SYNCROPROST®

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Product information

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1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Syncroprost, 0.250 mg/ml solution for injection for cattle, horses, pigs and goats.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Cloprostenol (equivalent to 0.263 mg cloprostenol sodium) ..... 0.250 mg

For the full list of excipients, see section 6.1. "List of excipients".

3. PHARMACEUTICAL FORM

Suspension for injection.

A clear, colourless solution, practically free from visible particles.

4. CLINICAL PARTICULARS

4.1 | Target species

Cattle (cows and heifers), horses (mares), pigs (sows and gilts) and goats (does).

4.2 | Indications for use, specifying the target species

Cattle (cows and heifers)

- Induction of luteolysis allowing resumption of oestrus and ovulation in cyclic females when used during dioestrus.
- Synchronisation of oestrus (within 2 to 5 days) in groups of cyclic females treated simultaneously.
- Treatment of suboestrus ("silent heat") and uterine disorders related to a functioning or persistent *corpus luteum* (endometritis, pyometra).
- Treatment of ovarian luteal cysts.
- Induction of abortion until day 150 of pregnancy.
- Expulsion of mummified foetuses.
- Induction of parturition.

Horses (mares)

- Induction of luteolysis in mares with a functional *corpus luteum.*
- Induction of the oestrus cycle during the breeding season.

Pigs (sows and gilts)

- Induction of luteolysis and parturition after day 114 of gestation.

Goats (does)

- Synchronisation of oestrus.

4.3 | Contraindications

Do not administer the veterinary medicinal product to pregnant animals unless the objective is to terminate the pregnancy.
Do not use in animals with cardiovascular, gastro-intestinal or respiratory problems.
Do not administer to induce parturition in animals with suspected dystocia due to mechanical obstruction or if problems are expected because of an abnormal position of the foetus.
Do not use in known 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

In cattle, for the termination of pregnancy, best results are obtained before day 100 of gestation. Results are less reliable between day 100 and 150 of gestation.
There is a refractory period of four to five days after ovulation when cattle are insensitive to the luteolytic effect of prostaglandins.

Induction of luteolysis in mares with a functional corpus luteum.
Some animals may present, on gynecological examination, a functioning or persistent *corpus luteum* or, simply, normal ovarian cycles with little or even absent behavioral manifestations (“silent heat”).
In such cases it is advisable to induce luteolysis for a return to normal heat.

Induction of the oestrus cycle in mares during the breeding season
In the context of a scheduled work program, oestrus can be induced to facilitate reproductive efficiency and better exploitation of stallions during the mating season. The oestrus resulting from the treatment with the veterinary medicinal product is perfectly normal both in terms of external manifestations and duration, and in the maturation of the follicles, their number and size.

4.5 | Special precautions for use

Special precautions for use in animals

In case of oestrus induction: from the 2nd day after injection, adequate heat detection is necessary.

Induction of parturition and abortion may increase the risk of complications, retained placenta, foetal death and metritis.

Induction of parturition in sows before day 114 of gestation may result in an increased risk of stillbirths and the need for manual assistance at farrowing.

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 taken 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.

Direct contact with skin or mucous membranes of the user should be avoided. Benzyl alcohol may cause allergic reactions. People with known hypersensitivity to benzyl alcohol should avoid contact with the veterinary medicinal product.

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 tract diseases should exercise caution when handling 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.

In case of accidental self-injection or spillage onto the skin, seek urgent medical advice, particularly if shortness of breath occurs, and show the package leaflet or label to the physician.

Wash hands after use.

iii Other precautions

None.

4.6 | Adverse reactions (frequency and seriousness)

In horses, slight sweating and muscle tremors may occur after treatment. This appears to be transient and resolves without any treatment. In some cases, soft faeces may be passed shortly after treatment. Other possible reactions are increased heart and respiratory rate, abdominal discomfort, locomotor incoordination and lying down.

Occurrence of bacterial infections is likely if anaerobic bacteria penetrate the tissue of the injection site.

Typical local reactions due to anaerobic infection are swelling and crepitus at the injection site. When used in cattle for induction of parturition and dependent on the time of treatment relative to the date of conception, the incidence of retained placenta may be increased.

In very rare cases, anaphylactic-type reactions can be observed which might be life-threatening and require rapid medical care.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 | Use during pregnancy, lactation or lay

Do not administer the veterinary medicinal product to pregnant animals unless the objective is to terminate the pregnancy.

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 | Amounts to be administered and administration route

For intramuscular use only.

Cattle:

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

Synchronisation of oestrus
Administer one dose of the veterinary medicinal product twice at 11-14 days interval.

Treatment of suboestrus ("silent heat") and uterine disorders related to a functioning or persistent *corpus luteum* (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.

Induction of parturition

Administer one dose of the veterinary medicinal product within 10 days before the expected date of parturition.

Horses:

Ponies: 0.125-0.250 mg cloprostenol/animal corresponding to 0.5-1 ml of the veterinary medicinal product per animal.

Light horses: 0.25 mg of 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.

If there is no sign of oestrus, the treatment may be repeated 14 days after the first injection.

Pigs

0.175 mg cloprostenol/animal corresponding to 0.7 ml of the veterinary medicinal product per animal, preferably with a needle at least 4 cm long.

The administration of a single dose at the end of pregnancy, one or two days before the expected date of parturition, causes luteolysis and the completion of parturition in the 36 hours following the treatment.

Goats

0.100 to 0.200 mg cloprostenol/animal corresponding to 0.4 to 0.8 ml of the veterinary medicinal product per animal.

Administer one dose of the veterinary medicinal product. If there is no sign of oestrus, the treatment may be repeated 9-10 days after the first injection.

The rubber stopper may safely be punctured up to 10 times. Otherwise, the use of a multiple dose syringe is recommended.

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 the mares, if the indicated dosage is exceeded, clinical signs such as sweating, diarrhoea, dyspnoea, tachycardia, colics can occasionally be observed.

4.11 | Withdrawal period

Cattle, goats, horses:

Meat and offal: 1 day
Milk: zero days

Pigs:

Meat and offal: 1 day

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic Group: prostaglandins and synthetic analogue.
ATCvet code: QG02AD90

5.1 | Pharmacodynamic properties

Cloprostenol is a synthetic prostaglandin analogue structurally related to Prostaglandin F2α (PGF2α). As a potent luteolytic agent, which provokes morphological regression (luteolysis) of the *corpus luteum*.

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

Cloprostenol does not demonstrate any androgenic, oestrogenic or anti-progesterone activity and its effects on pregnancy is due to its luteolytic property.

Unlike other prostaglandin analogues, cloprostenol has not tromboxane 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

Studies of metabolism, using 15-14C-cloprostenol sodium, were conducted in swine and cattle (following I.M. administration) to determine residual levels. Cloprostenol sodium is rapidly absorbed from the injection site. It is then metabolised and finally excreted practically similarly between urine and stool. In cattle and pigs the majority of the administered dose is excreted within 0-4 hours after injection and in practice the whole compound is excreted and metabolized within 24 hours.

The main pathway of metabolization in all animal species appears to be that of β-oxidation with formation of the Tetranor-or dinor-acids of cloprostenol.

The values at the peak of radioactivity in the blood are observed within 1 hour of parenteral administration of sodium cloprostenol and tend to decrease with a $T_{1/2}$ between 1 and 3 hours (depending on the animal species).

6. PHARMACEUTICAL PARTICULARS

6.1 | List of excipients

Benzyl alcohol (E1519)
Sodium citrate
Citric acid (for pH adjustment)
Sodium chloride
Sodium hydroxide (for pH adjustment)
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

Keep vial in the outer carton in order to protect from light.

6.5 | Nature and composition of immediate packaging

Type I colourless glass vials sealed with bromo-butyl rubber stoppers closed by aluminium flip-off caps.
Box with one 10- or 20-ml vial.
Box with 10 x 20 ml vials
Not all pack sizes may be marketed.

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 material derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

The veterinary medicinal product should not enter water courses as this may be dangerous for fish and other aquatic organisms.