ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS
1. **NAME OF THE VETERINARY MEDICINAL PRODUCT**

Suprelorin 4.7 mg implant for dogs

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

**Active substance:**

Deslorelin (as deslorelin acetate) 4.7 mg

For the full list of excipients, see section 6.1.

3. **PHARMACEUTICAL FORM**

Implant.

White to pale yellow cylindrical implant.

4. **CLINICAL PARTICULARS**

4.1 **Target species**

Dogs (male).

4.2 **Indications for use, specifying the target species**

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

4.3 **Contraindications**

None.

4.4 **Special warnings for each target species**

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. If lack of treatment efficacy is suspected, then the dog’s implant (e.g. presence) should be checked.

Any mating that occurs more than 6 months after the administration of the veterinary medicinal product may result in pregnancy. However, it is not necessary to keep bitches away from treated dogs following subsequent implantations, provided that the veterinary medicinal product is administered every 6 months.

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

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

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

During clinical trials, most of the smaller size dogs (<10 kg bodyweight) maintained suppressed levels of testosterone for more than 12 months following implantation. For very large dogs (>40 kg bodyweight), data are limited but duration of testosterone suppression was comparable to that seen in medium and large dogs. The use of the veterinary medicinal product in dogs of less than 10 kg or more than 40 kg bodyweight, therefore, should be subject to a risk/benefit assessment performed by the veterinarian.

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

4.5 Special precautions for use

Special precautions for use in animals

The use of the veterinary medicinal product 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.

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

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

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

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

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

4.6 Adverse reactions (frequency and seriousness)
Moderate swelling at the implant site was commonly observed for 14 days during safety/efficacy studies.

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). In very rare cases, a testicle may be able to ascend the inguinal ring.

In very rare cases, there has been transitory increased sexual interest, increased testicle size and testicular pain immediately after implantation. These signs resolved without treatment.

In very rare cases, a transient behavioural change has been reported with the development of aggression (see section 4.4).

In humans and animals, testosterone modulates seizure susceptibility. On very rare occasions (<0.01%) transient occurrence of seizure has been reported shortly after implantation, though the casual relationship with the application of the implant has not been established. In some cases, the dog had displayed epileptic seizure prior to the implant administration or was diagnosed as suffering from epilepsy.

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

4.7 Use during pregnancy, lactation or lay

Not applicable.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Subcutaneous use.

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

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

The veterinary medicinal product should be implanted subcutaneously 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 6 months to maintain efficacy.

![Preloaded implanter](image)

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.

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

No clinical adverse reactions other than those described in section 4.6 have been observed following simultaneous subcutaneous administration of up to 10 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 10 times the recommended dose.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

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

5.1 Pharmacodynamic properties

The GnRH agonist, deslorelin, acts by suppressing the function of the pituitary-gonadal axis when applied in a low, continuous dose. This suppression results in the failure of treated animals 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 4-6 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 following administration of the veterinary medicinal product.

5.2 Pharmacokinetic particulars

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.
6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrogenated palm oil
Lecithin
Sodium acetate anhydrous

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

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

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

Not all pack sizes may be marketed.

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

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

7. MARKETING AUTHORISATION HOLDER

VIRBAC
1ère avenue 2065 m LID
06516 Carros
FRANCE

8. MARKETING AUTHORISATION NUMBER(S)

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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10/07/2007
Date of latest renewal: 17/05/2017
10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.
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

For the full list of excipients, see section 6.1.

3. **PHARMACEUTICAL FORM**

Implant

White to pale yellow cylindrical implant.

4. **CLINICAL PARTICULARS**

4.1 **Target species**

Dogs (male) and ferrets (male).

4.2 **Indications for use, specifying the target species**

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

4.3 **Contraindications**

None.

4.4 **Special warnings for each target species**

**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.

### 4.5 Special precautions for use

**Special precautions for use in animals**

**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.

**4.6 Adverse reactions (frequency and seriousness)**

In dogs: Moderate swelling at the implant site was commonly observed for 14 days during safety/efficacy studies.

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). In very rare cases, a testicle may be able to ascend the inguinal ring.

In very rare cases, there has been transitory increased sexual interest, increased testicle size and testicular pain immediately after implantation. These signs resolved without treatment.

In very rare cases, a transient behavioural change has been reported with the development of aggression (see section 4.4).

In humans and animals, testosterone modulates seizure susceptibility. On very rare occasions (<0.01%) transient occurrence of seizure has been reported shortly after implantation, though the casual relationship with the application of the implant has not been established. In some cases, the dog
had displayed epileptic seizure prior to the implant administration or was diagnosed as suffering from epilepsy.

In ferrets: Transient moderate swelling, pruritus and erythema at the implant site were commonly observed during clinical studies.

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, including isolated reports treated).

4.7 Use during pregnancy, lactation or lay

Not applicable.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Dogs:

Subcutaneous use.

The recommended dose is one implant per dog, irrespective of the size of the dog (see also point 4.4). Disinfection of the implantation site should be undertaken prior to implantation to avoid introduction of infection. If the hair is long, a small area should be clipped, if required.

The veterinary medicinal product should be implanted subcutaneously 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 4.4.

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.

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

Ferrets: There is no information available in ferrets.

Dogs: No clinical adverse reactions other than those described in section 4.6 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.

4.11 Withdrawal period(s)

Not applicable.

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

5.1 Pharmacodynamic properties

The GnRH agonist, deslorelin, acts by suppressing the function of the pituitary-gonadal axis when applied in a low, continuous dose. This suppression results in the failure of treated animals 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.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrogenated palm oil
Lecithin

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

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

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

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

7. MARKETING AUTHORISATION HOLDER

VIRBAC
1ère avenue 2065 m LID
06516 Carros
FRANCE

8. MARKETING AUTHORISATION NUMBER(S)

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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10/07/2007
Date of latest renewal: 17/05/2017

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu
ANNEX II

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE
B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY OR USE
C. STATEMENT OF THE MRLs
A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

VIRBAC
1ère avenue 2065 m LID
06516 Carros
FRANCE

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY OR USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.
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

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
Dogs (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
1ère avenue 2065 m LID
06516 Carros
FRANCE

16. MARKETING AUTHORISATION NUMBER(S)

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

17. MANUFACTURER’S BATCH NUMBER

Batch
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<th>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</th>
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<td>FOIL POUCH</td>
</tr>
<tr>
<td>1.</td>
<td>NAME OF THE VETERINARY MEDICINAL PRODUCT</td>
</tr>
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<td></td>
<td>Suprelorin 4.7 mg implant for dogs</td>
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<td>2.</td>
<td>QUANTITY OF THE ACTIVE SUBSTANCE(S)</td>
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<td>Deslorelin (as deslorelin acetate) 4.7 mg</td>
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<td>3.</td>
<td>CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES</td>
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<td>One implant preloaded in one implanter.</td>
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<td>4.</td>
<td>ROUTE(S) OF ADMINISTRATION</td>
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<td>Subcutaneous use.</td>
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<td>5.</td>
<td>WITHDRAWAL PERIOD(s)</td>
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<td>7.</td>
<td>EXPIRY DATE</td>
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<td>EXP {month/year}</td>
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<td>8.</td>
<td>THE WORDS “FOR ANIMAL TREATMENT ONLY”</td>
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<td>For animal treatment only.</td>
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</tbody>
</table>
PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 9.4 mg implant for dogs and ferrets

2. STATEMENT OF ACTIVE SUBSTANCES

Deslorelin (as deslorelin acetate) 9.4 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

Dogs (male) and ferrets (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
1er avenue 2065 m LID
06516 Carros
FRANCE

16. **MARKETING AUTHORISATION NUMBER(S)**

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

17. **MANUFACTURER’S BATCH NUMBER**

Batch
<table>
<thead>
<tr>
<th><strong>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOIL POUCH</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>1. NAME OF THE VETERINARY MEDICINAL PRODUCT</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Suprelorin 9.4 mg implant for dogs and ferrets.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>2. QUANTITY OF THE ACTIVE SUBSTANCE(S)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Deslorelin (as deslorelin acetate) 9.4 mg</td>
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</table>

<table>
<thead>
<tr>
<th><strong>3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>One implant preloaded in one implanter</td>
</tr>
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<table>
<thead>
<tr>
<th><strong>4. ROUTE(S) OF ADMINISTRATION</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous route</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>5. WITHDRAWAL PERIOD(S)</strong></th>
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</thead>
</table>

<table>
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<tr>
<th><strong>6. BATCH NUMBER</strong></th>
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<tbody>
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<td>Batch {number}</td>
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</tbody>
</table>

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<tr>
<th><strong>7. EXPIRY DATE</strong></th>
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<td>EXP {month/year}</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>8. THE WORDS “FOR ANIMAL TREATMENT ONLY”</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>For animal treatment only.</td>
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</tbody>
</table>
B. PACKAGE LEAFLET
1. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT**

Marketing authorisation holder:
VIRBAC
1ère avenue 2065 m LID
06516 Carros
FRANCE

Manufacturers responsible for batch release:
VIRBAC
1ère Avenue 2065 m LID
06516 Carros
FRANCE

2. **NAME OF THE VETERINARY MEDICINAL PRODUCT**

Suprelorin 4.7 mg implant for dogs

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)**

For the induction of temporary infertility in healthy, non-castrated, sexually mature male dogs.

5. **CONTRAINDICATIONS**

None.

6. **ADVERSE REACTIONS**

Moderate swelling at the implant site was observed for 14 days during safety/efficacy studies.

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 (decrease in testicle size, reduced activity, weight gain). In very rare cases, a testicle may be able to ascend the inguinal ring.

In very rare cases there has been transitory increased sexual interest, increased testicle size and testicular pain immediately after implantation. These signs resolved without treatment.

In very rare cases, a transient behavioural change has been reported with development of aggression (see “Special warnings”).
In humans and animals, testosterone modulates seizure susceptibility. On very rare occasions (<0.01%) transient occurrence of seizure has been reported shortly after implantation, though the casual relationship with the application of the implant has not been established. In some cases, the dog had displayed epileptic seizure prior to the implant administration or was diagnosed as suffering from epilepsy.

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**

Dogs (male).

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

Administer one implant only, irrespective of the size of the dog (see also “Special warnings”). Repeat treatment every 6 months to maintain efficacy.

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

One implant should be administered subcutaneously between the shoulder blades of the dog.

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 midway between the shoulder blades. 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 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*. 

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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.

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

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. If lack of treatment efficacy is suspected, then the dog’s implant (e.g. presence) should be checked.

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.

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 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.

Special precautions for use in animals

The use of the veterinary medicinal product 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 product will reduce the libido of the dog.

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.

Overdose (symptoms, emergency procedures, antidotes)

No clinical adverse reactions other than those described in the section “Adverse reactions” have been observed following subcutaneous administration of up to 10 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 10 times the recommended dose.
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

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

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.

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

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Latvija
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FR-06516 Carros
Tel: +33-(0)4 92 08 73 00

United Kingdom
VIRBAC LTD
Suffolk, IP30 9UP – UK
Tel: +44 (0)-1359 243243
PACKAGE LEAFLET FOR:
Suprelorin 9.4 mg implant for dogs and ferrets

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

Marketing authorisation holder:
VIRBAC
1ère avenue 2065 m LID
06516 Carros
FRANCE

Manufacturers responsible for the batch release:
VIRBAC
1ère Avenue 2065 m LID
06516 Carros
FRANCE

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Suprelorin 9.4 mg implant for dogs and ferrets

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

Suprelorin is a white to pale yellow cylindrical implant containing 9.4 mg deslorelin (as deslorelin acetate).

4. INDICATION(S)

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

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

In dogs: Moderate swelling at the implant site was commonly observed for 14 days during safety/efficacy studies.

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). In very rare cases, a testicle may be able to ascend the inguinal ring.

In very rare cases there has been transitory increased sexual interest, increased testicle size and testicular pain immediately after implantation. These signs resolved without treatment.
In very rare cases, a transient behavioural change has been reported with the development of aggression (see “Special warnings”). In humans and animals, testosterone modulates seizure susceptibility. On very rare occasions (<0.01%) transient occurrence of seizure has been reported shortly after implantation, though the casual relationship with the application of the implant has not been established. In some cases, the dog had displayed epileptic seizure prior to the implant administration or was diagnosed as suffering from epilepsy.

In ferrets: Transient moderate swelling, pruritus and erythema at the implant site were commonly observed during clinical studies.

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, including isolated reports treated).

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

7. TARGET SPECIES

Dogs (male) and ferrets (male).

8. DOSAGE FOR EACH SPECIES, ROUTE(S) 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.

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”.

Tissue glue can be used to close the site of administration if required.
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 after the expiry date which is stated on the carton.

12. SPECIAL WARNING(S)

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.

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.

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**

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.
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.

Dogs: No adverse reactions other than those described in section “Adverse effects” 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.

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

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

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.

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

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<table>
<thead>
<tr>
<th>Country</th>
<th>Address</th>
<th>Phone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Республика България</td>
<td>VIRBAC 1ª avenue 2065 m LID FR-06516 Carros Франция</td>
<td>Тел: +33-(0)4 92 08 73 00</td>
</tr>
<tr>
<td>Česká republika</td>
<td>VIRBAC 1ª avenue 2065 m LID FR-06516 Carros Francie</td>
<td>Tel: +33-(0)4 92 08 73 00</td>
</tr>
<tr>
<td>Danmark</td>
<td>VIRBAC Danmark A/S Profilvej 1 DK-6000 Kolding Tlf: +45 75521244</td>
<td></td>
</tr>
<tr>
<td>Deutschland</td>
<td>VIRBAC Tierarzneimittel GmbH Rögen 20 DE-23843 Bad Oldesloe Tel: +49-(4531) 805 111</td>
<td></td>
</tr>
<tr>
<td>Eesti</td>
<td>VIRBAC 1ª avenue 2065 m LID FR-06516 Carros Prantsusmäe Tel: +33-(0)4 92 08 73 00</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>España</td>
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<td></td>
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<td></td>
</tr>
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</tr>
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</tbody>
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