Chorionic Gonadotropin for Injection, USP is a water-soluble polypeptide hormone produced by the human placenta composed of an alpha and a beta sub-unit. The alpha sub-unit is essentially identical to the alpha-subunits 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.

**INDICATIONS AND CLINICAL USE**

Chorionic Gonadotropin for Injection (hCG) is biologically standardized and the potency is declared in terms of the USP Reference Standard.

**DESCRIPTION**

Chorionic Gonadotropin for Injection, USP (hCG) is a water-soluble polypeptide hormone derived from the urine of pregnant women. It is a hyaluronic acid-like substance that is produced by the fetal placenta and is not detectable in the urine of non-pregnant women. The hormone is composed of an alpha subunit (hCGα) and a beta subunit (hCGβ), which are structurally similar to the corresponding subunits of human chorionic gonadotropin (hCG). The hCGα subunit is comprised of 97 amino acids, while the hCGβ subunit is composed of 111 amino acids. The hormone is produced in the placenta during pregnancy and is released into the circulation through the maternal circulation.

**CONTRAINDICATIONS**

Chorionic Gonadotropin for Injection, USP is contra-indicated in the treatment of:

- pituitary tumour, ovarian tumour, prostatic carcinoma and androgen-dependent neoplasms, uncontrolled endocrine disorders (e.g. hyperprolactinaemia, thyroid and adrenal dysfunction);
- in female, primary ovarian failure (ovarian dysgenesis and premature menopause), tubal occlusion unless the patient is undergoing superovulation for in vitro fertilization;
- urinary-hCG (u-hCG) will not be effective in men, in cases where the FSH level is raised as this is indicative of primary testicular failure;
- u-hCG is not effective and is not indicated for weight reduction;
- precocious puberty;
- active thrombophlebitis or thromboembolic event;
- allergy to u-hCG.

**WARNINGS**

**Female:**

- **Overhyperstimulation syndrome (OHSS)**
  An excessive ovarian response to follicular stimulating agents, in women undergoing ovulation induction, may lead to the development of ovarian hyper-stimulation syndrome if u-hCG is given to induce ovulation or to support the corpus luteum. It is of utmost importance that u-hCG be withheld in such cases.
  OHSS is generally categorized as mild, moderate or severe.
  - **Mild OHSS symptoms:** some abdominal distension; nausea; vomiting; occasional diarrhea; ovaries enlarged to about 5 cm diameter appear 3 - 6 days after u-hCG administration.
  - **Moderate OHSS symptoms:** oedema; diarrhoea; ovaries enlarged to about 10 cm. Therapy: bed rest; close observation in the case of conception occurring to detect any progression to severe hyper-stimulation. In order to avoid rupture of ovarian cysts, pelvic examination of enlarged ovaries should be gentle. Symptoms subside spontaneously over 2 - 3 weeks.
  - **Severe OHSS:** a rare (less than 2% of cases when patients are normally monitored) but serious complication. Symptoms: ovaries enlarge to in excess of 12 cm diameter; pronounced abdominal distension; ascites; pleural effusion; decreased blood volume; reduced urine output; electrolyte imbalance and sometimes shock. Diuretics should not be used in the primary phase of the syndrome, since they may precipitate cardiovascular shock in a patient who already has plasma hypovolemia. However, diuretics may be used during the resolution phase of OHSS to help mobilize and eliminate fluid sequestered during the first phase. Therapy: hospitalization, treatment should be conservative and concentrate on restoring fluid depletion and preventing shock. Acute symptoms subside over several days if conception has not occurred. Symptoms may persist longer if conception has occurred.
  - **Rupture of ovarian cysts with resultant haemoperitoneum.**
  - **Thromboembolic complications:** Thromboembolic events have been reported after gonadotropin/u-hCG therapy both in association with and separated from OHSS. These included thrombophlebitis, pulmonary embolism, stroke, and arterial occlusion resulting in loss of a limb. In rare instances, thromboembolic events have resulted in death.
  - **Multiple pregnancy:** The incidence of multiple pregnancies and births increases after gonadotropin/u-hCG therapy stimulation and ovulation induction in patients attempting in vivo conception. The risk of multiple pregnancy following
ART is related to the number of oocytes/embryos replaced. However, the majority of multiple pregnancies are twins. Multiple pregnancies might result in premature deliveries.

- Pregnancy testing: A false positive test result may be obtained if the patient has recently undergone (over the last 7 days) u-hCG administration or is still receiving the drug.

Male:
- Fluid retention: If high doses of u-hCG are administered in males, the androgens may cause fluid retention. In such instances, the dose should be reduced considerably, particularly in patients with cardiac or renal disease, epilepsy, migraine or asthma.
- Sexual precocity: u-hCG may cause sexual precocity when given to young patients for cryptorchidism. If signs are observed, cease treatment. If continued therapy is considered necessary, a reduced dosage regimen should be used.
- Gynecomastia: Gynecomastia may be induced by u-hCG.

PRECAUTIONS
The drug substance of this drug product is manufactured from human urine. Although the risk is theoretical, and no case of transmission of an infectious agent linked to the use of urine-derived gonadotropins has ever been identified, the risk of transmitting infectious agents cannot be completely excluded. Drug Interaction: No clinically significant drug interactions have been reported during u-hCG therapy.

ADVERSE REACTIONS
The following adverse reactions have been associated with the administration of Chorionic Gonadotropin for Injection, USP: headache, irritability, restlessness, depression, fatigue, edema, precocious puberty, gynecomastia, pain at the site of injection.

Ovarian cancer has been reported in a very small number of infertile women who have been treated with fertility drugs. A causal relationship has not been established between treatment with fertility drugs and ovarian cancer.

DOSAGE AND ADMINISTRATION
Dose
The dosage regimen used in any particular case depends upon the indication for use, the age and weight of the patient, and the physician’s preference.

Male:
1. Prepubertal Cryptorchidism (not due to anatomical obstruction)
   a) 4,000 USP units, three times weekly, for two to three weeks; or
   b) 1,000 USP units, three times weekly, for six to eight weeks.
   The dosage schedule may vary to some extent depending upon the age when treatment is given. If the dose is adequate, there will usually be some indication, following one such course of therapy, whether descent will occur or surgery be required.
   A therapeutic trial with Chorionic Gonadotropin for Injection, USP may constitute a valuable diagnostic aid to determine the need for surgery. Lack of response is usually an indication of anatomic obstruction. Furthermore, when surgery is required, this preliminary treatment may facilitate the procedure by increasing the size of the testes and the length of the cords. Postoperative gonadotropic therapy has also been suggested to prevent retraction of the testes.

2. Delayed Adolescence
   4,000 to 5,000 USP units three times weekly for six to eight weeks with a rest period of two to three weeks between courses of therapy.

3. Dwarfism (pituylary)
   1,000 to 5,000 USP units three times weekly.

4. Hypogonadotropic Eunuchoidism
   4,000 to 5,000 USP units three times weekly for six to eight weeks with a rest period of two to three weeks between courses of therapy.

5. Hypogonadism (after sexual maturity)
   4,000 to 5,000 USP units three times weekly for six to eight weeks with a rest period of two to three weeks between courses of therapy.

Female:
1. Ovulation Induction
   (For the gonadotropins dosage, see the prescribing information for that drug product.)
   5,000 to 10,000 USP units one day following the last dose of gonadotropins.

2. Abortion (habitual)
   1,000 to 2,000 USP units, or more, one or more times daily combined with other recognized therapeutic measures until the danger of abortion has passed.

3. Infrequent Scanty Bleeding (functional)
   Oligomenorrhea, amenorrhea (primary and secondary), and Frohlich’s Syndrome: see dosage for Functional Sterility.

4. Functional Sterility
   500 to 1,000 USP units Chorionic Gonadotropin for Injection may be given daily from the 15th to the 24th day. An alternative schedule is 1,500 USP units every other day, three times in all, on the 16th, 18th, and 20th day of the cycle.

Administration
Chorionic Gonadotropin for Injection is for subcutaneous or intramuscular use only.

Preparation of Solution: Using a syringe, withdraw the sterile air from the vial containing the lyophilized Chorionic Gonadotropin for Injection and inject it into the diluent vial. Remove up to 10 mL from the diluent vial (see table below) and add to the Chorionic Gonadotropin for Injection vial; mix gently until reconstitution is complete. Parenteral drug products should be inspected visually prior to administration. Do not inject if the reconstituted product contains particulate matter or is discoloured. Chorionic Gonadotropin for Injection may be reconstituted by adding the required amount of diluent to obtain the desired dosage.

Table of Reconstitution and Administration Volumes

<table>
<thead>
<tr>
<th>Desired Dosage (units)</th>
<th>Diluent Volume Options (mL)</th>
<th>Injection Volume (mL)</th>
</tr>
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<tbody>
<tr>
<td>10,000</td>
<td>10 5 2.5 1.0</td>
<td>10 5 2.5 1.0</td>
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<tr>
<td>5,000</td>
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<td>4,000</td>
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<td>1,000</td>
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STORAGE
Chorionic Gonadotropin for Injection, USP sterile lyophilized powder should be stored at controlled room temperature (less than 25°C) until the expiry date indicated on the label. When reconstituted, the solution should be kept refrigerated (2 - 8°C) and should be used within 30 days.

Each vial of Chorionic Gonadotropin for Injection, USP contains:
Chorionic gonadotropin 10,000 USP units; mannitol 100 mg; sodium phosphate monobasic and sodium phosphate dibasic for adjustment of pH. In addition, when reconstituted with the diluent provided (Bacteriostatic Water for Injection, USP containing 0.9% benzyl alcohol), each vial contains benzyl alcohol 0.9%.

AVAILABILITY OF DOSAGE FORMS
C25021 Each package contains one vial of Chorionic Gonadotropin for Injection, USP (10,000 USP units) and one 10 mL multiple-dose vial of Sterile Diluent (Bacteriostatic Water for Injection, USP containing 0.9% benzyl alcohol).