

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Estrumate 250 µg/ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substances:

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

Excipients:

Benzyl alcohol (E1519) 20 mg/ml

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
A clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, horses

4.2 Indications for use, specifying the target species

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

- As an aid to stud management.

4.3 Contraindications

None.

4.4 Special warnings for each target species

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

4.5 Special Precautions for Use

- Special precautions for use in animals
Do not administer intravenously.
- Special Safety Precautions to be taken by the Person Administering the Medicinal Product to animals

Direct contact with skin or mucous membranes of the user should be avoided. Prostaglandins of the F2 α 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.

4.6 Adverse reactions (frequency and seriousness)

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).

4.7 Use During Pregnancy, lactation or lay

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

4.8 Interactions with other medicinal products and other forms of interaction

None described.

4.9 Amounts to be administered and administration route

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 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:

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.

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 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.

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

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

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.

4.11 Withdrawal period(s):

Cattle

Meat: 1 day

Milk: zero hours

Horses

Not to be used in horses intended for human consumption.

Treated horses may never be slaughtered for human consumption.

The horse must have been declared as not intended for human consumption under national horse passport legislation.

5. PHARMACOLOGICAL PROPERTIES

ATCvet Code: QG02AD90

Cloprostenol is a synthetic prostaglandin analogue structurally related to Prostaglandin F_{2α} (PGF_{2α}), for use in cattle and horses. As a potent luteolytic agent 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. Estrumate 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.

5.1 Pharmacokinetic Properties

After its administration by injection, cloprostenol is metabolised to acid 9, 11, dihydroxy-15-ceto prost-5-enoic and 9, 11, 15-trihydroxyprost-5-enoic which rapidly disappear from the blood, being excreted via the urine in 5-6 hours.

Radiolabelled studies show blood levels between 0.0014 and 0.002 µg per ml at 20 minutes - 2 hours after its administration. Subsequently, blood levels fall rapidly, having an apparent half life of 1-3 hours, falling below 0.00004 µg/ml at 8 hours. No significant concentrations are found at 24 hours in the liver, muscle, heart, kidneys, uterus, ovaries, skin, brain and fat, nor in milk after 4 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Sodium citrate
Citric acid anhydrous
Sodium chloride
Water for injections

6.2 Incompatibilities

Strong acid/alkaline products

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

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

Keep vial in the outer carton in order to protect from light.

Following withdrawal of the first dose, use the product within 28 days. Discard unused material.

6.5 Nature and composition of immediate packaging

10 ml and 20 ml Type I colourless glass vials sealed with synthetic ethyl tetrafluoroethylene (ETFE) coated bromobutyl rubber stoppers secured with aluminium collars with flip-seal caps.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products if appropriate

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

7. MARKETING AUTHORISATION HOLDER

MSD Animal Health UK Limited
Walton Manor
Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

8. MARKETING AUTHORISATION NUMBER

Vm 01708/4598

9. DATE OF FIRST AUTHORISATION

18 December 1997

10. DATE OF REVISION OF THE TEXT

April 2021

Approved: 28/04/21

D. Austin