

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Delvosteron 100 mg/ml Suspension for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance

Proligestone 100 mg

Preservatives

Methyl Parahydroxybenzoate 1.02 mg

Propyl Parahydroxybenzoate 0.12 mg

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection.

White to off-white, aqueous, sterile suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Cats, dogs and ferrets.

4.2 Indications for use, specifying the target species

The safety of progestogens is related to their molecular structure. Proligestone has a unique molecular configuration which makes it possible to administer Delvosteron at any stage of the oestrous cycle with little risk of undesirable effects on the endometrium.

Oestrus control

(i) Bitches

Permanent postponement of heat (repeat injections given in 'anoestrus'/metoestrus induced by the previous administration of Delvosteron).

Temporary postponement of heat (a single injection given in anoestrus).

Suppression of heat (a single injection given at the beginning of pro-oestrus).

(ii) Queens

Permanent postponement of calling (repeat injections given in 'anoestrus'/di-oestrus induced by the previous administration of Delvosteron).

Temporary postponement of calling (a single injection given during di-oestrus or anoestrus).

Suppression of calling (a single injection given at the onset of calling).

(iii) Ferrets

To prevent the problems, such as vaginal and uterine infection and bone marrow depression associated with prolonged oestrus and persistently high oestrogen levels.

False pregnancy: treatment and prevention

It has been shown that in most bitches, a single injection of Delvosteron will effectively alleviate both the nervous signs and lactation associated with false pregnancy. Trial results have indicated that the incidence of false pregnancy is markedly reduced following the use of Delvosteron for oestrus control irrespective of the bitch's previous history in respect of this condition.

Feline miliary dermatitis (miliary eczema): treatment and prevention.

4.3 Contraindications

Although Delvosteron may be used to medicate bitches at their first oestrus, this regime is not normally recommended. Similarly medication before a bitch's first oestrus is not generally advised.

4.4 Special warnings for each target species

Delvosteron has been used to control heat in diabetic animals without altering insulin requirement. However in other animals, the administration of Delvosteron has led to an increased insulin requirement. It is advised therefore that the product is used with caution in such animals and that urine sugar levels are observed carefully during the month after dosing.

Cases of false pregnancy that recur after a second dose of Delvosteron are better treated conservatively (restricted water intake, low carbohydrate diet, increased exercise, etc) rather than being given further hormone medication.

Delvosteron should not be administered to bitches which have been treated previously with oestrogens or other progestogens for the current false pregnancy.

Bitches may accept the male for some days after medication with Delvosteron in pro-oestrus (suppression of heat). Thus contact with dogs should be prevented, wherever possible, until the signs of heat, vulval swelling and bleeding have fully regressed. This usually occurs within 5 days of dosing. In bitches, the duration of postponement of oestrus following a dose of Delvosteron may on occasion be shorter than expected where the medicated animal is housed with other bitches. In such cases contact the Company for advice on possible alternative dosage regimes.

4.5 Special precautions for use

Special precaution(s) for use in animals

See also 4.4. above.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

None.

4.6 Adverse reactions (frequency and seriousness)

As with all progestogens, the possibility exists that the CEH/pyometra complex may be seen as a side effect of the medication. In the clinical trials carried out with Delvosteron, however, the incidence of uterine disorders including pyometra, was only 0.3% overall and no cases occurred in bitches injected in pro-oestrus. The incidence of uterine changes was higher (1.4%) in animals which had previously received depot progestogens containing medroxy-progesterone acetate. A transient increased appetite, lethargy and weight gain may be seen in some animals medicated with Delvosteron, but these side effects occur less frequently than with the first generation progestogens such as medroxyprogesterone acetate or megestrol acetate.

A brief pain reaction may be seen immediately after injection. Since a slight local reaction, skin thinning and 'pitting' together with some discolouration and loss of hair may occur very occasionally, it is advisable to inject Delvosteron subcutaneously on the medial side of the flank fold in thin skinned or show animals.

Very occasionally a local or systemic allergic/anaphylactic reaction may occur, necessitating immediate treatment with an appropriate corticosteroid, antihistamine or adrenaline.

A few cases of mammary hypertrophy following the use of Delvosteron in entire and neutered queens have been recorded, but proligestone appears less likely to induce the condition than first generation progestogens.

Delvosteron, in common with other progestogens, may cause adrenal suppression in some animals. It may be sensible therefore to administer glucocorticoids to animals being given the product for the permanent postponement of heat if they are subjected to excessive trauma, stress or require major surgery. However no problems have been reported by veterinary surgeons in practice in this respect.

4.7 Use during pregnancy, lactation or lay

Delvosteron is not indicated for use in pregnant animals.

4.8 Interaction with other medicinal products and other forms of interaction

Delvosteron should not be administered to bitches which have been treated previously with oestrogens or other progestogens for the current false pregnancy.

4.9 Amounts to be administered and administration route

Bitches: 10-33 mg/kg body weight. The recommended average doses are as follows:

Bodyweight (kg)	Dose (ml)
< 5	1 - 1.5
5 - 10	1.5 - 2.5
10 - 20	2.5 - 3.5
20 - 30	3.5 - 4.5
30 - 45	4.5 - 5.5
45 - 60	5.5 - 6.0
thereafter	10 mg/kg

Cats: oestrus control - 1 ml for the average 3 kg cat
feline miliary dermatitis - 33 - 50 mg/kg, or 1.5 ml for the average 3 kg cat

Ferrets: 0.5 ml per jill

Delvosteron should be given by subcutaneous injection taking special care to ensure that the product is not deposited intradermally or into a pad of subcutaneous fat or scar tissue. The usual aseptic precautions should be observed, i.e. the site to be used should be cleansed and swabbed with spirit. It is helpful to massage the injection site following administration to promote dispersion of the product.

Shake well before use. Use a sterile needle and syringe. Avoid the introduction of contamination during use. Should any apparent growth or discolouration occur, the product should be discarded.

Dosage schedule

Bitches

Permanent postponement of heat: It is recommended that injections are given as follows:

1 st injection	- in pro-oestrus (see suppression of heat, below), or in anoestrus (see temporary postponement of heat, below).
2 nd injection	- 3 months after 1 st injection
3 rd injection	- 4 months after 2 nd injection
subsequent injections	- at 5 monthly intervals

An injection of Delvosteron may be given to maintain postponement of heat in bitches that are presented late, provided that postponement has not been interrupted by heat.

If anoestrus is not fully maintained, i.e. a 'breakthrough' oestrus occurs in bitches on the permanent postponement regime described above, then immediate re-injection is suggested followed by dosing at intervals described above, but starting one step back in the duration of intervals between injections.

For example if a breakthrough heat occurs in a bitch being given injections at 5 monthly intervals, an immediate dose is given, the next dose 4 months later and the subsequent doses at 5 monthly intervals. Following termination of a permanent postponement course, the next oestrus will occur generally 6-7 months after the last injection. In approximately 4% of cases the interval may be less than 5 months and in 7% it may be longer than 12 months. Up to 3% of bitches may fail to come on heat again when a permanent postponement course is terminated.

Temporary postponement of heat: A single injection given at any time in anoestrus but preferably not more than one month before the effect is required. The subsequent oestrus will occur on average 6 months after the injection. In about 3% of cases the interval will be shorter than 3 months and in up to 4% of bitches the delay will be longer than 12 months.

Suppression of heat: A single injection as soon as possible after the signs of pro-oestrus are seen. Following the injection, bleeding, vulval swelling and attractiveness to dogs gradually decrease and stop within 5-7 days. The times for return to oestrus in the majority of bitches will be 5-6 months on average, but in approximately 3% of bitches the interval will be shorter than 3 months and in 1% it will be longer than 12 months.

Treatment of false pregnancy: A single dose, given preferably as soon as the signs are seen. In most cases nervous signs will disappear within 6 days and lactation will have stopped or be much reduced by day 9 after injection. In approximately 20% of cases the signs will recur within one month of treatment, about 70% of these cases will respond to a second dose.

Prevention of false pregnancy: Medication for permanent postponement of oestrus as advocated above.

Queens

Oestrus control: Dosage regimes similar to those given for bitches are advised for permanent postponement, temporary postponement or the suppression of calling, except that for temporary postponement of calling the injections may be given in either di-oestrus or anoestrus. Following injection at the onset of calling, the signs will usually abate within 1-4 days, but in a few cases such a response may not be seen for 7 days.

As cats are seasonally polyoestrus, the recurrence of calling after treatment is very variable. However in one study 11% and 30% of cats called within 5 months after medication in anoestrus and pro-oestrus respectively. The return to calling will be further delayed if the non breeding season (anoestrus) intervenes.

Treatment and prevention of feline miliary dermatitis: A single injection is often sufficient but a second dose may be given 14 days later if the clinical response is not adequate. Dosing may need to be repeated 4 monthly, or more frequently if necessary depending on the clinical response obtained.

Jills

Oestrus control: Delvosteron can be used to suppress or postpone heat in jills during the breeding season. Following injection in jills showing prolonged oestrus (suppression) the signs will usually abate within 10-11 days. Injections given just before the onset of the breeding season (postponement) or during the breeding season (suppression or postponement) will usually maintain the jill in anoestrus for the remainder of the breeding season.

Further information:

Delvosteron may be safely used in breeding bitches, queens or jills; fecundity at the oestrus following the cessation of medication is not adversely affected. Delvosteron is not contra-indicated in bitches with a history of abnormal cycles or those which have shown or are showing signs of urogenital tract disorders. Indeed there is an indication that the product may be used beneficially in such cases; for example the permanent postponement of oestrus with Delvosteron may prevent the recurrence of endometritis.

Delvosteron generally has little effect on the performance of racing greyhounds.

When using Delvosteron for the suppression of heat, it is important to ensure that the bitch is still in the early stages of pro-oestrus as injection given in the later stages of pro-oestrus is unlikely to be effective at suppressing heat.

In trials, 65% of cases of allergic skin condition in dogs responded well to a single dose of 10-33 mg/kg, as recommended for oestrus control in bitches, although not unexpectedly the response was only maintained in just over one third of the cases. Cases of flea hypersensitivity responded particularly well. Dosing with Delvosteron may thus be a useful alternative to medication with glucocorticoids whilst the underlying cause is being eliminated.

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

No treatment or antidote is recommended.

4.11 Withdrawal Period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Progestogens

ATCvet Code: QG03DA90

5.1 Pharmacodynamic properties

The hormonal profile of proligestone was investigated in pharmacological studies in some of which progesterone and medroxyprogesterone acetate were used as reference compounds.

Proligestone was shown to:

- delay pregnancy in rats for prolonged periods
- possess antigonadotrophic activity
- possess clear progestational activity
- possess only very weak oestrogenic activity
- possess no androgenic activity
- possess negligible corticosteroid activity

5.2 Pharmacokinetic properties

After subcutaneous injection in bitches, the maximum plasma concentration (29 ± 12 ng/ml)

is reached 3.5 ± 2 days after treatment. The decline in proligestone concentrations is then biphasic.

The half-life of proligestone during its alpha phase is approx. 9 ± 5 days, while it lasts 150 ± 75 days for the later beta phase. This long term activity is provided by the formulation and results from a probable accumulation in the fatty tissue and an enterohepatic circulation.

Proligestone is eliminated via the faecal route.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl Parahydroxybenzoate

Propyl Parahydroxybenzoate

Sorbitan Palmitate

Polysorbate 40

Soya Lecithin

Sodium Citrate

Potassium Dihydrogen Phosphate

Macrogol 3350

Water for Injections

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 36 months.

Shelf-life after first opening the immediate packaging: use immediately.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate.

6.5 Nature and composition of immediate packaging

Colourless Type I glass vial with halogenated bromobutyl rubber stopper secured with an aluminium overseal.

Pack size 20 ml.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

7 MARKETING AUTHORISATION HOLDER

Intervet Ireland Ltd.,
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8 MARKETING AUTHORISATION NUMBER(S)

VPA 10996/065/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

1st October 2007

10 DATE OF REVISION OF THE TEXT

March 2012