Human Chorionic Gonadotropin (hCG) for Non-fertility

The following coverage policy criteria addresses the use of human chorionic gonadotropin (hCG) for indications other than fertility. The use of hCG for fertility is addressed in a separate coverage policy. Please refer to the related coverage policy link above (Infertility Injectables).

Human chorionic gonadotropin (chorionic gonadotropin, Novare®®, Pregnyl®) is considered medically necessary when BOTH of the following criteria are met:

- Individual is between the ages of 4 to 9 years old
- Diagnosis of prepubertal cryptorchidism not due to anatomical obstruction

Initial and reauthorization is up to 6 months unless otherwise stated.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Human chorionic gonadotropin (hCG) is considered experimental, investigational or unproven for ANY other non-fertility use including the following:
• Obesity
• In combination with testosterone therapy
• Sexual dysfunction, including erectile dysfunction
• Treatment of low testosterone in the absence of hypogonadotropic hypogonadism

**Note: If hCG is being used for the stimulation of spermatogenesis in hypogonadotropic hypogonadism please refer to the related coverage policy link Infertility Injectables (1012)**

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

### FDA Approved Indications

Human chorionic gonadotropin has not been demonstrated to be effective adjunctive therapy in the treatment of obesity. There is no substantial evidence that it increases weight loss beyond that resulting from caloric restriction, that it causes a more attractive or “normal” distribution of fat, or that it decreases the hunger and discomfort associated with calorie restricted diets.

1. Prepubertal cryptorchidism not due to anatomical obstruction. In general, HCG is thought to induce testicular descent in situations when descent would have occurred at puberty. HCG thus may help predict whether or not orchiopexy will be needed in the future. Although, in some cases, descent following HCG administration is permanent, in most cases, the response is temporary. Therapy is usually instituted in children between the ages of 4 and 9.

2. Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males.

3. 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.

Note: This coverage policy only addresses non-fertility uses. The use of hCG for fertility is addressed in a separate coverage policy (Infertility Injectables).

### Recommended Dosing

**FDA Recommended Dosing**

Intramuscular Use Only. The dosage regimen employed in any particular case will depend upon the indication for use, the age and weight of the patient, and the physician’s preference. The following regimens have been advocated by various authorities.

Prepubertal cryptorchidism not due to anatomical obstruction:

1. 4,000 USP Units three times weekly for three weeks.
2. 5,000 USP Units every second day for four injections.
3. 15 injections of 500 to 1,000 USP Units over a period of six weeks.
4. 500 USP Units three times weekly for four to six weeks. If this course of treatment is not successful, another is begun one month later, giving 1,000 USP Units per injection.

**Drug Availability**

**Chorionic Gonadotropin**

Chorionic Gonadotropin for Injection, 10,000 USP Units in a 10mL multiple dose vial with accompanying diluent in packages of 10

**Novarel**

Chorionic Gonadotropin 10,000 USP Units, Mannitol 100 mg, Dibasic Sodium Phosphate 16 mg, and Monobasic Sodium Phosphate 4 mg
**Pregnyl**  
Two-vial package containing: 1-10 mL lyophilized multiple dose vial containing: 10,000 USP Units chorionic gonadotropin per vial. 1-10 mL vial of solvent containing: water for injection with sodium chloride 0.56% and benzyl alcohol 0.9%

### General Background

#### Disease Overview

At 1 year of age, cryptorchidism or undescended testis affects approximately 1% of full-term male infants. It is one of the most common congenital anomaly affecting the genitalia of newborn males. Boys with undescended testes have lower fertility and paternity rates. They also have an increased risk of developing testicular malignancy.

#### Professional Societies/Organizations

#### Guidelines

**American Urological Association Evaluation and Treatment of Cryptorchidism**

The AUA’s evaluation and treatment of Cryptorchidism states that Providers should not use hormonal therapy to induce testicular descent as evidence shows low response rates and lack of evidence for long-term efficacy. (Standard; Evidence Strength: Grade B) Therapy with hCG or luteinizing hormone-releasing hormone (LHRH or gonadotropin-releasing hormone (GnRH)) has been used for numerous years. However, the studies published have provided divergent results based on differences in study characteristics such as patient age, treatment schedules, poor follow-up and possible inclusion of retractile testes. Studies have shown a significant risk of recurrence. AUA states that although an individual study may have demonstrated a reasonable result in testicular descent induction, the overall review of all studies in aggregate does fail to demonstrate long-term efficacy. (Kolon, 2014)

**Canadian Urological Association-Pediatric Urologists of Canada (CUA-PUC) guideline for the diagnosis, management, and follow up of cryptorchidism**

CUA-PUC states that the treatment for undescended testis with human chorionic gonadotropin or luteinizing hormone-releasing hormone does not appear to cause harm and might be effective; however, there are inconsistent data with success rates of between 9 and 62 percent with no single agent standing out. Therefore, this group recommends that hormone therapy have a limited role in the management of cryptorchidism and should not be recommended as first-line therapy (Level 2 evidence, Grade B recommendation). (Braga, 2016)

**The European Association of Urology (EAU)**

The European Association of Urology (EAU) 2018 guidelines note that the treatment of choice is surgical replacement in the scrotum (orchidopexy). There is no consensus on the use of hormonal treatment (hCG or gonadotropin-releasing hormone [GnRH]) for cryptorchidism. Hormonal therapy has a limited success rate of 20%, while surgery for palpable testis can be up to 92%. There are no long-term follow-up data available on the use of hormonal therapy for cryptorchidism. (Radmayr, 2018)

**American Association of Clinical Endocrinologists (AACE) Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 Update**

Although the AACE guidelines state that cryptorchidism is beyond the scope of these adult guidelines and recommend specialty consultation, the guidelines do state there are problems associated with both the management of cryptorchidism and medical treatment recommendations with using hCG versus surgical therapy. The general objective is to improve fertility potential by bringing the undescended testicle into the scrotum before 1 to 2 years of age. Surgical placement into the scrotum offers the chance for thorough examination which is useful because there is a small risk of a malignant lesion that is associated with undescended testicles. Treatment with hCG in prepubertal boys may be used for 4 weeks to determine whether testicular descent occurs before a surgery option is considered.

Clinical practice guidelines do not advocate the use of one product over another.

**The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative**
No recommendations are available for human chorionic gonadotropin (hCG).

**Centers for Medicare & Medicaid Services - National Coverage Determinations (NCDs)**

There are no CMS National Coverage Determinations for human chorionic gonadotropin (hCG).

**Clinical Efficacy**

**Prepubertal cryptorchidism**

A 2012 systematic review by Penson et al evaluated seven studies that evaluated hormonal treatment of cryptorchidism (995 boys, 1215 testes). The systematic review found that hormonal treatment was associated with slightly higher rates of testicular descent when compared to placebo (approximately 10%). However, testicular descent reported rates in individual studies varied widely with ranges from 9% to 62%. The initial location of the testis may influence the likelihood of success and greater rates of descent are usually achieved with more distally located testes. Insufficient evidence exists to suggest that a particular agent is superior. GnRH analogs and urine-derived hCG appeared to be similarly effective in achieving testicular descent (6% to 35% range). (Penson 2013, Forest 1998)

Wei et al conducted a meta-analysis of randomized controlled trials to evaluate the efficacy and safety of human chorionic gonadotropin for treatment of cryptorchidism. The researchers stated that the overall quality of the studies was low. The analysis pulled data from seven studies. The results were then separated into three subgroups: two studies compared hCG with a placebo, and three studies compared hCG with gonadotropin-releasing hormone (GnRH) in unilateral cryptorchidism, with two other studies compared hCG with GnRH in bilateral cryptorchidism. The identified trials revealed no significant differences between the effectiveness of hCG treatment and GnRH treatment in bilateral as well as unilateral cryptorchidism. In addition, these identified studies showed that hCG treatment is not superior to treatment with placebo. (Wei, 2018)

**Off Label Uses**

AHFS Drug Information 2019 Edition does not support any off-label uses of human chorionic gonadotropin (hCG) and recommends against the off-label use of hCG for the treatment of obesity.

**Experimental, Investigational, Unproven Uses**

FDA states that human chorionic gonadotropin has not been demonstrated to be effective adjunctive therapy in the treatment of obesity. There is no substantial evidence that it increases weight loss beyond that resulting from caloric restriction, that it causes a more attractive or normal distribution of fat, or that it decreases the hunger and discomfort associated with calorie restricted diets (Pregnyl Package Insert, 2015).

A randomized controlled trial has investigated human chorionic gonadotropin for erectile dysfunction but the study was limited by a small patient population. (Buvat, 1987)

There is insufficient evidence in the peer-reviewed published scientific literature to support safety and efficacy of human chorionic gonadotropin in the treatment of low testosterone in the absence of hypogonadotropic hypogonadism, in combination with testosterone therapy, or for erectile dysfunction.

**Coding/ Billing Information**

**Note:** 1. This list of codes may not be all-inclusive. 2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**If benefit coverage is available for injectable fertility medications, the following may be considered for coverage:**

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J0725</td>
<td>Injection, chorionic gonadotropin, per 1,000 USP units</td>
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References


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