SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prinocate 40 mg/4 mg Spot-on Solution for Small Cats and Ferrets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.4 ml pipette contains:

Active substances:

Imidacloprid	40 mg
Moxidectin	4 mg

Excipients:

Butylhydroxytoluene (E 321)	0.4 mg
Benzyl alcohol (E 1519)	329 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

Small cats (≤ 4 kg) and ferrets.

4.2 Indications for use, specifying the target species

For cats suffering from, or at risk from, mixed parasitic infections:

The treatment and prevention of flea infestation (*Ctenocephalides felis*),
The treatment of ear mite infestation (*Otodectes cynotis*),
The treatment of notoedric mange (*Notoedres cati*),
The treatment of the lungworm *Eucoleus aerophilus* (syn. *Capillaria aerophila*) (adults),
The prevention of lungworm disease (L3/L4 larvae of *Aelurostrongylus abstrusus*),
The treatment of the lungworm *Aelurostrongylus abstrusus* (adults),
The treatment of the eye worm *Thelazia callipaeda* (adults),
The prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*),
The treatment of infections with gastrointestinal nematodes (L4 larvae, immature adults and adults of *Toxocara cati* and *Ancylostoma tubaeforme*).

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

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

Treatment and prevention of flea infestation (*Ctenocephalides felis*),
Prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*).

4.3 Contraindications

Do not use in kittens under 9 weeks of age.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
For ferrets: Do not use the veterinary medicinal product for large cats (0.8 ml) or for dogs (any size).
For dogs, the corresponding veterinary medicinal product, which contains 100 mg/ml imidacloprid and 25 mg/ml moxidectin, must be used.
Do not use on canaries.

4.4 Special warnings for each target species

Please refer to section 4.5.
The product's efficacy has not been tested in ferrets weighing over 2 kg and therefore the duration of effect might be shorter in these animals.
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).

4.5 Special precautions for use

<u>Special precautions for use in animals</u>

The treatment of cats weighing less than 1 kg and ferrets weighing less than 0.8 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.
The product should only be applied to undamaged skin.
Care should be taken that the content 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. Oral uptake by Collie or Old English Sheep dogs and related breeds or crossbreeds should be prevented.

It is recommended that cats and ferrets living in, or travelling to areas endemic for heartworm are treated monthly with the product to protect them from heartworm disease.
Whilst the accuracy of diagnosis of heartworm infection is limited, it is recommended that attempts be made to check the heartworm status of any cat and ferret aged over 6 months, before beginning prophylactic treatment, as use of the product on cats or ferrets which have adult heartworms may cause serious adverse effects, including death. If adult heartworm infection is diagnosed, the infection should be treated in accordance with current scientific knowledge.
In certain individual cats *Notoedres cati* infestation may be severe. In these severe cases concomitant supportive treatment is necessary as treatment with the product alone may not be sufficient to prevent death of the animal.
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 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 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 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.

4.6 Adverse reactions (frequency and seriousness)

Use of the product may result in transient pruritus in cats. On rare occasions greasy fur, 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 site.

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.

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 interaction

During treatment with the veterinary medicinal product no other antiparasitic macrocyclic lactone should be administered.
No interactions between the veterinary medicinal product and routinely used veterinary medicinal products or medical or surgical procedures have been observed.

4.9 Amounts to be administered and administration route

For external use only (spot-on use).

Dosage schedule for cats:

The recommended minimum doses are 10 mg/kg bodyweight imidacloprid and 1.0 mg/kg bodyweight moxidectin, equivalent to 0.1 ml/kg bodyweight of the veterinary medicinal product.

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

Administer in accordance with the following table:

Cats [kg]	Pipette size to be used	Volume [ml]	Imidacloprid [mg/kg b.w.]	Moxidectin [mg/kg b.w.]
≤4	imidacloprid/moxidectin 40 mg/4 mg spot-on solution for small cats and ferrets	0.4	minimum of 10	minimum of 1

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 this 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 ear mite infestation (*Otodectes cynotis*):

A single dose of the product should be administered. 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 notoedric mange (*Notoedres cati*):

A single dose of the product should be administered.
Treatment of the lungworm *Eucoleus aerophilus* (syn. *Capillaria aerophila*) (adults):

A single dose of the product should be administered.

Prevention of *Aelurostrongylus abstrusus*:

The product should be administered monthly.

Treatment of *Aelurostrongylus abstrusus*:

The product should be administered monthly for three consecutive months.

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

A single dose of the product should be administered.

Heartworm prevention (*Dirofilaria immitis*):

Cats 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 product, the advice provided in section 4.5 should be considered.
For prevention of heartworm disease, the product must be applied at regular monthly intervals during the time of the year when mosquitoes (the intermediate hosts which carry and transmit heartworm 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 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 cats having heartworm. Therefore they can be treated without special precautions.

Roundworm and hookworm treatment (*Toxocara cati and Ancylostoma tubaeforme*):

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

Dosage schedule for ferrets:

One pipette of the product for use in small cats and ferrets (0.4 ml) should be administered per animal.
Do not exceed the recommended dose.
The treatment schedule should be based on the local epidemiological situation.

Flea treatment and prevention (*Ctenocephalides felis*):

One treatment prevents future flea infestation for 3 weeks. Under heavy flea pressure it may be necessary to repeat administration after 2 weeks.

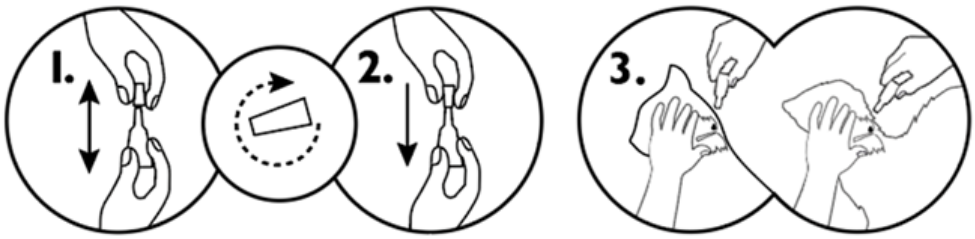
Heartworm prevention (*Dirofilaria immitis*):

Ferrets 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 product, the advice provided in section 4.5 should be considered.
For prevention of heartworm disease, the product must be applied at regular monthly intervals during the time of the year when mosquitoes (the intermediate hosts which carry and transmit heartworm 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. In non-endemic areas there should be no risk of ferrets having heartworm. Therefore they can be treated without special precautions.

Method of administration:

1. Remove the pipette from its packaging. Hold the pipette in an upright position, twist and pull the cap off.
2. Turn the cap around and place the other end of the cap back on the pipette. Push and twist the cap to break the seal, then remove the cap from the pipette.
3. Part the coat on the animal’s neck at the base of the skull until the skin is visible. Place the tip of the pipette onto the skin and squeeze the pipette several times to

empty its contents completely and directly onto the skin in one spot. Avoid contact between the product and your fingers.



Application at the base of the skull will minimise the opportunity for the animal to lick the product. The product should only be applied to undamaged skin.

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

Up to 10 times the recommended dose was tolerated in cats with no evidence of adverse effects or undesirable clinical signs.
The combination of imidacloprid and moxidectin was administered to kittens 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.
The combination of imidacloprid and moxidectin was administered to ferrets at 5 times the recommended dose, every 2 weeks for 4 treatments, and there was no evidence of adverse effects or undesirable clinical signs.
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 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 (L3, L4) of *Dirofilaria immitis.* 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 product has a persistent action and protects cats for 4 weeks after a single application against reinfection with *Dirofilaria immitis*.

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 1 to 2 days after treatment in cats. Following absorption from the skin, moxidectin is distributed systemically and is slowly eliminated from the plasma as manifested by detectable moxidectin concentrations in plasma throughout the treatment interval of one month.

The mean T ½ in cats ranges between 18.7 and 25.7 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 cats.

Environmental properties

See section 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: 3 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 product 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
Smarjeska Cesta 6
8501 Novo Mesto
Slovenia

8. MARKETING AUTHORISATION NUMBER

Vm 01656/4181

9. DATE OF FIRST AUTHORISATION

20 January 2020

10. DATE OF REVISION OF THE TEXT

November 2023

Approved 30 November 2023