

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

PREGNYL® 1500 IU powder for injection

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2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PREGNYL consists of a freeze-dried powder for injection and a solvent for reconstitution. The active ingredient [human chorionic gonadotrophin (hCG)] which is obtained from the urine of pregnant women, has luteinizing hormone (LH) activity.

An ampoule or vial contains 1500 or 5000 IU hCG.

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection. The powder is a white, dry powder or cake. The solvent is a clear and colourless aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

In the female

- Ovulation induction in subfertility due to anovulation or impaired follicle-ripening.
- Preparation of follicles for puncture in controlled ovarian hyperstimulation programmes (for medically assisted reproductive techniques).
- Luteal phase support.

In the male

- Hypogonadotropic hypogonadism (also cases of idiopathic dysspermias have shown a positive response to gonadotrophins).
- Delayed puberty associated with insufficient gonadotrophic pituitary function.
- Cryptorchidism, not due to anatomical obstruction.

4.2 Dose and method of administration

Dosage in the female

Ovulation induction in subfertility due to anovulation or impaired follicle-ripening

Usually, one injection of 5,000-10,000 IU PREGNYL to complete treatment with an FSH-containing preparation.

Preparation of follicles for puncture in controlled ovarian hyperstimulation programs

Usually, one injection of 5,000-10,000 IU PREGNYL to complete treatment with an FSH-containing preparation.

Luteal phase support

Two to three repeat injections of 1,000 to 3,000 IU each may be given within nine days following ovulation or embryo transfer (for example, on day 3, 6 and 9 after ovulation induction).

Dosage in the male

Hypogonadotropic hypogonadism

1,000-2,000 IU PREGNYL, two to three times per week. If the main complaint is subfertility, PREGNYL may be given with an additional follitropin (FSH)-containing preparation two to three times per week. 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.

Delayed puberty associated with insufficient gonadotrophic pituitary function

1,500 IU two to three times a week for at least six months.

Cryptorchidism not due to anatomical destruction

Under 2 years of age: 250 IU twice weekly for six weeks.

Under 6 years of age: 500-1,000 IU twice weekly for six weeks.

Over 6 years of age: 1,500 IU twice weekly for six weeks.

If necessary, this treatment can be repeated.

Method of Administration

After addition of the solvent to the freeze-dried substance, the reconstituted PREGNYL solution should be slowly administered intramuscularly or subcutaneously

4.3 Contraindications

- Hypersensitivity to human gonadotrophins or any of the excipients (see section 4.4 Special warnings and precautions for use).
- Known or suspected sex hormone-dependent tumours, such as ovary, breast and uterine carcinoma in female and prostatic or breast carcinoma in the male.
- Malformations of the reproductive organs incompatible with pregnancy.
- Fibroid tumours of the uterus incompatible with pregnancy.
- Abnormal (not menstrual) vaginal bleeding without a known/diagnosed cause.

4.4 Special warnings and precautions for use

The active ingredient in this preparation is extracted of human urine. Therefore the risk of a transmission of a pathogen (known or unknown) cannot be completely excluded.

For males and females:

Hypersensitivity reactions:

- Hypersensitivity reactions, both generalised and local; anaphylaxis; and angioedema have been reported. If a hypersensitivity reaction is suspected, discontinue PREGNYL and assess for other potential causes for the event. (See section 4.3 Contraindications).

General

- Patients should be evaluated for uncontrolled non-gonadal endocrinopathies (e.g. thyroid, adrenal or pituitary disorders) and appropriate specific treatment given.
- PREGNYL should not be used for body weight reduction. HCG has no effect on fat metabolism, fat distribution or appetite.

In the female:

Multi-foetal gestation and birth:

- In pregnancies occurring after induction of ovulation with gonadotrophic preparations, there is an increased risk of multiple pregnancies.

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.

Pregnancy loss:

- Rates of pregnancy loss in women undergoing ART are higher than in the normal population.

Congenital Malformations:

- The incidence of congenital malformations after Assisted Reproductive Technologies (ART) may be slightly higher than after spontaneous conceptions. This slightly higher incidence is thought to be related to differences in parenteral characteristics (e.g. maternal age, sperm characteristics) and to the higher incidence of multiple gestations after ART. There are no

indications that the use of gonadotrophins during ART is associated with an increased risk of congenital malformations.

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, diarrhoea, 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, dyspnoea, oliguria, haematological 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.

Adherence to the recommended Pregnyl dose and treatment regimen is advised. Care should be taken with the administration of Pregnyl because OHSS may be triggered by administration of human Chorionic Gonadotrophin (hCG). OHSS may also be triggered by pregnancy (endogenous hCG). Early OHSS usually occurs within 10 days after hCG administration and may be associated with an excessive ovarian response to gonadotrophin 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 PREGNYL. 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.

Follow current clinical practice for reducing the risk of OHSS during Assisted Reproductive Technology (ART). Careful monitoring of ovarian response is important to reduce the risk of OHSS. To monitor 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. For patients at increased risk of OHSS or if OHSS develops, standard and appropriate management of OHSS should be implemented and followed.

Ovarian torsion:

- Ovarian torsion has been reported after treatment with gonadotrophins, including PREGNYL. 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.

Vascular complications:

Thromboembolic events, both in association with and separate from OHSS, have been reported following treatment with gonadotrophins including PREGNYL. 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 recognized 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.

In the male:

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.
- 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 medicines and other forms of interaction

Interactions of PREGNYL with other medicines have not been investigated; interactions with commonly used medicinal products can therefore not be excluded.

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

4.6 Fertility, pregnancy and lactation

PREGNYL may be used for luteal phase support, but should not be used later on in pregnancy. It must not be used during lactation.

4.7 Effects on ability to drive and use machines

As far as known this medicine has no influence on alertness and concentration

4.8 Undesirable effects

Immune system disorders

In rare cases generalized rash or fever may occur.

General disorders and administrative site conditions

PREGNYL may cause reactions at the site of injection, such as bruising, pain, redness, swelling and itching, have been reported with the use of urinary gonadotrophin preparations. Occasionally allergic reactions have been reported, mostly manifesting as pain and/or rash at the injection site.

In the female

Vascular disorders

In rare instances, thromboembolism has been associated with FSH/hCG therapy, usually associated with severe OHSS (see section 4.4 Special warnings and precautions for use).

Respiratory, thoracic and mediastinal disorders

Hydrothorax, as a complication of severe OHSS.

Gastrointestinal disorders

Abdominal pain and gastrointestinal symptoms such as nausea and diarrhoea, related to mild OHSS. Ascites, as a complication of severe OHSS.

Reproductive system and breast disorders

Unwanted ovarian hyperstimulation, mild or severe ovarian hyperstimulation syndrome (OHSS, see section 4.4 Special warnings and precautions for use).

Painful breasts, mild to moderate enlargement of ovaries and ovarian cysts related to mild OHSS. Large ovarian cysts (prone to rupture), usually associated with severe OHSS.

Investigation

Weight gain as a characteristic of severe 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.

Reproductive system and breast disorders

hCG treatment may sporadically cause gynaecomastia.

4.9 Overdose

The acute toxicity of urinary gonadotrophin preparations has been shown to be very low. Nevertheless, there is a possibility that too high a dosage of hCG may lead to ovarian hyperstimulation syndrome (OHSS; see section 4.4 Special warnings and precautions for use).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

PREGNYL contains hCG which has LH activity. LH is indispensable in normal female and male gamete growth and maturation, and gonadal steroid production.

In the female

PREGNYL is given as a substitute for the endogenous mid-cycle LH surge to induce the final phase of follicular maturation, leading to ovulation. PREGNYL is also given as a substitute for endogenous LH during the luteal phase.

In the male

PREGNYL is given to stimulate Leydig cells to promote the production of testosterone.

5.2 Pharmacokinetic properties

Maximal hCG plasma levels will be reached in males approximately six and sixteen hours after a single IM or SC injection of hCG respectively, and in females after approximately 20 hours. 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. HCG is approximately 80 per cent metabolized, predominantly in the kidneys. 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. On the basis of the recommended dose regimens and elimination half-life, accumulation does not occur.

5.3 Preclinical safety data

No information

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The powder for injection contains mannitol, dibasic sodium phosphate dihydrate, sodium phosphate – monobasic dihydrate, and carmellose sodium.

The ampoule or vial of solvent contains 9 mg sodium chloride and 1 mL water for injections.

6.2 Incompatibilities

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

6.3 Shelf life

3 years

6.4 Special precautions for storage

PREGNYL should be stored in the dark between 2°C and 8°C. (Refrigerate. Do not freeze). Store in original package.

6.5 Nature and contents of container

Packs containing 3 ampoules of 1500 IU hCG and 3 ampoules solvent.

Packs containing 3 vials of 1500 IU hCG and 3 vials solvent.

Packs containing 1 ampoule of 5000 IU hCG and 1 ampoule solvent.

Packs containing 1 vial of 5000 IU hCG and 1 vial solvent.

6.6 Special precautions for use and handling and disposal

The powder for injection is reconstituted by adding the solvent.

Do not use if the solution contains particles or if the solution is not clear.

The solution should be used immediately after reconstitution.

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

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

Merck Sharp & Dohme (NZ) Ltd

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9. DATE OF FIRST APPROVAL

31 December 1969

10. DATE OF REVISION OF THE TEXT

21 August 2019

SUMMARY TABLE OF CHANGES

Version #	CCDS document	Release Date	Sections revised	Brief Description of Change
6	S-CCDS-MK8829-SOi-062019	June 2019	4.4 Special warnings and precautions for use	<ul style="list-style-type: none">• Revised subsection "Ovarian Hyperstimulation Syndrome (OHSS)"• Replaced text that describes clinical measures to be considered to reduce the risk of OHSS with language to direct the healthcare provider to follow current clinical practice for reducing the risk of OHSS during Assisted Reproductive Technology (ART).