SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dalmaprost 0.075 mg/ml solution for injection for cattle, pigs and horses (ES, IE, IT, PL, SI, UK)

Dalmazin SYNCH 0.075 mg/ml solution for injection for cattle, pigs and horses (AT, BE, BG, CY, CZ, DE, DK, EE, EL, HR, HU, IS, LT, LU, LV, MT, NL, PT, RO, SK)

Reprostenol SYNCH 0.075 mg/ml solution for injection for cattle, pigs and horses (FR)

Dalmaprost vet 0.075 mg/ml solution for injection for cattle, pigs and horses (FI, NO, SE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
d-cloprostenol …….0.075 mg
(equivalent to d-cloprostenol sodium……..0.079 mg)

Excipients:
chlorocresol ……..……..…1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution, with no visible particles.

4. CLINICAL PARTICULARS

4.1. Target species

Cattle (cows), pigs (sows) and horses (mares).

4.2. Indications for use, specifying the target species

The product is indicated for:

Cows:

- Synchronisation or induction of oestrus;
- Induction of parturition after day 270 of gestation;
- Treatment of ovarian dysfunction (persistent *corpus luteum*, luteal cyst);
- Treatment of clinical endometritis with the presence of a functional *corpus luteum* and pyometra;

- Treatment of delayed uterine involution;
- Induction of abortion up to day 150 of gestation;
- Expulsion of mummified foetuses.

Sows:

- Induction of parturition after day 114 of gestation.

Mares:

- Induction of luteolysis with a functional *corpus luteum*.

4.3. Contraindications

Do not use in pregnant females, unless it is desirable to induce parturition or induction of abortion.
Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not administer to animals with cardiovascular, respiratory or gastrointestinal problems.
Do not administer to induce parturition in sows and cows with suspected dystocia due to mechanical obstruction or if problems are expected because of an abnormal position of the foetus.

4.4. Special warnings for each target species

The response of cows to the synchronization protocols is not homogenous nor between the herds, neither within the same herd, and may vary depending on the physiological state of the animal at the time of treatment (sensitivity and a functional state of the *corpus luteum*, age, physical condition, interval from calving, etc.).

4.5. Special precautions for use

Special precautions for use in animals

Induction of parturition and abortion may increase the risk of complications, retained placenta, foetal death and metritis.
To reduce the risk of anaerobic infections, which might be related to the pharmacological properties of prostaglandins, care should be taken to avoid injection through contaminated areas of skin. Clean and disinfect injection sites thoroughly before administration.
In case of oestrus induction in cows: from the 2nd day after injection, adequate heat detection is necessary.
Induction of parturition in sows before day 114 of gestation may result in an increased risk of stillbirths and the need for manual assistance at farrowing.

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

Prostaglandins of the F2α type can be absorbed through the skin and may cause bronchospasm or miscarriage.
Pregnant women, women of child-bearing age, asthmatics and people with bronchial or other respiratory problems, should avoid contact with, or wear disposable impervious-gloves when administering the product. Care should be taken when handling the product to avoid self-injection or skin contact.

In case of accidental spillage onto the skin, the area involved should be washed immediately with soap and water.
Should shortness of breath result from accidental inhalation or injection, seek medical advice and show the package leaflet or the label to the physician.

4.6. Adverse reactions (frequency and seriousness)

Occurrence of anaerobic infection is common if anaerobic bacteria penetrate the tissue of the injection site. This applies especially to intramuscular injection and in particular to cows. Typical local reactions due to anaerobic infection are swelling and crepitus at the injection site. When used for induction of parturition and depending on the moment of treatment relative to the date of conception, increase of placental retention rate can occur.

Behavioural changes in sows observed after treatment for induction of farrowing are similar to those changes associated with natural farrowing and usually cease within 1 hour.

Adverse reactions in horses including sweating (occurring within 20 minutes of treatment), increased respiratory and cardiac rates, signs of abdominal discomfort, watery diarrhoea and depression may occur when exceptionally high doses are given. However adverse reactions are usually mild and transient

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports)

4.7. Use during pregnancy, lactation or lay

Do not administer to pregnant animals unless the objective is to terminate the pregnancy.
The product can be used safely during lactation.

4.8. Interaction with other medicinal products and other forms of interaction

Do not administer the product together with nonsteroidal anti-inflammatory drugs since they inhibit endogenous prostaglandin synthesis. The activity of other oxytocic agents can be increased after the administration of the product.

4.9. Amounts to be administered and administration route

For intramuscular administration only.

COWS:
Administer one dose (2 ml) per animal of product (equivalent to 150 µg of d-cloprostenol per animal):

- **Induction of oestrus** (also in cows showing weak or silent heat): administer one dose of the product after having established the presence of a *corpus luteum* (6th -18th day of the cycle). Heat usually appears within 48-60 hours. Proceed with insemination 72-96 hours

after injection. If oestrus is not evident, administration of the product needs to be repeated 11 days after the first injection.

- **Synchronisation of oestrus:** administer one dose of the product twice (with an interval of 11 days between each dose). Proceed therefore with two artificial inseminations at intervals of 72 and 96 hours from the second injection.

  D-cloprostenol may be used in combination with GnRH, with or without progesterone, in the protocols for synchronization of the ovulation (Ovsynch protocols). The responsible veterinarian shall decide the protocol to be used, basing on the objective of the treatment, and on the herd and animals to be treated. The following protocols have been evaluated and may be used:

  In cycling cows:
  - Day 0: inject GnRH (or analogous).
  - Day 7: inject d-cloprostenol (one dose of the product).
  - Day 9: inject GnRH (or analogous).
  - 16-24 hours later perform artificial insemination.

  Alternatively in cycling or not-cycling cows and heifers:
  - Day 0: insert the intravaginal device for progesterone delivery and inject GnRH (or analogous).
  - Day 7: remove the intravaginal device and inject d-cloprostenol (one dose of the product).
  - Day 9: inject GnRH (or analogous).
  - 16-24 hours later perform artificial insemination.

- **Induction of parturition:** administer one dose of the product. Birth usually occurs within 30-60 hours of treatment.

- **Ovarian dysfunction (persistent *corpus luteum*, luteal cyst)**: once a *corpus luteum* has been detected, administer on dose of the product and inseminate at the first oestrus after injection. If oestrus is not evident, conduct a further gynaecological examination, and repeat the injection 11 days after the first administration. Insemination must be carried out 72-96 hours after injection.

- **Clinical endometritis with the presence of a functional *corpus luteum*, pyometra**: administer one dose of the product. If necessary, repeat the treatment after 10 days.

- **Delayed uterine involution**: administer one dose of the product and, if considered necessary, carry out one or two successive treatments at 24 hours intervals.

- **Induction of abortion**: administer one dose of the product in the first half of pregnancy.

- **Mummified foetus:** expulsion of the foetus is observed within 3-4 days after administration of one dose of the product.

MARES:
For the induction of luteolysis in mares with a functional *corpus luteum*: administer a single injection of 1 ml of product/animal (equivalent to 75 µg of d-cloprostenol).

SOWS:
For the **i**nduction of parturition in sows: administer 1 ml of the veterinary medicinal product, equivalent to 75 micrograms of d-cloprostenol/animal, by intramuscular route, not earlier than 114 days of pregnancy. The injection can be repeated after 6 hours.

The rubber stopper of the vial can be safely punctured up to 20 times. Otherwise, for the 100 ml vials automatic syringe equipment, or a suitable draw-off needle, should be used to prevent excessive puncture of the closure.

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

At 10 times the therapeutic dose, no adverse reactions were reported in cows and sows.
In general, a large overdose could result in the following symptoms: increased pulse and breathing rate, bronchoconstriction, increased body temperature, increased amounts of loose faeces and urine, salivation and vomiting. As no specific antidote has been identified, in the case of overdose, symptomatic therapy is advisable. An overdose will not accelerate *corpus luteum* regression.
In mares, moderate sweating and soft faeces were detected when the product was administered at 3 times the therapeutic dose.

4.11. Withdrawal periods

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

Pigs
Meat and offal: 1 day

Horses
Meat and offal: 2 days
Milk: zero hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: other gynecologicals, prostaglandins.
ATCvet code: QG02AD90

5.1. Pharmacodynamic properties

The veterinary medicinal product is a sterile aqueous solution containing dextrorotatory cloprostenol, a synthetic analogue of the prostaglandin F2α. The dextrorotatory enantiomer, d-cloprostenol, constitutes the biologically active (luteolytic) component of the racemic cloprostenol molecule. The veterinary medicinal product is approximately 3.5 times more active than similar veterinary medicinal products containing racemic cloprostenol, thus it can be administered at a proportionally lower dose level.
During the luteal phase of the oestrus cycle, d-cloprostenol induces a reduction of the number of receptors for luteinizing hormone (LH) in the ovary, which leads to a rapid regression of the *corpus luteum*.

5.2. Pharmacokinetic particulars

In cows, the highest plasma concentration of d-cloprostenol was found at 90 minutes after injection (approximately 1.4 µg/l). Elimination half-life is 1 h 37 minutes.
In sows, the highest plasma concentration is reached within 30 - 80 minutes after the injection. The elimination half-life is approximately 3 h and 12 minutes.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Chlorocresol
Sodium hydroxide
Citric acid
Ethanol (96 per cent)
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:
- glass vials: 30 months;
- HDPE containers: 18 months.

Shelf life after first opening the immediate packaging: 28 days.

6.4. Special precautions for storage

Store below 25 °C.
Keep the vial in the outer carton in order to protect from light.

6.5. Nature and composition of immediate packaging

Colourless type I glass vial (2 ml), colourless type II glass vials (10 ml and 20 ml) and transparent high density polyethylene (HDPE) container (100 ml), closed with a chlorobutyl type I stopper coated with a fluoroplastic film and a flip-off aluminium collar, in cardboard box.

Pack sizes:
Box with 15 vials of 2 ml
Box with 60 vials of 2 ml
Box with 1 vial of 10 ml
Box with 1 vial of 20 ml
Box with 1 HDPE container of 100 ml

Not all pack sizes may be marketed.

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.
{Invented name} should not enter water courses as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

Fatro S.p.A
Via Emilia, 285
Ozzano dell'Emilia (Bologna)
Italy

8. MARKETING AUTHORISATION NUMBERS

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31/07/2019

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]

PROHIBITION OF SALE, SUPPLY AND/OR USE