

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prolusyn 50 micrograms/ml solution for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Gonadorelin (as gonadorelin acetate) 50.0 micrograms

Excipient:

Benzyl alcohol (E1519) 9.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (cows, heifers).

4.2 Indications for use, specifying the target species

Induction and synchronisation of oestrus and ovulation in combination with prostaglandin F_{2α} (PGF_{2α}) or analogue with or without progesterone as part of Fixed Time Artificial Insemination (FTAI) protocols.

Treatment of delayed ovulation.

4.3 Contraindications

Do not use in known cases of hypersensitivity to the active substance or to any of the excipients.

Do not use during infectious diseases and other relevant health disorders.

4.4 Special warnings for each target species

The response of dairy cows to synchronisation protocols may be influenced by the physiological state at the time of treatment, which includes age of the cow, body condition, health status and interval from calving.

Responses to treatment are not uniform either across herds or across cows within herds.

Where a period of progesterone treatment is included in the protocol, the percentage of cows displaying oestrus within a given period is usually greater than in untreated cows and the subsequent luteal phase is of normal duration.

4.5 Special precautions for use

Special precautions for use in animals

Not applicable.

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

Gonadorelin is a Gonadotropin Releasing Hormone (GnRH) analogue which stimulates the release of sex hormones. The effects of accidental exposure to GnRH analogues in pregnant women or in women with normal reproductive cycles are unknown; therefore it is recommended that pregnant women should not administer the product, and that women of child-bearing age should administer the product with caution.

Care should be taken when handling the product 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.

Since GnRH analogues can be absorbed through the skin and benzyl alcohol may cause mild local irritation, care should be taken to avoid skin and eyes contact. In case of skin and/or eye contact, rinse immediately and thoroughly with plenty of water.

GnRH analogues and benzyl alcohol may cause hypersensitivity (allergy). People with known hypersensitivity to GnRH analogues or benzyl alcohol should avoid contact with the veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy or lactation or lay

Can be used during lactation.

Laboratory studies in rats and rabbits have not produced any evidence of a teratogenic or embryotoxic effects.

Observations in pregnant cows receiving the product in early pregnancy have not shown evidence of negative effects on bovine embryos.

Inadvertent administration to a pregnant animal is unlikely to result in adverse effects.

4.8 Interaction with other medicinal products and other forms of interaction

A synergistic effect is possible when used in combination with FSH. Simultaneous use of human or equine chorionic gonadotropin can lead to ovarian overstimulation.

4.9 Amounts to be administered and administration route

Intramuscular use.

100 µg of gonadorelin (as acetate) per animal in a single injection.
i.e. 2 ml of the product per animal.

Judgement on the protocol to be used should be made by the veterinarian responsible for treatment, on the basis of the treatment objectives of the individual herd or cow. The following protocols have been evaluated and could be used:

Induction and synchronisation of oestrus and ovulation in combination with a prostaglandin F_{2α} (PGF_{2α}) or analogue:

- Day 0: First injection of gonadorelin (2 ml of the product)
- Day 7: Injection of prostaglandin (PGF_{2α}) or analogue
- Day 9: Second injection of gonadorelin (2 ml of the product) should be done.

The animal should be inseminated within 16-20 hours after the last injection of the product or at observed oestrus if sooner.

Induction and synchronisation of oestrus and ovulation in combination with a prostaglandin F_{2α} (PGF_{2α}) or analogue and a progesterone releasing intravaginal device:

The following FTAI protocols have been commonly reported in the literature:

- Insert progesterone releasing intravaginal device for 7 days.
- Inject gonadorelin (2 ml of the product) at the progesterone device insertion.
- Inject a prostaglandin (PGF_{2α}) or analogue 24 hours prior to device removal
- FTAI 56 hours after removal of the device, or
- Inject gonadorelin (2 ml of the product) 36 hours after progesterone releasing intravaginal device removal and FTAI 16 to 20 hours later.

Treatment of delayed ovulation:

GnRH is injected during oestrus.

To improve the pregnancy rates, the following timing of injection and insemination should be followed:

- injection should be performed between 4 and 10 hours after oestrus detection
- an interval of at least 2 hours between the injection of GnRH and artificial insemination is recommended
- artificial insemination should be carried out in accordance with the usual field recommendations, i.e., 12 to 24 hours after oestrus detection.

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

Up to 5 times the recommended dose and in a regimen extended from one to three daily administrations, no measurable signs of either local or general clinical intolerance are observed.

4.11 Withdrawal periods

Meat and offal: zero days

Milk: zero hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:
Pituitary and hypothalamic hormones and analogues, gonadotropin-releasing hormones

ATC vet code: QH01CA01.

5.1 Pharmacodynamic properties

Gonadorelin is an agonist of the natural gonadotropin releasing hormone (GnRH) formed in the hypothalamus that is excreted in a pulsatile manner into the pituitary portal vein circulation and controls the synthesis of the follicle stimulating hormone (FSH) and luteinising hormone (LH) in the gonadotropic cells of the anterior pituitary gland as well as LH secretion. The pulse frequency and amplitude of the GnRH excretion are dependent on the stage of the cycle. Along with FSH, LH stimulates the release of estrogens from maturing follicles in the ovaries and induces ovulation in the female organism.

Gonadorelin acetate has the same effect as endogenous GnRH: the LH peak in the spontaneous cycle is imitated and causes follicular maturation and ovulation or stimulates a new follicle maturation wave.

With high dosage repeated or continuous application of an agonist, the gonadotropic cells in the pituitary become temporarily refractory.

In animals with delayed ovulation or anovulation, one of the most prominent findings is the delayed and smaller preovulatory LH surge. Injection of GnRH during oestrus increases the spontaneous LH peak and prevents delay in ovulation.

5.2 Pharmacokinetic particulars

Absorption

After intramuscular administration of 100 µg of gonadorelin (as acetate) to the animal, absorption of GnRH is rapid.

The maximum concentration (C_{max}) of 120.0 ± 34.2 ng / litre is obtained after 15 min (T_{max}). Concentrations of GnRH decreased rapidly in plasma.

The absolute bioavailability of gonadorelin (IM versus IV) was estimated to be around 89%.

Distribution

24 hours after intramuscular administration of 100 µg of radiolabelled gonadorelin (as diacetate), the greatest amounts of radioactivity in tissues were measured in the main organs of excretion: liver, kidney and lungs.

8 or 24 hours after the administration, gonadorelin shows an extensive plasma protein binding of 73%.

Metabolism

Gonadorelin is a naturally occurring peptide which is rapidly broken down into inactive metabolites.

Elimination

After intramuscular administration of gonadorelin to the dairy cow, the principal excretion route is milk followed by urine and faeces. A high percentage of the administered dose is excreted as carbon dioxide in expired air.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Potassium dihydrogen phosphate
Dipotassium phosphate
Sodium chloride
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Keep vial in outer carton in order to protect from light.
Do not store above 25 °C.

6.5 Nature and composition of immediate packaging

Amber glass type I vials closed with a grey bromobutyl elastomeric rubber plug, sealed with a plastic flip off button and an aluminium capsule.

Box containing 1 vial of 20 ml.

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

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

7. MARKETING AUTHORISATION HOLDER

Syn Vet-Pharma Ireland Limited
Business Service Group
7A Durands Court
45 Parnell Street
Waterford X91 P381
Ireland

8. MARKETING AUTHORISATION NUMBER

Vm 54400/4000

9. DATE OF FIRST AUTHORISATION

08 April 2020

10. DATE OF REVISION OF THE TEXT

March 2021

Approved: 04/03/21

