1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fixplan 200 IU/ml lyophilisate and solvent for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Lyophilisate vial contains:

Active substances:
Gonadotrophin, equine serum 5000 IU

Solvent vial contains 25 ml

Each ml of the reconstituted solution contains:

Active substances:

Gonadotrophin, equine serum 200 IU

Excipients:

Qualitative composition of excipients and other constituents
Lyophilisate:
Mannitol
Disodium phosphate
Sodium dihydrogen phosphate dihydrate
Solvent:
Disodium phosphate dihydrate
Sodium dihydrogen phosphate dihydrate
Water for injections

Lyophilisate and solvent for solution for injection.
Lyophilisate: white powder
Solvent: clear colourless solution
Reconstituted solution: clear colourless solution free from visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, sheep and pigs.

3.2 Indications for use for each target species

To stimulate the development of the ovarian follicle in the female.

Cows: Treatment of anoestrus/ induction of oestrus, induction of superovulation and increase in fertility rates after progestagen pre-treatment.
Ewes: Increase in fertility rates after progestagen pre-treatment.

Sows: Treatment of anoestrus post-weaning/ induction of oestrus.

3.3 Contraindications

None.

3.4 Special warnings

Especially in sheep, dosing of eCG should be adapted to the breed (doses should be lower in prolific breeds) and to the breeding season of animals (higher when used off season).

3.5 Special precautions for use

Special precautions for safe use in the target species:
In case of anaphylactic shock, symptomatic treatment (e.g. adrenaline or corticosteroids) should be administered.
Where the possibility of multiple ovulations has not been excluded by clinical examination following administration of the veterinary medicinal product 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:
Studies in laboratory animals exhibited teratogenic effects after the administration of eCG.
Pregnant women, those intending to become pregnant, or whose pregnancy status is unknown, should not handle the product.
The veterinary medicinal product 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 the label to the physician.
Accidental spillage on the skin should be washed immediately with soap and water.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cattle, sheep and pigs:

Rare (more than 1 but less than 10 animals in 10,000 animals treated)	Anaphylactic-type reaction[1]

[1]May occur shortly after injection, as with all protein preparations.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:
Do not use (during the whole or part of the pregnancy).
Studies in laboratory animals exhibited teratogenic effects after the administration of eCG.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cattle and sheep: intramuscular (**i.m**) use.
Pigs: intramuscular (**i.m**) or subcutaneous (**s.c**) use.

Reconstitution: Reconstitute the lyophilisate with the solvent provided. Dissolve the lyophilisate with a small quantity of solvent. Mix to obtain a homogenous solution. Transfer this solution into the vial that contains the rest of the solvent and mix until completely dissolved.
Ensure the lyophilisate has fully dissolved before use.
Use normal aseptic precautions. Avoid the introduction of contamination.

Female animals	Indication	Dosage and administration
Cattle	Anoestrus/oestrus induction	500 – 1,000 IU (*i.e.* 2.5 to 5 ml of product), **i.m**
	Superovulation	1,500 – 3,000 IU (*i.e.* 7.5 to 15 ml of product), **i.m** between day 8– 13 of the cycle, followed by prostaglandin, **i.m** 48 hours later
	Increase in fertility rate after progestagen pre-treatment	300 – 750 IU (*i.e.* 1.5 to 3.75 ml of product), **i.m** at the end of a progestagen treatment
Sheep	Increase in fertility rate after progestagen pre-treatment (in and out of breeding season)	400 - 750 IU (*i.e.* 2.0 to 3.75 ml of product), **i.m** at time of progestagen removal
Pig	Anoestrus post-weaning (induction of oestrus is difficult until 40 days post partum)	1000 IU (*i.e.* 5 ml of product), **s.c or i.m** 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.

Equine serum gonadotropin is a protein hormone which acts on the ovary to stimulate the production of follicles. The number of follicles produced can be influenced by the dose of equine serum gonadotropin administered and this must be taken into account when, for instance, calculating the dose for a particular flock of ewes in which oestrus synchronisation is desired. In general, the further out of season that breeding is attempted and the lower the normal prolificacy of the flock, the more equine serum gonadotropin that will be required.

An average dose of 500 IU / ewe is recommended as a useful starting point but doses ranging from 400 - 750 IU have been used on occasion. It is therefore recommended that accurate flock records are kept of breed, dose given, time of injection and lambs produced so that in future seasons the amount can, if necessary, be adjusted for optimum results.

<u>Superovulation in cattle</u>
The veterinary medicinal product may be used for the superovulation of female donor cattle prior to embryo transfer.
The following is an example, of a regime that has successfully been applied in the field:

- A single dose of the veterinary medicinal product (1,500 - 3,000 IU) is injected between day 8 and 13 of a normal oestrus cycle. NB: the exact dose of the veterinary medicinal product 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 and is subject to individual variation.
- 48 hours after injection of the veterinary medicinal product, 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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No specific treatment or antidote is recommended.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

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

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

Pigs:
Meat and offal: Zero days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QG03GA03

4.2 Pharmacodynamics

Equine serum gonadotropin 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.
Equine serum gonadotropin 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 equine serum gonadotropin. As equine serum gonadotropin binds to FSH and LH receptors, it stimulates follicular growth and follicular maturation in the days preceding oestrus and ovulation. Limited amounts of equine serum gonadotropin 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 equine serum gonadotropin will result in superovulation, therefore resulting in the numerous blastocysts needed for embryo transfer.

4.3 Pharmacokinetics

The pharmacokinetic profile observed following injection of equine serum gonadotropin is characterised by the very long half-life generated by the glycosylation (N and O glycosylation) of the equine serum gonadotropin molecule. It also explains why a single equine serum gonadotropin 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 equine serum gonadotropin is rapid. In all three species studied, equine serum gonadotropin 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 %).
Equine serum gonadotropin elimination is slow. The elimination half-life has been shown to range between 34 and 150 hours depending on the species.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product, except solvent or other component supplied for use with the veterinary medicinal product.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after reconstitution according to directions: 24 hours.

5.3 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Keep the vials in the outer carton in order to protect from light.
The reconstituted solution should be stored in the refrigerator (2 °C – 8 °C).

5.4 Nature and composition of immediate packaging

Lyophilisate: 8 ml colourless type I glass vial closed with a grey bromobutyl rubber stopper, aluminium seals and prolypropylene caps.
Solvent: 30 ml colourless type II glass vial closed with a grey bromobutyl rubber stopper, aluminium seals and polypropylene caps.

Package sizes:
Cardboard box with 1 vial of 5,000 IU lyophilisate and 1 vial of solvent (25 ml).

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Syn Vet-Pharma Ireland Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA23174/002/001

8. DATE OF FIRST AUTHORISATION

05/03/2021

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

09/11/2026

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).