ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE

100 ml vial - Outer box + Label

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enzaprost Bovis 12.5 mg/ml solution for injection for cattle
dinoprost

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains 12.5 mg of dinoprost (as dinoprost trometamol)

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Cattle (heifers and cows)

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal periods:
Meat and offal: 2 days. Milk: zero days

9. SPECIAL WARNING(S), IF NECESSARY

Not required on the immediate label

This product may be harmful to the unborn child.
Read the package leaflet before use.

10. EXPIRY DATE

EXP:
Once broached, use within 3 months by __/__/__.

11. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.

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

Not required on the immediate label
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 15052/4152

17. MANUFACTURER'S BATCH NUMBER

Lot:

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Outer box 2 ml / 10 ml / 20 ml / 50 ml / 10 x 2 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enzaprost Bovis 12.5 mg/ml solution for injection for cattle
dinoprost

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains 12.5 mg of dinoprost (as dinoprost trometamol)

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

2 ml
10 ml
20 ml
50 ml
10 x 2 ml

5. TARGET SPECIES

Cattle (heifers and cows)

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal periods:
Meat and offal: 2 days. Milk: zero days

9. SPECIAL WARNING(S), IF NECESSARY

This product may be harmful to the unborn child.
Read the package leaflet before use.

10. EXPIRY DATE

EXP:
Not applicable on the 2 ml outer package
Once broached, use within 3 months by __/__/__

11. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.

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 15052/4152

17. MANUFACTURER'S BATCH NUMBER

Lot:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

2 ml vial
10 ml vial
20 ml vial
50 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enzaprost Bovis 12.5 mg/ml solution for injection for cattle
dinoprost

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Dinoprost (as dinoprost trometamol): 12.5 mg/ml

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

2 ml
10 ml
20 ml
50 ml

4. ROUTE(S) OF ADMINISTRATION

IM

5. WITHDRAWAL PERIOD(S)

Withdrawal periods:
Meat and offal: 2 days. Milk: zero days

6. BATCH NUMBER

Lot:

7. EXPIRY DATE

EXP:

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For 2 ml: leave blank for lack of space on final artwork.
For 10 ml, 20 ml 50 ml: For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Enzaprost Bovis 12.5 mg/ml solution for injection for cattle

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

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enzaprost Bovis 12.5 mg/ml solution for injection for cattle
dinoprost

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

Each ml contains:
Active substance: Dinoprost (as dinoprost trometamol): 12.5 mg
Excipients: Benzyl alcohol (E1519): 16.5 mg
Clear colourless to pale brownish yellow solution.

4. INDICATION(S)

The veterinary medicinal 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.

5. 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.

6. ADVERSE REACTIONS

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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle (heifers and cows).

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

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 the ovary should be determined and normal cyclic ovarian activity must be confirmed. Optimal results will be achieved in healthy normal cyclic cows.

- Treatment of sub-oestrusor 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.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD(S)

Meat and offal: 2 days. Milk: zero days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not store above 30°C.
Do not use this veterinary medicinal product after the expiry date which is stated on the container after EXP. The expiry date refers to the last day of that month.
Shelf life after first broaching the vial: 3 months.

12. SPECIAL WARNING(S)

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.

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.

Pregnancy and lactation:
Do not use in pregnant cows, unless abortion or parturition is intended.

Interaction with other medicinal products and other forms of interaction:
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.

Overdose (symptoms, emergency procedures, antidotes):
Increased rectal temperature has been very rarelyobserved 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.

Incompatibilities:
In the absence of incompatibility 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 MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product 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 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.

Approved 21 September 2022