ANNEX I

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

Excipients:

Qualitative composition of excipients and other constituents
Hydrogenated palm oil
Lecithin
Sodium acetate anhydrous

White to pale yellow cylindrical implant.

3. CLINICAL INFORMATION

3.1 Target species

Dogs, cats (male).

3.2 Indications for use for each target species

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

Prepubertal female dogs:
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 cats:
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.

3.3 Contraindications

None.

3.4 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 dogs

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 ($\geq$ 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 dogs

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 cats

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.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Male dogs

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 dogs

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 cats

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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs (male and female):

Common (1 to 10 animals / 100 animals treated):	Implant site swelling, Implant site scab[1] Dermatitis[2]
Rare (1 to 10 animals / 10,000 animals treated):	Hair change (Hair loss, Alopecia, Hair modification) Urinary incontinence Reduced testicle size Decreased activity, Weight gain
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Ascending testicle[3], Increased testicle size[4], Testicular pain[4] Increased sexual interest[5], Aggression[5] Epileptic seizures[6]
Undetermined frequency (Cannot be estimated from the available data):	Delayed growth plates closure[7]

[1]Moderate, for 14 days
[2]Local, lasting up to 6 months

[3]Through the inguinal ring
[4]Immediately following implantation, transitory, resolving without treatment
[5]Transient
[6]On average 40 days after implantation, 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. Sexual hormones (testosterone and progesterone) modulate seizure susceptibility in humans and animals.
[7]In long-bones without clinical or pathological consequences

Cats:

Common (1 to 10 animals / 100 animals treated):	Increased appetite[1], Weight gain[1] Implant site reaction (Implant site redness[2], Implant site pain[2], Implant site warmth[2], Implant site swelling[3,4])
Undetermined frequency (Cannot be estimated from the available data):	Increased sexual interest, Roaming[5] Delayed growth plates closure[6]

[1]Up to 10 % during the period of effect
[2]On the day of implantation, transient
[3]Swelling < 5 mm, for up to 45 days
[4]Severe swelling (> 4 cm) lasting for more than 7 months reported in 1 out 18 cats in a laboratory study
[5]During the first weeks post implantation, transiently in mature male cats
[6]In long-bones without clinical or pathological consequences

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

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 3.4).

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.

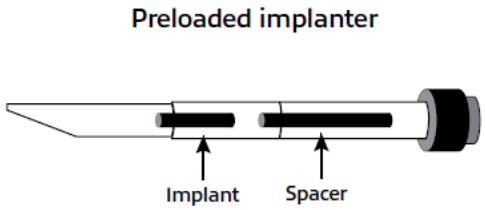
3. Lift the loose skin between the shoulder blades. Insert the entire length of the needle subcutaneously.

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 1 year 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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Dogs:
No clinical adverse reactions other than those described in section 3.6 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.

Cats:
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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QH01CA93.

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

Dogs:
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 cats:
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).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

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

5.3 Special precautions for storage

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

5.4 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.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

The actuator can be re-used.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

VIRBAC

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/07/072/001
EU/2/07/072/002

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 10/07/2007

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 9.4 mg implant for dogs and ferrets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Deslorelin (as deslorelin acetate) 9.4 mg

Excipients:

Qualitative composition of excipients and other constituents
Hydrogenated palm oil
Lecithin

White to pale yellow cylindrical implant.

3. CLINICAL INFORMATION

3.1 Target species

Dogs (male) and ferrets (male).

3.2 Indications for use for each target species

For the induction of temporary infertility in healthy, entire, sexually mature male dogs and ferrets.

3.3 Contraindications

None.

3.4 Special warnings

Dogs

Infertility is achieved from 8 weeks up to at least 12 months after initial treatment. Treated dogs should therefore still be kept away from bitches on heat within the first 8 weeks after initial treatment.

In 2 out of 30 dogs in the clinical trial infertility was not achieved until approximately 12 weeks after initial treatment, but in most cases these animals were not capable of successfully siring offspring. Should a treated dog mate with a bitch between 8 and 12 weeks after treatment, appropriate measures should be taken to rule out the risk of pregnancy.

Uncommonly, lack of expected efficacy has been reported in dogs (in the majority of reports a lack of reduction in 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. If lack of treatment efficacy is suspected, then the dog's implant (e.g. presence) should be checked.

Any mating that occurs more than 12 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 for the initial 8 week period, provided that the veterinary medicinal product is administered every 12 months.

In certain cases, the implant may be lost from a treated dog. If loss of the implant is suspected in connection with the first implantation, this can be confirmed by observing no reduction in scrotal circumference or plasma testosterone levels after 8 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 12 months, 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 68 % of dogs administered one implant, returned to fertility within 2 years of implantation. 95 % of dogs had returned to normal plasma testosterone levels within 2.5 years 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 12 months, or repeated implantation, are limited. In very rare cases the temporary infertility may last more than 18 months.

Due to limited data, the use of Suprelorin in dogs of less than 10 kg or more than 40 kg bodyweight should be subject to a risk/benefit assessment performed by the veterinarian. During clinical trials with Suprelorin 4.7 mg, the mean duration of testosterone suppression was 1.5 times longer among smaller size dogs (< 10 kg) compared with all larger dogs.

Surgical or medical castration might have unexpected consequences (i.e. improvement or worsening) on aggressiveness. 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.

Ferrets

Infertility (suppression of spermatogenesis, reduced testis size, levels of testosterone below 0.1 ng/ml, and suppression of musky odour) is achieved between 5 weeks and 14 weeks after initial treatment under laboratory conditions. Treated ferrets should therefore still be kept away from jills on heat within the first weeks after initial treatment.
Levels of testosterone remain below 0.1 ng/ml for at least 16 months. Not all parameters of sexual activity have been tested specifically (seborrhoea, urine marking, and aggressiveness). Any mating that occurs more than 16 months after the administration of the product may result in pregnancy.

The need for subsequent implantations should be based on the increase in testis size and/or increase in plasma testosterone concentrations and return to sexual activity.

The reversibility of effects and ability of treated hobs to produce offspring subsequently has not been investigated. Therefore, the use of Suprelorin should be subject to a benefit/risk assessment performed by the responsible veterinarian.

In certain cases, the implant may be lost from a treated ferret. If loss of the first implant is suspected, then this can be confirmed by observing no reduction in testis size or plasma testosterone levels as both should reduce under correct implantation. If loss of the implant is suspected following re-implantation, then a progressive increase will be seen in testis size and/or plasma testosterone levels. In both of these circumstances a replacement implant should be administered.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Dogs

The use of Suprelorin in pre-pubertal dogs has not been investigated. It is therefore recommended that 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 dog.

Ferrets

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

Treatment in ferrets should be initiated at the beginning of the breeding season.

The treated hobs may remain infertile up to four years. The veterinary medicinal product should therefore be used prudently in hobs intended for future reproduction.

The safety after repeated implantations with Suprelorin in ferrets has not been investigated.

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 and show the package leaflet or the label to the physician, with a view to having the implant removed.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Implant site swelling[1]
Rare (1 to 10 animals / 10,000 animals treated):	Hair change (Hair loss, Alopecia, Hair modification) Urinary incontinence Reduced testicle size Decreased activity, Weight gain

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Ascending testicle[2], Increased testicle size[3], Testicular pain[3] Increased sexual interest[3], Aggression[4] Epileptic seizures[5]

[1]Moderate, for 14 days
[2]Through the inguinal ring
[3]Immediately following implantation, transitory, resolving without treatment
[4]Transient
[5]On average 40 days after implantation, 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.

Ferrets:

Common (1 to 10 animals / 100 animals treated):	Implant site swelling[1], Implant site pruritus[1], Implant site erythema[1]

[1]Transient, moderate

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Not applicable.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Dogs:

Subcutaneous use.

The recommended dose is one implant per dog, irrespective of the size of the dog (see also point 3.4). 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 in 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 ascertain 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 12 months to maintain efficacy.

Ferrets:

Subcutaneous use.

The recommended dose is one implant per ferret, irrespective of the size of the ferret.
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.

It is recommended that the product should be administered under general anaesthesia in ferrets.

The product should be implanted subcutaneously in the loose skin on the back in the intrascapular space. 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.

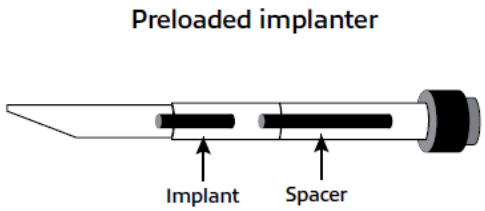
3. Lift the loose skin between the shoulder blades. Insert the entire length of the needle subcutaneously.

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 ascertain 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*. Tissue glue is recommended to close the site of administration if required.

The need for subsequent implantations should be based on the increase of testis size and/or increase in plasma testosterone concentrations as well as return to sexual activity. See also point 3.4.



Dogs and ferrets:

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

The biocompatible implant does not require removal. However, should it be necessary to end treatment, implants may be surgically removed by a veterinarian. Implants may be located using ultrasound.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Ferrets:
There is no information available in ferrets.

Dogs:
No clinical adverse reactions other than those described in section 3.6 have been observed following subcutaneous administration of up to 6 times the recommended dose. 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 6 times the recommended dose.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QH01CA93.

4.2 Pharmacodynamics

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 to synthesise and/or release follicle stimulating hormone (FSH) and luteinising hormone (LH), the hormones responsible for the maintenance of fertility.

The continuous low dose of deslorelin will reduce the functionality of the male reproductive organs, libido and spermatogenesis and lower the plasma testosterone levels, from 4 to 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 12 months following administration of the veterinary medicinal product.

4.3 Pharmacokinetics

It has been shown in dogs 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

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

5.3 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

5.4 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.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

The actuator can be re-used.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

VIRBAC

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/07/072/003
EU/2/07/072/004

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 10/07/2007

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

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

2. STATEMENT OF ACTIVE SUBSTANCES

Deslorelin (as deslorelin acetate) 4.7 mg

3. PACKAGE SIZE

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

4. TARGET SPECIES

Dogs, cats (male)

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store in a refrigerator.
Do not freeze.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

VIRBAC

14. MARKETING AUTHORISATION NUMBERS

EU/2/07/072/001
EU/2/07/072/002

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

FOIL POUCH

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

4.7 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 9.4 mg implant

2. STATEMENT OF ACTIVE SUBSTANCES

Deslorelin (as deslorelin acetate) 9.4 mg

3. PACKAGE SIZE

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

4. TARGET SPECIES

Dogs (male) and ferrets (male)

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store in a refrigerator.
Do not freeze.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

VIRBAC

14. MARKETING AUTHORISATION NUMBERS

EU/2/07/072/003
EU/2/07/072/004

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

FOIL POUCH

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

9.4 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Suprelorin 4.7 mg implant for dogs and cats

2. Composition

Active substance:

Deslorelin (as deslorelin acetate) 4.7 mg

White to pale yellow cylindrical implant.

3. Target species

Dogs and cats (male)

4. Indications for use

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. Special warnings

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 occured 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 bitched 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 safe use in the target species:

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 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 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 and lactation:

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

Overdose:

Dog:
No clinical adverse reactions other than those described in section “Adverses events” 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 ine one mature cat.

7. Adverse events

Dogs (male and female):

Common (1 to 10 animals / 100 animals treated):

Implant site swelling, Implant site scab[1] Dermatitis[2]
Rare (1 to 10 animals / 10,000 animals treated):
Hair change (Hair loss, Alopecia, Hair modification) Urinary incontinence Reduced testicle size Decreased activity, Weight gain
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Ascending testicle[3], Increased testicle size[4], Testicular pain[4] Increased sexual interest[5], Aggression[5] Epileptic seizures[6]
Undetermined frequency (Cannot be estimated from the available data):
Delayed growth plates closure[7]

[1]Moderate, for 14 days
[2]Local, lasting up to 6 months
[3]Through the inguinal ring
[4]Immediately following implantation, transitory, resolving without treatment
[5]Transient
[6]On average 40 days after implantation, 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. Sexual hormones (testosterone and progesterone) modulate seizure susceptibility in humans and animals.
[7]In long-bones without clinical or pathological consequences

Cats:

Common (1 to 10 animals / 100 animals treated):
Increased appetite[1], Weight gain[1] Implant site reaction (Implant site redness[2], Implant site pain[2], Implant site warmth[2], Implant site swelling[3,4])
Undetermined frequency (Cannot be estimated from the available data):
Increased sexual interest, Roaming[5] Delayed growth plates closure[6]

[1]Up to 10 % during the period of effect
[2]On the day of implantation, transient
[3]Swelling < 5 mm, for up to 45 days
[4]Severe swelling (> 4 cm) lasting for more than 7 months reported in 1 out 18 cats in a laboratory study
[5]During the first weeks post implantation, transiently in mature male cats
[6]In long-bones without clinical or pathological consequences

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes 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.

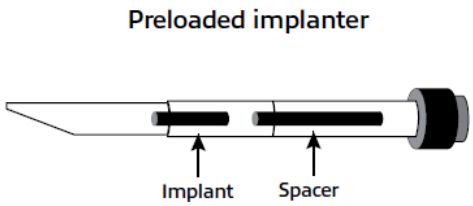
2. Attach the actuator to the implanter using the Luer Lock connection.

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 periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach 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 precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

The actuator can be re-used.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/07/072/001-002

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

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release:

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1ère Avenue 2065 m LID
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Local representatives and contact details to report suspected adverse reactions:

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For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Suprelorin 9.4 mg implant for dogs and ferrets

2. Composition

Active substance:

Deslorelin (as deslorelin acetate) 9.4 mg

White to pale yellow cylindrical implant.

3. Target species

Dogs (male) and ferrets (male).

4. Indications for use

For the induction of temporary infertility in healthy, entire, sexually mature male dogs and ferrets.

5. Contraindications

None.

6. Special warnings

Special warnings:

Dogs

Infertility is achieved from 8 weeks up to at least 12 months after initial treatment. Treated dogs should therefore still be kept away from bitches on heat within the first 8 weeks after initial treatment.

In 2 out of 30 dogs in the clinical trial infertility was not achieved until approximately 12 weeks after initial treatment, but in most cases these animals were not capable of successfully siring offspring. Should a treated dog mate with a bitch between 8 and 12 weeks after treatment, appropriate measures should be taken to rule out the risk of pregnancy.

Uncommonly, lack of expected efficacy has been reported in dogs (in the majority of reports a lack of reduction in 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. If lack of treatment efficacy is suspected, then the dog's implant (e.g. presence) should be checked.

Any mating that occurs more than 12 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 for the initial 8 week period, provided that the veterinary medicinal product is administered every 12 months.

In certain cases, the implant may be lost from a treated dog. 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 8 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 12 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 (i.e. an established surrogate marker of fertility), during clinical trials 68 % of dogs administered one implant, returned to fertility within 2 years of implantation. 95 % of dogs had returned to normal plasma testosterone levels within 2.5 years 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 12 months, or repeated implantation, are limited. In very rare cases the temporary infertility may last more than 18 months.

Due to limited data, the use of Suprelorin in dogs of less than 10 kg or more than 40 kg bodyweight should be subject to a risk/benefit assessment performed by the veterinarian. During clinical trials with Suprelorin 4.7 mg, the mean duration of testosterone suppression was 1.5 times longer among smaller size dogs (< 10 kg) compared with all larger dogs.

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.

Ferrets

Infertility (suppression of spermatogenesis, reduced testis size, levels of testosterone below 0.1 ng/ml, and suppression of musky odor) is achieved between 5 weeks and 14 weeks after initial treatment under laboratory conditions. Treated ferrets should therefore still be kept away from jills on heat within the first weeks after initial treatment.
Levels of testosterone remain below 0.1 ng/ml for at least 16 months. Not all parameters of sexual activity have been tested specifically (seborrhoea, urine marking and aggressiveness). Any mating that occurs more than 16 months after the administration of the product may result in pregnancy.

The need for subsequent implantations should be based on the increase in testis size and/or increase in plasma testosterone concentrations and return to sexual activity.

The reversibility of effects and ability of treated hobs to produce offspring subsequently has not been investigated. Therefore, the use of Suprelorin should be subject to a benefit/risk assessment performed by the responsible veterinarian.

In certain cases, the implant may be lost from a treated ferret. If loss of the first implant is suspected, then this can be confirmed by observing no reduction in testis size or plasma testosterone levels as both should reduce under correct implantation. If loss of the implant is suspected following re-implantation, then a progressive increase will be seen in testis size and/or plasma testosterone levels. In both of these circumstances a replacement implant should be administered.

Special precautions for safe use in the target species:

Dogs

The use of Suprelorin in pre-pubertal dogs has not been investigated. It is therefore recommended that 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 dog.

Ferrets

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

Treatment in ferrets should be initiated at the beginning of the breeding season.

The safety after repeated implantations with Suprelorin in ferrets has not been investigated.

The treated hobs may remain infertile up to four years. The veterinary medicinal product should therefore be used prudently in hobs intended for future reproduction.

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 and show the package leaflet or the label to the physician, with a view to having the implant removed.

Overdose:

Dogs: No adverse reactions other than those described in section “Adverse events” have been observed following subcutaneous administration of up to 6 times the recommended dose. 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 6 times the recommended dose.

Ferrets: There is no information available in ferrets concerning overdose.

7. Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):
Implant site swelling[1]

Rare (1 to 10 animals / 10,000 animals treated):
Hair change (Hair loss, Alopecia, Hair modification)[2] Urinary incontinence[2] Reduced testicle size[2,3] Decreased activity[2,3], Weight gain[2,3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Ascending testicle[4], Increased testicle size[5], Testicular pain[5] Increased sexual interest[5], Aggression[6] Epileptic seizures[7]

[1]Moderate, for 14 days
[2]During the treatment period
[3]Down-regulation associated signs
[4]Through the inguinal ring
[5]Immediately following implantation, transitory, resolving without treatment
[6]Transient
[7]On average 40 days after implantation, 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. In humans and animals, sexual hormones (testosterone and progesterone) modulate seizure susceptibility.

Ferrets:

Common (1 to 10 animals / 100 animals treated):
Implant site swelling[1], Implant site pruritus[1], Implant site erythema[1]

[1]Transient, moderate

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

Dogs

Administer one implant only, irrespective of the size of the dog (see also “Special warnings”). Repeat treatment every 12 months to maintain efficacy.

Ferrets

Administer one implant only, irrespective of the size of the ferret. Repeat treatment every 16 months to maintain efficacy.

Dogs and ferrets

The implant should be administered subcutaneously between the shoulder blades of the dog or ferret. Do not use the veterinary medicinal product if the foil pouch is broken.

The biocompatible implant does not require removal. However, should it be necessary to end treatment, implants may be surgically removed by a veterinarian. Implants may be located using ultrasound.

9. Advice on correct administration

Dogs

Subcutaneous use.

The recommended dose is one implant per dog, irrespective of the size of the dog (see also "Special warnings").

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 in 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 ascertain 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 12 months to maintain efficacy.

Ferrets

Subcutaneous use.

The recommended dose is one implant per ferret, irrespective of the size of the ferret.

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.

It is recommended that the product should be administered under general anaesthesia in ferrets.

The product should be implanted subcutaneously in the loose skin on the back in the intrascapular space. 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.

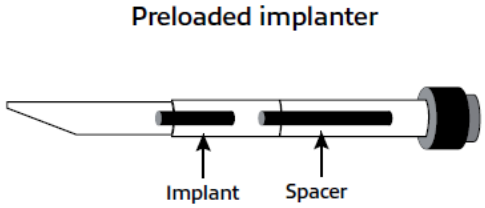
3. Lift the loose skin between the shoulder blades. Insert the entire length of the needle subcutaneously.

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 ascertain 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*.
Tissue glue can be used to close the site of administration if required.

Subsequent implantations should be based on the increase in testis size and/or increase in plasma testosterone concentrations as well as return to sexual activity. See also “Special warnings”.



10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach 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 precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

The actuator can be re-used.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/07/072/003-004

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

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release:

VIRBAC
1ère Avenue 2065 m LID
06516 Carros
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Local representatives and contact details to report suspected adverse reactions:

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For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.