

# NEW ZEALAND DATA SHEET

## **PREGNYL**

Human chorionic gonadotrophin (hCG) injection – 1500 i.u., 5000 i.u.

### **Presentation**

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.

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

An ampoule contains 1500 or 5000 IU hCG.

For excipients see **List of Excipients**.

### **Uses**

#### **Actions**

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.

#### **Pharmacokinetics**

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.

#### **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 gonadotropins).
- Delayed puberty associated with insufficient gonadotropic pituitary function.
- Cryptorchidism, not due to anatomical obstruction.

### **Dosage And Administration**

#### **Dosage In The Female**

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

Usually, one injection of 5,000-10,000 I.U 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 I.U. 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 I.U. 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 gonadotropic 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 I.U. twice weekly for six weeks.

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

Over 6 years of age: 1,500 I.U. 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.

## **Contraindications**

- Hypersensitivity to human gonadotropins or any of the excipients.
- 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 sexual organs incompatible with pregnancy.
- Fibroid tumours of the uterus incompatible with pregnancy.

## **Warnings And Precautions**

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.

### **In the female:**

- In pregnancies occurring after induction of ovulation with gonadotropic preparations, there is an increased risk of multiples.
- Since infertile women undergoing assisted reproduction, and particularly 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 ART are higher than in the 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 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.
- Unwanted ovarian hyperstimulation  
In patients treated for subfertility due to anovulation or impaired follicular ripening, the prior administration of an FSH-containing preparation may lead to unwanted ovarian hyperstimulation. Therefore, ultrasonic assessment of follicular development and determinations of oestradiol levels should be performed prior to FSH-treatment and at regular intervals during FSH-treatment. Oestradiol levels may rise very rapidly, e.g. more than a daily doubling for two or three consecutive days, and possibly reach excessively high values. The diagnosis of unwanted ovarian hyperstimulation may be confirmed by ultrasound examination. If this unwanted ovarian hyperstimulation occurs (i.e. not as part of a treatment preparing for IVF/ET, GIFT or ICSI), the administration of the FSH-containing preparation should be discontinued immediately. In that case pregnancy should be avoided and PREGNYL must not be given, because the administration of an LH-active gonadotropin at this stage may induce, in addition to multiple ovulations, the ovarian hyperstimulation syndrome (OHSS). This warning is particularly important with respect to 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. In rare cases severe ovarian hyperstimulation syndrome occurs, which may be life-threatening. This is characterized by large ovarian cysts (prone to rupture), ascites, weight gain, often hydrothorax and occasionally thromboembolic phenomena.
- Women with generally recognized risk factors for thrombosis, such as a personal or family history, severe obesity (Body Mass Index  $>30\text{kg/m}^2$ ) or thrombophilia, may have an increased risk of venous or arterial thromboembolic events, during or following treatment with gonadotropins. 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.
  - PREGNYL should not be used for body weight reduction. HCG has no effect on fat metabolism, fat distribution or appetite.

### **In The Male**

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.

### **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.

### **Effects On Ability To Drive And Use Machines**

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

### **Adverse 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 gonadotropin 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.

#### **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

### **Warnings and 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 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.

### **Interactions**

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.

### **Overdosage**

The acute toxicity of urinary gonadotropin 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 **Warnings and Precautions** section).

### **Pharmaceutical Precautions**

The shelf-life of PREGNYL is 3 years. PREGNYL should be stored in the dark between 2°C and 8°C. (Refrigerate. Do not freeze).

### **List of Excipients**

The powder for injection contains mannitol, disodium hydrogen phosphate, sodium dihydrogen phosphate and sodium carboxymethylcellulose.

The ampoule of solvent contains sodium chloride (9mg) and water for injections (1ml).

### **Incompatibilities**

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

### **Instructions for Use/Handling**

The powder for injection is reconstituted by adding the solvent.

Since an opened ampoule cannot be resealed in such a way to further guarantee the sterility of the contents, the solution should be used immediately after reconstitution.

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

### **Medicine Classification**

Prescription Medicine.

### **Package Quantities**

Packs containing 3 ampoules of 1500 i.u. hCG and 3 ampoules solvent.

Packs containing 1 ampoule of 5000 i.u. hCG and 1 ampoule solvent.

### **Further Information**

Nil.

### **Name and Address**

Merck Sharp & Dohme (NZ) Ltd

P O Box 99 851

Newmarket

Auckland 1149

Tel: 0800 500 673

### **Date of Preparation**

14 July 2011

(RA 2400 OS S2 Ref 2.0)