SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Choragon® 5000

2. Qualitative und quantitative composition

1 ampoule of Choragon 5000 contains 5000 IU chorionic gonadotrophin.

For excipients, see section 6.1.

3. Pharmaceutical form

Powder and solvent for solution for injection.

4. Clinical particulars

4.1 Therapeutic indications

Choragon 5000

Therapy

Gynaecology

- Ovulation induction, if necessary after stimulation of follicle growth
  Maintenance of the corpus luteum function in female patients with luteal phase insufficiency.

Paediatrics

- Delayed puberty in boys.

Diagnostics

Differential diagnosis of cryptorchism and anorchism.
Assessment of the function of the testes in patients with hypogonadotropic hypogonadism before a planned long-term stimulation treatment.

4.2 Posology and method of administration

Method of administration

After solution in the enclosed solvent, Choragon is injected intramuscularly

Dosage, duration of administration

Choragon 5000

Gynaecology

For ovulation induction once 1 or 2 ampoules of Choragon 5000, if the dominant follicle has reached a diameter of more than 18mm.

For maintenance of the corpus luteum function, three times I ampoule Choragon 5000, e.g. on the 3rd, 6th and 9th day following ovulation.

Paediatrics and andrology
For induction of puberty in boys with delayed puberty 1 ampoule of Choragon 5000 per week over a period of 3 months.

Once 1 ampoule of Choragon 5000
- for differential diagnosis in boys with undescended testicle as well as
- for assessment of the function of the testes in patients with hypogonadotropic hypogonadism.

4.3 Contraindications

General
Hypersensitivity against chorionic gonadotrophin or any of the excipients of Choragon.

Gynaecology
- Tumours of the pituitary or hypothalamic glands,
- Ovarian cysts or enlarged ovaries not due to polycystic ovarian disease,
- Gynaecological haemorrhage of unknown aetiology,
- Ovarian, uterine or mammary carcinoma,
- Extrauterine pregnancy in the previous 3 months,
- Active thromboembolic diseases

Choragon must not be administered in case the treatment outcome is unlikely to be favourable, e.g. in case of
- Primary ovarian failure,
- Malformations of sexual organs incompatible with pregnancy,
- Uterine myoma incompatible with pregnancy,
- Women after the menopause.

Choragon should not be administered for ovulation induction in women with ovarian hyperstimulation.

Paediatrics and andrology
Choragon must not be used in case of sexual hormone-dependent tumors and in case of undescended testicle known to be of organic origin (inguinal hernia, surgery in the inguinal region, ectopic testicle).

4.4 Special warnings and precautions for use

General
Choragon is not induced for reduction of the body weight. HCG does not have any influence of the lipometabolism, fat distribution, appetite or sensation of hunger.

Gynaecology
Before starting treatment, the couple's infertility should be assessed as appropriate and putative contraindications for pregnancy evaluated. In particular, patients should be

evaluated for hypothyroidism, adrenocortical deficiency, hyperprolactinemia and pituitary or hypothalamic tumours, and appropriate specific treatment given.

Patients undergoing stimulation of follicular growth may have a higher risk of ovarian hyperstimulation syndrome (OHSS) due to multifollicle development.

An ovarian hyperstimulation syndrome can manifest itself as a severe medical event which is marked by ovarian cysts tending to rupture and the occurrence of ascites together with

circulatory disorder. Ovarian hyperstimulation syndrome due to an excessive ovarian reaction may be avoided by withholding hCG. In this case, the patients are to be advised to refrain from coitus for at least 4 days or to use appropriate barrier methods.

Close monitoring of the estradiol levels and the ovarian reaction by means of sonography before and during the stimulation therapy is recommended for all patients.

The risk of multiple pregnancies after assisted reproduction techniques is related to the number of embryos replaced. Patients undergoing an ovulation induction have a higher risk of multiple pregnancy and/or multiple delivery (mostly twins) compared to the normal conception.

In order to minimize OHSS and multiple pregnancy, ultrasound examinations and estradiol measurements are recommended.

Adherence to recommended Choragon dosage, regimen of administration and careful monitoring of therapy will minimise the incidence of ovarian hyperstimulation or multiple pregnancy

The incidence of pregnancy wastage in anovulatory patients and patients undergoing ART is higher than in the normal population, but comparable to the pregnancy wastage rate of women with other fertility disorders.

Special information for the treatment

For treatment of sterile women, close monitoring is necessary:

- Prior to administration of Choragon, examinations of follicle growth (ultrasound) and the cervix index (over a period of two days until a stimulation effect is achieved) have to be carried out.
- When stimulation symptoms appear during treatment, daily ultrasound examinations and estradiol analyses should be carried out (additionally, the ovarian reaction can be measured by the cervix index).

In case of unintentional hyperstimulation, treatment should be stopped.

Ovarian hyperstimulation

In case of slight hyperstimulation (level I) with slight enlargement of the ovaries (ovary size 5- 7 cm), excessive steroid secretion and abdominal pain, no therapy is necessary. However, the patient should be informed and carefully monitored.

In case of medium hyperstimulation (level II) with ovarian cysts (ovary size 8- 10 cm) together with abdominal symptoms, nausea and vomiting, clinical supervision, symptomatic treatment and perhaps an intravenous volume replacement in case of high

hemoglobin concentration is necessary.

In case of serious hyperstimulation (level III) with large ovarian cysts (ovary size above 10 cm), ascites, hydrothorax, enlarged abdomen, abdominal pain, dyspnea, salt retention, hemoglobin concentration, increased blood viscosity and increased platelet aggregation with the danger of thromboembolisms, hospitalisation is imperative.

4.5. Interaction with other medicinal products and other forms of interaction

No clinically significant drug interactions have been observed.

4.6. Pregnancy and lactation

The administration of Choragon for luteal phase insufficiency supports the endometrium and optimizes the implantation area in the periimplantation phase by stimulating progesterone production.
Moreover, there is no indication for the use of Choragon during normal pregnancy and nursing.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8. Undesirable effects

Gynaecology:
After use of hCG (urinary or recombinant), the following undesirable effects may occur:
- headache, fatigue
- vomiting, nausea, diarrhoea
- abdominal pain
- depressions, irritability, restlessness
- exanthem, urticaria, Quincke's oedema
- local reactions at the injection site: bruise, pain, redness, swelling, itching
- allergic reactions, fever

Paediatrics and androIogy
Temporary or long-term gynaecomastia due to the estrogen release and/or proliferative change in the prostate.

Acne vulgaris as well as electrolyte and water retention due to stimulation of testosterone secretion.

Increase in size of penis and erections due to increased testosterone secretion caused by induction.

Occasionally, minor emotional changes in boys similar to those at the beginning of puberty may occur which are limited to the course of treatment.

4.9 Overdose

No cases of overdose have been reported.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gonadotrophins
ATC-Code: GO3GAOI

Human chorionic gonadotrophin (HCG) is a glucoprotein and represents the association between an alpha and a beta chain. HCG is obtained from the urine of pregnant women and is not homogeneous. Also highly purified drugs contain several fractions differing from sialic acid and in the biologic action. The amount of HCO is indicated in units of the biological action.

The hormonal effect of chorionic gonadotrophin is based on its ability to stimulate the biosynthesis of sexual steroids in the gonads (ovaries and testes). The action of HCO is qualitatively the same as that of the pituitary gonadotrophin (LH). However, HCG has a

significantly longer half-life which leads to a stronger action in case of cumulative administration.

In the ovaries, HCG stimulates the granulosa, theca and stroma or luteal cells to support the production of progesterone and estradiol. In the granulosa cells of the small follicles, the biosynthesis of the estradiol is preferably stimulated by high HCG-doses. However, in the granulosa cells of the mature, dominant follicles and/or in the luteinizing granulosa cells, the biosynthesis of the progesterone is stimulated by high HCO-doses. Furthermore, HCG stimulates the production of biologically active peptides in the ovary that are important for the regulation of reproduction (e.g. inhibin, relaxin, prorenin, plasminogen-activator-inhibitor). The administration of 5000 IU up to 10,000 IU HCG to women with mature follicles (e.g. after stimulation with HMG or Chlomiphen) induces ovulation abt. 36 hours after the intramuscular injection. Repeated injections (3 to 7 times) of HCG (1500 IU up to 10,000 IU) in the luteal phase may extend the life-time of the corpus luteum and thus the secrectory phase of the endometrium.

In the Leydig cells, HCG stimulates the production of testosterone and other sexual steroids such as dihydrotestosterone, 17 OH-progesterone and estradiol. The single administration of 5000 IU HCG to boys and men raises testosterone secretion in a bi-phasal manner with a first maximum after 2 to 4 hours and a second maximum between 48 and 72 hours. The maximum amount of estradiol in serum is reached approximately 24 hours after the administration of HCG. This principle is used for the differential diagnosis of cryptorchism in order to differentiate between cryptorchism and anorchism. In boys during puberty, HCG is suitable for treatment of retarded descensus of the testicle.

5.2. Pharmacokinetic properties

HCG is administered by intramuscular injection. The maximum serum level of HCG is reached after 4 to 12 hours (dose-dependent) and decreases afterwards with a half-life of 29 to 36 hours. Due to the slow elimination, HCG may cumulate in serum after several (e.g. daily) intramuscular injections.

HCG is metabolized renally whereby about 10- 20 % can be found in its original form in urine, while the main amount is probably excreted as the beta-core fragment.

5.3. Preclinical safety data

Animal experiments in mice showed dose-dependent increased embryonic fetal death, smaller fetuses, less fetuses per liner as well as a significant increase of congenital malformations (open eyelids, cleft palates) after administration of HCG for ovulation induction in the therapeutic range.

In investigations in women, a higher abortion rate compared to the normal population was determined. However, there is no information of a higher malformation rate after ovulation induction with HCG in women.

6. Pharmaceutical particulars

6.1. List of excipients

Powder: Mannitol, sodium hydroxide
Solvent: Sodium chloride, dilute hydrochloric acid 10 %, water for injections

6.2. Incompatibilities

Not known.

6.3. Shelf life

The shelf life is 3 years.
This medicinal products must not be used after the expiry date.

6.4 Special precautions for storage

Do not store Choragon above + 25^0C.

6.5 Nature and contents of container

Powder:
The powder for solution for injection is supplied in brown 1 ml ampoules, type I glass.

Solvent.
The solvent for solution for injection is supplied in colourless 1 ml ampoules, type I glass.

Choragon is supplied in the following pack sizes:

Choragon 5000
Package with 3 ampoules with 5000 IU powder and 3 ampoule with 1 ml solvent each.

6.6 Instructions for handling

None.

7. Marketing authorisation holder

Ferring S.p.A.
Via Senigallia 18/2
Milan
Italy

8. Marketing authorisation number

MA461/00302

9. Date of first authorisation / renewal of the authorisation

20th September 2006

10. Date of revision of the text

1ST December 2010

11. Prescription status

Prescription only