**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

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## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dalmarelin 25 micrograms/ml solution for injection for cattle and rabbits (AT, BE, BG, CY, CZ, DE, DK, ES, FI, HR, HU, IE, IS, IT, LU, MT, NL, NO, PL, PT, RO, SI, SK)

Reproréline 25 micrograms/ml solution for injection for cattle and rabbits (FR)

Dalmarelin Vet 25 micrograms/ml solution for injection for cattle and rabbits (SE)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

**Active substance:**

lecirelin 25 µg (as lecirelin acetate)

**Excipients:**

| **Qualitative composition of excipients and other constituents** | **Quantitative composition if that information is essential for proper administration of the veterinary medicinal product** |
|---|---|
| benzyl alcohol (E1519) | 20 mg |
| glacial acetic acid (E 260) | |
| disodium phosphate dodecahydrate (E339ii) | |
| sodium chloride | |
| water for injections | |

Clear, colourless solution, with no visible particles.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cattle (cows) and rabbits.

### 3.2 Indications for use for each target species

<u>Cattle</u>

- Treatment of follicular ovarian cysts.
- Cycle induction in early post-partum cows from day 14 post-partum.
- Induction of ovulation at the time of insemination in cases of short, silent heat or prolonged heat.
- Induction of ovulation in cycling cows in association with artificial insemination to optimise the time of ovulation.
- Induction and synchronisation of oestrus and ovulation in combination with prostaglandin F2α (PGF2α) or PGF2α analogue, with or without progesterone, as part of fixed time artificial insemination (FTAI) protocols.

Rabbits

- Induction of ovulation.
- Conception rate enhancement.

### 3.3 Contraindications

None.

### 3.4 Special warnings

The veterinary medicinal product should be administered to cows with normal ovaries at least 14 days after calving due to the absence of receptivity of the hypophysis before that time.
The veterinary medicinal product should be administered at least 35 days post-partum for the induction of ovulation in association with artificial insemination (with or without FTAI protocols).
The OvSynch procedure may not be as efficacious in heifers as in cows.

### 3.5 Special precautions for use

Special precautions for safe use in the target species:

Animals in poor condition, whether from illness, inadequate nutrition, or other factors, may respond poorly to treatment.

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

- People with known hypersensitivity to GnRH analogues and benzyl alcohol should avoid contact with the veterinary medicinal product.
- Lecirelin has been shown to be foetotoxic in rats; therefore, pregnant women should not handle the veterinary medicinal product. Women of child-bearing age should administer the veterinary medicinal product with caution.
- Avoid eye and skin contact with the veterinary medicinal product. In case of accidental contact, rinse thoroughly with water. Should skin contact with the veterinary medicinal product occur, wash the exposed area immediately with soap and water, as lecirelin, like all GnRH analogues, may be absorbed through the skin. Wash hands after use.
- When administering the veterinary medicinal product, care should be taken to avoid accidental self-injection by ensuring that animals are suitably restrained and the application needle is shielded until the moment of injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- Do not eat, drink or smoke while handling the veterinary medicinal product.

Special precautions for the protection of the environment:

Not applicable.

### 3.6 Adverse events

Cattle (cows) and rabbits: none known.

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 package leaflet for respective contact details.

### 3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The use is not recommended during pregnancy.
Can be used during lactation.

### 3.8 Interaction with other medicinal products and other forms of interaction

None known.

### 3.9 Administration routes and dosage

For intramuscular use.
The posology varies according to the indications and the animal species, as follows.

Cattle

- Treatment of follicular ovarian cysts: 4 ml of the veterinary medicinal product (100 µg of lecirelin).
- Cycle induction in early post-partum cows from day 14 post-partum: 2 ml of the veterinary medicinal product (50 µg of lecirelin).
- Induction of ovulation at the time of insemination in cases of short, silent heat or prolonged heat: 2 ml of the veterinary medicinal product (50 µg of lecirelin).
- Induction of ovulation in cycling cows in association with artificial insemination to optimise the time of ovulation: 2 ml of the veterinary medicinal product (50 µg of lecirelin). After oestrus detection, the veterinary medicinal product should be administered at the time of the artificial insemination (AI) or up to 8 hours beforehand. No more than 20 hours should elapse between onset of observable oestrus and AI.
- Induction and synchronisation of oestrus and ovulation in combination with prostaglandin F2α (PGF2α) or PGF2α analogue, with or without progesterone, as part of fixed time artificial insemination (FTAI) protocols: 2 ml of the veterinary medicinal product (50 µg of lecirelin).

On the basis of results of clinical studies and scientific literature, lecirelin can be used in combination with prostaglandin F2α (PGF2α)/PGF2α analogue, with or without progesterone, in protocols of induction and synchronization of ovulation (e.g. OvSynch) with fixed time artificial insemination (AI) in cattle.

The OvSynch (i.e. GnRH/prostaglandin/GnRH) protocol for breeding dairy cows at a pre-planned time without the need for specific heat detection is summarised below:

| | |
|---|---|
| Day 0 | 2 ml of the veterinary medicinal product (50 µg of lecirelin) |
| Day 7 | PGF2α/PGF2α analogue at luteolytic dose |
| Day 9 | 2 ml of the veterinary medicinal product (50 µg of lecirelin) |
| AI | 16 - 20 hours after the second lecirelin injection, or at observed oestrus if sooner |

The OvSynch protocol combined with progesterone supplementation for breeding dairy cows at a pre-planned time without the need for specific heat detection is summarised below:

| | |
|---|---|
| Day 0 | Insert progesterone releasing intravaginal device<br>Administer 2 ml of the veterinary medicinal product (50 µg of lecirelin) |
| Day 7 | Remove device<br>Administer PGF2α/PGF2α analogue at luteolytic dose |
| Day 9 | 2 ml of the veterinary medicinal product (50 µg of lecirelin) |

AI 16 - 20 hours after the second lecirelin injection, or at observed oestrus if sooner

Other protocols may be equally relevant in a given herd. Judgement on the protocol to be used should be made by the veterinarian responsible, on the basis of the characteristics of the individual herd.

Rabbits

- Induction of ovulation: 0.2 ml.
- Conception rate enhancement: 0.3 ml.

Treatment may be administered 24 h postpartum.
Mating or insemination must take place immediately after administration.

The closures should not be punctured more than 25 times.

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

No adverse reactions were recorded in cattle with up to 3 times the recommended dose and in rabbits with up to 2 times the recommended dose.

### 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

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

## 4. PHARMACOLOGICAL INFORMATION

### 4.1 ATCvet code: QH01CA92

### 4.2 Pharmacodynamics

Lecirelin is a synthetic analogue of gonadotropin releasing hormone (GnRH). It differs by substitution of D-tertiary leucine for glycine at position 6 and replacement of glycine by ethyl amide at position 10. Consequently, it is a nonapeptide.
Due to structural differences between lecirelin and natural GnRH, the lecirelin molecule shows greater persistence at the site of the specific hypophyseal receptors.

The physiological action of the gonadotropins results from stimulating the maturation of the follicle, inducing ovulation and the appearance of corpora lutea in the ovary.

### 4.3 Pharmacokinetics

Lecirelin, administered by the intramuscular route, is rapidly absorbed.
Plasma elimination occurs rapidly, whilst the hormonal action persists for several hours, because of greater persistence in binding to the receptor site.
However, pharmacokinetics is species and dose dependent.

GnRH-analogues accumulate primarily in the liver, kidney and hypophysis whereupon they are metabolised enzymatically, producing compounds devoid of pharmacological activity, which are subsequently excreted in the urine.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major incompatibilities

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

### 5.2 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.

### 5.3 Special precautions for storage

Do not store above 25 °C.

### 5.4 Nature and composition of immediate packaging

4, 10, 20 ml type I or type II neutral colourless glass vials, closed with a type I chlorobutyl rubber stopper and an aluminium overseal, in a cardboard box.
100 ml High Density Polyethylene (HDPE) collapsible container closed with a type I chlorobutyl rubber stopper and an aluminium overseal, in a cardboard box.

Package sizes:
- Cardboard box with 1 vial of 4 ml
- Cardboard box with 10 vials of 4 ml
- Cardboard box with 1 vial of 10 ml
- Cardboard box with 5 vials of 10 ml
- Cardboard box with 1 vial of 20 ml
- Cardboard box with 1 collapsible container of 100 ml

Not all pack sizes may be marketed.

### 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

FATRO S.p.A.

## 7. MARKETING AUTHORISATION NUMBERS

| | |
|---|---|
| Box with 1 vial of 4 ml | Marketing Authorisation No. : |
| Box with 10 vials of 4 ml | Marketing Authorisation No. : |
| Box with 1 vial of 10 ml | Marketing Authorisation No. : |
| Box with 5 vials of 10 ml | Marketing Authorisation No. : |
| Box with 1 vial of 20 ml | Marketing Authorisation No. : |
| Box with 1 collapsible container of 100 ml | Marketing Authorisation No. : |

## 8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

MM/YYYY

## 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*).