SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Procox 0.9 mg/ml + 18 mg/ml oral suspension for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

Active substances:

emodepside	0.9 mg
toltrazuril	18 mg

Excipients:

butylhydroxytoluene (E321; as antioxidant)	0.9 mg
sorbic acid (E200; as preservative)	0.7 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension.
White to yellowish suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For dogs, when mixed parasitic infections caused by roundworms and coccidia of the following species are suspected or demonstrated:

Roundworms (Nematodes):
- *Toxocara canis* (mature adult, immature adult, L4)
- *Uncinaria stenocephala* (mature adult)
- *Ancylostoma caninum* (mature adult)
- *Trichuris vulpis* (mature adult)

Coccidia:
- *Isospora ohioensis* complex
- *Isospora canis*

Procox is effective against the replication of *Isospora* and also against the shedding of oocysts. Although treatment will reduce the spread of infection, it will not be effective against the clinical signs of infection in already infected animals.

4.3 Contraindications

Do not use in dogs/puppies which are under 2 weeks of age or weigh less than 0.4 kg.

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings

Procox is effective against the replication of coccidia and against the shedding of oocysts. Replication of the parasite damages the dog's intestinal mucosa, which may cause enteritis. Therefore, treatment with Procox does not resolve clinical symptoms arising from mucosal damage (e.g. diarrhoea) that have arisen before treatment. In such cases supportive treatment may be necessary.

Treatment against *Isospora* should aim to minimize the shedding of oocysts into the environment, thereby reducing the risk for reinfection in groups/kennels with known and recurring *Isospora* infections.
A prevention strategy, including efforts to eliminate the infection, should be initiated. Treatment with Procox is included as one of several measures necessary in such a strategy.

It is important that hygienic measures are implemented, in particular to ensure the environment is as dry and clean as possible, in order to prevent reinfection from the environment. *Isospora* oocysts are resistant to many disinfectants and can survive in the environment for extensive periods of time. Prompt removal of faeces before oocyst sporulation (within 12 hours) reduces the likelihood of transmission of infection. One administration of Procox to a litter/group is generally sufficient to reduce the shedding of *Isospora* oocysts within it. In kennels with recurring outbreaks of clinical disease due to *Isospora* infection, each litter should be treated for an extended period of time in order to control, and gradually reduce, the level of infection. All dogs at risk of infection within the group should be treated at the same time, including adult animals as they may be subclinically infected. Diagnostic methods (faecal flotation) to determine the presence and level of oocyst shedding within groups of animals could be useful at the end of a control program in order to monitor its success.

As with any parasiticide product, the frequent and long term use of anthelmintics or antiprotozoals may lead to the development of resistance. An appropriate treatment regimen established by a veterinarian will ensure adequate parasite control and reduce the likelihood of resistance developing. Unnecessary use of the product should be avoided. Repeated treatment is indicated only if mixed infection with coccidia and nematodes, as described in section 4.2, is still suspected or demonstrated.

4.5 Special precautions for use

Special precautions for use in animals

Procox is not recommended to be used in dogs of Collie or related breeds that carry or are suspected to carry the mdr1 -/- mutation, because the tolerance of the product in mdr1 -/- mutant puppies has been shown to be lower than in other puppies. Emodepside is a substrate for P-glycoprotein.

There is limited experience with severely debilitated dogs or dogs with seriously compromised kidney or liver function. Therefore, the veterinary medicinal product should only be used in such animals according to a benefit/risk assessment by the responsible veterinarian.

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

Do not eat, drink or smoke while handling the veterinary medicinal product.
Wash hands after use.
In case of accidental spillage onto skin, wash off immediately with soap and water.
If the veterinary medicinal product accidentally gets into the eyes, they should be thoroughly flushed with plenty of water.
In case of accidental ingestion, especially in the case of children, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Slight and transient digestive tract disorders (e.g., vomiting or loose stools) may occur in very rare cases.

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 investigated in pregnant dogs and lactating dogs. Use in pregnant dogs and lactating dogs during the first two weeks of their lactation is therefore not recommended.

4.8 Interaction with other medicinal products and other forms of interaction

Emodepside is a substrate for P-glycoprotein. Co-treatment with other veterinary medicinal products that are P-glycoprotein substrates/inhibitors (for example, ivermectin and other antiparasitic macrocyclic lactones, erythromycin, prednisolone and cyclosporine) could give rise to pharmacokinetic interactions. The potential clinical consequences of such interactions have not been investigated.

4.9 Amounts to be administered and administration route

Dose and Treatment Schedule

For oral use in dogs from 2 weeks of age and weighing at least 0.4 kg.

The recommended minimum dose is 0.5 ml/kg bodyweight (bw), equivalent to 0.45 mg emodepside / kg bw and 9 mg toltrazuril / kg bw.

Recommended dose volumes are given in the table below:

Weight [kg]	Dose [ml]
0.4	0.2
> 0.4 – 0.6*	0.3
> 0.6 – 0.8	0.4
> 0.8 – 1	0.5
> 1.0 – 1.2	0.6
> 1.2 – 1.4	0.7
> 1.4 – 1.6	0.8
> 1.6 – 1.8	0.9
> 1.8 – 2	1.0
> 2.0 – 2.2	1.1
> 2.2 – 2.4	1.2
> 2.4 – 2.6	1.3
> 2.6 – 2.8	1.4
> 2.8 – 3	1.5
> 3.0 – 3.2	1.6
> 3.2 – 3.4	1.7
> 3.4 – 3.6	1.8
> 3.6 – 3.8	1.9
> 3.8 – 4	2.0
> 4 – 5	2.5
> 5 – 6	3.0
> 6 – 7	3.5
> 7 – 8	4.0
> 8 – 9	4.5
> 9 – 10	5.0
> 10 kg: Continue with dose of 0.5 ml / kg bw	

***** = more than 0.4 and up to 0.6 kg

One administration is generally sufficient to reduce the shedding of *Isospora* oocysts. Repeated treatment is indicated only if mixed infection with coccidia and nematodes, as described in section 4.2, continues to be suspected or demonstrated. Depending on the infection pressure in the environment, treatment strategies should be tailored to each kennel (see also section 4.4).

Method of administration

Shake well before use.

Remove screw cap. Use a standard disposable syringe with Luer nozzle for each treatment. To ensure precise dosing when treating dogs up to 4 kg, use a syringe with 0.1 ml graduations. For dogs weighing more than 4 kg, a syringe with 0.5 ml graduations can be used. Place the syringe nozzle firmly into the opening of the bottle. Then turn the bottle upside down, and withdraw the necessary volume. Turn the bottle back into an upright position before removing the syringe. Replace screw cap after use. Administer the suspension into the mouth of the dog.

Dispose of the syringe after treatment (as it is not possible to clean it).

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

The safety of the recommended dose has been demonstrated in puppies treated every two weeks, on up to five occasions.

Slight and transient digestive tract disorders such as loose faeces and vomiting occurred occasionally when the veterinary medicinal product was administered at repeated doses of up to five times the recommended dose.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antiparasitic product, other anthelmintic agents.
ATCvet code: QP52AX60

5.1 Pharmacodynamic properties

Emodepside is a semi-synthetic compound belonging to the chemical group of depsipeptides. It is active against roundworms (ascarids, hookworms and whipworms). In this product, emodepside is responsible for the efficacy against *Toxocara canis, Uncinaria stenocephala, Ancylostoma caninum* and *Trichuris vulpis*. It acts at the neuromuscular junction by stimulating presynaptic receptors belonging to the secretin receptor family which results in paralysis and death of the parasites.

Toltrazuril is a triazinon derivative. It acts against coccidia of the genera *Eimeria* and *Isospora*. It is acting against all intracellular development stages of coccidia of the merogony (asexual multiplication) and gamogony (sexual phase). All stages are destroyed, thus the mode of action is coccidiocidal.

5.2 Pharmacokinetic particulars

After oral application in the rat, emodepside is distributed to all organs. Highest concentration levels are found in the fat. Unchanged emodepside and hydroxylated derivatives are the major excretion products.

In mammals toltrazuril is absorbed slowly after oral administration. The main metabolite is characterised as toltrazuril sulfone.

Kinetics of oral suspension:
After treatment of one year old dogs with a dose of approximately 0.45 mg emodepside and 9 mg toltrazuril per kg bodyweight, geometric mean maximum serum concentrations of 39 µg emodepside/l and 17.28 mg toltrazuril/l were observed. Maximum concentrations of emodepside and toltrazuril were reached 2 hours and 18 hours after treatment respectively. Emodepside was eliminated from the serum with a half-life of 10 hours while the half life of toltrazuril was 138 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321)
Sorbic acid (E200)
Sunflower oil
Glyceryl dibehenate

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product.

6.3 Shelf life

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

Shelf-life after first opening the immediate packaging: 10 weeks

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Amber glass bottle with a polyethylene Luer adapter and a tamper-proof polypropylene child resistant closure containing 7.5 ml or 20 ml.

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

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

7. MARKETING AUTHORISATION HOLDER

Vetoquinol SA
34 Rue de Chene Sainte-Anne
Magny-Vernois
70200 Lure
France

8. MARKETING AUTHORISATION NUMBER

Vm 06462/5005

9. DATE OF FIRST AUTHORISATION

20 April 2011

10. DATE OF REVISION OF THE TEXT

November 2023

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

Approved 07 November 2023