancement of weight loss, improvement of muscle development and muscle injury
Recovery have been reported (1-3).

**Regulatory Status**
FDA-approved indications: HCG products are purified preparations obtained from the urine of pregnant women and standardized for injection by a biological assay. Chorionic gonadotropin (HCG powder, Novarel, Pregnyl) is approved for prepubertal cryptorchidism not due to anatomic obstruction, selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males, and the induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins (1-3).

For the treatment of cryptorchidism therapy is usually instituted in children between the ages of 4 and 9 (1-3).

Choriogonadotropin alfa (Ovidrel) is indicated for the 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. Ovidrel is also indicated for the induction of ovulation (OI) and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure (3).

Novarel and Pregnyl may also be used to induce puberty in boys and to treat androgen deficiency in hypogonadotropic hypogonadism; the major use of these preparations is in the initiation and maintenance of spermatogenesis in hypogonadotropic men who desire fertility. It may take 2 to 3 months to achieve normal levels of testosterone (4).

**Related policies**

*Policy*

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

HCG powder, Novarel and Pregnyl, may be considered **medically necessary** for male patients who are diagnosed with hypogonadotrophic hypogonadism or prepubertal cryptorchidism not caused by anatomic obstruction; and HCG, Novarel, Pregnyl and Ovidrel in female patients for use in ovulation induction.
HCG powder may be considered **medically necessary** if the requested dose is **NOT** commercially available, the requested dose/strength does **NOT** exceed the maximum FDA-approved dose/strength for the requested ingredient, and the requested dosage form is a FDA approved dosage form.

HCG powder, Novarel, Pregnyl, and Ovidrel may be considered **investigational** for all other indications.

Use in erectile or sexual dysfunction, weight loss, performance enhancement, chronic pain management/neurogenesis and for anti-aging effects is excluded by benefit design.

HCG powder, Novarel, Pregnyl, and Ovidrel used in conjunction with assisted reproductive technology (ART) procedures are not a covered benefit.

**Prior-Approval Requirements**

**Diagnoses**

**Male** patients must have one of the following (Novarel and Pregnyl ONLY):

1. Hypogonadotrophic hypogonadism (hypogonadism secondary to pituitary deficiency)
2. Prepubertal cryptorchidism not caused by anatomic obstruction

**AND NOT** being used to treat:

1. Erectile or sexual dysfunction
2. Weight loss
3. Performance (athletic) enhancement
4. Anti-aging effects
5. Chronic pain management / neurogenesis

**Female** patients must have one of the following:

1. Ovulation induction

**AND NOT** being used to treat:

1. Assisted reproductive techniques (ART)
2. Weight loss
3. Performance (athletic) enhancement
4. Anti-aging effects
5. Chronic pain management / neurogenesis

AND ALL of the following for HCG powder

1. The requested dose is NOT commercially available
2. The requested dose/ strength does NOT exceed the maximum FDA-approved dose/strength for the requested ingredient
3. The requested dosage form is a FDA approved dosage form

Prior – Approval Renewal Requirements

Diagnoses

Male patients must have one of the following (Novarel and Pregnyl only):

1. Prepubertal cryptorchidism not caused by anatomic obstruction

AND NOT being used to treat:

1. Erectile or sexual dysfunction
2. Weight loss
3. Performance (athletic) enhancement
4. Anti-aging effects
5. Chronic pain management / neurogenesis

Female patients must have one of the following:

1. Ovulation induction

AND NOT being used to treat:

1. Assisted reproductive techniques (ART)
2. Weight loss
3. Performance (athletic) enhancement
4. Anti-aging effects
5. Chronic pain management / neurogenesis

AND ALL of the following for HCG powder

1. The requested dose is NOT commercially available
2. The requested dose/ strength does NOT exceed the maximum FDA-approved dose/strength for the requested ingredient
3. The requested dosage form is a FDA approved dosage form
**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**

**Females**

| Duration | 6 months |

**Males**

| Quantity | Novarel | 18 vials/ 84 days |
| Quantity | Pregnyl | 18 vials /84 days |

| Duration | 12 months |

**Prior – Approval Renewal Limits**

**Females**

| Duration | 6 months |

**Males**

**Prepubertal cryptorchidism only**

| Quantity | Novarel | 18 vials/ 84 days |
| Quantity | Pregnyl | 18 vials /84 days |

| Duration | 12 months |

**Rationale**

**Summary**

Human chorionic gonadotropin (HCG), a polypeptide hormone produced by the human placenta, is composed of an alpha and a beta sub-unit. The alpha sub-unit is essentially identical to the alpha sub-units of the human pituitary gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH). The action of HCG is virtually identical to LH and, therefore, has therapeutic potential (1-3).
Chorionic gonadotropin (HCG powder, Novarel, Pregnyl) is approved for prepubertal cryptorchidism not due to anatomic obstruction, selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males, and the induction of ovulation and pregnancy. Choriogonadotropin alfa (Ovidrel) is indicated for the induction of final follicular maturation and early luteinization in infertile women who have undergone pituitary desensitization (1-3).

Chorionic gonadotropin is used off-label for weight loss, erectile or sexual dysfunction, anti-aging effects, chronic pain management / neurogenesis, and performance enhancement. Such uses are excluded from the benefit.

The use of HCG preparations in conjunction with assisted reproductive technology (ART) is excluded from the benefit.

Prior authorization is required for chorionic gonadotropin and choriogonadotropin alfa to ensure their safe, clinically appropriate and cost effective use while maintaining optimal therapeutic outcomes.

References
4. American Association of Clinical Endocrinologists (AACE); Medical guidelines for clinical practice for the evaluation and treatment of hypogonadism. 2002;8(No.6).

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
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<tbody>
<tr>
<td>March 2011</td>
<td>Adding human chorionic gonadotropin (HCG) powder to the list of drugs used in infertility and ART; HCG is used to induce ovulation and spermatogenesis.</td>
</tr>
<tr>
<td>September 2011</td>
<td>Weight loss, performance enhancing, and anti-aging are not covered benefits. To date no clinical evidence has established clinical efficacy of the use of HCG in any formal study to be used in weight loss therapy (3). Prior approval is required to exclude coverage of use in weight loss, performance enhancing, anti-aging, and in conjunction with ART.</td>
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### 5.30.43

<table>
<thead>
<tr>
<th>Section:</th>
<th>Prescription Drugs</th>
<th>Effective Date:</th>
<th>October 1, 2016</th>
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<tr>
<td>Subsection:</td>
<td>Endocrine and Metabolic Drugs</td>
<td>Original Policy Date:</td>
<td>March 14, 2011</td>
</tr>
<tr>
<td>Subject:</td>
<td>HCG</td>
<td>Page:</td>
<td>7 of 7</td>
</tr>
</tbody>
</table>

- December 2012: Annual editorial review and update
- March 2013: Interval editorial review and update
- September 2014: Annual editorial review and reference update
- May 2015: Reference update, addition of quantity limits to males, removal of renewal for hypogonadotropic hypogonadism, additional criteria for powder for compounding
- June 2015: Annual editorial review
- September 2016: Annual editorial review and reference update

**Keywords**

Policy number change from 5.08.09 to 5.30.43

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**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 15, 2016 and is effective on October 1, 2016.**

**Deborah M. Smith, MD, MPH**