ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bioestrovet 0.250 mg/ml solution for injection for cattle
cloprostenol

2. STATEMENT OF ACTIVE SUBSTANCES

Active substance:

Cloprostenol	0.250 mg/ml
(eq Cloprostenol Sodium	0.263 mg/ml)

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

20 ml
50 ml
100 ml

5. TARGET SPECIES

Cattle (heifers, cows)

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular injection.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 1 day
Milk: Zero hours

9. SPECIAL WARNING(S), IF NECESSARY

User warnings: Prostaglandins can cause severe adverse reactions.
Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached, use within 28 days
Once broached, use by: …

11. SPECIAL STORAGE CONDITIONS

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

Vetoquinol UK Limited
Steadings Barn
Pury Hill Business Park
Nr Alderton
Towcester
Northants
NN12 7LS

16. MARKETING AUTHORISATION NUMBER(S)

Vm 08007/4147

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vial of 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bioestrovet 0.250 mg/ml solution for injection for cattle
cloprostenol

2. STATEMENT OF ACTIVE SUBSTANCES

Active substance:

Cloprostenol	0.250 mg/ml
(eq Cloprostenol Sodium)	0.263 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Cattle (heifers, cows)

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular injection.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 1 day
Milk: Zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached, use within 28 days
Once broached, use by:

11. SPECIAL STORAGE CONDITIONS

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

Vetoquinol UK Limited
Steadings Barn
Pury Hill Business Park
Nr Alderton
Towcester
Northants
NN12 7LS

16. MARKETING AUTHORISATION NUMBER(S)

Vm 08007/4147

17. MANUFACTURER'S BATCH NUMBER

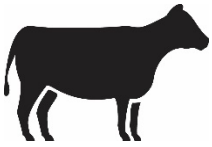
Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of 20 ml
Vial of 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bioestrovet 0.250 mg/ml solution for injection for cattle
cloprostenol



2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Active substance:

Cloprostenol	0.250 mg/ml
(equivalent to Cloprostenol sodium	0.263 mg/ml)

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

20 ml
50 ml

4. ROUTE(S) OF ADMINISTRATION

i.m.

5. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 1 day
Milk: Zero hours

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once broached, use within 28 days
Once broached, use by: …

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

Bioestrovet 0.250 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:
Vetoquinol UK Limited
Steadings Barn
Pury Hill Business Park
Nr Alderton
Towcester
Northants
NN12 7LS

Manufacturer responsible for batch release:
Vetoquinol S.A.
Magny-Vernois
70200 Lure
FRANCE

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bioestrovet 0.250 mg/ml solution for injection for cattle
cloprostenol

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

Each ml contains:

Active substance:

Cloprostenol	0.250 mg
(equivalent to Cloprostenol Sodium)	0.263 mg

Excipients:

Chlorocresol	1.00 mg

Solution for injection
A clear colourless aqueous solution.

4. INDICATION(S)

Cattle (heifers, cows):
- Induction of luteolysis allowing resumption of oestrus and ovulation in cyclic females when used during luteal phase
- Synchronisation of oestrus (within 2 to 5 days) in groups of cyclic females treated simultaneously
- Treatment of suboestrus 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 calving

5. CONTRAINDICATIONS

Do not administer to pregnant animals unless the objective is to terminate the pregnancy.
Do not use in animals with cardiovascular, gastro-intestinal or respiratory disturbances.
Do not administer to induce calving in cattle with suspected calving difficulties 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.

6. ADVERSE REACTIONS

Localised post-injection bacterial infections, which may spread throughout the body, are occasionally reported.
When used in cattle for induction of calving and dependent on the time of treatment relative to the date of conception, the incidence of retained placenta may be increased.
Anaphylactic-type reactions can be observed in very rare cases, 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 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.

Alternatively you can report via your national reporting system *{national system details}*.

7. TARGET SPECIES

Cattle (heifers, cows)

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

For intramuscular use.
0.5 mg cloprostenol/animal corresponding to 2 ml product per animal.
In order to synchronise oestrus in cattle, it is recommended that the product is administered on two occasions with an interval of 11 days between treatments.
Termination of abnormal pregnancy: between day 5 and 150 after insemination.
Induction of calving: within 10 days before the expected date of calving.
It is recommended that the vial is not broached more than 10 times and that the appropriate vial size is used for prevailing usage conditions. Otherwise, automatic syringe equipment, or a suitable draw-off needle, should be used for the 50 ml and 100 ml vials to avoid excessive puncturing of the stopper.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIOD

Meat and offal: 1 day
Milk: Zero hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Keep the vial in the outer carton in order to protect from light.
This veterinary medicinal product does not require any special temperature storage conditions.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 28 days

12. SPECIAL WARNING(S)

Special warnings for each target species:
There is a refractory period of four to five days after ovulation when cattle are insensitive to the luteolytic effect of prostaglandins.

Special precautions for use in animals:

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

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Prostaglandins of the $F_{2\alpha}$-type, such as cloprostenol, can be absorbed through the skin and mucous membrane and may cause bronchospasm or miscarriage.
Direct contact with skin or mucous membranes of the user should be avoided.
Care should be taken when handling the 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 product.
Wear disposable impervious gloves when administering the product.
Wash hands after use.
Do not eat, drink or smoke while handling the 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 medical advice immediately, particularly as shortness of breath may occur, and show the package leaflet or label to the physician.

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

Lactation:
Use only according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Do not administer the 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.

Overdose (symptoms, emergency procedures, antidotes):
Overdose may be associated with uneasiness, increased heart rate, increased respiratory rate, bronchoconstriction, increased rectal temperature, increased urination, salivation and diarrhoea. These effects are usually transient, and will resolve without treatment.
No antidotes are available.

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 MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

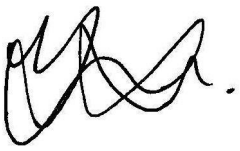
February 2022

15. OTHER INFORMATION

Cardboard box with 1 vial of 20 ml
Cardboard box with 1 vial of 50 ml
Cardboard box with 1 vial of 100 ml

Not all pack sizes may be marketed.

For any information about this veterinary medicinal product, please contact the local representative
of the marketing authorisation holder.



Approved: 15 March 2022