SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Luteoplan 0.25 mg/ml solution for injection for cattle and horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each ml contains:

Cloprostenol	0.25 mg
(as cloprostenol sodium	0.263 mg)

Excipients:

Chlorocresol	1.0 mg/ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution for injection.

4. CLINICAL PARTICULARS

4.1 Target species

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

4.2 Indications for use, specifying the target species

Cattle (heifers, cows):
- Synchronisation or induction of oestrus;
- Treatment of ovarian dysfunction (persistent corpus luteum, luteal cyst);
- Treatment of uterine disorders related to a functioning or persistent corpus luteum (endometritis, pyometra);
- Induction of abortion until day 150 of pregnancy;
- Expulsion of mummified foetuses;
- Induction of parturition

Horses (mares):
Induction of luteolysis with a functional corpus luteum

4.3 Contraindications

Do not use in pregnant animals unless the objective is to induce parturition or abortion. Do not use in animals with cardiovascular, gastro-intestinal or respiratory problems.
Do not administer to induce parturition in cattle with suspected dystocia due to mechanical obstruction or if problems are expected because of an abnormal position of the foetus.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not administer intravenously.

4.4 Special warnings for each target species

There is a refractory period of four to five days after ovulation when cattle and horses are insensitive to the luteolytic effect of prostaglandins.

Cattle:

For the induction of abortion, best results are obtained before day 100 of gestation. Results are less reliable between day 100 and 150 of gestation.
In case of oestrus induction in cattle: from the 2nd day after injection, adequate heat detection is necessary.

4.5 Special precautions for use

i). 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 (e.g. swelling, crepitus), 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.
All animals should receive adequate supervision after treatment.

ii). Special precautions to be take by the person administering the veterinary medicinal product to animals

Prostaglandins of the F2α type, such as cloprostenol, can 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 child-bearing age, asthmatics and people with bronchial or other respiratory problems should avoid any contact with the veterinary medicinal product.

Wear disposable impervious gloves when administering the veterinary medicinal product.

Accidental spillage on the skin should be washed off 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.

Do not eat, drink or smoke while handling the veterinary medicinal product. Chlorocresol may cause irritation and allergic reactions. People with known hypersensitivity to chlorocresol should administer the veterinary medicinal product with caution.

4.6 Adverse reactions (frequency and seriousness)

In cattle:

Rare (1 to 10 animals / 10,000 animals treated):	Injection site infection (which may become generalised)[*1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylaxis[*2]
Undetermined frequency	Dystocia, foetal death, retained placenta and/or metritis[*3]

[*1] Typical local reactions due to anaerobic infection are swelling and crepitus at the injection site.
[*2] Anaphylactic reactions require immediate medical attention.
[*3] These adverse events may be observed when used in cattle for induction of parturition or abortion, dependent on the time of treatment relative to the date of conception.

In horses:

Rare (1 to 10 animals / 10,000 animals treated):	Injection site infection (which may become generalised)[*1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylaxis[*2]
Undetermined frequency	Increased sweating[*3] Incoordination, muscle tremors[*3] Increased heart rate Increased respiratory rate Abdominal discomfort, loose stool[*4] Lying down.

[*1] Typical local reactions due to anaerobic infection are swelling and crepitus at the injection site.
[*2] Anaphylactic reactions require immediate medical attention.
[*3] Mild sweating and muscle tremors that may occur after treatment appear to be transient and resolve without any treatment.
[*4] Loos stool may be passed shortly after treatment.

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 also the last section of the package leaflet for respective contact details.

4.7 Use during pregnancy, lactation or lay

Do not administer to pregnant animals unless the objective is to induce parturition or abortion.

The veterinary medicinal product can be used safely during lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer the veterinary medicinal product 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.

4.9 Amount(s) to be administered and administration route

Intramuscular use.

Cattle:

0.5 mg cloprostenol/animal corresponding to 2 ml of the veterinary medicinal product per animal.

Induction of oestrus: Administer one dose of the veterinary medicinal product after determination of the presence of a functional corpus luteum (6th to 18th day of cycle). Heat usually appears within 2 to 5 days. Proceed to insemination 72 to 96 hours after treatment. If there is no sign of oestrus, treatment may be repeated 11 days after the first injection.

Synchronisation of oestrus: Administer one dose of the veterinary medicinal product on two occasions with an 11 day interval between treatments. Proceed with insemination 72 to 96 hours after the second injection.

Treatment of ovarian dysfunction (persistent corpus luteum, luteal cyst): Administer one dose of the veterinary medicinal product after determination of presence of the corpus luteum. Then, proceed to inseminate at the first oestrus after injection. If oestrus does not take place, conduct a further gynaecological examination, and repeat the injection 11 days after the first administration.

Treatment of uterine disorders (clinical endometritis, pyometra): Administer one dose of the veterinary medicinal product preferably before the 60th day post-partum. If necessary, repeat the treatment at the latest after 10-11 days.

Induction of abortion: Administer one dose of the veterinary medicinal product until day 150 after insemination.

Expulsion of mummified foetuses: Administer one dose of the veterinary medicinal product.

Induction of parturition: Administer one dose of the veterinary medicinal product within 10 days before the expected date of parturition. Birth usually occurs within 30-60 hours of treatment.

Horses:
Ponies: 0.125 to 0.250 mg cloprostenol/animal corresponding to 0.5 to 1 ml of the veterinary medicinal product per animal.
Light horses: 0.250 mg cloprostenol/animal corresponding to 1 ml of the veterinary medicinal product per animal.
Heavy horses: 0.500 mg cloprostenol/animal corresponding to 2 ml of the veterinary medicinal product per animal.
It is recommended that the vial is not broached more than 10 times.

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

Overdose may be associated with uneasiness and diarrhoea. These effects are usually transient and will resolve without treatment.
In mares, if the indicated dosage is exceeded, clinical signs such as sweating, diarrhoea, dyspnoea, tachycardia and colic can occasionally be observed.

4.11 Withdrawal period(s)

Cattle
Meat and offal: 1 day.
Milk: Zero hours.

Horses
Not authorised for use in horses and ponies intended for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Genito urinary system and sex hormones, other gynecologicals, uterotonics, prostaglandins, cloprostenol.

ATC Vet Code: QG02AD90.

5.1 Pharmacodynamic properties

Cloprostenol sodium is a (racemic) analogue of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$).
This veterinary medicinal product is a potent luteolytic agent. It causes functional and morphological regression of the corpus luteum (luteolysis) in cattle and horses followed by return to oestrus and normal ovulation.

Furthermore, this group of substances has a contractile effect on the smooth muscles (uterus, gastro-intestinal 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.

At pharmacological doses, no obvious ill effects have been observed. Unlike other prostaglandin analogues, cloprostenol has no thromboxane A2 activity and does not cause platelet aggregation. Cloprostenol has a good safety margin and does not impair fertility. No deleterious effects have been reported on the progeny conceived at the oestrus following treatment.

5.2 Pharmacokinetic particulars

Metabolism studies, using 15-^{14}C-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 followed by excretion in approximately equal proportion in urine and faeces. In the cow, a major portion of the dose is excreted within 0 - 4 hours and most of the dose is eliminated within 24 hours. 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol
Citric acid anhydrous
Sodium hydroxide
Anhydrous ethanol
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: 2 years
Shelf life after first opening the immediate packaging: 28 days

6.4 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions.
This veterinary medicinal product should be stored upright.

6.5 Nature and composition of immediate packaging

Container size: 20 ml.
Container material: Amber Type I glass vials in a cardboard box.
Closure: Grey elastomeric bromobutyl rubber stoppers sealed with a plastic flip off button and an aluminium cap.

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.

7. MARKETING AUTHORISATION HOLDER

Syn Vet-Pharma Ireland Limited
7 A Durands Court
45 Parnell Street
X91 P381
Ireland

8. MARKETING AUTHORISATION NUMBER

Vm 54400/5000

9. DATE OF FIRST AUTHORISATION

18 October 2023

10. DATE OF REVISION OF THE TEXT

October 2023

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Approved 18 October 2023