ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton for individual 20 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

JURAMATE 250 µg/ml Solution for Injection
cloprostenol

2. STATEMENT OF ACTIVE SUBSTANCES

Cloprostenol 250 µg/ml
(equivalent to Cloprostenol Sodium 263 µg/ml)
Preservative: Chlorocresol

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

20 ml

5. TARGET SPECIES

Cattle and horses

6. INDICATION(S)

Prostaglandin injection

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intramuscular injection.

8. WITHDRAWAL PERIOD(S)

Cattle:
Meat and offal: 1 day
Milk: zero hours

Do not administer to horses intended for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Operator warnings
Prostaglandins of the $F_{2\alpha}$ type can 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.
Women of child-bearing age, asthmatics and persons with bronchial or other respiratory problems should avoid contact with the product, and should wear disposable plastic gloves when administering the product.

The possible incidence of bronchospasm with the product is unknown. Should shortness of breath result from accidental inhalation of injection, seek urgent medical advice and show the doctor this warning.
Accidental spillage on the skin should be washed off immediately with soap and water.
Wash hands after use. Do not eat, drink or smoke when handling the product.

10. EXPIRY DATE

EXP. (MM/YY)
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.
Discard unused material.

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

Dispose of waste material in accordance with local requirements.

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

For animal treatment only
POM-V 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

Jurox (UK) Limited
Second Floor, Richmond House
105 High Street
Crawley
West Sussex
RH10 1DD
United Kingdom.
+44 1293 510681

16. MARKETING AUTHORISATION NUMBER(S)

Vm 25296/4001

17. MANUFACTURER'S BATCH NUMBER

BN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Label for 20 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

JURAMATE 250 µg/ml Solution for Injection
cloprostenol

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Cloprostenol 250 µg/ml

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

20 ml

4. ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intramuscular use.

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

BN

7. EXPIRY DATE

EXP:

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
JURAMATE 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 and manufacturer responsible for batch release:
Jurox (UK) Limited
Second Floor, Richmond House
105 High Street
Crawley
West Sussex
RH10 1DD

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

JURAMATE 250 µg/ml Solution for Injection
cloprostenol

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

Contains cloprostenol 250 µg/ml (equivalent to cloprostenol sodium 263 µg/ml) and chlorocresol 1 mg/ml as preservative.
Clear, colourless solution.

4. INDICATION(S)

Cloprostenol is a synthetic prostaglandin analogue structurally related to Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$). As a potent luteolytic agency it causes functional and morphological regression of the corpus luteum (luteolysis) in cattle and horses followed by return to oestrus and normal ovulation.

Note: There is a refractory period of four to five days after ovulation when cattle and horses are insensitive to the luteolytic effect of prostaglandins. Juramate has a good safety margin and does not impair fertility. No deleterious effects have been reported on the progeny conceived at the oestrus following treatment.

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

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 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 and horses

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

CATTLE
(Single or repeated 2mL doses (equivalent to 500 µg. 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 non-cycling (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.

A recommended guideline for use of the product in dairy cows would be as follows:

i) After the first injection, inseminate any cows showing signs of heat.
ii) Animals that do not show signs of heat should be injected 11 days after the first injection and then inseminated 72-96 hours later.

Control of the oestrous cycle is of value in:-

1) The dairy herd:
   a) To control oestrus in the individual animal giving better control of the individual calving index and reducing the number of cows culled as barren.
   b) To control oestrus in groups of cows to promote management of the herd in groups of suitable size and facilitate the maintenance of a seasonal calving pattern.
   c) To permit the use of artificial insemination (AI) in dairy heifers.

2) The beef herd:
   a) To facilitate the use of AI to obtain better progeny by use of high quality bulls.
   b) To enable the most effective use of available bulls where natural service is preferred.
   c) To permit better herd management at conception and calving.

HORSES

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

As an aid in stud management: mares may be brought into oestrus on a planning timing schedule (singly or in groups), to facilitate more efficient use and management of stallions during the breeding season.

9. ADVICE ON CORRECT ADMINISTRATION

Careful aseptic techniques should be employed to decrease the possibility of infection at the site of injection. See 6. Adverse Reactions above.

10. WITHDRAWAL PERIOD(S)

Cattle:
Meat and offal: 1 day
Milk: zero hours

Do not administer to horses intended for human consumption.

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.
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 insert, the date on which any product remaining in the container should be worked out. This discard date should be written in the space provided on the carton.

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 after “EXP:”. <The expiry date refers to the last day of that month.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Due to the possibility of post-injection bacterial infections, careful aseptic techniques should be employed.

Special precautions for use in animals:
Do not administer intravenously.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Prostaglandins of the $F_{2\alpha}$ type can 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.
Women of child-bearing age, asthmatics and persons with bronchial or other respiratory problems should avoid contact with, and should wear disposable plastic gloves, when administering the product.

The possible incidence of bronchospasm with the product is unknown. Should shortness of breath result from accidental inhalation of injection, seek urgent medical advice and show the doctor this warning.
Accidental spillage on the skin should be washed off immediately with soap and water.
Wash hands after use. Do not eat, drink or smoke when handling the product.

Use during pregnancy and lactation:
Do not administer to pregnant animals unless the objective is to terminate pregnancy.

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

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:
Strong acid/alkaline products.

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

Medicines should not be disposed of via wastewater.
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

15. OTHER INFORMATION

POM-V To be supplied only on veterinary prescription.
Vm 25296/4001.
For animal treatment only.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder:
Jurox (UK) Limited, Tel +44 1293 510 681

Approved 11 October 2019