SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prinovox 400 mg + 100 mg spot-on solution for extra-large dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 4.0 ml pipette contains:

Active substance(s):
Imidacloprid 400.0 mg
Moxidectin 100.0 mg

Excipient(s):
Butylhydroxytoluene (E 321) 4.0 mg
Benzyl alcohol 3229.2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on solution.
Clear yellow to brownish solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs (> 25–40 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*), demodicosis (caused by *Demodex canis*),
- the prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*),
- the 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),
- the 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 known 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 “Prinovox for cats” 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 Prinovox for dogs. Only “Prinovox for small cats and ferrets” (0.4 ml) must 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

i) Special precautions for use in animals

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.

Do not apply in the mouth, in the eyes or the ears of the animal.

Care should be taken that the product is not ingested by animals and does not come into contact with the eyes or mouth of the recipient and/or other animals.

When the product is applied in 3 to 4 separate spots (see section 4.9), specific care should be taken to prevent the animal licking the application sites.

Do not allow recently treated animals to groom each other. Do not allow treated animals to come into contact with untreated animals until the application site is dry.

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 this product has not been evaluated when administered on the same day as an adulticide.

Imidacloprid is toxic for birds, especially canaries.

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

Avoid contact with skin, eyes or mouth.
Do not eat, drink or smoke during application.
Ingestion of the product is harmful. In order to prevent children getting access to pipettes, keep the pipette in the original packaging until ready for use and dispose of used pipettes immediately.
Wash hands thoroughly after use.

After application, treated animals should not be handled, especially by children, until the application site is dry. This may be ensured by treating animals in the evening.
Do not allow recently treated animals to sleep with owners, especially children.
In case of accidental spillage onto skin, wash off immediately with soap and water.
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.
In case of accidental ingestion of the product or if skin or eye symptoms persist, seek medical advice immediately and show the package leaflet or label to the physician.

iii) 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)

Vomiting can occur on rare occasions. Use of the product may result in transient pruritus in dogs. The product may, in rare cases, cause local hypersensitivity reactions. Transient local skin sensitivity reactions including increased itching, hair loss, greasy fur and redness at application site have been reported in very rare cases. These signs disappear without further treatment. In very rare cases, diarrhoea may occur after application of the product. Neurological signs such as ataxia and muscle tremor (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. in the target species. Therefore, the use of the product is not recommended in animals intended for breeding or during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

During treatment with this veterinary medicinal product no other antiparasitic macrocyclic lactone should be administered.

No interactions between this veterinary medicinal product and routinely used veterinary medicinal products or medical or surgical procedures have been observed.

Safety of this veterinary medicinal 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

Dosage schedule:

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

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

Weight of dog [kg]	Pipette size to be used	Volume [ml]	Imidacloprid [mg/kg bw]	Moxidectin [mg/kg bw]
> 25–40 kg	Prinovox for extra-large dogs	4.0	10–16	2.5–4
> 40 kg	the appropriate combination of pipettes			
Dogs weighing less than 25 kg bodyweight: use the appropriate Prinovox spot-on solution for dogs				

Flea treatment and prevention (Ctenocephalides felis)

One treatment prevents future flea infestation for 4 weeks. 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 the treatment with the 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.

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 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)

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 this 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 *D. immitis* larvae) are present. The product may be administered throughout the year. The first dose may be given after first possible exposure to mosquitoes, but not more than one month after this exposure. 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 dogs having heartworm. Therefore they can be treated without special precautions.

Prevention of cutaneous dirofilariosis (skinworm) (D. repens)

For prevention of 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. 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.

Treatment of microfilariae (D. immitis)

The product should be administered monthly for two consecutive months.

Treatment of cutaneous dirofilariosis (adult stages of Dirofilaria repens)

The product should be administered monthly for six consecutive months.

Reduction of microfilariae (D. repens)

The 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 Spirocerca lupi

The product should be administered monthly.

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

The 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 product should be administered.

Roundworm, hookworm and whipworm treatment

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-

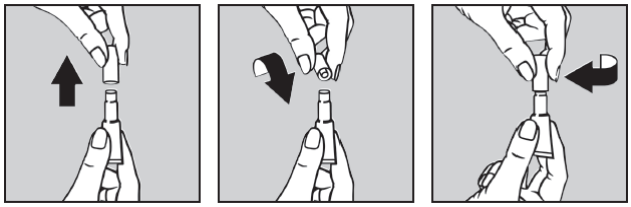
endemic for heartworm, the product can be used as part of a seasonal prevention programme against fleas and gastrointestinal nematodes.

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

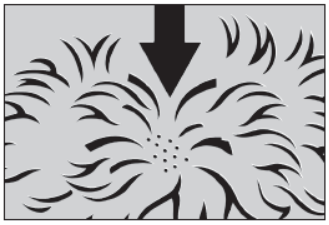
Method of administration

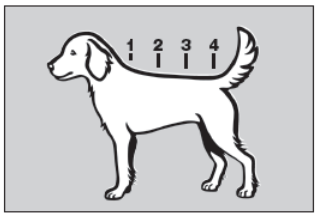
For external use only.

Remove one pipette from the package. Then hold the pipette in an upright position, and twist and pull off the cap. Reverse the cap and use it to twist and remove the seal from the pipette, as shown.



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. Wherever possible apply to undamaged skin. Place the tip of the pipette on the skin and gently squeeze the pipette to expel a portion of its contents directly onto 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.





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

Up to 10 times the recommended dose 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 product 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 PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, insecticides and repellents, macrocyclic lactones, milbemycins.
ATCvet 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 re-infection 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.

5.3 Environmental properties

Moxidectin fulfils the criteria for a persistent, bioaccumulative and toxic substance; therefore, exposure of the environment to moxidectin should be minimised as much as possible. 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. See also section 6.6.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E 321)
Benzyl alcohol
Propylene carbonate

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and composition of immediate packaging

White polypropylene pipettes closed with a screw cap.
Blister packs containing 1, 2, 3, 4, 6 or 21 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

Elanco Europe Ltd.
Form 2, Bartley Way
Bartley Wood Business Park
Hook
RG27 9XA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

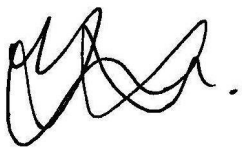
Vm 00879/4157

9. DATE OF FIRST AUTHORISATION

17 December 2014

10. DATE OF REVISION OF THE TEXT

February 2022



Approved: 09 February 2022