1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Imoxicate 100 mg/25 mg spot-on solution for medium dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml pipette contains:

Active substances:
Imidacloprid 100 mg
Moxidectin 25 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl Alcohol (E 1519)	807 mg
Propylene Carbonate	
Butylhydroxytoluene (E 321)	1 mg
Trolamine	

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

3. CLINICAL INFORMATION

3.1 Target species

Medium dogs (>4-10 kg).

3.2 Indications for use for each target species

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*), sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*), demodicosis (caused by *Demodex 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 veterinary medicinal product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

3.3 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 veterinary medicinal 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 veterinary medicinal product for small cats and ferrets (0.4 ml) should be used.
Do not use on canaries.

3.4 Special warnings

Brief contact of the animal with water on one or two occasions between monthly treatments is unlikely to significantly reduce the efficacy of the veterinary medicinal product. However, frequent shampooing or immersion of the animal in water after treatment may reduce the efficacy of the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product should be based on the confirmed diagnosis of mixed infection (or risk of infection, where prevention applies) at the same time (see also sections 3.2 and 3.9). Efficacy against adult *Dirofilaria repens* has not been tested under field conditions.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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 veterinary medicinal product in sick and debilitated animals, thus the veterinary medicinal 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.
The veterinary medicinal product should only be applied to undamaged skin.
This veterinary medicinal 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 veterinary medicinal product as described under section 3.9; in particular, oral uptake by the recipient and/or other animals in close contact should be prevented.
The safety of the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal 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 known hypersensitivity to benzyl alcohol, imidacloprid or moxidectin should administer the veterinary medicinal product with caution. In very rare cases the veterinary medicinal product may cause skin sensitisation or transient skin reactions (for example numbness, irritation or burning/tingling sensation).
In very rare cases the veterinary medicinal product may cause respiratory irritation in sensitive individuals.
If the veterinary medicinal 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 the 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 veterinary medicinal product in the evening. Recently treated animals should not be allowed to sleep in the same bed as their owner, especially children.

Special precautions for the protection of the environment:

The veterinary medicinal 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.

Other precautions:

The solvent in the veterinary medicinal 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.

3.6 Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Diarrhoea[1], Vomiting[1] Cough[1], Dyspnoea[1], Tachypnoea[1] Inappetence[1], Lethargy[1]
Rare (1 to 10 animals / 10,000 animals treated):	Vomiting[2] Application site greasy fur[2], Application site erythema[2], Hypersensitivity reaction[3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Behavioural disorders (e.g. agitation)[4] Inappetence[4], Lethargy[4] Neurological signs[5]

Undetermined frequency (cannot be estimated from the available data):	Pruritus[6] Hypersalivation[7]

[1]These signs are common in heartworm positive dogs with microfilaraemia. In a case of severe respiratory signs (cough, dyspnoea, tachypnoea) prompt veterinary treatment may be required.
[2]These signs disappear without further treatment.
[3]Local.
[4]Transient and related to sensation at application site.
[5]Most occur transiently and if animal licks the application site after treatment (see section 3.10).
[6]Transient.

[7]Occurs if the animal licks the application site immediately after treatment. This is not a sign of intoxication and disappears within minutes without treatment. Correct application will minimise licking of the application site.

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

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.

3.8 Interaction with other medicinal products and other forms of interaction

During treatment with the veterinary medicinal 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. Safety of the veterinary medicinal product when administered on the same day as an adulticide to remove adult heartworms has not been evaluated.

3.9 Administration routes and dosage

Spot-on use. For external use only.

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.]

>4-10	imidacloprid/moxidectin 100 mg/25 mg spot-on solution for medium dogs	1	10-25	2.5-6.25

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 veterinary medicinal 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 veterinary medicinal 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.

Treatment of demodicosis (caused by *Demodex canis*)

The administration of a single dose every 4 weeks for 2 to 4 months is efficacious against *Demodex canis* and leads to a marked improvement of clinical signs particularly in mild to moderate cases. Especially severe cases may require more prolonged and more frequent treatment. To achieve the best possible response in these severe cases, at the discretion of the veterinarian, the veterinary medicinal product can be applied once a week and for a prolonged time. In all cases it is essential that the treatment should be continued until skin scrapings are negative on at least 2 consecutive monthly occasions. Treatment should be stopped in dogs that show no improvement or do not respond in mite count after 2 months treatment. Alternative treatment should be administered. Seek the advice of your veterinarian. As demodicosis is a multi-factorial disease, where possible, it is advisable to also treat any underlying disease appropriately.

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 section 3.5 should be considered. For prevention of heartworm disease and cutaneous dirofilariosis, the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product in a heartworm prevention programme, the first treatment with this 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.

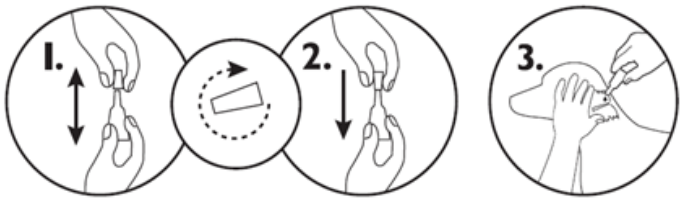
Roundworm, hookworm and whipworm treatment (*Toxocara canis, Ancylostoma caninum, Uncinaria stenocephala, Toxascaris leonina* and *Trichuris vulpis*).

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 veterinary medicinal 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.*

Method of 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.
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.



3.10 Symptoms of overdose (and where applicable, emergency procedures and 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.

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 : QP54AB52.

4.2 Pharmacodynamics

Imidacloprid, 1-(6-Chloro-3-pyridylmethyl)-N-nitro-imidazolidin-2-ylideneamine is an ectoparasiticide belonging to the chloronicotinyl group of compounds. Chemically, it is more accurately described as a chloronicotinyl nitroguanidine. 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 veterinary medicinal product. Imidacloprid has a high affinity for the nicotinergic acetylcholine receptors in the post-synaptic region of the central nervous system (CNS) of the flea. The ensuing inhibition of cholinergic transmission in insects results in paralysis and death. Due to the weak nature of the interaction with mammalian nicotinergic receptors and the postulated poor

penetration through the blood-brain barrier in mammals, it has virtually no effect on the mammalian CNS. Imidacloprid has minimal pharmacological activity in mammals.

Moxidectin, 23-(O-methyloxime)-F28249 alpha is a second-generation macrocyclic lactone of the milbemycin family. It is a parasiticide which is active against many internal and external parasites. Moxidectin is active against larval stages of *Dirofilaria immitis* (L1, L3, L4) and *Dirofilaria repens* (L1, L3). It is also active against gastrointestinal nematodes. Moxidectin interacts with GABA and glutamate-gated chloride channels. This leads to opening of the chloride channels on the postsynaptic junction, the inflow of chloride ions and induction of an irreversible resting state. The result is flaccid paralysis of affected parasites, followed by their death and/or expulsion.
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*.

4.3 Pharmacokinetics

After topical administration of the veterinary medicinal product, imidacloprid is rapidly distributed over the animal's skin within one day of application. It can be found on the body surface throughout the treatment interval. Moxidectin is absorbed through the skin, reaching maximum plasma concentrations approximately 4 to 9 days after treatment in dogs. Following absorption from the skin, moxidectin is distributed systemically throughout the body tissues but due to its lipophilicity it is concentrated mainly in the fat. It is slowly eliminated from the plasma as manifested by detectable moxidectin concentrations in plasma throughout the treatment interval of one month. The T ½ in dogs is about 28.4 days. 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

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 the original package in order to protect from light and moisture. This veterinary medicinal product does not require any special temperature storage conditions.

5.4 Nature and composition of immediate packaging

A white polypropylene (PP) unit dose pipette with a closure with a spike composed of high density polyethylene (HDPE) or polyoxymethylene (POM) or polypropylene (PP) packed into a laminated triplex bag composed of polyester (PETP), aluminium (Al) and low density polyetylene (LDPE).

Cardboard box containing 1, 3, 4, 6, 24 or 48 pipettes.
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.

The veterinary medicinal product should not enter water courses as imidacloprid and moxidectin may be dangerous for fish and other aquatic organisms.

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.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

KRKA, d.d., Novo mesto

7. MARKETING AUTHORISATION NUMBER(S)

VPA10774/067/002

8. DATE OF FIRST AUTHORISATION

13/03/2020

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

05/02/2025

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).