Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Prinocate 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:		
Butylhydroxytoluene (E 321)	1	mg
Benzyl alcohol (E 1519)	807	mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Spot-on solution.
Clear, slightly yellow to yellow or to brownish yellow solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Medium dogs (>4-10 kg).

4.2 Indications for use, specifying the 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*),
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).

4.3 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 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.

4.4 Special warnings for each target species

Please refer to section 4.5.
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 sections 4.2 and 4.9). Efficacy against adult *Dirofilaria repens* has not been tested under field conditions.

4.5 Special precautions for use

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.
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 4.9; 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.

Other precautions
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.
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.

4.6 Adverse reactions (frequency and seriousness)

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) may be observed in very rare cases (see section 4.10).
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.

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

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.

4.8 Interaction with other medicinal products and other forms of interactions

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

4.9 Amounts to be administered and administration route

For external use only (spot-on use).

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 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 section 4.5 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 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.

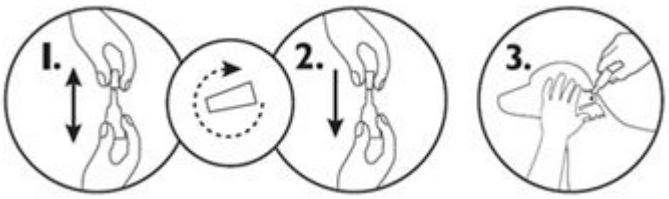
Treatment of the eye worm *Thelazia callipaeda* (adults)
A single dose of the veterinary medicinal product should be administered.

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 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.



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

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.

4.11 Withdrawal period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, insecticides and repellents, macrocyclic lactones, milbemycins, moxidectin, combinations.
ATC vet code: QP54AB52.

5.1 Pharmacodynamic properties

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 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*.

5.2 Pharmacokinetic particulars

After topical administration of the 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.

Environmental properties
See sections 4.5 and 6.6.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol (E 1519)
Propylene Carbonate
Butylhydroxytoluene (E 321)
Trolamine

6.2 Major incompatibilities

Not applicable

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

6.4 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.

6.5 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.

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

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.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER(S)

VPA10774/070/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 May 2020

10 DATE OF REVISION OF THE TEXT