

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box:
1 x 2 ml vial + syringe
15 x 2 ml vials
60 x 2 ml vials
1 x 10 ml vial
10 x 10 ml vials
1 x 20 ml vial
Aluminium box
5 x 20 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains d-cloprostenol 75 µg

3. PACKAGE SIZE

1 x 2 ml + syringe
15 x 2 ml
60 x 2 ml
1 x 10 ml
10 x 10 ml
1 x 20 ml
5 x 20 ml

4. TARGET SPECIES

Cattle (cows) and pigs (sows and young females).

5. INDICATIONS

--- --- ---

6. ROUTES OF ADMINISTRATION

For intramuscular use.

7. WITHDRAWAL PERIODS

Withdrawal period:

Meat and offal:

cattle Zero days

pigs 1 day

Milk: Zero hours

8. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

Use by _____

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

To be supplied only on veterinary prescription.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

FATRO S.p.A.

14. MARKETING AUTHORISATION NUMBERS

1 vial of 2 ml + syringe	Marketing Authorisation No.: Vm 11557/3001
15 vials of 2 ml	Marketing Authorisation No.: Vm 11557/3001
60 vials of 2 ml	Marketing Authorisation No.: Vm 11557/3001
1 vial of 10 ml	Marketing Authorisation No.: Vm 11557/3001
10 vials of 10 ml	Marketing Authorisation No.: Vm 11557/3001
1 vial of 20 ml	Marketing Authorisation No.: Vm 11557/3001
5 vials of 20 ml	Marketing Authorisation No.: Vm 11557/3001

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

10 ml vial - 20 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains d-cloprostenol 75 µg

3. TARGET SPECIES

Cattle (cows) and pigs (sows and young females).

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.
For intramuscular use.

5. WITHDRAWAL PERIODS

Withdrawal period:

Meat and offal:

cattle Zero days

pigs 1 day

Milk: Zero hours

6. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

Use by _____

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

FATRO S.p.A.

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

2 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dalmazin

Reprosténol

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

d-cloprostenol 75 µg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days

Use by_____

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

Each ml contains:

Active substance: d-cloprostenol 75 µg

Excipients: chlorocresol 1 mg

Clear, colourless solution for injection with no visible particles.

3. Target species

Cattle (cows) and pigs (sows and young females).

4. Indications for use

Cows

Indications for reproduction: synchronisation or induction of oestrus. Induction of parturition after day 270 of gestation.

Therapeutic indications: ovarian dysfunction (persistent corpus luteum, luteal cyst), endometritis/pyometra, delayed uterine involution, induction of abortion in the first half of pregnancy and expulsion of mummified fetuses.

Sows and young females

Indications for reproduction: induction of parturition.

5. Contraindications

Do not use in pregnant females, unless it is desirable to induce parturition or induction of abortion.

Do not use in sows which are expected to have a distocic parturition due to abnormal position 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.

6. Special warnings

None.

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 labour before the 111th day of gestation may cause mortality in piglets and an increase in the number of sows that require manual assistance.

Do not administer by intravenous route.

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.

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.

Pregnancy and lactation:

Do not use in gestating animals unless it is desirable to induce parturition or therapeutic induction of abortion.

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.

Overdose:

At 10 times the therapeutic dose, no adverse reactions were reported. 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.

Special restrictions for use and special conditions for use:

Not applicable.

Major incompatibilities:

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

7. Adverse events

Cattle (cows) 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 product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or to the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system {national system details}.

8. Dosage for each species, routes and method of administration

For intramuscular use.

Cows

Administer 2 ml of the veterinary medicinal product, equivalent to 150 micrograms of d-cloprostenol/animal by intramuscular route. Repeat after 11 days for the synchronisation of oestrus.

The dose of 2 ml equivalent to 150 micrograms of d-cloprostenol/animal by intramuscular route can be repeated for the induction of oestrus and for the treatment of ovarian dysfunction, endometritis/pyometra and delayed uterine involution.

In particular:

- Induction of oestrus (also in cows showing weak or silent heat): 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 of parturition: administer the veterinary medicinal product after 270 days of pregnancy. Birth usually results within 30-60 hours of treatment.
- 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.
- 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.
- Delayed uterine involution: administer the veterinary medicinal product and, if considered necessary, carry out one or two successive treatments at 24 hour intervals.

Sows and young females

Administer 1 ml of the veterinary medicinal product, equivalent to 75 micrograms of d-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.

9. Advice on correct 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 20 times

10. Withdrawal periods

Meat and offal:

cattle	Zero days
pigs	1 day

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 label after Exp.

The expiry date refers to the last day of that month.

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

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

1 vial of 2 ml + syringe	Marketing Authorisation No. : Vm 11557/3001
15 vials of 2 ml	Marketing Authorisation No. : Vm 11557/3001
60 vials of 2 ml	Marketing Authorisation No. : Vm 11557/3001
1 vial of 10 ml	Marketing Authorisation No. : Vm 11557/3001
10 vials of 10 ml	Marketing Authorisation No. : Vm 11557/3001
1 vial of 20 ml	Marketing Authorisation No. : Vm 11557/3001
5 vials of 20 ml	Marketing Authorisation No. : Vm 11557/3001

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

March 2023

Detailed information on this veterinary medicinal product is available in the Union Product Database.
(<https://medicines.health.europa.eu/veterinary>).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release:

Fatro S.p.A
Via Emilia, 285
40064 Ozzano Emilia
Bologna
Italy

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information

The veterinary medicinal product is a sterile aqueous solution containing 75 micrograms/ml of dextrorotatory cloprostenol, a synthetic analogue of the prostaglandin F_{2α}.
d-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, d-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.

Pharmacokinetic studies demonstrate a rapid absorption of d-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 d-cloprostenol in the cows, the peak plasma level (C_{max}) of 1.4 micrograms/l is reached after approximately 90 minutes, while the elimination half life ($t_{1/2\beta}$) is in the order of 1 hour 37 minutes. In sows, a C_{max} of approximately 2 micrograms/l is observed between 30 and 80 minutes following administration of 75 micrograms d-cloprostenol, with an elimination half life in the order of 3 hours 10 minutes.



Approved: 02 June 2023