

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Luteoplan 250 micrograms/ml solution for injection for cattle and horses.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Cloprostenol 250 micrograms
(equivalent to 263 micrograms cloprostenol sodium)

Excipients:

| Qualitative composition of excipients and other constituents | Quantitative composition if that information is essential for proper administration of the veterinary medicinal product |
|--|---|
| Chlorocresol | 1.0 mg |
| Citric acid | |
| Sodium hydroxide (for pH adjustment) | |
| Ethanol, anhydrous | |
| Water for injections | |

Clear, colourless solution for injection.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (cows and heifers) and horses (mares).

3.2 Indications for use for each target species

Cattle (cows and heifers):

- Oestrus induction and synchronisation in cows and heifers with a functional corpus luteum.
- Induction of oestrus as an aid to management of suboestrus ('silent heat').
- Treatment of clinical and subclinical endometritis in the presence of a functional corpus luteum.
- Treatment of ovarian luteal cysts.
- Induction of parturition after day 270 of gestation.
- Induction of abortion up to day 150 of gestation.

Horses (mares):

- Oestrus induction and synchronisation in mares with a functional corpus luteum.
- Termination of early pregnancy between day 5 and day 120 of gestation.

3.3 Contraindications

Do not use in pregnant animals in which the induction of abortion or parturition is not intended.

Do not administer to induce parturition in animals with suspected dystocia due to mechanical obstruction or abnormal position, presentation and/or posture of the foetus.

Do not use in animals with compromised cardiovascular function, bronchospasm or gastrointestinal dysmotility.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

There is a refractory period of several days after ovulation (e.g. four to five days in cattle and horses), when females are insensitive to the luteolytic effect of prostaglandins.

For the termination of gestation in cattle, best results are obtained before day 100 of gestation. Results are less reliable between day 100 and 150 of gestation.

3.5 Special precautions for use

Special precautions for safe use in the target species:

To reduce the risk of anaerobic infections arising from vasoconstriction at the injection site, injections into contaminated (wet or dirty) skin areas should be avoided. Thoroughly clean and disinfect injection sites prior to administration.

Do not administer intravenously.

All animals should receive adequate supervision after treatment.

Induction of parturition or abortion may cause dystocia, stillbirth and/or metritis. The incidence of retained placenta may be increased depending on the time of treatment relative to the date of conception.

Injection into adipose tissue can result in incomplete absorption of the veterinary medicinal product.

Cloprostenol may cause effects related to Prostaglandin F_{2α} activity in the smooth muscles, such as increased frequency of urination and defecation.

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

Prostaglandins of the F_{2α} type, such as cloprostenol, may be absorbed through the skin and may cause bronchospasm or miscarriage. Care should be taken when handling the veterinary medicinal product to avoid self-injection or skin contact.

Pregnant women, women of childbearing age, asthmatics and persons with other respiratory tract diseases should avoid contact when handling this veterinary medicinal product. Personal protective equipment consisting of impervious gloves should be worn when handling the veterinary medicinal product.

Accidental spillage on the skin should be washed immediately with soap and water. If accidental contact with eyes occurs, rinse the affected eyes thoroughly with clean, fresh water. In case of accidental self-injection or spillage onto the skin seek medical advice immediately, particularly as shortness of breath may occur, and show the package leaflet or label to the physician.

Chlorocresol may cause irritation and allergic reactions. People with known hypersensitivity to chlorocresol should administer the veterinary medicinal product with caution.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle (cows and heifers):

| | |
|--|---|
| Rare (1 to 10 animals / 10,000 animals treated): | Injection site infection ¹ |
| Very rare (<1 animal / 10,000 animals treated, including isolated reports): | Anaphylaxis ² ; Increased respiratory rate ³ ; Increased heart rate ³ ; Abdominal pain ³ , Diarrhoea ^{3,5} ; Incoordination ³ ; Lying down ³ ; Retained placenta ⁴ , Metritis ⁴ , Dystocia ⁴ , Stillbirth ⁴ ; Restlessness, Frequent urination ^{3,5} ; |

¹ May occur if anaerobic bacteria enter the injection site, especially following intramuscular injection, and may become generalized. Aggressive antibiotic therapy, particularly covering clostridial species, should be employed at the first sign of infection. Careful aseptic techniques should be employed to decrease the possibility of these infections.

² Requiring immediate medical attention. Can be life-threatening.

³ Cloprostenol may cause effects similar to Prostaglandin F_{2α} activity in the smooth muscles.

⁴ May be caused by induction of parturition or abortion. As part of induction of parturition, depending on the date of treatment versus the date of conception, the incidence of placental retention may be increased.

⁵ In case of occurrence, these effects are observed within 15 minutes post-injection and usually disappear after one hour.

Horses (mares):

| | |
|--|--|
| Uncommon (1 to 10 animals / 1,000 animals treated): | Abnormal oestrus ¹ ; |
| Rare (1 to 10 animals / 10,000 animals treated): | Injection site infection ² |
| Very rare (<1 animal / 10,000 animals treated, including isolated reports): | Anaphylaxis ³ ; Increased respiratory rate ⁴ ; Increased heart rate ⁴ ; Increased sweating ^{4,5} ; Abdominal pain ⁴ , Colic ⁶ , Diarrhoea ^{4,8} ; Incoordination ⁴ , Muscle tremor ⁵ ; Lying down ⁴ , Decreased body temperature ⁴ ; Retained placenta ⁷ , Metritis ⁷ , Dystocia ⁷ , Stillbirth ⁷ ; Restlessness, Frequent urination ^{4,8} ; |

¹ Haemorrhagic (anovular) follicles and multiple ovulations are reported in literature for horses treated with cloprostenol.

² May occur if anaerobic bacteria enter the injection site, especially following intramuscular injection, and may become generalized. Aggressive antibiotic therapy, particularly covering clostridial species, should be employed at the first sign of infection. Careful aseptic techniques should be employed to decrease the possibility of these infections.

³ Requiring immediate medical attention. Can be life-threatening.

⁴ Cloprostenol may cause effects similar to Prostaglandin F_{2α} activity in the smooth muscles.

⁵ Appears to be transient and resolves without any treatment.

⁶ Mild.

⁷ May be caused by termination of gestation, depending on the date of treatment versus the date of conception, the incidence of placental retention may be increased.

⁸ In case of occurrence, these effects are observed within 15 minutes post-injection and usually disappear after one hour.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal 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 the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:

Do not use in pregnant animals in which the induction of abortion or parturition is not intended.

Lactation:

The product can be used during lactation.

Fertility:

Cloprostenol has a large safety margin and does not negatively affect fertility in cattle. Nor have any harmful effects been reported in the offspring of an insemination or mating following treatment with this veterinary medicinal product for conception products obtained after treatment.

3.8 Interaction with other medicinal products and other forms of interaction

The concomitant use of oxytocin and cloprostenol increases the effects on the uterus.

The concomitant use of progestogens decreases the effect of cloprostenol.

Do not administer with non-steroidal anti-inflammatory drugs (NSAIDs) since they inhibit endogenous prostaglandin synthesis.

3.9 Administration routes and dosage

Intramuscular use.

Cattle (cows and heifers):

One dose equals 500 micrograms of cloprostenol per animal, corresponding to 2 ml of the veterinary medicinal product.

Oestrus induction and synchronisation:

Administer one dose per animal. When no oestrus symptoms are observed, a second dose can be administered after 11 days.

Treatment of clinical and subclinical endometritis in the presence of a functional corpus luteum:

Administer one dose per animal. If necessary, repeat the treatment 10-14 days later.

Treatment of ovarian luteal cysts:

Administer a single dose per animal.

Induction of parturition:

Administer a single dose per animal, not earlier than 10 days before the expected date of calving.

Induction of abortion up to day 150 of gestation:

Administer a single dose per animal, between the 5th and the 150th day of gestation.

Horses (mares):

Ponies and horses weighing less than 500 kg bodyweight:

One dose equals 125 – 250 micrograms of cloprostenol per animal, corresponding to 0.5 – 1 ml of the veterinary medicinal product.

Horses weighing more than 500 kg bodyweight:

One dose equals 250 – 500 micrograms of cloprostenol per animal, corresponding to 1 – 2 ml of the veterinary medicinal product.

Oestrus induction and synchronisation:
Administer a single dose per animal.

Termination of early gestation between day 5 and day 120:

Administer a single dose per animal, not earlier than 5 days after ovulation.

The stopper may be safely punctured up to 10 times. When treating groups of animals in one run, use a draw-off needle that has been placed in the vial stopper to avoid excess broaching of the stopper. The draw-off needle should be removed after treatment.

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

Cattle: At 5x to 10x overdose the most frequent side effect is increased rectal temperature. This is usually transient, however, and not detrimental to the animal. Limited salivation or transient diarrhoea may also be observed in some animals.

Horses: The most frequently observed side effects are sweating and decreased rectal temperatures. These are usually transient, however, and not detrimental to the animal. Other possible reactions are increased heart rate, increased respiratory rate, abdominal discomfort, locomotor incoordination and lying down. If these occur, they are likely to be seen within 15 minutes of injection and disappear within 1 hour. Mares usually continue to eat throughout.

There are no antidotes available, treatment should be symptomatic, assuming that prostaglandin F_{2α} influences the smooth muscle cells.

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:

Meat and offal: 1 day.

Milk: Zero hours.

Horses:

Meat and offal: 2 days.

Milk: 24 hours.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QG02AD90

4.2 Pharmacodynamics

Cloprostenol sodium, a (racemic) analogue of prostaglandin F_{2α} (PGF_{2α}), is a very potent luteolytic agent. It causes functional and morphological regression of the corpus luteum (luteolysis) followed by return to oestrus and normal ovulation.

Furthermore, this group of substances has a contractile effect on the smooth muscles (uterus, gastrointestinal tract, respiratory tract, vascular system).

The veterinary medicinal product does not demonstrate any androgenic, oestrogenic or anti progesterone activity and its effect on pregnancy is due to its luteolytic property.

Unlike other prostaglandin analogues, cloprostenol has no thromboxane A₂ activity and does not cause platelet aggregation.

4.3 Pharmacokinetics

Metabolism studies, using 15-¹⁴C-cloprostenol have been performed in cattle (by IM administration) to determine residue levels.

The kinetic studies indicate that the compound is rapidly absorbed from the site of injection, is metabolised then excreted in approximately equal proportion in urine and faeces. In cattle, less than 1% of the administered dose is eliminated via milk. The major route of metabolism appears to be β-oxidation to the tetranor or dinor acids of cloprostenol.

Peak values of radioactivity in blood were observed within 1 hour of a parenteral dose and declined with a t_½ of between 1 – 3 hours depending on species.

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: 2 years.

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

5.3 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions.

This veterinary medicinal product should be stored upright.

5.4 Nature and composition of immediate packaging

Amber Type I glass vial with grey elastomeric bromobutyl rubber stoppers sealed with a plastic flip off button and an aluminium cap.

Package size:

Cardboard box with 1 vial of 20 ml.

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 veterinary medicinal product should not enter water courses as cloprostenol 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

Syn Vet-Pharma Ireland Limited.

7. MARKETING AUTHORISATION NUMBER(S)

VPA23174/004/001

8. DATE OF FIRST AUTHORISATION

13/10/2023

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

12/02/2026

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 \(https://medicines.health.europa.eu/veterinary\)](https://medicines.health.europa.eu/veterinary).