SUMMARY OF PRODUCT CHARACTERIZATION

(Chorionic Gonadotropin for Injection USP, 5000 IU/Vial)

1. NAME OF THE MEDICINAL PRODUCT

Chorionic Gonadotropin for Injection USP 5000 IU/Vial & Subcutaneous (S.C.) and intramuscular (I.M.)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient

Each vial of sterile freeze-dried product contains: Chorionic Gonadotropin 5000 IU.

For a full list of excipients, see section 6.1.

Product Description

A white or practically white freeze-dried product sealed in a 2 mL USP Type-I clear glass vial.

Reconstitution Solution:

A clear, colourless solution is filled and duly sealed in a 2 mL USP Type-I clear glass ampoule.

After Reconstitution: Clear colourless solution.

3. PHARMACEUTICAL FORM

Freeze-dried product for Injection and Sodium Chloride Injection for reconstitution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

In the female

Sterility due to the absence of follicle-ripening or ovulation.

In combination with FSH or HMG, promotion of controlled superovulation in medically assisted reproduction programmes.

In the male

Hypogonadotrophic hypogonadism.

Delayed puberty associated with insufficient gonadotrophic pituitary function.

Sterility in selected cases of deficient spermatogenesis.

4.2 Posology and method of administration

Dosage

In the female

Sterility due to the absence of follicle-ripening or ovulation.

5,000–10,000 IU hCG to induce ovulation, following treatment with an FSH (Follicle Stimulating Hormone) or HMG (Human Menopausal Gonadotrophins) preparation.

In combination with FSH or HMG, promotion of controlled superovulation in medically assisted reproduction programmes.

5,000–10,000 IU hCG 30 - 40 hours after the last FSH or HMG injection. Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial should not be administered if the following criteria have not been met: at least 3 follicles greater than 17mm in diameter are present with 17ß estradiol levels of at least 3500 pmol/L (920 picogram/ml). Oocyte collection is carried out 32 - 36 hours after the hCG injection.

As luteal phase support, two to three injections of 1,000 to 3,000 IU hCG each may be given within nine days of ovulation or embryo transfer, for example on day 3, 6 and 9 after ovulation induction or embryo transfer.

In the male

Hypogonadotrophic hypogonadism.

500–1,000 IU hCG 2-3 times weekly.

Delayed puberty associated with insufficient gonadotrophic pituitary function.

1,500 IU hCG twice weekly for at least 6 months.

Sterility in selected cases of deficient spermatogenesis.

Usually, 3,000 IU hCG per week in combination with an FSH or HMG preparation.

This treatment should be continued for at least three months before any improvement in spermatogenesis can be expected. During this treatment testosterone replacement therapy should be suspended. Once achieved, the improvement may sometimes be maintained by hCG alone.

Method of Administration

After addition of the solvent to the freeze-dried substance, the solution should be given immediately by intramuscular or subcutaneous injection. Any unused solution should be discarded. Subcutaneous injection may be carried out by patient or partner, provided that proper instruction is given by the physician. Self-administration of Chorionic Gonadotropin

for Injection USP, 5000 IU/ Vial should only be performed by patients who are well-motivated, adequately trained and with access to expert advice.

4.3 Contraindications

- Hypersensitivity to human gonadotrophins or any of the excipients of Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial.
- Presence of uncontrolled non-gonadal endocrinopathies (e.g. thyroid, adrenal or pituitary disorders).
- Breast, uterine, ovarian tumours.
- Vaginal bleeding of unknown cause.
- Known or suspected androgen-dependent tumours such as testicular tumours, carcinoma of the prostate or mammary carcinoma in males.
- Malformations of the sexual organs incompatible with pregnancy.
- Fibroid tumours of the uterus incompatible with pregnancy.

4.4 Special warnings and precautions for use

In males and females:

Hypersensitivity reactions:

- Hypersensitivity reactions, both generalised and local; anaphylaxis; and angioedema have been reported. If a hypersensitivity reaction is suspected, discontinue Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial and assess for other potential causes for the event (see section 4.3).

General:

- Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial should not be used for body weight reduction. HCG has no effect on fat metabolism, fat distribution or appetite.

Additionally in females:

Ectopic pregnancy:

- Infertile women undergoing Assisted Reproductive Technologies (ART) have an increased incidence of ectopic pregnancy. Early ultrasound confirmation that a pregnancy is intrauterine is therefore important.
- Prior to treating patients for inadequate endogenous stimulation of the gonads, an examination should be performed to exclude anatomical abnormalities of the genital organs or nongonadal endocrinopathies (e.g. thyroid or adrenal disorders, diabetes). Primary ovarian failure should be excluded by the determination of gonadotrophin

levels.

Multi-fetal gestation and birth:

- In the pregnancies occurring after induction of ovulation with gonadotrophic preparations, there is an increased risk of abortion and multiplets. Multiple pregnancy, especially high order, carries an increased risk in adverse maternal and perinatal outcomes. The parents should be advised of the potential risks of multiple pregnancies before starting treatment.

Congenital Malformations:

- The incidence of congenital malformations after Assisted Reproductive Technologies (ART) may be higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics (e.g. maternal age, sperm characteristics) and an increased incidence of multiple gestations.

Vascular Complications:

- Thromboembolic events, both in association with and separate from OHSS, have been reported following treatment with gonadotropins, including Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial. Intravascular thrombosis, which may originate in venous or arterial vessels, can result in reduced blood flow to vital organs or the extremities. Women with generally recognised risk factors for thrombosis, such as a personal or family history, severe obesity or thrombophilia, may have an increased risk of venous or arterial thromboembolic events, during or following treatment with gonadotrophins. In these women the benefits of IVF treatment need to be weighed against the risks. It should be noted, however, that pregnancy itself also carries an increased risk of thrombosis.
- There have been reports of ovarian and other reproductive system neoplasms, both benign and malignant, in women who have undergone multiple drug regimens for infertility treatment. It is not yet established whether or not treatment with gonadotrophins increases the baseline risk of these tumours in infertile women.

Medical examinations:

- For up to ten days after administration of Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial, a pregnancy test may give a false-positive result.

Ovarian Hyperstimulation Syndrome (OHSS):

OHSS is a medical event distinct from uncomplicated ovarian enlargement. Clinical signs and

symptoms of mild and moderate OHSS are abdominal pain, nausea, diarrhea, mild to moderate enlargement of ovaries and ovarian cysts. Severe OHSS may be life-threatening. Clinical signs and symptoms of severe OHSS are large ovarian cysts, acute abdominal pain, ascites, pleural effusion, hydrothorax, dyspnea, oliguria, hematological abnormalities and weight gain. In rare instances, venous or arterial thromboembolism may occur in association with OHSS. Transient liver function test abnormalities suggestive of hepatic dysfunction with or without morphologic changes on liver biopsy have also been reported in association with OHSS.

OHSS may be caused by administration of human Chorionic Gonadotropin (hCG) and by pregnancy (endogenous hCG). Early OHSS usually occurs within 10 days after hCG administration and may be associated with an excessive ovarian response to gonadotropin stimulation. Late OHSS occurs more than 10 days after hCG administration, as a consequence of the hormonal changes with pregnancy. Because of the risk of developing OHSS, patients should be monitored for at least two weeks after hCG administration.

Women with known risk factors for a high ovarian response may be especially prone to the development of OHSS during or following treatment with Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial. For women having their first cycle of ovarian stimulation, for whom risk factors are only partially known, close observation for early signs and symptoms of OHSS is recommended.

To reduce the risk of OHSS, ultrasonographic assessments of follicular development should be performed prior to treatment and at regular intervals during treatment. The concurrent determination of serum estradiol levels may also be useful. In ART, there is an increased risk of OHSS with 18 or more follicles of 11 mm or more in diameter. When there are 30 or more follicles in total, it is advised to withhold hCG administration.

Depending on the ovarian response, the following measures can be considered to reduce the risk of OHSS:

- withhold further stimulation with a gonadotropin for a maximum of 3 days (coasting);
- withhold hCG and cancel the treatment cycle;
- administer a dose lower than 10,000 IU of urinary hCG for triggering final oocyte

maturation, e.g. 5,000 IU urinary hCG or 250 micrograms rec-hCG (which is equivalent to approximately 6,500 IU of urinary hCG);

- cancel the fresh embryo transfer and cryopreserve embryos;
- avoid administration of hCG for luteal phase support.

Adherence to the recommended Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial dose and treatment regimen and careful monitoring of ovarian response is important to reduce the risk of OHSS. If OHSS develops, standard and appropriate management of OHSS should be implemented and followed.

Ovarian torsion:

- Ovarian torsion has been reported after treatment with gonadotropins, including Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial. Ovarian torsion may be related to other conditions, such as OHSS, pregnancy, previous abdominal surgery, past history of ovarian torsion, and previous or current ovarian cysts. Damage to the ovary due to reduced blood supply can be limited by early diagnosis and immediate detorsion.

***Additionally in males*:**

Antibody formation:

- Administration of hCG can provoke the formation of antibodies against hCG. In rare cases, this may result in an ineffective treatment. Treatment with hCG leads to increased androgen production. Therefore:
- Patients with latent or overt cardiac failure, renal dysfunction, hypertension, epilepsy or migraine (or a history of these conditions) should be kept under close medical supervision, since aggravation or recurrence may occasionally be induced as a result of increased androgen production.

***Male paediatric patient*:**

- HCG should be used cautiously in prepubertal boys to avoid premature epiphyseal closure or precocious sexual development. Skeletal maturation should be monitored regularly.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed; interactions with commonly used medicinal products can therefore not be excluded.

Following administration, Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial may

interfere for up to ten days with the immunological determination of serum/urinary hCG, leading to a false positive pregnancy test.

4.6 Pregnancy and lactation

Not applicable.

4.7 Effects on ability to drive and use machines

As far as known Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Frequency is unknown for all undesirable effects described below (cannot be determined with available data).

Immune system disorders

In rare cases generalized rash or fever may occur.

General disorders and administrative site conditions

Local site reactions such as bruising, pain, redness, swelling and itching. Oedema. Occasionally allergic reactions have been reported, mostly manifesting as pain and/or rash at the injection site. Tiredness.

Nervous system disorders

Headache.

Psychiatric disorders

Mood changes.

In the female

Reproductive system and breast disorders

Unwanted ovarian hyperstimulation, mild or severe ovarian hyperstimulation syndrome (OHSS, see section 4.4):

Mild OHSS: Painful breasts
Mild to moderate enlargement of ovaries Ovarian cysts
Abdominal pain
Abdominal discomfort
Gastrointestinal symptoms such as nausea, diarrhoea and bloating
Severe Large ovarian cysts (prone to rupture)

OHSS: Acute abdominal pain Ascites

Weight gain

Hydrothorax

In rare instances, thromboembolism has been associated with FSH/hCG therapy

Not all symptoms described are always associated to OHSS.

In the male

Metabolism and nutrition disorders

Water and sodium retention is occasionally seen after administration of high dosages; this is regarded as a result of excessive androgen production.

Reproduction system and breast disorders

HCG treatment may sporadically cause gynaecomastia.

Skin and subcutaneous tissue disorders

Acne may occur occasionally during hCG therapy.

4.9 Overdose

The toxicity of human chorionic gonadotrophic hormone is very low. However, too high a dose may lead to hyperstimulation of the ovaries.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: gonadotrophins: ATC code G03G A01

Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial is a preparation of human chorionic gonadotrophin obtained from the urine of pregnant women. It stimulates the steroidogenesis in the gonads by virtue of a biological effect similar to that of LH (Luteinizing hormone, which is the same as interstitial cell stimulating hormone). In the male it promotes the production of testosterone and in the female the production of estrogens and particularly of progesterone after ovulation. In certain cases, this preparation is used in combination with human menopausal gonadotrophin (HMG).

Because HCG is of human origin, no antibody formation is to be expected.

5.2 Pharmacokinetic properties

In healthy male subjects, maximal hCG plasma levels were reached after a single IM or SC injection of hCG at approximately six and sixteen hours respectively; in addition, maximum concentrations and areas under the concentration curves were higher after the IM than after the SC injection. However, these differences did not translate into significant differences in terms of testicular steroidogenic response.

In female subjects under oral contraceptives, IM and SC administration of hCG were found to be bioequivalent regarding the extent of absorption and the apparent elimination half-lives of approximately 33 hours; maximal hCG plasma levels were reached after approximately 20 hours regardless of the route of administration. Although high intersubject variability was observed, the difference related to gender after IM injection may be caused by gluteal fat thickness in women which exceeds that in men. In another study performed in female patients in the early follicular phase of their menstrual cycle, the bioavailability of a single dose of hCG was higher with the IM route than with the SC route and lower in obese women than in non-obese women.

HCG is approximately 80 percent metabolized, predominantly in the kidneys.

On basis of the recommended dose regimens and elimination half-life, accumulation is not expected to occur.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Freeze-dried product: mannitol, potassium di-hydrogen phosphate and di-potassium hydrogen phosphate.

Sodium Chloride Injection: Isotonic sodium chloride solution (0.9% w/w), dilute hydrochloric acid for pH-adjustment and water for Injection.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Shelf-Life of Chorionic Gonadotropin for Injection is 3 years when stored at a temperature between 2°C - 8°C

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C).

6.5 Nature and contents of container

Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial5000 IU is available in the following containers and pack sizes:

Product:

Chorionic Gonadotropin for Injection USP, 5000 IU/ Vial is filled in the 2 mL USP Type I clear glass vial and stoppered with 13mm bromobutyl rubber stopper and then sealed with 13mm aluminium flip-off seals.

Reconstitution Solution:

0.9% w/v Sodium Chloride Injection USP is filled in 2 mL USP Type I clear glass yellow dot ampoule.

6.6 Special precautions for disposal and other handling

The Powder should only be reconstituted with the solvent provided in the package .

Attach a reconstitution needle to the syringe. Withdraw the entire content from the ampoule with solvent and inject the total contents into the vial containing the powder. The powder should dissolve quickly to a clear solution. Shaking should be avoided and administer immediately.

The reconstituted solution should not be administered if it contain particles or is not clear.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT / HOLDER OF CERTIFICATE F PRODUCT REGISTRATION

IGINITE Pharma Nigeria

30, Ajegunle village

Magboro, Ogun state. Nigeria

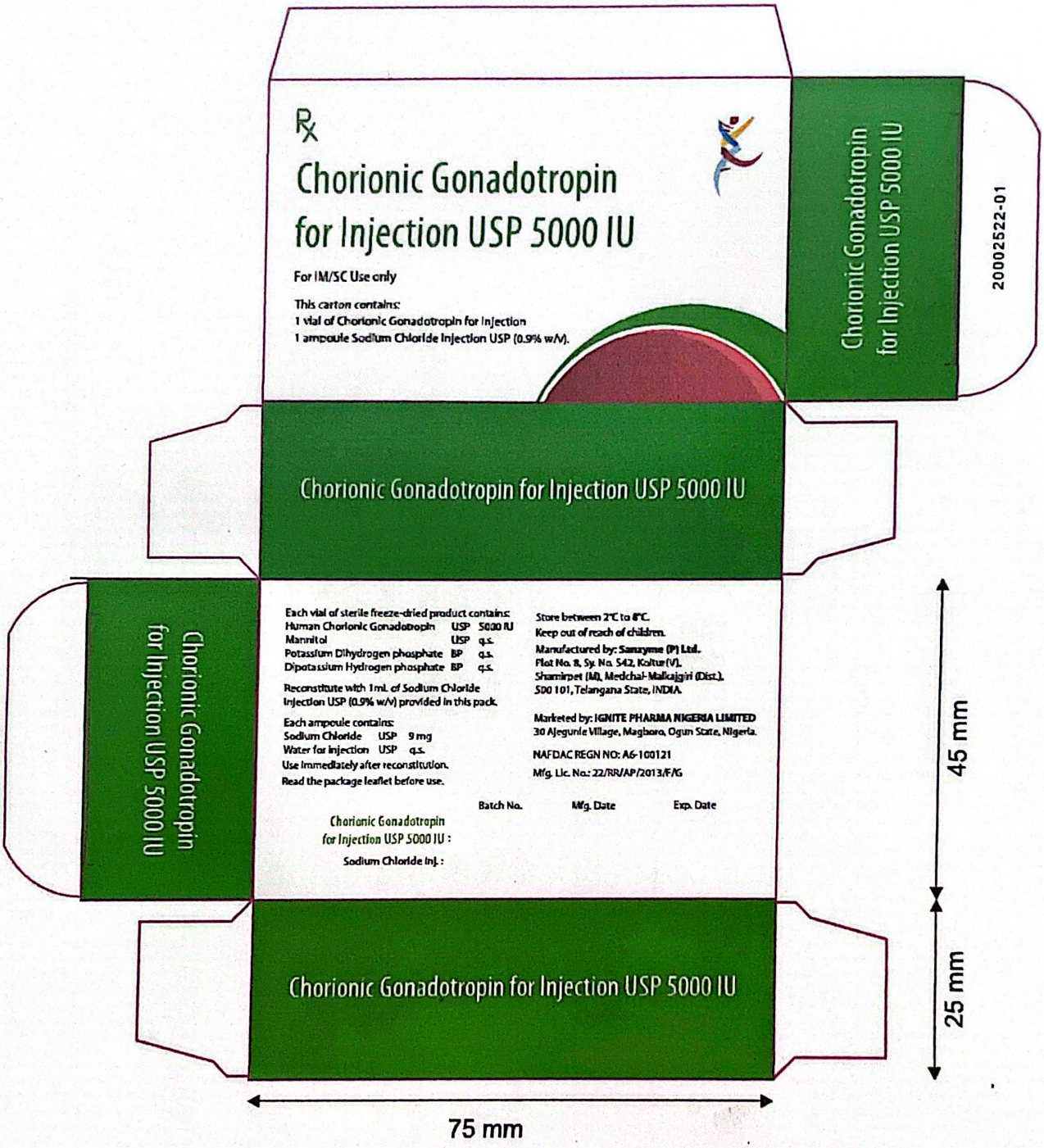
8. DRUG PRODUCT MANUFACTURER

Sanzyme (P) Ltd.

Plot No. 8, Sy. No. 542, Koltur Village,
Shamirpet Mandal,Medchal-Malkajgiri
District – 500101, Telangana State, India

9. NAFDAC REGISTRATION NUMBER(S)

A6-100121



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Date

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Chorionic Gonadotropin for Injection USP 5000 IU

For IM/SC Use only

Each vial of sterile freeze-dried product contains:

Human Chorionic Gonadotropin	USP	5000 IU
Mannitol	USP	q.s.
Potassium Dihydrogen phosphate	BP	q.s.
Dipotassium Hydrogen phosphate	BP	q.s.

Reconstitute with 1mL of Sodium Chloride Injection USP (0.9%w/v) provided in this pack.

Use immediately after reconstitution.
Read the package leaflet before use.
Store between 2°C to 8°C.
Keep out of reach of children.

Manufactured by: **Sanzyme (P) Ltd.**
Plot No. 8, Sy. No. 542, Koltur(V),
Shamirpet (M), Medchal-Malkajgiri (Dist.),
500 101, Telangana State, INDIA.

Marketed by: **IGNITE PHARMA NIGERIA LIMITED**
30 Ajegunle Village, Magboro,
Ogun State, Nigeria.

20002521-01

NAFDAC REGN NO: A6-100121
Mfg. Lic. No.: 22/RR/AP/2013/F/G
Batch No. :
Mfg. Date :
Exp. Date :

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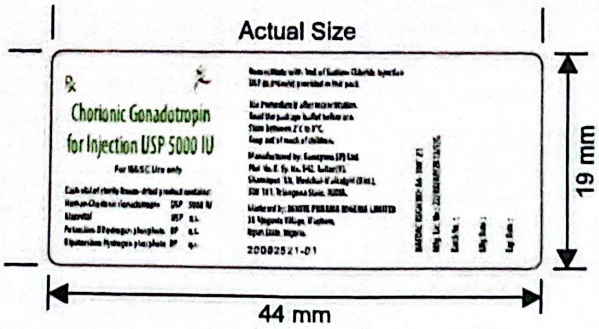
44 mm

Actual Size



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Chorionic Gonadotrophin for Injection USP 5000 IU/Vial

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