LABELLING AND PACKAGE LEAFLET

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard boxes of 10, 20 ml or 10x20ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cevaprost 250 µg/ml Solution for Injection
cloprostenol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Cloprostenol 0.250 mg/ml
(as 0.263 mg/ml cloprostenol sodium)

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

10 ml
20 ml
10x20 ml

5. TARGET SPECIES

Cattle

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Cattle: Intramuscular

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Cattle
Meat : 1 day
Milk : zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Prostaglandins can cause severe adverse reactions. See package leaflet for user warnings.

10. EXPIRY DATE

EXP:
Once broached, use within 28 days by: ___/___/___

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C. Keep the vial in the outer carton in order to protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read package leaflet

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Ceva Animal Health Ltd
Explorer House
Mercury Park
Wycombe Lane
Wooburn Green
High Wycombe
Buckinghamshire
HP10 0HH
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

Vm 15052/4159

17. MANUFACTURER'S BATCH NUMBER

Lot:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of 10 and 20 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cevaprost 250 µg/ml Solution for Injection
cloprostenol

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Cloprostenol 0.250 mg/ml
(as 0.263 mg/ml cloprostenol sodium)

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

10 ml
20 ml

4. ROUTE(S) OF ADMINISTRATION

Cattle: IM

5. WITHDRAWAL PERIOD

Cattle
Meat : 1 day
Milk : zero hours

6. BATCH NUMBER

Lot:

7. EXPIRY DATE

EXP:

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR

Cevaprost 250 µg/ml Solution for Injection

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Ceva Animal Health Ltd
Explorer House
Mercury Park
Wycombe Lane
Wooburn Green
High Wycombe
Buckinghamshire
HP10 0HH
United Kingdom

Manufacturer responsible for the batch release:
Vetem S.p.A, Lungomare Pirandello, 8, 92014 Porto Empedocle (AG), Italy

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cevaprost 250 µg/ml Solution for Injection
cloprostenol

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains: 0.250 mg Cloprostenol (as 0.263 mg cloprostenol sodium)
The product is a clear, colourless solution for injection.

4. INDICATION(S)

Cattle (heifers, cows)
- Silent heat
- Ovarian luteal cysts
- Termination of pregnancy
- Induction of parturition
- Removal of mummified foetus
- Chronic endometritis (pyometra)
- Synchronisation of oestrus (within 2 to 5 days) in groups of cyclic females treated Simultaneously

5. CONTRAINDICATIONS

Do not administer the product to pregnant cows unless you wish to induce parturition or therapeutic abortion, as luteolysis may result in loss of the foetus.
Do not use in animals in cases of dystocic delivery, in case of abnormal position of the foetus or of mechanical obstruction.
Do not administer to animals with known hypersensitivity to the active substance or one of the excipients.

Do not use in animals with cardiovascular, gastro-intestinal or respiratory problems.
Do not administer intravenously.

6. ADVERSE REACTIONS

In very rare cases, anaphylactic-type reactions can be observed which require immediate medical care.
Anaerobic infection may occur 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 for the induction of parturition and dependent on the time of treatment relative to the date of conception, the incidence of retained placenta may be increased.

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).

7. TARGET SPECIES

Cattle

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Cattle
Single or repeated 2ml doses (equivalent to 500 mcg of cloprostenol) by intramuscular injection).

Therapeutic indications:

A) Silent heat
This condition is particularly common in heavy producing dairy cows, which have normal ovarian cycles but slightly express or do not express behavioural manifestations. These animals can be treated only after checking the cycle activity and the presence of the corpus luteum. Animals treated with the product may be bred (natural service or artificial insemination) 72 and 96 hours after treatment.
If the animal has been treated in the absence of a corpus luteum, another injection of the product is required 11 days after the first injection.

B) Ovarian luteal cysts
The product has demonstrated its efficacy in restoring normal the oestrus cycle in case of absence of heat caused by ovarian cysts (characterized by the presence of persistent luteal tissue).

C) Termination of pregnancy
The condition may occur in case of immature calves.

The pregnancy can be interrupted starting from one week after its establishment until day 150 of pregnancy. Before day 100, abortion can be induced quickly and effectively while between day 100 and day 150, results may be less significant because some cows may become progressively less sensitive to the action of corpus luteum maintaining pregnancy. The animals must be kept under observation until foetus and placental membranes complete expulsion.

D) Induction of parturition
From day 270 of pregnancy, the administration of the product induces parturition 30 – 60 hours of treatment. The induction of parturition should take place as close as possible to the expected date of spontaneous parturition. The induction of parturition should not be induced before day 270 day of pregnancy. All treated animals must be kept under observation. As with all other methods of shortening the pregnancy period, placental retention rate may be increased.

E) Removal of mummified foetus
Foetus death may be followed by dehydration and degeneration. The induction of luteolysis at any stage of pregnancy causes the expulsion of mummified foetuses from the uterus to the vagina, from which it is possible to make manual removal. Usually, normal cyclic activity follows.

F) Chronic Endometritis (Pyometra)
Reproduction system lesions caused during parturition or placental retention may cause uterine inflammation and infections known as endometritis. Acute or sub-acute endometritis, which may occur shortly after parturition, may require both local and general antibiotic treatments. This condition is known as pyometra and is characterised by the absence of annual cyclic activity and the presence of a persistent corpus luteum. The condition can be successfully treated by inducing the regression of the corpus luteum. If necessary, the treatment may be repeated after 10-14 days.

Controlled breeding:

A treatment consisting of two injections of the product at 11 days interval is highly effective for oestrus synchronization in healthy cycling cows. Two artificial inseminations at 72 and 96 hours after the second injection, involve a normal fertility rate. For economic reasons, if only one insemination is performed, this must be done after 72-84 hours but this may involve fewer pregnancies. Of cause, such protocol can vary. For example, it is possible to inseminate all animals in heat after the first injection and limit the second treatment, to the cows in which the first had no effect.

9. ADVICE ON CORRECT ADMINISTRATION

Administer the product intramuscularly by observing normal aseptic rules to reduce the risk of anaerobic infections. Clean and disinfect the injection site prior to administration. Avoid administration through wet or dirty skin.

10. WITHDRAWAL PERIOD

Cattle
Meat : 1 day
Milk : zero hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not store at temperature above 25°C.
Keep vial in the outer carton in order to protect from light.

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 container: 28 days

When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the carton.

12. SPECIAL WARNING(S)

Special warnings for each target species:
The product should not be administered to pregnant animal if you do not wish abortion, as luteolysis may result in foetus loss. The administration must be carried out only intramuscularly, other routes of administration may not be efficient.
Do not perform the treatment at the same time as non-steroidal anti-inflammatory drugs: as non-steroidal anti-inflammatory drugs may inhibit the endogenous prostaglandin synthesis, concomitant administration of these compounds with the product may decrease the luteolytic effects.
After treatment, the animals must remain under observation to detect any adverse reaction.

Special precautions for use in animals
Administer the product intramuscularly by observing normal aseptic rules to reduce the risk of anaerobic infections. Clean and disinfect the injection site prior to administration. Avoid administration through wet or dirty skin.
In cows when used for induction of pregnancy, abortion at the most advanced stage, complications such as dystocia and increased placental retention are possible.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Direct contact with skin or mucous membranes of the user should be avoided. Prostaglandins of the F2α type may be absorbed through the skin and **may cause bronchospasm or miscarriage.** Care should be taken when handling the product to **AVOID SELF-INJECTION OR SKIN CONTACT.** Pregnant women, women of childbearing age, asthmatics and persons with other respiratory tract diseases should exercise caution when handling cloprostenol. Those persons should avoid contact or wear disposable gloves during administration of the product. Accidental spillage on the skin should be washed immediately with soap and water. The possible incidence of bronchospasm with the product is unknown. Should shortness of breath result from accidental inhalation or injection, seek urgent medical advice and show the doctor this warning. Wash hands after use.

Pregnancy
Do not administer to pregnant animals unless the objective is to terminate pregnancy.

Interaction with other medicinal products and other forms of interaction.
Do not perform the treatment at the same time as non-steroidal anti-inflammatory drugs as non-steroidal anti-inflammatory drugs may inhibit the endogenous prostaglandin synthesis: concomitant administration of these compounds with the product may decrease the luteolytic effects. The activity of other oxytocin agents can be increased after the administration of cloprostenol.

Overdose
At x5 to x10 overdose the most frequent side effect is increased rectal temperature. This is usually transient, however, and not detrimental to the animal. Limited salivation may also be observed in some animals.
Five animals treated with 40 mg cloprostenol (80 times the therapeutic dose) showed only slight symptoms of restlessness: two animals presented a slight sialorrhea and only one had diarrhoea.
These symptoms were moderate and were observed only after careful clinical examination. They disappeared definitively within 8 hours of administration.
One animal treated with 100 mg cloprostenol (200 times the therapeutic dose) by intramuscular injection showed only a slight form of transient diarrhoea, confirming that the drug presents a high safety margin.
In case of signs, a symptomatic treatment is recommended.

Incompatibilities
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIAL, IF ANY

Any unused veterinary medicinal product or waste material derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

September 2022

15. OTHER INFORMATION

Pack size:
10 ml and 20 ml Type I colourless glass vials sealed with halogen-butyl rubber stoppers closed by aluminium flip-off caps.

Boxes with one 10 or 20ml vial.
Boxes with 10 x 20ml vials

Not all pack sizes may be marketed

For Animal treatment only
To be supply only on veterinary prescription.

Approved 30 September 2022