1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dalmazin, 75 micrograms/ml, solution for injection for cattle, buffaloes and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

(+)-Cloprostenol ..... 75 µg
(equivalent to (+)-Cloprostenol sodium salt…..79 µg)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Ethanol 96 per cent	
Chlorocresol	1 mg
Sodium hydroxide (for pH adjustment)	
Citric acid (for pH adjustment)	
Water for injections	

Clear, colourless solution for injection with no visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (cows), buffaloes (female) and pigs (sows and young females).

3.2 Indications for use for each target species

Cattle (cows) and buffaloes (female)

Zootechnical indications: synchronisation or induction of oestrus.
Induction and synchronisation of oestrus and ovulation in combination with GnRH or GnRH analogues, with or without progesterone, as part of fixed time artificial insemination (FTAI) protocols.
Induction of parturition after day 270 of gestation in cattle and within 10-15 days before expected calving in buffaloes.

Therapeutic indications: ovarian dysfunction (persistent corpus luteum, lutealcyst), treatment of uterine disorders related to a functioning or persistent corpus luteum (endometritis/pyometra).

Cattle (cows)

Zootechnical indications: induction of abortion in the first half of pregnancy.

Therapeutic indications: delayed uterine involution and expulsion of mummified foetuses.

Pigs (sows and young females)

Zootechnical indications: induction of parturition.

3.3 Contraindications

Do not use in pregnant females, unless it is desirable to induce parturition or induction of abortion.
Do not use in animals which are expected to have dystocia due to abnormal position/presentation of the foetus, mechanical obstruction, etc.
Do not use in animals suffering cardiovascular or respiratory diseases.
Do not use in animals with spastic diseases of the respiratory or gastrointestinal tract.
Do not administer by intravenous route.

3.4 Special warnings

The response of animals to the synchronisation protocols is not homogeneous between herds, nor 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.).
The efficacy of cloprostenol treatment in buffaloes may show a wide variation throughout the year as climate and particularly the photoperiod plays a pivotal role in the reproductive seasonality.

3.5 Special precautions for use

Special precautions for safe use in the target species:
As with parenteral administration of any substance, basic antiseptic rules should be observed.
The injection site must be thoroughly cleaned and disinfected in order to reduce the risk of infection with anaerobic bacteria.
Induction of parturition before the 111th day of gestation may cause mortality in piglets and an increase in the number of sows that require manual assistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Prostaglandins of the $F_{2\alpha}$ type can be absorbed through the skin and may cause bronchospasm or miscarriage.
Chlorocresol may cause irritation and allergic reactions. People with known hypersensitivity to chlorocresol should administer the veterinary medicinal product with caution.
Care should be taken when handling the product to avoid self-injection or skin contact.
Pregnant women, women of child-bearing age, asthmatics and people with bronchial or other respiratory problems, should avoid contact with, or wear disposable plastic gloves when administering the product.
Accidental spillage on the skin should be washed off immediately with soap and water.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Should shortness of breath result from accidental inhalation or injection, seek urgent medical advice and show the doctor this warning.
Do not eat, drink or smoke while handling the product.

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

3.6 Adverse events

Cattle (cows), buffaloes (female) and pigs (sows and young females):

Undetermined frequency	Injection site infection[a]. Injection site swelling[a]. Crepitus[a]. Retained placenta[b]. Behavioural changes[c].

[a] due to anaerobic infection, especially after intramuscular injection in cows.

[b] dependent on the time of treatment relative to the date of conception, the incidence in cows may be increased.

[c] similar to those changes associated with natural farrowing in sows usually ceasing within one hour.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinarymedicinal 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:

Do not use in pregnant animals unless it is desirable to induce parturition or abortion.

3.8 Interaction with other medicinal products and other forms of interaction

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

3.9 Administration routes and dosage

For intramuscular use.

Cattle (cows) and buffaloes (female)

Administer 2 ml of the veterinary medicinal product, equivalent to 150 micrograms of (+)-Cloprostenol/animal by intramuscular route.

In particular:

- Induction of oestrus: administer the veterinary medicinal product after having established the presence of a corpus luteum (6-18th day of the cycle); heat usually appears within 48-60 hours. Proceed, therefore, 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 the veterinary medicinal 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.
- Induction and synchronisation of oestrus and ovulation in combination with GnRH or GnRH analogue, with or without progesterone, as part of fixed time artificial insemination (FTAI) protocols (e.g. OvSynch).
  Judgment on the protocol to be used should be made by responsible veterinarian, on the basis of the intended objective and characteristics of the individual herd or animal.

  The following protocols have been evaluated and could be used:

  The OvSynch (i.e. GnRH/prostaglandin/GnRH) protocol for breeding dairy cows and female

buffaloes at a pre-planned time without the need for specific heat detection is summarised below:

Day 0	GnRH or GnRH analogue
Day 7	2 ml of the product (150 micrograms of (+)-Cloprostenol)
Day 9	GnRH or GnRH analogue
AI	16 - 20 hours after the second GnRH or GnRH analogue injection, or at observed oestrus if sooner

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

Day 0	Insert progesterone releasing intravaginal device Administer GnRH or GnRH analogue
Day 7	Remove device Administer 2 ml of the product (150 micrograms of (+)-Cloprostenol)
Day 9	GnRH or GnRH analogue
AI	16 - 20 hours after the second GnRH or GnRH analogue injection, or at observed oestrus if sooner

Other protocols may be equally relevant.

- Induction of parturition: administer the veterinary medicinal product after 270 days of pregnancy in cattle and within 10-15 days before expected calving in buffaloes. Birth usually results within 30-60 hours of treatment.
- Ovarian dysfunction (persistent corpus luteum, luteal cysts): administer the veterinary medicinal product, then proceed to 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 always be carried out 72-96 hours after injection.
- Endometritis, pyometra: administer the veterinary medicinal product and if necessary repeat the treatment after 10-11 days.

Cattle (cows)
- Mummified foetus: expulsion of the foetus is observed within 3-4 days after administration of the veterinary medicinal product.
- Induction of abortion: administer the veterinary medicinal product in the first half of pregnancy.
- Delayed uterine involution: administer the veterinary medicinal product and, if considered necessary, carry out one or two successive treatments at 24 hour intervals.

<u>Pigs (sows and young females)</u>
Administer 1 ml of the veterinary medicinal product, equivalent to 75 micrograms of (+)-Cloprostenol/animal, by intramuscular route, not earlier than 112 days of pregnancy. Repeat after 6 hours. Alternatively, 20 hours after the initial dose of the veterinary medicinal product, a myometrial stimulant (oxytocin or carazolol) may be administered.
Following the protocol of the double administration, approximately 70-80% of the animals will give birth during the interval between 20 and 30 hours after the first administration.

As with every prostaglandin-based product, injection in contaminated skin areas is to be avoided in order to reduce the risk of infection with anaerobic bacteria.

The injection site must be thoroughly cleaned and disinfected before administration.

The closures should not be punctured more than 25 times for all the pack sizes from 10 ml to 100 ml and more than 2 times for the 2 ml pack size.

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

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.

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 (cows): Meat and offal: Zero days
Milk: Zero hours

Buffaloes (female): Meat and offal: 1 day
Milk : Zero hours

Pigs (sows and young females): Meat and offal: 1 day

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QG02AD90

4.2 Pharmacodynamics

The veterinary medicinal product is a sterile aqueous solution containing 75 micrograms/ml of dextrorotatory cloprostenol, a synthetic analogue of the prostaglandin $F_{2\alpha}$.
(+)-Cloprostenol, the dextrorotatory enantiomer, constitutes the biologically active component of the racemic cloprostenol molecule and results in an approximate 3.5-fold increase in activity. Administered in the luteal phase of the oestrus cycle, (+)-Cloprostenol induces functional and morphological regression of the corpus luteum (luteolysis) resulting in a sharp fall in progesterone levels. The increased release of the follicle stimulating hormone (FSH), induces the follicular maturation followed by signs of oestrus and by ovulation.

4.3 Pharmacokinetics

Pharmacokinetic studies demonstrate a rapid absorption of (+)-Cloprostenol. The peak blood level is reached a few minutes following intramuscular administration, as well as a rapid diffusion to the ovaries and uterus, the organs in which the maximum concentration is reached 10-20 minutes after administration.
Following intramuscular administration of 150 micrograms of (+)-Cloprostenol in cows, the peak plasma level (C_{max}) of 1.4 micrograms/l is reached after approximately 90 minutes, while the elimination half life ($t_{½\beta}$) is in the order of 1 hour 37 minutes. In sows, a C_{max} of approximately 2micrograms/l is observed between 30 and 80 minutes following administration of 75 micrograms (+)- Cloprostenol, with an elimination half life in the order of 3 hours 10 minutes.

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

5.3 Special precautions for storage

Store below 25°C.

5.4 Nature and composition of immediate packaging

Colourless type I glass vials (2 ml) closed with a chlorobutyl type I rubber stopper coated with a fluoroplastic film and an aluminium overseal, placed in polyvinyl chloride (PVC) blisters, in a cardboard box.
Colourless type II glass vials (10 ml, 20 ml and 50 ml), transparent high density polyethylene (HDPE) multidose container (100 ml), closed with a chlorobutyl type I rubber stopper coated with a fluoroplastic film and an aluminium overseal in a cardboard or an aluminium box.

Package sizes:
Cardboard box with 1 blister of 15 vials of 2 ml solution for injection
Cardboard box with 4 blister of 15 vials of 2 ml solution for injection (60 vials)
Cardboard box with 1 vial of 10 ml solution for injection
Cardboard box with 10 vials of 10 ml solution for injection
Cardboard box with 1 vial of 20 ml solution for injection
Aluminium box with 5 vials of 20 ml solution for injection
Cardboard box with 1 vial of 50 ml solution for injection
Cardboard box with 1 HDPE multidose container of 100 ml solution for injection

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.
The product should not enter water courses as this may be dangerous for fish and other aquatic organisms.
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 NUMBER(S)

VPA10836/001/001

8. DATE OF FIRST AUTHORISATION

13/10/2000

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

28/07/2025

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*).