Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Enzaprost Bovis 12.5 mg/ml solution for injection for cattle

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Dinoprost (as dinoprost trometamol) 12.5 mg

Excipients:
Benzyl alcohol (E1519) 16.5 mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.
Clear colourless to pale brownish yellow solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle (heifers and cows).

4.2 Indications for use, specifying the target species

The veterinary medicinal product is used in the following indications:
- Induction of oestrus,
- Controlled breeding in normally-cycling dairy cows:
    - oestrus synchronisation,
    - ovulation synchronisation in combination with GnRH or GnRH analogues as part of timed artificial insemination protocols.
- Treatment of sub-oestrus or silent heat in cows which have a functional corpus luteum,
- As supportive treatment of endometritis with the presence of functional corpus luteum and pyometra,
- Induction of abortion,
- Induction of parturition, including cases with complications such as hydrops amnii, etc,
- Expulsion of mummified foetuses.

4.3 Contraindications

Do not use in animals suffering from either acute or sub-acute disorders of the vascular system, gastro-intestinal tract or respiratory system.
Do not use in pregnant cows unless abortion or parturition is intended.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not administer by the intravenous route.

4.4 Special warnings for each target species

Do not administer more than 2 ml per single injection.
The veterinary medicinal product is ineffective when administered prior to day 5 after ovulation in cattle.

4.5 Special precautions for use

Special precautions for use in animals
Pregnancy status should be determined prior to injection since the veterinary medicinal product is indicated for abortion or parturition induction.
Induction of abortion or parturition by using exogenous substances can increase the risk for dystocia, fetal death, retention of the placenta and/or metritis.
Accidental administration to non-cycling cattle has no adverse effects on future fertility.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Prostaglandins of the F2α type may cause bronchospasms or miscarriage and can be absorbed through the skin.
Pregnant women, women of child-bearing age and people with bronchial or other respiratory problems should avoid contact with the product, or wear disposable gloves when administering the product.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
This product may cause irritation and/or hypersensitivity reactions. Avoid exposure to the skin and eyes. People with known hypersensitivity to benzyl alcohol should avoid exposure.
Wash hands after use.
In case of accidental spillage on the skin, wash off immediately with water.
In case of accidental contact with the eyes, rinse immediately with plenty of water.

4.6 Adverse reactions (frequency and seriousness)

Small transient swelling can sometimes be observed after injection.
In very rare cases, localised post injection bacterial infections that may become generalised have been reported. 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 post injection bacterial infections.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Do not use in pregnant cows, unless abortion or parturition is intended.

4.8 Interaction with other medicinal products and other forms of interactions

As non-steroidal anti-inflammatory drugs may inhibit endogenous prostaglandin synthesis, concomitant administration of these compounds with the product may decrease the luteolytic effects. As oxytocin stimulates the production of prostaglandins, concomitant administration of these compounds with the product may exacerbate the luteolytic effects.

4.9 Amounts to be administered and administration route

For intramuscular use only.

The dosage for all indications in cattle is 25 mg of dinoprost equivalent to 2 ml of the veterinary medicinal product per animal.

Induction of oestrus:
Cows and heifers treated during dioestrus will normally return to oestrus and ovulate within two to four days after treatment.

Controlled breeding in normally-cycling dairy cows:
- Oestrus synchronisation:
After injection, inseminate as soon as the animals are in oestrus. If necessary, repeat treatment after 10-12 days.
- Ovulation synchronization in combination with GnRH or GnRH analogues, as part of timed artificial insemination protocols, at any time of lactation. The following protocols are often mentioned in the literature:

Protocol 1:
Day 0 Inject GnRH or analogue
Day 7 Inject 2 ml of this veterinary medicinal product intramuscularly
Day 9 Inject GnRH or analogue
Artificial insemination 16-20 hours later, or if earlier, when observing oestrus.

Protocol 2:
Day 0 Inject GnRH or analogue
Day 7 Inject 2 ml of this veterinary medicinal product intramuscularly
Artificial insemination and inject GnRH or analogue 60-72 hours later, or if earlier, when observing oestrus.

To maximize the conception rates of the cows to be treated, the status of theovary should be determined and normal cyclic ovarian activity must be confirmed. Optimal results will be achieved in healthy normal cyclic cows.

-Treatment of sub-oestrus or silent heat in cows which have a functional corpus luteum:
If necessary, repeat treatment after 10-12 days.
Breeding of cattle with the product for the above indication may be by natural service or artificial insemination, at the usual time in relation to observed oestrus, or by fixed time insemination (78 hours or 72 and 90 hours post-treatment).

- As supportive treatment of endometritis with the presence of a functional corpus luteum and pyometra:
Treatment may have to be repeated after 10-12 days where the condition is long standing.

- Induction of abortion:
Between the 5th and 120th day of gestation, the administration of the veterinary medicinal product usually results in abortion within 4 days after treatment. The more advanced the gestation, the more difficult the induction of the abortion. Therefore, abortion always has to be checked by observation of the oestrus or by gestation check.

- Induction of parturition:
The administration of the veterinary medicinal product on or after Day 270 of gestation induces parturition which occurs 1 to 8 days (on average 3 days) after the administration.

The rubber stopper of the vial can be safely punctured up to 30 times. Otherwise, for the 100 ml vials automatic syringe equipment, or a suitable draw-off needle, should be used to prevent excessive puncturing of the closure.

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

Increased rectal temperature has been very rarely observed at 5 or 10 times the recommended dosage in cattle; and this effect was transient in all cases.
In some instances, there was a slight salivation noted.
The safety margin in cattle is at least 10 times the therapeutic dose.

4.11 Withdrawal period(s)

Meat and offal: 2 days
Milk: zero days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: prostaglandins.
ATC vet code: QG02AD01

5.1 Pharmacodynamic properties

Dinoprost has luteolytic activity. It causes the involution of the corpus luteum in most mammals and induces the appearance of estrus and ovulation in females with cyclic sexual activity. The administration of dinoprost causes abortion or induction of parturition in cattle. In addition, it has other activities that vary according to the species considered, such as an increase in blood pressure and bronchoconstriction. Dinoprost is also a stimulant of smooth muscle fibers.

5.2 Pharmacokinetic particulars

Dinoprost is rapidly absorbed after intramuscular administration. Peak plasma concentration is observed a few tens of minutes after administration. It has an extremely short half-life of just a few minutes and is fully cleared via one or two passages through the liver and/or the lungs.
Upon exogenous administration of prostaglandin F2 α (dinoprost) concentrations are reached equal to natural occurring concentrations in uterus and blood shortly before partum.
Dinoprost is a natural prostaglandin, therefore enzyme systems necessary for degradation and metabolism are present in the body.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
Water for injections

6.2 Major incompatibilities

In the absence of incompatibility 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: 24 months.
Shelf-life after first broaching the vial: 3 months.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and composition of immediate packaging

Nature of container
Colourless type I glass vial closed with a bromobutyl rubber stopper and aluminium and plastic flip capsule.
Translucent multi layer (polypropylene/ ethylene vinyl alcohol/ polypropylene) vial closed with a bromobutyl rubber stopper and aluminium and plastic flip capsule.

Pack sizes:
Cardboard box containing 1 glass vial of 2 ml,
Cardboard box containing 10 glass vials of 2 ml
Cardboard box containing 1 glass vial of 10 ml,
Cardboard box containing 1 glass vial of 20 ml,
Cardboard box containing 1 plastic vial of 50 ml.
Cardboard box containing 1 plastic vial of 100 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Ceva Santé Animale
10, avenue de La Ballastière
33500 Libourne
France

8 MARKETING AUTHORISATION NUMBER(S)

VPA10815/056/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th December 2020

10 DATE OF REVISION OF THE TEXT