ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Imidamox 400 mg/100 mg spot-on solution for extra-large dogs
Imidacloprid/Moxidectin

2. STATEMENT OF ACTIVE SUBSTANCES

Each 4 ml pipette contains:

Active substances:
Imidacloprid 400 mg
Moxidectin 100 mg

3. PHARMACEUTICAL FORM

Spot-on solution

4. PACKAGE SIZE

1x 4 ml
3 x 4 ml
4 x 4 ml
24 x 4 ml
42 x 4 ml

5. TARGET SPECIES

Extra large dogs (>25-40 kg)

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Spot-on use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP

11. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture and light.

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

Krka, d.d, Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

16. MARKETING AUTHORISATION NUMBER(S)

Vm 01656/4207

17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

FOIL LABEL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Imidamox 400 mg/100 mg spot-on solution for extra-large dogs
Imidacloprid/Moxidectin

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

400 mg/100 mg

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

4 ml

4. ROUTE(S) OF ADMINISTRATION

Spot on use.

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot

7. EXPIRY DATE

EXP

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

PIPETTE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Imidamox 400 mg/100 mg
Imidacloprid/Moxidectin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

KRKA, d.d., Novo mesto

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Imidamox 40 mg/10 mg spot-on solution for small dogs
Imidamox 100 mg/25 mg spot-on solution for medium dogs
Imidamox 250 mg/62.5 mg spot-on solution for large dogs
Imidamox 400 mg/100 mg spot-on solution for extra-large dogs

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

Marketing authorisation holder:
Krka, d.d, Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

Manufacturer responsible for batch release:
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Imidamox 40 mg/10 mg spot-on solution for small dogs
Imidamox 100 mg/25 mg spot-on solution for medium dogs
Imidamox 250 mg/62.5 mg spot-on solution for large dogs
Imidamox 400 mg/100 mg spot-on solution for extra-large dogs
Imidacloprid/Moxidectin

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

Each pipette contains:

Active substances, excipients:

	Imidacloprid [mg]	Moxidectin [mg]	Butylhydroxytoluene (E 321) [mg]	Benzyl alcohol (E 1519)	Volume [ml]
Imidamox 40 mg/10 mg spot-on solution for small dogs	40	10	0.4	323 mg	0.4
Imidamox 100 mg/25 mg spot-on solution for medium dogs	100	25	1	807 mg	1
Imidamox 250 mg/62.5 mg spot-on solution for large dogs	250	62.5	2.5	2018 mg	2.5
Imidamox 400 mg/100 mg spot-on solution for extra-large dogs	400	100	4	3229 mg	4

Clear, slightly yellow to yellow or to brownish yellow solution.

4. INDICATION(S)

For dogs suffering from, or at risk from, mixed parasitic infections.

The treatment and prevention of flea infestation (*Ctenocephalides felis*). 
The treatment of biting lice (*Trichodectes canis*). 
The treatment of ear mite infestation (*Otodectes cynotis*) and sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*). 
The prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*). 
Treatment of circulating microfilariae (*Dirofilaria immitis*). 
The treatment of cutaneous dirofilariosis (adult stages of *Dirofilaria repens*). 
The prevention of cutaneous dirofilariosis (L3 larvae of *Dirofilaria repens*). 
The reduction of circulating microfilariae (*Dirofilaria repens*). 
The prevention of angiostrongylosis (L4 larvae and immature adults of *Angiostrongylus vasorum*). 
The treatment of *Angiostrongylus vasorum* and *Crenosoma vulpis*. 
The prevention of spirocercosis (*Spirocerca lupi*). 
The treatment of *Eucoleus* (syn. *Capillaria*) *boehmi* (adults). 
The treatment of the eye worm *Thelazia callipaeda* (adults). 
Treatment of infections with gastrointestinal nematodes (L4 larvae, immature adults and adults of *Toxocara canis, Ancylostoma caninum* and *Uncinaria stenocephala*, adults of *Toxascaris leonina* and *Trichuris vulpis*). 

The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

5. CONTRAINDICATIONS

Do not use in puppies under 7 weeks of age.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Do not use in dogs classified as Class 4 for heartworm disease as the safety of the product has not been
evaluated in this animal group.
For cats, the corresponding veterinary medicinal product (0.4 or 0.8 ml), which contains 100 mg/ml imidacloprid and 10 mg/ml moxidectin, must be used.
For ferrets: Do not use the veterinary medicinal product for dogs. Only the product for small cats and ferrets (0.4 ml) should be used.
Do not use on canaries.

6. ADVERSE REACTIONS

Use of the product may result in transient pruritus in dogs. On rare occasions greasy hair, erythema and vomiting can occur. These signs disappear without further treatment. The product may, in rare cases, cause local hypersensitivity reactions.

If the animal licks the application site after treatment, neurological signs (most of which are transient) such as ataxia, generalised tremors, ocular signs (dilated pupils, little pupillary reflex, nystagmus), abnormal respiration, salivation and vomiting may be observed in very rare cases).

The product tastes bitter. Salivation may occasionally occur if the animal licks the application site immediately after treatment. This is not a sign of intoxication and disappears within some minutes without treatment. Correct application will minimise licking of the application sites.

The product may in very rare cases cause at the application site a sensation resulting in transient behavioural changes such as lethargy, agitation, and inappetence.
A field study has shown that in heartworm positive dogs with microfilaraemia there is a risk of severe respiratory signs (coughing, tachypnea and dyspnea) that may require prompt veterinary treatment. In the study these reactions were common (seen in 2 of 106 treated dogs). Gastrointestinal signs (vomiting, diarrhoea, inappetence) and lethargy are also common adverse reactions following treatment in such dogs.

In case of accidental oral uptake, symptomatic treatment should be performed by a veterinary surgeon. There is no known specific antidote. The use of activated charcoal may be beneficial.

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 side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs.

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

For external use only.
Apply topically to the skin between the shoulder blades.

Dosage schedule:

The recommended minimum doses are 10 mg/kg bodyweight imidacloprid and 2.5 mg/kg bodyweight moxidectin, equivalent to 0.1 ml/kg bodyweight.

The treatment schedule should be based on individual veterinary diagnosis and on the local epidemiological situation.

Administer in accordance with the following table:

Dogs [kg]	Pipette size to be used	Volume [ml]	Imidacloprid [mg/kg b.w.]	Moxidectin [mg/kg b.w.]
≤4	imidacloprid/moxidectin 40 mg/10 mg spot-on solution for small dogs	0.4	minimum of 10	minimum of 2.5
>4-10	imidacloprid/moxidectin 100 mg/25 mg spot-on solution for medium dogs	1	10-25	2.5-6.25
>10-25	imidacloprid/moxidectin 250 mg/62.5 mg spot-on solution for large dogs	2.5	10-25	2.5-6.25
>25-40	imidacloprid/moxidectin 400 mg/100 mg spot-on solution for extra-large dogs	4	10-16	2.5-4
>40	the appropriate combination of pipettes to provide the recommended dose (the minimum recommended dose is 0.1 ml product/kg bodyweight)			

Flea treatment and prevention (*Ctenocephalides felis*) 

One treatment prevents future flea infestation for 4 weeks. Pre-existing pupae in the environment may emerge for 6 weeks or longer after treatment is initiated, depending upon climatic conditions. Therefore, it may be necessary to combine treatment with the veterinary medicinal product with environmental treatments aimed at breaking the flea life cycle in the surroundings. This can result in a more rapid reduction in the household flea population. The product should be administered at monthly intervals when used as part of a treatment strategy for flea allergy dermatitis.

Treatment of biting lice (*Trichodectes canis*) 

A single dose should be administered. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

Treatment of ear mite infestation (*Otodectes cynotis*) 

A single dose of the product should be administered. Loose debris should be gently removed from the external ear canal at each treatment. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment. Do not apply directly to the ear canal.

Treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*) 

A single dose should be administered twice 4 weeks apart.

Prevention of heartworm disease (*D. immitis*) and cutaneous dirofilariosis (skinworm) (*D. repens*)

Dogs in areas endemic for heartworm, or those which have travelled to endemic areas, may be infected with adult heartworms. Therefore prior to treatment with the veterinary medicinal product, the advice provided in the 'Special precautions for use in animals' section should be considered. For prevention of heartworm disease and cutaneous dirofilariosis, the product must be applied at regular monthly intervals during the time of the year when mosquitoes (the intermediate hosts which carry and transmit *D. immitis* and *D. repens* larvae) are present. The product may be administered throughout the year or at least 1 month before the first expected exposure to mosquitoes. Treatment should continue at regular monthly intervals until 1 month after the last exposure to mosquitoes. To establish a treatment routine, it is recommended that the same day or date be used each month. When replacing another heartworm preventative product in a heartworm prevention programme, the first treatment with the veterinary medicinal product must be given within 1 month of the last dose of the former medication. In non-endemic areas there should be no risk of dogs having heartworm. Therefore they can be treated without special precautions.

Treatment of microfilariae (*D. immitis*)

The veterinary medicinal product should be administered monthly for two consecutive months.

Treatment of cutaneous dirofilariosis (skin worm) (adult stages of *Dirofilaria repens*)

The veterinary medicinal product should be administered monthly for six consecutive months.

Reduction of microfilariae (skin worm) (*D. repens*)

The veterinary medicinal product should be administered monthly for four consecutive months.

Treatment and prevention of *Angiostrongylus vasorum*

A single dose should be administered. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment. In endemic areas regular monthly applications will prevent angiostrongylosis and patent infection with *Angiostrongylus vasorum*.

Treatment of *Crenosoma vulpis*

A single dose should be administered.

Prevention of spirocercosis (*Spirocerca lupi*)

The veterinary medicinal product should be administered monthly.

Treatment of *Eucoleus* (syn. *Capillaria*) *boehmi* (adults)

The veterinary medicinal product should be administered monthly for two consecutive months. It is advisable to prevent auto-coprophagia between the two treatments in order to prevent possible reinfection.

Treatment of the eye worm *Thelazia callipaeda* (adults)

A single dose of the veterinary medicinal product should be administered.

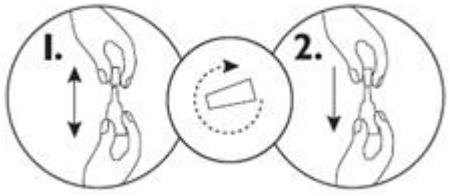
Roundworm, hookworm and whipworm treatment (*Toxocara canis, Ancylostoma caninum, Uncinaria stenocephala, Toxascaris leonina* and *Trichuris vulpis*).

In areas endemic for heartworm, monthly treatment may significantly reduce the risk of re-infection caused by the respective round-, hook- and whipworms. In areas non-endemic for heartworm, the product can be used as part of a seasonal prevention programme against fleas and gastrointestinal nematodes.

Studies have shown that monthly treatment of dogs will prevent infections caused by *Uncinaria stenocephala.*

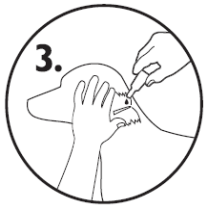
9. ADVICE ON CORRECT ADMINISTRATION

1. Remove one pipette from the package. Hold applicator pipette in an upright position. Twist and pull cap off.
2. Turn the cap around and place the other end of cap back on pipette. Push and twist the cap to break seal, and then remove the cap from the pipette.



For dogs up to 25 kg:

3. With the dog standing still, part the coat between the shoulder blades until the skin is visible. The product should only be applied to undamaged skin. Place the tip of the pipette on the skin and squeeze firmly several times to empty the contents directly onto the skin.



For dogs of more than 25 kg:

4. For easy application the dog should be standing. The entire contents of the pipette should be applied evenly as 3 or 4 spots along the top of the back, from between the shoulders to the base of the tail. At each spot, part the coat until the skin is visible. The product should only be applied to undamaged skin.. Place the tip of the pipette on the skin and gently squeeze the pipette to expel a portion of the solution on the skin. Do not apply an excessive amount of solution at any one spot, as that could cause some of the product to run down the animal's side.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store in the original package in order to protect from moisture and light. This veterinary medicinal product does not require any special temperature storage conditions.
Do not use this veterinary medicinal product after the expiry date which is stated on the packaging after EXP. The expiry date refers to the last day of that month.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Brief contact of the animal with water on one or two occasions between monthly treatments is unlikely to significantly reduce the efficacy of the product. However, frequent shampooing or immersion of the animal in water after treatment may reduce the efficacy of the product.
Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated
use of an anthelmintic of that class. Therefore, the use of this product should be based on the assessment of each individual case and on local epidemiological information about the current susceptibility of the target species in order to limit the possibility of a future selection for resistance.
The use of the product should be based on the confirmed diagnosis of mixed infection (or risk of infection, where prevention applies) at the same time (see also ‘Indication(s)’ and ‘Dosage for each species, route(s) and method of administration’ sections).
Efficacy against adult *Dirofilaria repens* has not been tested under field conditions.

Special precautions for use in animals:
The treatment of animals weighing less than 1 kg should be based on a benefit-risk assessment.
There is limited experience on the use of the product in sick and debilitated animals, thus the product should only be used based on a benefit-risk assessment for these animals.
Care should be taken that the contents of the pipette or the applied dose does not come into contact with the eyes or mouth of the recipient and/or other animals. Do not allow recently treated animals to groom each other. When the product is applied in 3 to 4 separate spots (see section “ADVICE ON CORRECT ADMINISTRATION”), specific care should be taken to prevent the animal licking the application sites.
The product should only be applied to undamaged skin.
This product contains moxidectin (a macrocyclic lactone), therefore special care should be taken with Collie or Old English Sheep dogs and related breeds or crossbreeds, to correctly administer the product as described under section “ADVICE ON CORRECT ADMINISTRATION”; in particular, oral uptake by the recipient and/or other animals in close contact should be prevented.
The safety of the product has only been evaluated in dogs classified as either Class 1 or 2 for heartworm disease in laboratory studies and in a few Class 3 dogs in a field study. Therefore the use in dogs with obvious or severe symptoms of the disease should be based on a careful benefit-risk assessment by the treating veterinarian.
Although experimental overdosage studies have shown that the product may be safely administered to dogs infected with adult heartworms, it has no therapeutic effect against adult *Dirofilaria immitis*. It is therefore recommended that all dogs 6 months of age or more, living in areas endemic for heartworm, should be tested for existing adult heartworm infection before being treated with the product. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to remove adult heartworms. The safety of the combination of imidacloprid and moxidectin has not been evaluated when administered on the same day as an adulticide.
Imidacloprid is toxic for birds, especially canaries.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
In order to prevent children from getting access to pipettes, keep the pipette in the original packaging until ready for use and dispose of used pipettes immediately.
Do not ingest. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
People with a known hypersensitivity to benzyl alcohol, imidacloprid or moxidectin should administer the product with caution. In very rare cases the product may cause skin sensitisation or transient skin reactions (for example numbness, irritation or burning/tingling sensation).
In very rare cases the product may cause respiratory irritation in sensitive individuals.
If the product accidentally gets into eyes, they should be thoroughly flushed with water.
Avoid contact with skin, eyes or mouth.
In case of accidental spillage onto skin, wash off immediately with soap and water.
Wash hands thoroughly after use.
If skin or eye symptoms persist, seek medical advice immediately and show the package leaflet or label to the physician.
Do not eat, drink or smoke during application.

Treated animals should not be handled, especially by children, until the application site is dry. Therefore, it is recommended to apply the product in the evening. Recently treated animals should not be allowed to sleep in the same bed as their owner, especially children.

The product should not enter water courses as it has harmful effects on aquatic organisms: moxidectin is highly toxic to aquatic organisms. Dogs should not be allowed to swim in surface waters for 4 days after treatment.

The solvent in the product may stain or damage certain materials including leather, fabrics, plastics and finished surfaces. Allow the application site to dry before permitting contact with such materials.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Laboratory studies with either imidacloprid or moxidectin in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.
Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
During treatment with the product no other antiparasitic macrocyclic lactone should be administered. No interactions between imidacloprid/moxidectin combination and routinely used veterinary medicinal products or medical or surgical procedures have been observed.

Overdose (symptoms, emergency procedures, antidotes):
Up to 10 times the recommended dose of the combination of imidacloprid and moxidectin was tolerated in adult dogs with no evidence of adverse effects or undesirable clinical signs. Five times the recommended minimum dose applied at weekly intervals for 17 weeks was investigated in dogs aged over 6 months and tolerated with no evidence of adverse effects or undesirable clinical signs.
The combination of imidacloprid and moxidectin was administered to puppies at up to 5 times the recommended dose, every 2 weeks for 6 treatments, and there were no serious safety concerns. Transient mydriasis, salivation, vomiting and transient rapid respiration were observed.
After accidental oral ingestion or overdose, neurological signs (most of which are transient) such as ataxia, generalised tremors, ocular signs (dilated pupils, little pupillary reflex, nystagmus), abnormal respiration, salivation and vomiting may occur in very rare cases.
Ivermectin-sensitive Collie dogs tolerated up to 5 times the recommended dose repeated at monthly intervals without any adverse effects, but the safety of application at weekly intervals has not been investigated in ivermectin-sensitive Collie dogs. When 40% of the unit dose was given orally, severe neurological signs were observed. Oral administration of 10% of the recommended dose produced no adverse effects.
Dogs infected with adult heartworms tolerated up to 5 times the recommended dose, every 2 weeks for 3 treatments, without any adverse effects. In case of accidental oral uptake, symptomatic treatment should be administered. There is no known specific antidote. The use of activated charcoal may be beneficial.

Incompatibilities:
None known.

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

The product should not enter water courses as this may be dangerous for fish and other aquatic organisms. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

June 2023

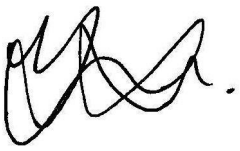
15. OTHER INFORMATION

Imidacloprid is effective against larval flea stages and adult fleas. Flea larvae in the pet's surroundings are killed after contact with a pet treated with the product.
The drug has a persistent action and protects dogs for 4 weeks after a single application against reinfection with the following parasites: *Dirofilaria immitis, Dirofilaria repens, Angiostrongylus vasorum*.
Studies evaluating the pharmacokinetic behaviour of moxidectin after multiple applications have indicated that steady state serum levels are achieved following approximately 4 consecutive monthly treatments in dogs.

Polypropylene unit dose pipette with polyethylene or polyoxymethylene or polypropylene closure with spike packed into a laminated triplex bag composed of polyester, aluminium and polyetylene.
Cardboard box containing 1, 3, 4, 24 or 48 pipettes.

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.



Approved: 22 June 2023