Product Information

NAME OF THE MEDICINE

Pregnyl®
(human chorionic gonadotrophin)

DESCRIPTION AND PHARMACOLOGY

Pregnyl is a preparation of human chorionic gonadotrophin (hCG) obtained from the urine of pregnant women. It stimulates steroidogenesis in the gonads by virtue of a biologic effect similar to that of LH (luteinising 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 a follicle stimulating hormone (FSH) containing preparation. Because hCG is of human origin, no antibody formation is to be expected.

INDICATIONS

In the female:

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

In the male:

- Hypogonadotrophic hypogonadism.
- Delayed puberty associated with insufficient gonadotrophic pituitary function.
- Cryptorchism, not due to an anatomic obstruction.
- Sterility, in selected cases of deficient spermatogenesis.

CONTRAINDICATIONS

- Hypersensitivity to human gonadotrophins or any of the ingredients in Pregnyl (see PRECAUTIONS).
- Known or suspected sex hormone-dependent tumours, such as ovary, breast and uterine carcinoma in female and prostatic carcinoma or mammary 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.

PRECAUTIONS

The active ingredient of this preparation is extracted from human urine. Therefore the risk of a transmission of a pathogen (known or unknown) can not 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 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 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 parental 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.

OHSS may be caused by administration of human Chorionic Gonadotrophin (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 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.

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 gonadotrophin 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 Pregnyl 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 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 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.

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:

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

- 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.

Use in Pregnancy

Category A

Pregnyl may be used for luteal phase support, but should not be used later on in pregnancy.

Use in Lactation

Pregnyl must not be used during lactation.

INTERACTIONS WITH OTHER MEDICINES

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 10 days with the immunological determination of serum/urinary hCG, leading to a false positive pregnancy test.

Effects on ability to drive and use machines
As far as is known this medicine has no influence on alertness and concentration.

ADVERSE EFFECTS

Immune system disorders
In rare cases generalised 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. 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 PRECAUTIONS).

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 PRECAUTIONS).

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.

Investigations
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.

DOSAGE AND ADMINISTRATION

In the male:

- Hypogonadotrophic hypogonadism:
  500-1000 IU 2-3 times per week;

- Delayed puberty associated with insufficient gonadotrophic pituitary function:
  1500 IU twice weekly for at least 6 months.

- Cryptorchism, not due to an anatomic obstruction;
  Under 6 years of age: 500 IU twice weekly for 6 weeks.
  Over 6 years of age: 1000 IU twice weekly for 6 weeks.
  If necessary, this treatment can be repeated.

- Sterility in selected cases of deficient spermatogenesis:
  Usually, 3000 IU per week in combination with a FSH containing preparation.

In the female:

Sterility due to the absence of follicle-ripening or ovulation: usually, 5000-10000 IU to complete treatment with a FSH containing preparation. A repeat injection of 5000 IU may be given 7 days later (or in accordance with individual patient needs) to prevent insufficiency of the corpus luteum.

Reconstitution
Do not use if the solution contains particles or if the solution is not clear.
After addition of the solvent to the freeze-dried substance, the reconstituted Pregnyl solution should be administered intramuscularly. The solution should be used immediately after reconstitution.

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

OVERDOSAGE

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 PRECAUTIONS).

PRESENTATION AND STORAGE CONDITIONS

Vials of Pregnyl 1500 IU and 5000 IU contain powder for injection corresponding to 1500 and 5000 IU hCG respectively.

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

Vials of solvent contain 9 mg sodium chloride and 1 mL Water for Injections.

Each mL of the reconstituted solution contains: 1500, 5000 IU of human chorionic gonadotrophin (hCG).

Vials 1500 IU/mL, 1mL: 3's
Vials 5000 IU/mL, 1mL: 1's and 3's*.

*Pack size not currently marketed in Australia.

Shelf Life:
The shelf life of Pregnyl is 3 years.
The contents of the vial should be used immediately after reconstitution.

Storage:
Store at 2^{o}C to 8^{o}C (Refrigerate. Do not freeze). Protect from light.
Store in the original package.

NAME AND ADDRESS OF THE SPONSOR

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POISON SCHEDULE OF THE MEDICINE

Prescription Only Medicine (Schedule 4)

DATE OF FIRST INCLUSION IN THE ARTG

20 September 1991

DATE OF MOST RECENT AMENDMENT

24 April 2017