

ESTROMIL INJECTION

Active constituent: ESTROMIL, a synthetic prostaglandin analogue for use in cattle and horses, is structurally related to Prostaglandin F_{2a} (PGF_a). Each mL of the colourless aqueous solution contains 263µg cloprostenol sodium equivalent to 250µg/mL cloprostenol.

Action: ESTROMIL is a potent luteolytic agent, i.e. it causes functional and morphological regression of the corpus luteum (luteolysis) in a variety of circumstances. Luteolysis is usually followed by return to oestrus two to four days after treatment, and normal ovulation. **Note:** There is a refractory period of four to five days after ovulation when cattle are insensitive to the luteolytic effect of prostaglandins. ESTROMIL 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.

In cattle adverse reactions have not been seen at up to 80 times the effective recommended dose (500µg). The only clinically apparent effect was mild and transient diarrhoea.

Directions for use:

ESTROMIL can be absorbed through the skin and therefore, care should be taken when handling this product, especially by women of child-bearing age and also by asthmatics. In case of accidental spillage on skin, wash immediately with water.

Prostaglandins of the F_{2a} type may cause broncho-spasm in man, although the possible incidence of this effect with ESTROMIL is not known. Should respiratory embarrassment result from accidental inhalation or injection, a rapid acting bronchodilator, e.g. isoprenaline or salbutamol by inhalation is indicated.

ESTROMIL should not be administered to pregnant animals where the foetus is not to be aborted, since luteolysis at some stages of gestation will result in the loss of the foetus.

Avoid intravenous injection.

In horses adverse reactions including sweating (occurring within the 20 minutes of treatment), increased respiratory and cardiac rates, signs of abdominal discomfort, watery diarrhoea and depression may occur when exceptionally high doses are given. However, adverse reactions are usually mild and transient. ESTROMIL should NOT be administered to:

- Mares suffering from acute or sub-acute disorders of the gastrointestinal tract.
- Mares suffering from acute or sub-acute respiratory disease. (This is a precautionary measure because in some species of animals, dosing with prostaglandins

Pregnant mares, since luteolysis at some stages of gestation will result in the loss of the foetus.

CATTLE

1. Therapeutic:

A single intramuscular dose of ESTROMIL is likely to be highly effective in the following clinical conditions of the cow.

Suboestrus (or non-detected oestrus – NDO):

This condition occurs in heavy yielding cows, usually at peak lactation, which have normal ovarian cyclicity but in which behavioural manifestations of oestrus are either very mild, transient or absent. Such animals can be treated with ESTROMIL following diagnosis of a corpus luteum by rectal palpation and then closely observed for oestrus. Those showing heat should be inseminated. Some animals may have been treated during the refractory period of the cycle and therefore will not respond. Animals not showing heat should receive a further single injection 11 days after the first and be inseminated 72 and 96 hours later.

Termination of Normal but Unwanted pregnancies:

Pregnancy can be terminated from one week after conception until the 150th day of gestation. Before 100 days gestation, abortion can be induced rapidly and efficiently. Between 100 and 150 days of gestation results are less reliable, probably because a proportion of cattle may become progressively less dependent upon the corpus luteum for the maintenance of pregnancy. Abortion should not be induced after day 150 of gestation. Treated animals should be kept under supervision until expulsion of the foetus and the placental membranes is complete, as an occasional animal may develop metritis following abortion. Most cows will abort in 3 – 5 days, if an animal has not aborted by the eight day, a second injection should be given.

Termination of Abnormal Pregnancy

Removal of mummified foetus:

Death of the conceptus may be followed by its dehydration and degeneration. Induction of luteolysis at any stage of pregnancy will result in the expulsion of this mummified foetus from the uterus into the vagina. Manual removal from the vagina may be necessary. Normal cyclical activity should then follow.

Hydrops of the Foetal Membranes:

Pathological accumulation of placental fluids – hydramnios of hydrallantois – can cause several physiological complications and death. Surgical drainage is not usually

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successful in alleviating the condition. A single dose of ESTROMIL may be used to induce parturition in such cases, success has been achieved as early as the sixth month of pregnancy.

Chronic Endometritis (Pyometra):

Damage to the reproductive tract at calving or post-partum retention of the placenta, frequently lead to infection and inflammation of the uterus. Acute or sub-acute endometritis occurring shortly after parturition may require both local and systemic antibiotic treatment and this often results in resolution of the condition. However, under certain circumstances the endometritis may progress until, at a few weeks post-partum the uterus is very swollen, of a soft doughy consistency and full of purulent discharge. This is characterised by a lack of cyclical oestrus behaviour and the presence of a persistent corpus luteum. This condition can be successfully treated by induction of luteal regression. Where necessary, treatment may be repeated at 10 to 14 days intervals.

Induction of Parturition:

Induction of parturition 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. All treated animals must receive adequate

supervision. In common with all other methods of shortening the gestation period a higher than usual incidence of retention of the foetal membranes is to be expected. It is now recognised that there may be a reduced survival rate in calves born as a result of early induction. Any increased mortality is due to lack of viability as a result of prematurity rather than any effect from the prostaglandins.

Ovarian Luteal Cysts:

Where cystic ovaries associated with persistent luteal tissue and absence of oestrus are diagnosed, ESTROMIL® has proven effective in correcting the condition and bringing about a return of cycling. Accurate diagnosis is essential if completely satisfactory results are to be achieved.

2. Controlled Breeding Programmes in Cattle:

The luteolytic activity of ESTROMIL can be harnessed to control the breeding patterns of cattle.

A variety of treatment regimes exists from which it is possible to choose the most appropriate for the characteristics and objectives of each particular individual, group or herd. ESTROMIL can be used to complement oestrus detection input or animals may be bred "on schedule" during critical times of the breeding season, without reference to oestrus detection. Use one of the following programs:

A	Day 1: ESTROMIL Injection		Day 11: ESTROMIL Injection	BREED: <ul style="list-style-type: none"> At the usual time, relative to detect heat OR At about 72 hours and 96 hours post-injection OR Mass AI at 72 hours, with re-insemination of those in Oestrus over the next 2 to 3 days.
B.	Palpate	All animals with Corpus luteum	ESTROMIL Injection	
C.	Day 1: ESTROMIL Injection	Detect heat and breed	Day 11: All animals not bred ESTROMIL Injection	
D.	Detect heat for 6 days and breed		Day 6: All animals not bred ESTROMIL Injection	

NOTE:

- Best results obtained where heat detection is utilised. This is generally assisted by the use of tail paint.
- Identification of animals is important.
- Conception rate may be about 20% less if insemination is carried out en masse 72 hours after injection with no following insemination.
- ESTROMIL can also be used in systems which include other treatment regimes, e.g. CIDR.

3. Dairy Herd:

To control oestrus in the individual animal giving better insemination without oestrus detection. The number of cows culled as barren is consequently reduced.

To synchronise oestrus in groups of cows to promote management of the herd in groups of suitable size for feeding, A.I. and "drying off". The chances of maintaining a strictly seasonal calving herd are improved and the number of barren cows at the end of the breeding program is reduced.

To permit the use of A.I. in dairy heifers which, in turn, allows the speeding up of the breeding program, the use of a bull known to produce few dystocia problems, better control of heifer management, and steaming up prior to calving.

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4. Beef Herd:

To facilitate the use of A.I. improving the progeny through the use of genetically superior bulls. The problems of oestrus detection are avoided and the labour involved in carrying out an A.I. program is reduced by allowing groups of cattle to be presented instead of single animals.

To permit better management at conception and calving: The calving pattern is altered, resulting in greater average and weight of calves at weaning. The peak calving period can be forecast more accurately in relation to other events in the farm calendar and there is an improved potential for "flushing" the cows prior to A.I.

Dosage and Administration:

Single or repeat doses of 2mL (500µg) by intramuscular injection.

HORSES

ESTROMIL as a potent luteolytic agent causes regression of the corpus luteum in MARES, in a variety of circumstances. Luteolysis is usually followed by oestrus, appearing 2 to 4 days after treatment, with ovulation during the induced oestrus. This sequence of events is seen for example, in mares treated with ESTROMIL during dioestrus (the progestational) phase of the oestrus cycle, but it should be noted that there is a refractory period of 4 to 5 days after ovulation when mares are not responsive to the luteolytic action of prostaglandins.

ESTROMIL has a wide margin of safety and has no deleterious effect on foals conceived and born as a result of mares being covered at the induced oestrus. This property of shortening the life span of the corpus luteum makes ESTROMIL of clinical value in:

Induction of Luteolysis following early foetal death and resorption: About 8 to 10 percent 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 of oestrus. Treatment before day 45 is recommended. After that time no response may be obtained due to the presence of circulating P.M.S.G.

Termination of Pseudopregnancy: Some mares 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 in most cases. Some variability does however occur.

Barren and Maiden Mares: Some of these animals will be found, on examination, to have a functional corpus luteum and are either suffering from abnormal persistence of oestrus behaviour ("silent heat") while ovarian cyclicity continues.

Synchronisation of Oestrus: Under some circumstances this may be a desirable objective in stud management. Treatment during dioestrus usually induces oestrus after 2

to 4 days, with ovulation occurring 8 to 12 days after treatment.

Nomination of the time of service: Mares may be brought into oestrus at will, simply as an aid to successful and economic management of stallions during the breeding season.

Dosage And Administration:

A single intramuscular injection of 0.5 to 1.0mL up to 400kg bodyweight. 1.0 to 2.0mL for horses weight 400 kg and above.

WITHHOLDING PERIODS:

MEAT: DO NOT USE less than one day before slaughter for human consumption

MILK: NIL

MEAT WITHHOLDING PERIOD (horses): 28 days

Pack: 20ml & 100ml.

Registered pursuant to the ACVM Act 1997,

No A8191

RESTRICTED VETERINARY MEDICINE

Estromil

For Animal Treatment Only



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