Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Folligon PMSG 200 IU/ml lyophilisate and solvent for solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, each ml contains:

Active substance:
Serum gonadotrophin 200 IU

Excipients:
For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Lyophilisate and solvent for solution for injection.

Lyophilisate: White powder.
Solvent: Clear, colourless.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle, sheep and pigs.

4.2 Indications for use, specifying the target species

To stimulate the development of the ovarian follicle in the female and has spermatogenic activity in the male by its effect on the seminiferous tubules.

Folligon PMSG is a complex glycoprotein obtained from the serum of pregnant mares. This substance is capable of supplementing and being substituted for follicle stimulating gonadotrophin of the anterior pituitary gland in both female and male animals.

4.3 Contraindications

None.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Where the possibility of multiple ovulations has not been excluded by clinical examination following administration of Folligon PMSG to uniparous species (unless to induce superovulation in cattle), it is inadvisable to permit service or to inseminate animals during the first heat produced.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

PMSG can influence fertility in humans after injection.
Administer the veterinary medicinal product with caution to avoid self-injection.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or label to the physician.
Accidental spillage on the skin should be washed immediately with soap and water.

4.6 Adverse reactions (frequency and seriousness)

In rare cases, as with all protein preparations, anaphylactic reactions may occur shortly after injection. Adrenaline injection (1: 1,000) given intravenously or intramuscularly when symptoms appear is the standard treatment. The administration of corticosteroid may also be indicated.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Do not use during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Dose: See table below.
Routes of administration: Cattle and sheep: intramuscular use; pigs: intramuscular or subcutaneous use.
Reconstitution: Reconstitute the lyophilisate with the solvent provided.
Ensure the lyophilisate has fully dissolved before use.
Depending on the presentation (pack size), reconstitute one vial of 1,000 IU lyophilisate with 5 ml of solvent, or reconstitute one vial of 5,000 IU lyophilisate with 25 ml of solvent.
Use normal aseptic precautions. Avoid the introduction of contamination.

Female animals	**Indication**	**Dosage and Administration**
Cattle	Anoestrus/oestrus induction	500 - 1,000 IU, IM
	Superovulation	1,500 - 3,000 IU, IM, between day 8 - 13 of the cycle, followed by prostaglandin, im, 48 hours later
	Increase in fertility rate after progestagen pre-treatment	300 - 750 IU, IM at the end of a progestagen treatment
Sheep	Increase in fertility rate after progesterone pre-treatment (in and out of breeding season)	400 - 750 IU, IM, at time of progestagen removal (see further information)
Pig	Anoestrus post-weaning (induction of oestrus is difficult until 40 days post partum)	1000 IU SC. or IM, fertile oestrus usually follows within 3 -7 days

Anoestrus is often caused by inadequate management (feeding and housing). Improvement of management is therefore a prerequisite for a successful treatment.

Superovulation in cattle
Folligon PMSG may be used for the superovulation of female donor cattle prior to embryo transfer.
The following is an example, of a regime that has been successfully been applied in the field:

- A single dose of Folligon PMSG (1,500 - 4,000 IU) is injected on day 9 - 13 of a normal oestrus. NB: the exact dose of Folligon PMSG required to achieve effective superovulation will depend upon a number of factors particularly the breed, age, reproductive history, general health and nutritional status of the donor female, is subject to individual variation.
- 48 hours after Folligon PMSG injection, luteolysis is induced by the injection of a prostaglandin analogue. Usually 1 ½ times the normal luteolytic dose is administered. Oestrus normally occurs approximately 48 hours after the prostaglandin injection.
- Insemination is carried out at 60 and 72 hours after prostaglandin injection.
- Collection of fertilised embryos (flushing) is carried out 6-8 days after insemination. Suitable embryos are transferred to female recipient cattle whose oestrus cycles have previously been synchronised with that of the donor female. Experience has shown that oestrus cycles in donor and recipient females should be synchronised within ± 24 hours if reasonable success is to be expected.
- A further prostaglandin treatment (usually 1 ½ times the luteolytic dose) should be administered at the time of embryo collection.

Note:
1. Despite the application of a suitable treatment regime certain individual donor cows may fail to respond.
2. Wide variations in response may be expected between individual animals. Repeated treatment of a single animal may also yield variable results.
3. The overall success of an embryo transfer protocol will be influenced by the availability of suitable equipment and the skill and experience of the operator.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No specific treatment or antidote is recommended.

4.11 Withdrawal Period(s)

Meat and offal: Zero days.
Milk: Zero days.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Gonadotropins and other ovulation stimulants, serum gonadotrophin.
ATC vet code: QG03GA03

5.1 Pharmacodynamic properties

PMSG is a potent gonadotrophin with dual FSH and LH activity. It is composed of two non-covalently associated alpha and beta subunits and is heavily glycosylated on its CTP tail. This extensive glycosylation is of key importance in obtaining the extended half-life in blood that is typical of PMSG. As PMSG binds to FSH and LH receptors, it stimulates follicular growth and follicular maturation in the days preceding oestrus and ovulation. Limited amounts of PMSG will result in induction and synchronisation of ovulation in cattle and small ruminants, irrespective of their cyclicity prior to treatment. Administration of slightly higher amounts will modestly increase ovulation rate and litter size. Administration of high amounts of PMSG will result in superovulation, therefore resulting in the numerous blastocysts needed for embryo transfer.

5.2 Pharmacokinetic properties

The pharmacokinetic profile observed following injection of PMSG is characterised by the very long half life generated by the glycosylation (N and O glycosylation) of the PMSG molecule. It also explains why a single PMSG administration has the ability to support follicular growth throughout the full duration of the follicular phase (2 to 5 days depending on the species).

Absorption of PMSG is rapid. In all three species studied, PMSG is rapidly absorbed from the injection site and Cmax is reached within 8 hours (pig/sheep) or 16 hours (cattle) following injection. Bioavailability following intramuscular injection (compared to intravenous administration) is high in all species (cattle: 72 %; pigs: 71.3 %; sheep: 92.6 %).

PMSG elimination is slow. The elimination half-life has been shown to range between 34 and 150 hours depending on the species.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Sodium dihydrogen phosphate dihydrate
Disodium hydrogen phosphate dihydrate
Water for injections

6.2 Incompatibilities

Do not mix with any other veterinary medicinal product except solvent supplied with the product.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after reconstitution according to directions: 24 hours.

6.4 Special precautions for storage

Store in a refrigerator (2 ºC - 8 ºC). Store reconstituted product in a refrigerator (2 ºC - 8 ºC). Protect from light.

6.5 Nature and composition of immediate packaging

Lyphilisate: Clear, type I (Ph. Eur.) glass vials with halogenobutyl rubber stopper, closed with a colour coded aluminium cap.

Solvent: Clear, type I (Ph. Eur) or type II (Ph. Eur.) glass vials with halogenobutyl rubber stopper, closed with a colour coded aluminium cap.

Pack sizes:
Cardboard box with 1 vial of 5,000 IU lyophilisate and 1 x 25 ml vial of solvent.
Cardboard box with 1 vial of 1,000 IU lyophilisate and 1 x 5 ml vial of solvent.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Intervet Ireland Ltd
Magna Drive
Magna Business Park
Citywest Road
Dublin 24

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10996/055/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19th September 1998

Date of last renewal: 30th September 2008

10 DATE OF REVISION OF THE TEXT

March 2017