[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dalmazin, 75 micrograms/ml, solution for injection for cattle, buffaloes and pigs (AT, BE, DE, IE, IT, LU, NI).

Reprosténol, 75 micrograms/ml, solution for injection for cattle, buffaloes and pigs (FR).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

d-cloprostenol..... 75 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	
Chlorocresol	1 mg
Sodium hydroxide	
Citric acid	
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 d-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 d-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 d-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 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.

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.

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 $F_{2\alpha}$.
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.

4.3 Pharmacokinetics

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 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 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.

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

Do not store above 25 °C

5.4 Nature and composition of immediate packaging

2 ml, 10 ml, 20 ml vials in glass type I or type II, closed with a chlorobutyl rubber stopper with an aluminium overseal in a cardboard or an aluminium box.

Package sizes:
Cardboard box with 1 vial of 2 ml + syringeCardboard box with 15 vials of 2 ml Cardboard box with 60 vials of 2 ml Cardboard box with 1 vial of 10 ml Cardboard box with 10 vials of 10 ml Cardboard box with 1 vial of 20 ml Aluminium box with 5 vials of 20ml

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)

1 vial of 2 ml + syringe	Marketing Authorisation No. :
15 vials of 2 ml	Marketing Authorisation No. :
60 vials of 2 ml	Marketing Authorisation No. :
1 vial of 10 ml	Marketing Authorisation No. :
10 vials of 10 ml	Marketing Authorisation No. :
1 vial of 20 ml	Marketing Authorisation No. :
5 vials of 20ml	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*).

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, buffaloes and pigs (AT, BE, DE, IE, IT, LU, NI).

Reprosténol, 75 micrograms/ml, solution for injection for cattle, buffaloes and pigs (FR).

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

5. INDICATIONS

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6. ROUTES OF ADMINISTRATION

For intramuscular use.

7. WITHDRAWAL PERIODS

Withdrawal period:

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

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.:
15 vials of 2 ml	Marketing Authorisation No.:
60 vials of 2 ml	Marketing Authorisation No.:
1 vial of 10 ml	Marketing Authorisation No.:
10 vials of 10 ml	Marketing Authorisation No.:
1 vial of 20 ml	Marketing Authorisation No.:
5 vials of 20 ml	Marketing Authorisation No.:

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

2 ml vial – 10 ml vial – 20 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, buffaloes and pigs (AT, BE, DE, IE, IT, LU, NI).

Reprosténol, 75 micrograms/ml, solution for injection for cattle, buffaloes and pigs (FR).

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

4. Indications for use

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, luteal cyst), 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.

5. 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.

6. Special warnings

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.

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.

Pregnancy and lactation:
Do not use in pregnant animals unless it is desirable to induce parturition or 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 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.

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 withother veterinary medicinal products.

7. 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 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.

Cattle (cows) and buffaloes (female)
Administer 2 ml of the veterinary medicinal product, equivalent to 150 micrograms of d-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 d-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 d-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.

Pigs (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

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

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

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

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.
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 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. :
15 vials of 2 ml	Marketing Authorisation No. :
60 vials of 2 ml	Marketing Authorisation No. :
1 vial of 10 ml	Marketing Authorisation No. :
10 vials of 10 ml	Marketing Authorisation No. :
1 vial of 20 ml	Marketing Authorisation No. :
5 vials of 20 ml	Marketing Authorisation No. :

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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 dell'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 $F_{2\alpha}$.
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 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 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.