SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DALMARELIN 25 micrograms/ml solution for injection for cattle and rabbits (AT, DE, ES, FI, IE, IT, LU, NL, PT)

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:
Active substance:
lecirelin acetate equivalent to lecirelin……..……..... 25 µg

Excipients:
benzyl alcohol (E1519)..……..…….20 mg

For a 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 (cow) and rabbits.

4.2 Indications for use, specifying the target species

Cattle
- 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.

4.3 Contraindications

None.

4.4 Special warnings for each target species

The 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 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.

4.5 Special precautions for use

Special precautions for use in animals

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

Women of childbearing age should administer Dalmarelin with caution since lecirelin has been shown to be foetotoxic in rats. In case of accidental self-injection, seek medical advice.
GnRH-analogues may be absorbed through intact skin. In case of dermal contact wash the exposed area immediately with soap and water.

4.6 Adverse reactions (frequency and seriousness)

None observed.

4.7 Use during pregnancy, lactation or lay

The use of Dalmarelin is not recommended during pregnancy.
Dalmarelin can be used during lactation.

4.8 Interactions with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Administer by the intramuscular route.
The closures should not be punctured more than 25 times.
The posology varies according to the indications and the animal species, as follows.

Cattle

- Treatment of follicular ovarian cysts: 4 ml of the product (100 µg of lecirelin).
- Cycle induction in early post-partum cows from day 14 post-partum: 2 ml of the 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 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 product (50 µg of lecirelin). After oestrus detection, the 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 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 product (50 µg of lecirelin)
Day 7	PGF2α/PGF2α analogue at luteolytic dose
Day 9	2 ml of the 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 Administer 2 ml of the product (50 µg of lecirelin)
Day 7	Remove device Administer PGF2α/PGF2α analogue at luteolytic dose
Day 9	2 ml of the 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.

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

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.

4.11 Withdrawal periods

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

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Gonadotropin-releasing hormones
ATC Vet Code: QHO1CA92.

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Glacial acetic acid (E 260)
Disodium phosphate dodecahydrate (E339ii)
Sodium chloride
Water for injections

6.2 Major incompatibilities

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

Do not store above 25 °C.

6.5 Nature and composition of immediate packaging

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

Package sizes:
- 1 x 4 ml vial of product per box
- 10 x 4 ml vials of product per box
- 1 x 10 ml vial of product per box

- 5 x 10 ml vials of product per box
- 1 x 20 ml vial of product per box
- 1 x 100 ml collapsible container

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

FATRO S.p.A. - Via Emilia, 285 - Ozzano Emilia (Bologna), Italy.

8. MARKETING AUTHORISATION NUMBERS

To be completed locally

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

To be completed locally

10. DATE OF REVISION OF THE TEXT

To be completed locally

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

PACKAGE LEAFLET

DALMARELIN 25 micrograms/ml solution for injection for cattle and rabbits (AT, DE, ES, FI, IE, IT, LU, NL, PT)

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

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

FATRO S.p.A. - Via Emilia, 285 - Ozzano Emilia (Bologna), Italy.

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

DALMARELIN 25 micrograms/ml solution for injection for cattle and rabbits
lecirelin

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

1 ml contains:
Active substance: lecirelin acetate equivalent to lecirelin 25 µg - **Excipients:** benzyl alcohol (E1519) 20 mg.

4. INDICATIONS

Cattle
- 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.

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

None observed.
If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle (cow) and rabbits.

8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

Administer by the intramuscular route.
The closures should not be punctured more than 25 times.

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

Cattle

- Treatment of follicular ovarian cysts: 4 ml of the product (100 µg of lecirelin).
- Cycle induction in early post-partum cows from day 14 post-partum: 2 ml of the 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 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 product (50 µg of lecirelin). After oestrus detection, the 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 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 product (50 µg of lecirelin)
Day 7	PGF2α/PGF2α analogue at luteolytic dose
Day 9	2 ml of the 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 Administer 2 ml of the product (50 µg of lecirelin)
Day 7	Remove device Administer PGF2α/PGF2α analogue at luteolytic dose
Day 9	2 ml of the 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.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIOD

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

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not store above 25 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton after "EXP". The expiry date refers to the last day of that month.

Shelf-life after first opening the container: 28 days.

12. SPECIAL WARNINGS

Special warnings for each target species
The 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 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.

Special precautions for use in animals
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
Women of childbearing age should administer Dalmarelin with caution since lecirelin has been shown to be foetotoxic in rats. In case of accidental self-injection, seek medical advice.
GnRH-analogues may be absorbed through intact skin. In case of dermal contact wash the exposed area immediately with soap and water.

Pregnancy and lactation
The use of Dalmarelin is not recommended during pregnancy.
Dalmarelin can be used during lactation.

Interactions with other medicinal products and other forms of interaction
None known.

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

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

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicine should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

……..

15. OTHER INFORMATION

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.

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.

Package sizes:
- 1 x 4 ml vial
- 10 x 4 ml vials
- 1 x 10 ml vial
- 5 x 10 ml vials
- 1 x 20 ml vial
- 1 x 100 ml collapsible container

Not all pack sizes may be marketed.

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carboard box:
1 x 4 ml vial
10 x 4 ml vials
1 x 10 ml vial
5 x 10 ml vials
1 x 20 ml vial
1 x 100 ml collapsible container

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DALMARELIN 25 micrograms/ml solution for injection for cattle and rabbits (AT, DE, ES, FI, IE, IT, LU, NL, PT)

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

lecirelin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml contains:
Active substance: lecirelin acetate equivalent to lecirelin 25 µg

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZES

1 x 4 ml vial
10 x 4 ml vials
1 x 10 ml vial
5 x 10 ml vials
1 x 20 ml vial
1 x 100 ml collapsible container

5. TARGET SPECIES

Cattle (cow) and rabbits.

6. INDICATION(S)

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7. METHOD AND ROUTE OF ADMINISTRATION

For intramuscular administration.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

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

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP …….
Shelf life after first opening the container: 28 days
Once opened, use by _____

11. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

FATRO S.p.A. - Via Emilia, 285 - Ozzano Emilia (Bologna), Italy.

16. MARKETING AUTHORISATION NUMBER(S)

To be completed locally

17. MANUFACTURER'S BATCH NUMBER

Batch ……

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Label

4 ml vial
10 ml vial
20 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DALMARELIN 25 micrograms/ml solution for injection for cattle and rabbits (AT, DE, ES, FI, IE, IT, LU, NL, PT)

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

lecirelin

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Lecirelin 25 µg/ml

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

4 ml vial
10 ml vial
20 ml vial

4. ROUTE OF ADMINISTRATION

For i.m. administration.

5. WITHDRAWAL PERIOD

Meat/offal/milk: Zero days.

6. BATCH NUMBER

Batch……

7. EXPIRY DATE

EXP …….
Shelf-life after first opening the container: 28 days
Once opened, use by _____

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGE
Label
100 ml collapsible container

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DALMARELIN 25 micrograms/ml solution for injection for cattle and rabbits (AT, DE, ES, FI, IE, IT, LU, NL, PT)

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

lecirelin

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains:
Active substance: lecirelin acetate equivalent to lecirelin 25 µg

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZES

100 ml collapsible container

5. TARGET SPECIES

Cattle (cow) and rabbits.

6. INDICATION(S)

---

7. METHOD AND ROUTE OF ADMINISTRATION

For intramuscular administration.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

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

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP …….
Shelf-life after first opening the container: 28 days
Once opened, use by_____

11. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

FATRO S.p.A. - Via Emilia, 285 - Ozzano Emilia (Bologna), Italy.

16. MARKETING AUTHORISATION NUMBER(S)

To be completed locally

17. MANUFACTURER'S BATCH NUMBER

Batch ……