ANNEX I

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:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Butylhydroxytoluene (E321)	0.9 mg
Sorbic acid (E200)	0.7 mg
Sunflower oil	
Glyceryl dibehenate	

Oral suspension.
White to yellowish suspension.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each 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.

3.3 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.

3.4 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.

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.

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 3.2, is still suspected or demonstrated.

3.5 Special precautions for use

Special precautions for safe use in the target species

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.

Special precautions for the protection of the environment:

Not applicable

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Lethargy Muscle tremor, ataxia, convulsion Digestive tract disorders (e.g., vomiting or loose stools)*

*Slight and transient

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 the national competent authority via the national reporting system. See also section 'Contact details' of the package leaflet.

3.7 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.

3.8 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.

3.9 Administration routes and dosage

Dose and treatment schedule

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

To ensure a correct dosage, body weight should be determined as accurately as possible.

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 3.2, 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 3.4).

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).

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

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:

QP52AX60

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product.

5.2 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

5.3. Special precautions for storage

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

5.4 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.

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 emodepside and toltrazuril 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

Vetoquinol S.A.

7. MARKETING AUTHORISATION NUMBERS

EU/2/11/123/001-002

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 20/04/2011

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

{MM/YYYY}

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).

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Outer Carton, 7.5 ml (or 20 ml) bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains:
Active substances: emodepside 0.9 mg, toltrazuril 18 mg

3. PACKAGE SIZE

7.5 ml
20 ml

4. TARGET SPECIES

For dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.
Shake well before use

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp {month/year}
Once opened, use within 10 weeks.

9. SPECIAL STORAGE CONDITIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetoquinol S.A.

14. MARKETING AUTHORISATION NUMBERS

EU/2/11/123/001 7.5 ml
EU/2/11/123/002 20 ml

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Bottle label

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCE(S)

0.9 mg/ml emodepside + 18 mg/ml toltrazuril.

3. TARGET SPECIES

Dogs

4. ROUTES OF ADMINISTRATION

Oral use.
Read the package leaflet before use

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Exp {month/year}
Once opened, use by…

7. SPECIAL STORAGE PRECAUTIONS

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetoquinol S.A.

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

1 ml contains:

Active substances:

emodepside	0.9 mg
toltrazuril	18 mg

Excipients:

butylhydroxytoluene (E321)	0.9 mg
sorbic acid (E200)	0.7 mg

White to yellowish suspension

3. Target species

Dogs.

4. Indications for use

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*

Treatment will reduce the spread of *Isospora* infection but will not be effective against symptoms in already infected animals.

5. 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.

6. Special warnings

Special warnings

Treatment will prevent the spread of *Isospora* infection but will not be effective against symptoms (e.g. diarrhoea) in already infected animals. Additional treatment (by a veterinarian) may be needed in animals with diarrhoea.

It is important to take hygienic measures 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 a long time. The prompt removal of faeces (within 12 hours) reduces the risk of transmission of infection. All dogs at risk of infection within the group should be treated at the same time.

As with any antiparasitic 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.

Special precautions for safe use in the target species

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.

There is limited experience with severely debilitated dogs or dogs with seriously compromised kidney or liver function. Please tell your veterinary surgeon if your dog has any of these.

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.

Pregnancy and lactation:

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 lactation is therefore not recommended.

Interactions with other medicinal products and other forms of interaction:

Emodepside may interact with other veterinary medicinal products using the same transport system (e.g. macrocyclic lactones). The potential clinical consequences of such interactions have not been investigated.

Overdose:

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.

Major incompatibilities:

Do not mix with any other veterinary medicinal product.

7. Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Lethargy Muscle tremor, ataxia (incoordination), convulsion Digestive tract disorders (e.g., vomiting or loose stools)*

*Slight and transient

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

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	

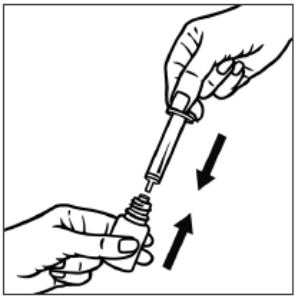
***** = more than 0.4 and up to 0.6 kg

One treatment is generally sufficient to reduce the spread of *Isospora* infection. Repeated treatment is indicated only if mixed infections with coccidia and roundworms continue to be suspected (by the veterinarian) or demonstrated.

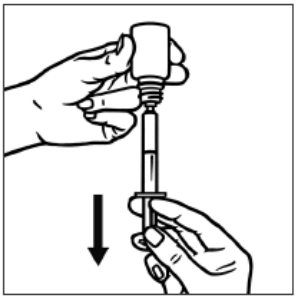
9. Advice on correct administration

1. Shake well before use.
2. 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.
3. 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.
4. Give Procox into the mouth of the dog. Dispose of the syringe after treatment (as it is not possible to clean it).

1. Shake well before use.



2. Place syringe nozzle firmly into opening of the bottle.



3. Turn bottle upside down and withdraw necessary volume.

4. Give Procox into the dog's mouth.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

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

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after Exp. The expiry date refers to the last day of that month.

Shelf-life after first opening the bottle: 10 weeks.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

This veterinary medicinal product should not enter water courses as emodepside and toltrazuril 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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/11/123/001-002

Procox oral suspension is supplied in two different pack sizes containing 7.5 or 20 ml.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database .(https://medicines.health.europa.eu/veterinary)

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Vetoquinol S.A.
Magny-Vernois
70200 Lure
France
Tel: + 33 3 84 62 55 55

Manufacturer responsible for batch release:

KVP Pharma + Veterinär Produkte GmbH
Projensdorfer Str. 324, Kiel
D-24106 Kiel
Germany

VETOQUINOL BIOWET Sp. z o.o.
Żwirowa 140
66-400 Gorzów Wlkp.,
Poland