Product Information

NAME OF PRODUCT

Pregnyl\textsuperscript{(R)}
(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 oestrogens 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 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.

In the female:

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

CONTRAINdications

- Hypersensitivity to human gonadotrophins or any of the ingredients in Pregnyl.
- 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 sexual organs incompatible with pregnancy.
- Fibroid tumours of the uterus incompatible with pregnancy.

WARNINGS AND PRECAUTIONS

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

In the male:
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 monitored, since salt and fluid retention has been observed after administration of high doses of hCG. This could cause an aggravation or recurrence of these medical conditions.

In the female:

- When treating anovulatory infertility, the stimulation of the ovaries by a FSH containing preparation may lead to very rapid rise in oestrogen levels e.g. more than a daily doubling for two or three days, and possibly lead to excessively high oestrogen levels. In such cases hCG should not be administered, since there is a risk of inducing multiple ovulation or the ovarian hyperstimulation syndrome. This warning is particularly important for patients with polycystic ovarian disease. Clinical symptoms of mild ovarian hyperstimulation syndrome are gastrointestinal problems (pain, nausea, diarrhoea), painful breasts, and mild to moderate enlargement of ovaries and ovarian cysts. Transient liver function test abnormalities suggestive of hepatic dysfunction, which may be accompanied by morphologic changes on liver biopsy, have been reported in association with ovarian hyperstimulation syndrome (OHSS). In rare cases severe ovarian hyperstimulation syndrome occurs, which may be life threatening. This is characterised by large ovarian cysts (prone to rupture, ascites, weight gain, often hydrothorax and occasionally thrombo-embolic phenomena.

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

- Since infertile women undergoing assisted reproduction, and particularly in vitro fertilisation (IVF), often have tubal abnormalities, the incidence of ectopic pregnancies might be increased. Early ultrasound confirmation that a pregnancy is intrauterine is therefore important.

- Rates of pregnancy loss in women undergoing assisted reproductive technologies (ART) are higher than in normal population.

- The presence of uncontrolled non-gonadal endocrinopathies (e.g thyroid, adrenal or pituitary disorders) should be ruled out.
• 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 amongst other factors, to differences in parental characteristics (e.g. maternal age, sperm characteristics) and by 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.

• Women with generally recognised risk factors for thrombosis, such as a personal or family history, severe obesity (Body Mass Index > 30 kg/m²) or thromboembolic events, during or following treatment with gonadotrophins. In these women the benefits of IVF treatment needs to be weighed against the risks. It should be noted, however, that pregnancy itself also carries an increased risk of thrombosis.

• Pregnyl should not be used for body weight reduction. hCG has no effect on fat metabolism, fat distribution or appetite.

**Use in Pregnancy**
Category A

**Use in Lactation**
Pregnyl must not be used during lactation.

**INTERACTIONS WITH OTHER DRUGS**

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

**Effect on laboratory tests**
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 REACTIONS**

**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.

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.

Investigation
Weight gain as a characteristic of severe OHSS.

In the male:

Metabolism and nutrition disorders
Water and salt retention is occasionally seen in males after administration of high doses; 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
After addition of the solvent to the freeze-dried substance, the reconstituted Pregnyl solution should be administered intramuscularly. Since an opened ampoule cannot be resealed in such a way as to guarantee the continued sterility of the contents, 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

Ampoules of Pregnyl 500 IU, 1500 IU and 5000 IU contain powder for injection corresponding to 500, 1500 and 5000 IU hCG respectively.

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

The ampoule of solvent contains sodium chloride (9 mg) and Water for Injections (1mL).

Each mL of the reconstituted solution contains: 500, 1500, 5000 IU of human chorionic gonadotrophin (hCG)
Ampoules 500 IU/mL, 1mL: 3's
Ampoules 1500 IU/mL, 1mL: 3's
Ampoules 5000 IU/mL, 1mL: 1's and 3's.

Shelf Life:
The shelf life of Pregnyl is 3 years.
**Storage:**
Store at 2°C to 8°C (Refrigerate. Do not freeze). Protect from light.

**Sponsor:**
Merck Sharp & Dohme (Australia) Pty Limited
54-68 Ferndell Street,
South Granville, NSW 2142
Australia

Merck Sharp & Dohme (New Zealand) Ltd
P O Box 99 851
Newmarket
Auckland 1149
New Zealand

TGA approval date: 11 September 2006
Date of Safety Related Notification: 23 December 2008

Date of Safety Related Notification: 1 April 2011
Date of most recent amendment: 2 September 2011