Prescribing information for MERIOFERT PFS 900 IU

Powder and solvent for solution for injection (Refer to Summary of Product Characteristics (SPC) for full information). Presentation: Each multidose vial contains freeze-dried powder with 900 IU human follicle stimulating hormone activity (FSH) and 900 IU human luteinising hormone activity (LH). Human menopausal gonadotrophin (HMG) is extracted from urine of post-menopausal women. Human chorionic gonadotrophin (hCG), extracted from urine of pregnant women, is added to contribute to the total LH activity.
Indications: *Ovulation induction:* for the induction of ovulation in amenorrhoeic or anovulatory women who have not responded to treatment with clomiphene citrate. *Controlled ovarian hyperstimulation (COH)* within a medically assisted reproduction technology (ART): induction of multiple follicular development in women undergoing assisted reproduction techniques such as in vitro fertilisation (IVF).
Dosage and administration: Treatment with MERIOFERT PFS should be initiated under the supervision of a physician experienced in the treatment of infertility problems. There are great inter- and intra-individual variations in the response of the ovaries to exogenous gonadotrophins. The dosage should, therefore, be adjusted individually depending on the ovarian response. This requires ultrasonography and may also include monitoring of oestradiol levels.

Females undergoing ovary stimulation for induction of multiple follicular development – as part of assisted reproductive technology: In a commonly used protocol the administration of MERIOFERT PFS begins approximately two weeks after the start of the agonist treatment, both treatments are then continued until adequate follicular development has been achieved. For example, following two weeks of pituitary down-regulation with agonist, 150 to 225 IU of MERIOFERT PFS are administered for the first five-seven days. The dose is then adjusted according to the patient's ovarian response. An alternative protocol for controlled ovarian hyperstimulation involves the administration of 150 to 225 IU of MERIOFERT PFS daily starting on the 2nd or 3rd day of the cycle. The treatment is continued until sufficient follicular development has been achieved (assessed by monitoring of serum oestrogen concentrations and/or ultrasound) with the dose adjusted according to the patient's response (usually not higher than 450 IU daily). Adequate follicular development is usually achieved on average around the tenth day of treatment (5 to 20 days). When an optimal response is obtained a single injection of 5 000 IU to 10 000 IU of hCG administered 24 to 48 hours after the last MERIOFERT PFS injection, to induce final follicular maturation. Oocyte retrieval is performed 34-35 hours later.

Method of administration: MERIOFERT PFS is intended for subcutaneous administration and is not intended for use in children. The injection should be performed slowly to prevent pain and backflow of product at the injection site. The injection site should be alternated to prevent lipoatrophy. As this vial contains medication for several days of treatment, 12 administration syringes graduated in FSH/LH IU units are provided to draw up the correct single dose of MERIOFERT PFS in IU (units). MERIOFERT PFS may be recommended for patient self-administration. Patients must be trained on appropriate reconstitution/injection techniques prior to use. (See SPC for full details).
Contraindications: Hypersensitivity to menotrophin or to any of the excipients, ovarian enlargement, or cysts not related to polycystic ovarian syndrome, gynaecological bleeding of unknown cause, ovarian, uterine or breast carcinoma tumours of the hypothalamus or pituitary gland MERIOFERT PFS is contraindicated when an effective response cannot be achieved, for example: Primary ovarian failure, malformations of sexual organs incompatible with pregnancy, fibroid tumours of the uterus incompatible with pregnancy.
Warnings and precautions: Anaphylactic reactions may occur, particularly in patients with known hypersensitivity to gonadotropins. The first injection of MERIOFERT PFS should be always performed under direct medical supervision and in settings with facilities for cardio-pulmonary resuscitation. The first injection of MERIOFERT PFS should be performed under direct medical supervision.
Before starting the treatment, the couple's infertility should be assessed as appropriate and above mentioned contraindications for pregnancy evaluated. In addition, patients should be evaluated for hypothyroidism, adrenocortical deficiency, hyperprolactinemia and pituitary or hypothalamic tumours, for which appropriate specific treatments are given (See SPC for full details).

Ovarian hyperstimulation syndrome (OHSS): Ultrasonographic assessment of follicular development, and determination of oestradiol levels should be performed prior to treatment and monitored at regular intervals during treatment. Apart from the development of a high number of follicles, oestradiol levels may

rise very rapidly and possibly reaching excessively high values. The diagnosis of ovarian hyperstimulation may be confirmed by ultrasound examination. If this unwanted ovarian hyperstimulation occurs, the administration of MERIOFERT PFS should be discontinued. In that case pregnancy should be avoided and hCG must be withheld, because it may induce, in addition to multiple ovulation, the ovarian hyperstimulation syndrome (OHSS). Clinical symptoms and signs of mild ovarian hyperstimulation syndrome are abdominal pain, nausea, diarrhoea, 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 characterised by large ovarian cysts (prone to rupture), ascites, often hydrothorax and weight gain. In rare instances, venous or arterial thromboembolism may occur in association with OHSS (see SPC section 4.8).
Multiple Pregnancies: In patients undergoing ART procedures the risk of multiple pregnancies is related mainly to the number of replaced embryos. To minimise the risk of multiple pregnancy, careful monitoring of ovarian response is recommended (see section 4.2 SPC).
Pregnancy wastage: The incidence of spontaneous miscarriage is higher in patients treated with FSH than in the general population, but it is comparable to the incidence found in women with other fertility disorders.
Ectopic pregnancy: Early ultrasound confirmation that a pregnancy is intrauterine, and not ectopic, is important.
Reproductive system neoplasms: There have been reports of ovarian and other reproductive system neoplasms, both benign and malignant, in women who have undergone multiple drug regimens for infertility treatment. It is not yet established if treatment with gonadotropins increases the baseline risk of these tumours in infertile women.
Congenital malformation: The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics
Thromboembolic events: Women with generally recognised risk factors for thromboembolic events, such as personal or family history, severe obesity (Body Mass Index > 30 kg/m2) 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 gonadotrophin administration need to be weighed against the risks (see section 4.8 SPC).

Interactions: No drug/drug interaction studies have been conducted for MERIOFERT PFS in humans. Although there is no clinical experience, it is expected that the concomitant use of MERIOFERT PFS 900 IU and clomiphene citrate may enhance the follicular response. When using GnRH agonist for pituitary desensitisation, a higher dose of MERIOFERT PFS 900 IU may be necessary to achieve adequate follicular response.
Pregnancy and Lactation: MERIOFERT PFS should not be used during pregnancy or during lactation.
Undesirable Effects: The most (non-serious) relevant occurring adverse drug reaction in clinical trials with MERIOFERT PFS is (dose-related) ovarian hyperstimulation (OHSS), generally mild with small ovarian enlargement, abdominal discomfort or pain. Two cases of OHSS were serious. The most frequent adverse reactions with MERIOFERT PFS were headache and abdominal distension as well as nausea, fatigue, dizziness, back/pelvic pain, breast tenderness, malaise, thirst and pain at the injection site (See SPC for full details).

Pack size and NHS List Price: The set contains the following:
- 1 vial containing powder
- 1 prefilled syringe containing solvent for reconstitution.

Price: 334.80
Marketing Authorisation Number: PLGB 21039/0076
Legal Classification: POM
Marketing Authorisation Holder: IBSA Farmaceutici Italia S.r.l, Via Martiri di Cefalonia 2, 26900 Lodi, Italy.
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