ANNEX II

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box (10 ml/ 20 ml or 5x10 ml 12x10 ml 5x20 ml 12x20 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Synchromate 0.25mg/ml, Solution for injection for cattle and horses

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml solution for injection contains:

Active substance(s):
Cloprostenol 0.25 mg
(as Cloprostenol sodium 0.263 mg)

Excipients:
Chlorocresol 1.0 mg

3. PHARMACEUTICAL FORM

Solution for Injection

4. PACKAGE SIZE

1 X 10 ml
5 X 10 ml
12 X 10 ml

1 X 20 ml
5 X 20 ml
12 X 20 ml

5. TARGET SPECIES

Cattle and horses

6. INDICATION(S)

For animal treatment only.
Keep out of the sight and reach of children.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Cattle
Meat and offal: 1 day
Milk: zero hours

Horses
Not authorised for use in horses intended for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet for full warnings.

10. EXPIRY DATE

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

11. SPECIAL STORAGE CONDITIONS

This veterinary medicinal product does not require any special temperature storage conditions.
Keep 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

Dispose of waste material in accordance with local requirements.
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. POM-V.

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

Alivira Animal Health UK Ltd
Hygeia Building, Rear Ground Floor
66-68 College Road
Harrow
Middlesex
HA1 1BE
United Kingdom

16. MARKETING AUTHORISATION NUMBER

Vm 54375/5000

17. MANUFACTURER'S BATCH NUMBER

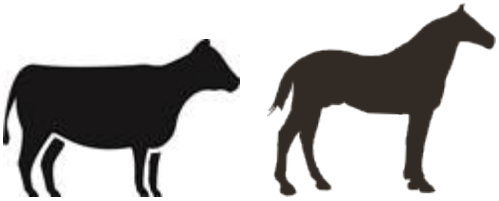
Batch no.{number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial (10 ml, 20ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Synchromate 0.25mg/ml, Solution for injection for cattle and horses



2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Cloprostenol 0.25 mg
(Corresponds to Cloprostenol sodium 0.263 mg)

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

10 ml
20 ml

4. ROUTE(S) OF ADMINISTRATION

5. WITHDRAWAL PERIOD(S)

Cattle
Meat and offal: 1 day
Milk: zero hours

Horses
Not authorised for use in horses intended for human consumption.

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {month/year}
Once broached use by

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Synchromate 0.25mg/ml, Solution for Injection for Cattle and Horses

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

Marketing authorisation holder:
Alivira Animal Health UK Ltd
Hygeia Building, Rear Ground Floor
66-68 College Road
Harrow
Middlesex
HA1 1BE
United Kingdom

Manufacturer responsible for batch release:

Bremer Pharma GmbH
Werkstrasse 42
34414 Warburg
GERMANY

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Synchromate 0.25mg/ml, Solution for injection for cattle and horses

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

Each ml contains:

Active substance:
Cloprostenol 0.25 mg
(as Cloprostenol sodium 0.263 mg)

Excipients:
Chlorocresol 1.0 mg

Clear colorless solution.

4. INDICATION(S)

Cattle:
- Suboestrus or non-detected oestrus
- Induction of parturition
- Termination of normal pregnancy
- Termination of abnormal pregnancy
    - Mummified foetus
    - Hydrops of the foetal membranes
- Chronic endometritis (pyometra)
- Ovarian luteal cysts
- Controlled breeding

Horses:
- Induction of luteolysis following early foetal death and resorption
- Termination of persistent dioestrus
- Termination of pseudopregnancy
- Treatment of lactation anoestrus
- Establishing oestrous cycles in barren/maiden mares.

5. CONTRAINDICATIONS

Do not administer intravenously.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

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'

6. ADVERSE REACTIONS

In very rare cases, anaphylactic-type reactions can be observed which require immediate medical care. On rare occasions severe life-threatening local bacterial infections may occur associated with clostridial proliferation at the injection site. It is important to keep treated animals under observation and, if such infection occurs aggressive antibiotic therapy, particularly covering clostridial species, should be employed as a matter of urgency. Careful aseptic techniques should be employed to decrease the possibility of these infections.

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 and horses

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

Sub-oestrus (or non detected oestrus)

After diagnosing the presence of a corpus luteum - by rectal palpation - treat with the product and inseminate those animals showing heat. Those animals which do not show heat to be re-examined 11 days later and may receive a second injection and be bred at oestrus or at fixed times; once at 72-84 hours or twice at 72 and 96 hours.

Induction of parturition

Induces parturition in the period around normal term. Induction should take place as close to the predicted calving date as possible and not more than 10 days before. Induction should not be attempted before day 270 of gestation measured from the confirmed day of conception, except in pathological conditions. All treated animals must receive adequate supervision. In common with other methods of shortening the gestation period a higher than usual incidence of retention of the foetal membranes is to be expected.

Termination of normal pregnancy

Normal pregnancy can be terminated in cattle from one week after conception until the 150th day of gestation. Best results are obtained during the first 100 days. Treated animals should be kept under observation until expulsion of the foetus and placenta is complete.

Termination of abnormal pregnancy

- Mummified foetus - induction of luteolysis at any stage of pregnancy will result in the expulsion of the mummified foetus from the uterus into the vagina from which manual removal may be necessary. Normal cyclical activity should then follow.

- Hydrops of the foetal membrane - Pathological accumulation of placental fluids can cause severe physiological complications and death. Surgical drainage is not usually successful in alleviating the condition. In such cases, a single dose may be used to induce parturition.

Chronic endometritis (Pyometra)

Treat with a single dose. In long-standing cases treatment may be repeated after 10-14 days.

Ovarian luteal cysts

Where cystic ovaries associated with persistent luteal tissue and absence of heat are diagnosed, the product has proved to be effective in correcting the condition and bringing about a return to cyclicity.

Other indications: Controlled breeding

Examples of programmes which have been used are:

i) A single treatment of cattle with palpable evidence of a corpus luteum, followed by breeding on detection of the subsequent oestrus.

ii) Detection of oestrus for 6 days, breeding those animals seen in heat; a single treatment is given to all non-served animals on the 6th day and these cattle are bred at subsequent oestrus.

iii) Two injections 11 days apart, breeding at oestrus or at fixed times (see below).

iv) As iii) above, but breeding any animals showing oestrus before the second injection. Thus the second dose is given only to those cattle not seen in oestrus during that time and is followed by breeding either on signs of oestrus or at fixed times (see below).

Cattle which respond to a single prostaglandin injection will normally do so within 6 days of treatment. The response time after two injections is more rapid. Animals may be inseminated on detection of oestrus in any of the breeding programmes. However, fixed time insemination should only be used following the second of a two injection programme (i.e. examples iii) and iv)). In the latter case insemination should be performed either once at 72-84 hours or twice at 72 and 96 hours after the second injection, as preferred.

Double ‘fixed-time’ insemination may give superior results to a single insemination. However, economic factors in the particular herd may outweigh such a benefit.

For successful treatment, animals should be cycling normally. Rectal examination before treatment should avoid the disappointment of treating noncycling (an-oestrus) or pregnant animals.

Attention should be directed to the diet and condition of the treated animals. Sudden changes in feeding levels, in feed constituents and in housing, etc should be avoided around the time of the breeding programme, as should any other factor, such as regrouping, which could reasonably be expected to lead to stress.

If artificial insemination is to be used, the quality of semen and insemination technique should be assured beforehand follows:

After the first injection, inseminate any cows showing signs of heat.

Animals that do not show signs of heat should be injected 11 days after the first injection and then inseminated 72-96 hours later.

Horses

(Ponies and donkeys: single dose of 0.5-1.0 ml (equivalent to 125-250 mcg of cloprostenol) by intramuscular injection. Thoroughbreds, hunters and heavy horses: 1-2 ml (equivalent to 250- 500 mcg cloprostenol) by intramuscular injection).

- Induction of luteolysis following early foetal death and resorption: about 8-10% of all mares which conceive lose the conceptus during the first 100 days of pregnancy.

Persistence of luteal function in the ovary precludes an early return to oestrus.

- Termination of persistent dioestrus: non-pregnant mares frequently and spontaneously go to and out of periods of prolonged dioestrus. A very high proportion of mares in this category i.e. not cycling, are in prolonged dioestrus rather than anoestrus, particularly in the latter part of the breeding season.

- Termination of pseudopregnancy: some mares which are covered at normal oestrus and subsequently found to be empty (but not having lost or resorbed a conceptus) display clinical signs of pregnancy. These animals are said to be “pseudopregnant”.

- Treatment of lactation anoestrus: failure of lactating mares to cycle again for several months after exhibiting an early ‘foal heat’ can be avoided.

- Establishing oestrous cycles in barren/maiden mares: some of these animals will be found, on examination, to have a functional corpus luteum and are suffering from abnormal persistence of luteal function or are simply failing to exhibit normal oestrous behaviour (“silent heat”) while ovarian cyclicity continues.

9. ADVICE ON CORRECT ADMINISTRATION

Due to the possibility of post-injection bacterial infections, careful aseptic techniques should be employed.

10. WITHDRAWAL PERIOD(S)

Cattle
Meat and offal: 1 day
Milk: zero hours

Horses
Not authorised for use in horses intended for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special temperature storage conditions. 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 the package leaflet, the date on which any product remaining in the container should be discarded should be determined. This discard date should be written in the space provided on the carton.

12. SPECIAL WARNING(S)

Special warnings for each target species
None.

Special precautions for use in animals:
Due to the possibility of post-injection bacterial infections, careful aseptic techniques should be employed.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
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 bronchial or other respiratory tract diseases should exercise caution when handling the product.
Wear disposable impervious gloves when administering the product.
People with a known hypersensitivity to cloprostenol or chlorocresol to avoid contact with the product.
Direct contact with the skin or eyes may cause irritation.
Accidental spillage on the skin should be washed immediately with soap and water.
If accidental contact with eyes occurs, rinse the affected eyes thoroughly with clean, fresh water.
The possible incidence of bronchospasm with the product is unknown.
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.
Do not eat, drink or smoke while handling the product.
Wash hands after use.

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

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose (*symptoms, emergency procedures, antidotes):*
Cattle:
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.
Horses:
The most frequently observed side effects are sweating and decreased rectal temperatures. These are usually transient, however, and not detrimental to the animal. Other possible reactions are increased heart rate, increased respiratory rate, abdominal discomfort, locomotor incoordination and lying down. If these occur, they are likely to be seen within 15 minutes of injection and disappear within 1 hour. Mares usually continue to eat throughout.

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

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

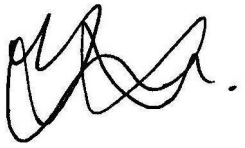
15. OTHER INFORMATION

For animal treatment only.

Pack Sizes:
20 ml: Clear Type I glass vial with bromobutyl stopper and bronze coloured aluminium cap.
10 ml: Clear Type I glass vial with laminated elastomeric bromobutyl stopper and aluminium cap.
Cardboard box containing 1 vial of 10 ml, 5 vials of 10 ml or 12 vials of 10 ml
Cardboard box containing 1 vial of 20 ml,5 vials of 20 ml or12 vials of 20 ml

Not all pack sizes maybe marketed

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



Approved: 02 November 2022