human chronic gonadotropin (Novarel®; Pregnyl®)
EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO127

Description
Human chorionic gonadotropin (hCG) stimulates production of gonadal steroid hormones by causing production of androgen by the testes and the development of secondary sex characteristics in males. In females, hCG acts as a substitute for luteinizing hormone (LH) to stimulate ovulation.

Length of Authorization
- Initial: 12 months (for hypogonadotropic hypogonadism); six months (for cryptorchidism)
- Renewal: 12 months (for hypogonadotropic hypogonadism)*
  * Other indications are not eligible for renewal

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
human chorionic gonadotropin (human chorionic gonadotropin)	10,000 unit vial	Hypogonadotropic hypogonadism Ovulation induction* Prepubertal cryptorchidism	5 vials/30 days
human chorionic gonadotropin (Novarel)	5,000 unit vial		10 vials/30 days
human chorionic gonadotropin (Pregnyl)	10,000 unit vial		5 vials/30 days

**Drugs used in the treatment of fertility are excluded from coverage. Please refer to the member handbook/certificate of coverage for further information.*

Initial Evaluation

I. Human chorionic gonadotropin (Novarel; Pregnyl) may be considered medically necessary when the following criteria below are met:
   A. A diagnosis of one of the following:
      1. **Hypogonadotropic hypogonadism; AND**
         i. Two sub-normal testosterone concentration levels taken on two separate mornings while fasting; **AND**
         ii. Treatment with **all** of the following has been ineffective, contraindicated, or not tolerated:
            a. Generic injectable testosterone (i.e. testosterone cypionate, testosterone enanthate); **AND**
            b. Generic topical testosterone (i.e. generic testosterone 1% gel); **OR**
      2. **Prepubertal cryptorchidism; AND**
         i. Not due to anatomical obstruction

II. Human chorionic gonadotropin (Novarel; Pregnyl) is considered not medically necessary when criteria above are not met and/or when used for:
   A. Men with low testosterone concentration and without clinical symptoms and signs consistent with testosterone deficiency. The routine assessment of testosterone level in the absence of hypogonadal symptoms is not advised.
   B. Men with a single, sub-normal testosterone concentration that is not repeatable per the U.S. Endocrine Society.
   C. Men with symptoms of hypogonadism; however, current testosterone level is within normal range.

III. Human chorionic gonadotropin (Novarel; Pregnyl) is considered investigational when used for all other conditions including but not limited to:
   A. Age-related hypogonadism
   B. Men with type 2 diabetes mellitus with low testosterone for the purpose of improving glycemic control
   C. Obesity

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. A diagnosis of **hypogonadotropic hypogonadism; AND**
IV. Member has exhibited improvement or stability of disease symptoms.

Supporting Evidence

I. Human chorionic gonadotropin (Novarel; Pregnyl) is FDA approved for the treatment of hypogonadotropic hypogonadism, prepubertal cryptorchidism, and ovulation induction. Coverage of medications used in the treatment of fertility is an excluded benefit; thus, criteria for coverage in the setting of ovulation induction is unrepresented within this policy.
II. There are several dosing regimen options in the setting of prepubertal cryptorchidism; however the label only supports a six week course with the potential of another series given one month later if the initial course was not successful.
III. Per the 2018 AUA guidelines, diagnosis of hypogonadism should be confirmed prior to initiating testosterone replacement therapy. Testosterone levels should be drawn ideally between 8 and 10 AM while fasting due to the diurnal fluctuation of testosterone and its sensitivity to glucose ingestion. A separate, confirmatory measurement is recommended.
IV. Thirty percent of men with an initial testosterone concentration in the hypogonadal range can have a measurement within the normal range on repeat measurement.
V. The Endocrine Society strongly advises against “trial periods” of testosterone in men with a single sub-normal testosterone concentration and vague symptoms of deficiency.

VI. In patients within normal range, or have low testosterone concentration due to age, obesity or otherwise, the benefit of increased testosterone has not been shown. Rather, in this patient population with low testosterone and an intact gonadal system, increasing testosterone is associated with an increase of certain health risks, including cardiovascular disease. Because of this, the FDA has required manufacturers to label testosterone products warning of the increased risk for heart attack and stroke.

Investigational or Not Medically Necessary Uses

I. All of the aforementioned conditions listed in the not medically necessary section are considered to be excluded from coverage.
II. In the conditions listed, there is insufficient information, or, information reports inconclusive evidence, to support the safety and efficacy of using human chorionic gonadotropin (Novarel; Pregnyl).

References

1. Novarel [Prescribing Information]. Parsippany, NJ: Ferring Pharmaceuticals, Inc. May 2018.
2. Pregnyl [Prescribing Information]. Whitehouse Station, NJ: Merck & Co., January 2015.
3. Bhasin S, Brito JP, Cunningham GR, et al. Testosterone Therapy in Men with Hypogonadism: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2018; 103:1715.
4. Yeap B, Wu F. Clinical practice update on testosterone therapy for male hypogonadism: Contrasting perspectives to optimize care. Clinical Endocrinology 2019; 56:65. Available at: DOI: 10.1111/cen.13888
5. Crowley, W. F. (2018, July 23). Approach to patient with delayed puberty. Retrieved from UpToDate.
6. Snyder, P. J. (2018, April 21). Clinical features and diagnosis of male hypogonadism. Retrieved from UpToDate.
7. National Institute on Aging. Scientific task force to examine usefulness of testosterone replacement therapy in older men. NIH News Release. November 6, 2002. Available at: http://www.nia.nih.gov/NewsAndEvents/PressReleases/PR20021106ScientificTask.htm (access date April 4, 2007).

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Action and Summary of Changes	**Date**