

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 per ml

Proligestone 100 mg

Preservatives

Methylparahydroxybenzoate 1.02 mg

Propylparahydroxybenzoate 0.12 mg

For 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 the product 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 the product).
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 the product).
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 the product 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 the product 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 Contra-indications

Although the product 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

The product has been used to control heat in diabetic animals without altering insulin requirement. However in other animals, the administration of the product 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 the product are better treated conservatively (restricted water intake, low carbohydrate diet, increased exercise, etc) rather than being given further hormone medication. The product 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 the product 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 the product 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

i. Special precautions for use in animals

See also 4.4. above.

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

Care should be taken to avoid accidental self-injection. If accidental self-injection occurs, seek medical advice immediately and show the doctor this leaflet.

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 the product, however, the incidence of uterine disorders including pyometra, as 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 medroxyprogesterone acetate.

A transient increased appetite, lethargy and weight gain may be seen in some animals medicated with the product, 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 the product 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 the product in entire and neutered queens have been recorded, but proligestone appears less likely to induce the condition than first generation progestogens.

The product, 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 or lactation

The product is not indicated for use in pregnant animals.

4.8 Interaction with other medicinal products and other forms of interaction

The product 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:

Body weight (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

The product 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.

Dosage schedule

Bitches

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

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

An injection of the product may be given to maintain permanent 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 time 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 polyoestrous, 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: The product 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:

The product may be safely used in breeding bitches, queens or jills; fecundity at the oestrus following the cessation of medication is not adversely affected. The product 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 the product may prevent the recurrence of endometritis.

The product generally has little effect on the performance of racing greyhounds.

When using the product 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 conditions 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 the product 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. The product is not indicated for use in any food-producing species.

5. PHARMACOLOGICAL PROPERTIES

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 antigenadotrophic activity
- possess clear progestational activity
- possess only very weak oestrogenic activity
- possess no androgenic activity
- possess negligible corticosteroid activity

ATC Vet Code: QG03DA90

5.2 Pharmacokinetic particulars

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

Methylparahydroxybenzoate
Propylparahydroxy benzoate
Sorbitan monopalmitate
Polysorbate 40
Soya lecithin
Sodium citrate dihydrate
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: 3 years.
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.
This product should be used immediately and not stored after opening.

6.5 Nature and composition of immediate packaging

Colourless glass (Type I) vial with halogenated bromobutyl rubber bung secured with an aluminium overseal. Pack size 20 ml.

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

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

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

Vm 01708/4321

9. DATE OF FIRST AUTHORISATION

31 March 1995

10. DATE OF REVISION OF THE TEXT

April 2021

Approved: 01/04/21

