TECHNICAL NOTES

elevet+ Cloprostenol Injection for Cattle & Horses

Active Constituents

250 µg/mL CLOPROSTENOL (as the sodium salt)

Indications

A luteolytic agent for clinical use and the control of the bovine and equine oestrous cycles.

For use by or under direction of a registered veterinarian.

General Directions

elevet+ Cloprostenol Injection is a synthetic prostaglandin analogue for use in cattle and horses. It is structurally related to Prostaglandin F2α (PGF2α). Each mL of the colourless aqueous solution contains 263 µg cloprostenol sodium, equivalent to 250 µg cloprostenol.

The solution also contains 2% benzyl alcohol Ph. Eur. as a bactericide.

Action:

elevet+ Cloprostenol Injection 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 a return to oestrus two to four days after treatment, and normal ovulation.

Dosage & Administration

Use the contents within 28 days of first broaching of the vial. Discard the unused portion.

CATTLE

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

I. Therapeutic

A single intramuscular dose of elevet+ Cloprostenol Injection 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 elevet+ Cloprostenol Injection 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 eighth 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 or hydrallantois - can cause severe physiological complications and death. Surgical drainage is not usually successful in alleviating the condition. A single dose of elevet+ Cloprostenol Injection 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 day 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, elevet+ Cloprostenol Injection has proved effective in correcting the condition and bringing about a return of cycling. Accurate diagnosis is essential if completely satisfactory results are to be achieved.

II. Controlled Breeding Programmes in Cattle

The luteolytic activity of elevet+ Cloprostenol Injection can be harnessed to control the breeding patterns of cattle. A variety of treatment regimes exist from which it is possible to choose the most appropriate for the characteristics and objectives of each particular individual, group or herd. elevet+ Cloprostenol Injection 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 programmes:

A	Day 1: elevet+ Cloprostenol Injection		Day 11: elevet+ Cloprostenol Injection	BREED: *At usual time, relative to detected 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 or 3 days.
B	Palpate	All animals with luteum elevet+ Cloprostenol Injection		
C	Day 1: elevet+ Cloprostenol Injection	Detect heat and breed	Day 11: All Animals not bred elevet+ Cloprostenol Injection	
D	Detect heat for 6 days and breed		Day 6: All Animals not bred elevet+ Cloprostenol 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.
- Elevet+ Cloprostenol Injection can also be used in systems which include other treatment regimes. e.g. CIDR.

III. Dairy Herd

To control oestrus in the individual animal giving better control of the calving index by allowing artificial 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 programme is reduced.

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

IV. 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. programme 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 age and weight of calves at weaning. The peak calving pattern 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.

HORSES

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

elevet+ Cloprostenol Injection 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 elevet+ Cloprostenol Injection 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.

elevet+ Cloprostenol Injection 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 lifespan of the corpus luteum makes elevet+ Cloprostenol Injection of clinical value in:

- Induction of Luteolysis following early foetal death and resorption: About 8 to 10 per cent 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 luteal function or are simply failing to exhibit normal 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.

Withholding Periods

MEAT (CATTLE, HORSES): DO NOT USE less than 1 day before slaughter for human consumption.

MILK: Zero (0) days.

Contraindications

This product should not be used in 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. This product should not be administered by intravenous injection.

Side Effects

Note: There is a refractory period of four to five days after ovulation when cattle are insensitive to the luteolytic effect of prostaglandins. elevet+ Cloprostenol Injection 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 (500 µg). The only clinically apparent effect was mild and transient diarrhoea. In horses, adverse reactions including sweating (occurring within about 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. elevet+ Cloprostenol Injection 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 can result in acute respiratory distress.)
- Pregnant mares, since luteolysis at some stages of gestation will result in the loss of the foetus.

First Aid

If poisoning occurs, contact a doctor or phone the Poisons Information Centre on 13 11 26 (Australia).

Additional user safety

elevet+ Cloprostenol Injection can be absorbed through the skin and therefore, care should be taken when handling this product, especially by women of childbearing age and also by asthmatics. In case of accidental spillage on skin, wash immediately with water.

Prostaglandins of the F2a type may cause broncho-spasm in man, although the possible incidence of this effect with elevet+ Cloprostenol Injection is not known. Should respiratory embarrassment result from accidental inhalation or injection, a rapid acting broncho-dilator, e.g. isoprenaline or salbutamol by inhalation is indicated.

Safety Data Sheet

For Safety Data Sheet see www.avet.health

Trade Advice

EXPORT SLAUGHTER INTERVAL (ESI): An ESI has not been established for this product. Note – observing the meat withholding period may not be sufficient to mitigate potential risks to export trade. Trade advice should be sought from AVet Health Ltd on 1300 28 38 28 before using this product.

Disposal

Dispose of container by wrapping with paper and putting in garbage.

Storage

Store below 30 ˚C (room temperature). Protect from light.

Poisons schedule

S4

Registration Number

APVMA Approval Number: 92214