SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 4.7 mg implant for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Deslorelin (as deslorelin acetate) 4.7 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Implant.
White to pale yellow cylindrical implant.

4. CLINICAL PARTICULARS

4.1 Target species

Dog, cat (male).

4.2 Indications for use, specifying the target species

Male dog:
For the induction of temporary infertility in healthy, intact, sexually mature male dogs.

Prepubertal female dog:
For the induction of temporary infertility to delay the first oestrus and heat signs, and to prevent pregnancy at a young age in intact and healthy sexually immature female dogs. The implant should be administered between 12 and 16 weeks of age.

Male cat:
For the induction of temporary infertility and suppression of urine odour and of sexual behaviours such as libido, vocalisation, urine marking, and aggressiveness in intact male cats from 3 months of age.

4.3 Contraindications

None.

4.4 Special warnings for each target species

All target species:
In certain cases, the implant may be lost from a treated animal. If lack of expected efficacy is suspected, then the subcutaneous presence of the implant should be checked.

Male dog:
Infertility is achieved from 6 weeks up to at least 6 months after initial treatment. Treated dogs should therefore still be kept away from bitches on heat within the first 6 weeks after initial treatment.

One out of 75 dogs treated with the veterinary medicinal product during clinical trials mated and tied with a bitch on heat within six months of implantation, but this did not result in pregnancy. Should a treated dog mate with a bitch between 6 weeks and 6 months after treatment, appropriate measures should be taken to rule out the risk of pregnancy.

In rare cases, suspected lack of expected efficacy has been reported (in the majority of cases a lack of reduction of testicle size was reported and/or a bitch was mated). Only testosterone levels (i.e. an established surrogate marker of fertility) could definitely confirm a lack of efficacy of the treatment.
Any mating that occurs more than 6 months after the administration of the veterinary medicinal product may result in pregnancy. However, it is not necessary to keep bitches away from treated dogs following subsequent implantations, provided that the veterinary medicinal product is administered every 6 months.

If loss of the first implant is suspected, then this can be confirmed by observing no reduction in scrotal circumference or plasma testosterone levels after 6 weeks from the suspected date of loss, as both should reduce under correct implantation. If loss of the implant is suspected following re-implantation after 6 months, then a progressive increase will be seen in scrotal circumference and/or plasma testosterone levels. In both of these circumstances a replacement implant should be administered.

The ability of dogs to sire offspring following their return to normal plasma testosterone levels, after the administration of the veterinary medicinal product, has not been investigated.

With respect to testosterone levels (an established surrogate marker of fertility), during clinical trials more than 80 % of dogs administered one or more implants, returned to normal plasma testosterone levels (≥0.4 ng/ml) within 12 months of implantation. Ninety-eight percent of dogs returned to normal plasma testosterone levels within 18 months of implantation. However, data demonstrating the complete reversibility of clinical effects (reduced testicular size, reduced ejaculation volume, reduced sperm count and reduced libido) including fertility after 6 months, or repeated implantation, are limited. In very rare cases, the temporary infertility may last more than 18 months.

During clinical trials, most of the smaller size dogs (<10 kg bodyweight) maintained suppressed levels of testosterone for more than 12 months following implantation.

For very large dogs (>40 kg bodyweight), data are limited but duration of testosterone suppression was comparable to that seen in medium and large dogs. The use of the veterinary medicinal product in dogs of less than 10 kg or more than 40 kg bodyweight, therefore, should be subject to a risk/benefit assessment performed by the veterinarian.

Surgical or medical castration might have unexpected consequences (i.e. improvement or worsening) on aggressive behaviour. Thus, dogs with sociopathic disorders and showing episodes of intra-specific (dog to dog) and/or inter-specific (dog to another species) aggressions should not be castrated either surgically or with the implant.

Prepubertal female dog:
During clinical trials, the first oestrus occured 6 to 24 months after administration of the product in 98.2% of animals; for one out of 56 female dogs (1.8%) suppression of oestrus lasted 5 months. Specifically, 44.6% of female dogs displayed their first oestrus between 6 and 12 months post-implantation, 53.6% between 12 and 24 months post-implantation.

The veterinary medicinal product should only be administered to prepubertal bitches aged 12-16 weeks, which do not display any signs of oestrus. Measurements of hormonal levels and vaginal smears can be used to confirm the absence of oestrus

Male cat:
In mature male cats, induction of infertility and suppression of urine odour and sexual behaviours are achieved from approximately 6 weeks up to 12 months after implantation. Should a male cat mate with a queen before 6 weeks or after 12 months of being implanted, appropriate measures should be taken to rule out the risk of pregnancy.

When implanted in 3-month old male kittens, suppression of fertility lasted at least for 12 months in 100% of cats and for more than 16 months in 20% of cats.

For most cats, within 2 weeks after implantation, testosterone levels drop, followed by reduced testicular volume and reduced size of penile spines from weeks 4-8 after implantation. Sexual behaviours begin to decrease within a week after treatment, starting with reduced vocalisation, followed by reduction in libido, urine odour, urine marking, and aggressiveness from 4 weeks after implantation. Some sexual behaviours, e.g., mounting and neck-biting, may also have a social component, however, the downregulated male cat cannot complete a mating or induce ovulation in the queen. Clinical effects on urine odour, urine marking, testicular volume, penile spine size, and sexual behaviours begin to wane after approximately 12 months post implantation.

The time-course and duration of down-regulation observed after treatment is variable with 28 months being the maximum duration observed to return to normal fertility following implantation.
In a field study, 22 male cats were administered a second implant 12 months after the first one which extended the duration of suppressed reproductive function and sexual behaviours for another year.

In 1-3% of male cats, lack of expected efficacy has been reported based on continued expression of sexual behaviours, mating resulting in pregnancy, and/or lack of suppression of plasma testosterone levels (an established surrogate marker of fertility). In case of doubt, the animal owner should consider keeping the treated tomcat separate from queens where pregnancy would be undesirable.

4.5 Special precautions for use

Special precautions for use in animals

Male dog:
The use of the veterinary medicinal product in pre-pubertal male dogs has not been investigated. It is therefore recommended that male dogs should be allowed to reach puberty before treatment with the veterinary medicinal product is initiated.

Data demonstrate that treatment with the veterinary medicinal product will reduce the libido of the male dog.

Prepubertal female dog:
In a study, out of the 34 female dogs that were implanted between 16 and 18 weeks of age, one animal implanted at 16 to 17 weeks of age and two animals implanted at 17 to 18 weeks of age displayed an implant-induced oestrus.
Repeated treatment has not been investigated in female dogs and is, therefore, not recommended.

After reaching sexual maturity following the end of the effect of one implant, information has been collected about heat cycles and the ability of female dogs to produce litters: no reproductive safety concerns were noticed. In a follow-up survey six pregnancies in five bitches were completed with one to nine alive puppies. Due to the limited amount of data, the use in prepubertal female dogs intended for breeding should be made according to a benefit/risk assessment by the responsible veterinarian.

The use in sexually mature female dogs to supress reproductive function and oestrus cycling is not recommended, due to the risk of inducing an oestrus, which may cause uterine and ovarian pathology (metropathy, cysts) and unwanted pregnancy.

Male cat:
No data is available in kittens with undescended testicles at implantation. It is recommended to wait until the testicles have descended before administering the product.
Limited data is available regarding return to normal fertility after repeated administrations of the veterinary medicinal product.
The ability of cats to sire offspring following their return to normal plasma testosterone levels, after the administration of the veterinary medicinal product, has not been fully demonstrated, especially in prepubertal cats. A decision to use the veterinary medicinal product in male cats that are intended to be used for breeding therefore needs to be made on a case by case basis.

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

Pregnant women should not administer the veterinary medicinal product. Another GnRH analogue has been shown to be foetotoxic in laboratory animals. Specific studies to evaluate the effect of deslorelin when administered during pregnancy have not been conducted.

Although skin contact with the veterinary medicinal product is unlikely, should this occur, wash the exposed area immediately, as GnRH analogues may be absorbed through the skin.

When administering the veterinary medicinal product, take care to avoid accidental self-injection by ensuring that animals are suitably restrained and the application needle is shielded until the moment of implantation.

In case of accidental self-injection, seek medical advice immediately, with a view to having the implant removed. Show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

All target species:
Prepubertal surgical gonadectomy as well as prepubertal hormonal suppression may delay physeal closure in long-bones, typically without clinical or pathological consequences.

Dog (male and female):

Moderate swelling or scabbing at the implant site was commonly observed for 14 days during safety/efficacy studies. Local dermatitis lasting up to 6 months was commonly reported in a field trial.

During the treatment period, rare clinical effects have been reported:
Hair coat disorders (e.g. hair loss, alopecia, hair modification), urinary incontinence, down-regulation associated signs (e.g. decrease in testicle size, reduced activity, weight gain) have been reported rarely during the treatment period.
A testicle may be able to ascend up through the inguinal ring , in very rare cases.
Transitory increased sexual interest, increased testicle size and testicular pain immediately following implantation were reported very rarely. These signs resolved without treatment.

Transient behavioural change with the development of aggression have been reported very rarely (see section 4.4).

In humans and animals, sexual hormones (testosterone and progesterone) modulate seizure susceptibility. Epileptic seizures have been observed very rarely and have been reported on average 40 days after implantation, the median time to onset of signs was 14 days after implantation, on the same
day of implantation at the earliest, and 36 weeks after implantation at the latest.

Cat:

Local reactions consisting of redness and pain or heat on the day of implantation, that were transient, were commonly observed. Swellings (<5mm) were commonly seen for up to 45 days, in a field study. Severe swelling (>4 cm) lasting for more than 7 months was reported in 1 out 18 cats in a laboratory study.

Increased sexual activity and roaming may be observed transiently in mature male cats during the first weeks post implantation

Increased food intake and increase of body weight are known to be associated with neutering. Some treated cats increase their body weight up to 10% during the period of effect.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Subcutaneous use.

The recommended dose is one implant per dog or cat, irrespective of the size of the dog or the cat (see also point 4.4).

Disinfection of the implantation site should be undertaken prior to implantation to avoid introduction of infection. If the hair is long, a small area should be clipped, if required.

The veterinary medicinal product should be implanted subcutaneously under the loose skin on the back between the lower neck and the lumbar area. Avoid injection of the implant into fat, as release of the active substance might be impaired in areas of low vascularisation.

1. Remove Luer Lock cap from the implanter.

2. Attach the actuator to the implanter using the Luer Lock connection.

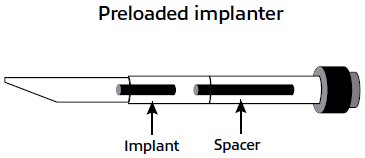
3. Lift the loose skin between the shoulder blades. Insert the entire length of the needle subcutaneously.

4. Fully depress the actuator plunger and, at the same time, slowly withdraw the needle.

5. Press the skin at the insertion site as the needle is withdrawn, and maintain pressure for 30 seconds.

6. Examine the syringe and needle to ensure that the implant has not remained within the syringe or needle, and that the spacer is visible. It may be possible to palpate the implant *in situ*.

Repeat administration every 6 months to maintain efficacy in male dogs and every 12 months to maintain efficacy in male cats.



Do not use the veterinary medicinal product if the foil pouch is broken.

The implant is biocompatible and does not require removal. However, should it be necessary to end treatment, the implant or its fragments may be surgically removed by a veterinarian. Implants may be located using ultrasound.

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

Dog:
No clinical adverse reactions other than those described in section 4.6 or a lump near the injection site have been observed following simultaneous subcutaneous administration of up to 10 times the recommended dose and up to 15 implants over one year, i.e. simultaneous administration of 5 implants every 6 months for 3 consecutive courses, or simultaneous administration of 3 implants every 3 months for 5 consecutive courses. Seizures were observed in one male dog and one female dog at 5 times the recommended dose. The seizures were controlled using symptomatic treatment. Histologically, mild local reactions with chronic inflammation of the connective tissue and some capsule formation and collagen deposition have been seen at 3 months after administration following simultaneous subcutaneous administration of up to 10 times the recommended dose.

Cat:
In a laboratory study, where male cats received 1 or 3 implants 3 times with 6 months intervals, 3 out of 8 developed severe swelling (> 4 cm) at the interscapular injection site that lasted at least 4 weeks after the 2nd and/or 3rd implantation
Cases of infertility have been reported following off-label overdose exposure in newborn kittens as well as in one mature cat.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Pituitary and hypothalamic hormones and analogues, Gonadotropin-releasing hormones (GnRH), ATCvet code: QH01CA93.

5.1 Pharmacodynamic properties

The GnRH agonist, deslorelin, acts by suppressing the function of the pituitary-gonadal axis when applied in a low, continuous dose. This suppression results in the failure of treated animals, intact or surgically neutered, to synthesise and/or release follicle stimulating hormone (FSH) and luteinising hormone (LH), the hormones responsible for the maintenance of fertility as well as secondary sexual behaviours.

In male dogs or cats, the continuous low dose of deslorelin will reduce the functionality and the size of the male reproductive organs, libido, and spermatogenesis, and lower the plasma testosterone levels, from 4-6 weeks after implantation. A short transient increase in plasma testosterone may be seen immediately after implantation. Measurement of plasma concentrations of testosterone has demonstrated the persistent pharmacological effect of the continuing presence of deslorelin in the circulation for at least six months in dogs and twelve months in cats following administration of the veterinary medicinal product.

In sexually immature female dogs, the continuous low dose of deslorelin maintains dogs in a physiologically immature state and prevents the increase of the plasma oestradiol and progesterone levels. This hormonal downregulation suppresses the development and function of the female reproductive organs and associated sexual heat behavioural signs and changes in vaginal cytology.

5.2 Pharmacokinetic particulars

Dog:
It has been shown that plasma deslorelin levels peak 7 to 35 days following administration of an implant containing 5 mg radiolabelled deslorelin. The substance can be directly measured in the plasma up to approximately 2.5 months post implantation. The metabolism of deslorelin is rapid.

Male cat:
In a study investigating pharmacokinetics in cats, it has been shown that plasma deslorelin concentrations peak at 2 hours (C_{max}) at around 100 ng/mL followed by a rapid decrease by 92%, 24 hours post implantation. After 48 hours, a slow and continuous decline of plasma deslorelin concentrations was observed. The duration of deslorelin release from Suprelorin implants, calculated as measurable plasma deslorelin concentrations, varied from 51 weeks to at least 71 weeks (the end of the study).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrogenated palm oil
Lecithin
Sodium acetate anhydrous

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.

6.5 Nature and composition of immediate packaging

The implant is supplied in a pre-loaded implanter. Each pre-loaded implanter is packaged in a sealed foil pouch, which is subsequently sterilised.

Cardboard carton containing either two or five individually foil wrapped implanters that have been sterilised, together with an implanting device (actuator) that is not sterilised. The actuator is attached to the implanter using the Luer Lock connection.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements. The actuator can be re-used.

7. MARKETING AUTHORISATION HOLDER

VIRBAC
1ère avenue 2065m LID
06516 Carros
France

8. MARKETING AUTHORISATION NUMBER

Vm 05653/5017

9. DATE OF FIRST AUTHORISATION

10 July 2007

10. DATE OF REVISION OF THE TEXT

January 2023

Approved 19 January 2023