

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 4.7 mg implant for dogs and cats

2. STATEMENT OF ACTIVE SUBSTANCES

Each implant contains Deslorelin (as deslorelin acetate) 4.7 mg

3. PHARMACEUTICAL FORM

Implant

4. PACKAGE SIZE

2 implants preloaded in implanters + 1 actuator
5 implants preloaded in implanters + 1 actuator

5. TARGET SPECIES

Dog. Cat (male).

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Do not use if the foil pouch is broken.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

VIRBAC
1^{ère} avenue 2065 m LID
06516 Carros
FRANCE

16. MARKETING AUTHORISATION NUMBER(S)

Vm 05653/5017

17. MANUFACTURER'S BATCH NUMBER

Batch

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

FOIL POUCH

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 4.7 mg implant for dogs and cats

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Deslorelin (as deslorelin acetate) 4.7 mg

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

One implant preloaded in one implanter.

4. ROUTE(S) OF ADMINISTRATION

Subcutaneous use.

5. WITHDRAWAL PERIOD(s)

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

**PACKAGE LEAFLET FOR:
Suprelorin 4.7 mg implant for dogs and cats**

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
VIRBAC
1^{ère} Avenue 2065 m LID
06516 Carros
FRANCE

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 4.7 mg implant for dogs and cats

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Suprelorin is a white to pale yellow cylindrical implant containing 4.7 mg deslorelin (as deslorelin acetate).

4. INDICATION(S)

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.

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

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 development of aggression have been reported very rarely (see "Special warnings").

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 (>4cm) lasting for more than 7 months was reported in 1 out of 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).

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dog. Cat (male).

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Administer one implant only, irrespective of the size of the dog or the cat (see also “Special warnings”). Repeat treatment every 6 months to maintain efficacy in male dogs and every 12 months to maintain efficacy in male cats.

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

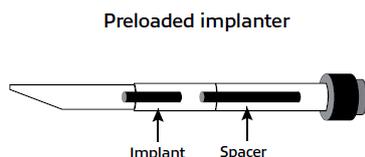
One implant should be administered subcutaneously.

9. ADVICE ON CORRECT ADMINISTRATION

Disinfection of the implantation site should be undertaken prior to implantation to avoid introduction of infection.

Select the implant site by locating the area of 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. If the hair is long, a small area may be clipped, if required.

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*.



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.

The actuator can be re-used.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.

Store in a refrigerator (2°C – 8°C)

Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton.

12. SPECIAL WARNING(S)

Special warnings

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 (>0.01 % to < 0.1%), 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 (< 0.01 %) the temporary infertility may last more than 18 months.

During clinical trials, most of the smaller size dogs (< 10 kg) maintained suppressed levels of testosterone for more than 12 months following implantation. For very large dogs (> 40 kg), 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 occurred at 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 bitch 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.

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 with the veterinary medicinal product has not been investigated in female dogs and therefore is 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 suppress 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 afterwards 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.

Pregnancy:

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

Overdose (symptoms, emergency procedures, antidotes)

Dog:

No clinical adverse reactions other than those described in section “Adverses reactions” 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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

January 2023

15. OTHER INFORMATION

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.



Approved: 28 February 2023