SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZIPYRAN TABLETS FOR DOGS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:

Praziquantel .....50 mg

Pyrantel (as pyrantel embonate).....50 mg

Febantel .....150 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Yellowish round scored tablet, divisible into four equal parts.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Treatment of mixed infections by adult cestodes and nematodes of the following species:

Nematodes:

Hookworms: *Ancylostoma caninum*

Uncinaria Stenocephala

Ascarids*: Toxocara canis*

Toxascaris leonina

Cestodes:

Tapeworms*: Taenia spp*

Dipylidium caninum

4.3 Contraindications

See section 4.7.

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

4.4 Special warnings for each target species

Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class.

Fleas serve as intermediate hosts and source of infection for one common type of tapeworm – *Dipylidium caninum*.

Tapeworm infestation may reoccur unless control of intermediate hosts as well as the environment is undertaken concurrently to the treatment.

4.5 Special precautions for use

Special precautions for use in animals

In debilitated or heavily infested animals, the product should be used only after evaluation of the risk / benefit by the veterinarian

Digestive haemorrhages (diarrhoea, bloody stools and even deaths) provoked by worm lysis may result from anthelminthic treatment in cases of heavy infestations.

In dogs less than 6 weeks old, tapeworm infections are highly uncommon. Treatment of animals less than 6 weeks old with a fixed combination product against cestodes and nematodes may, therefore, not be necessary.

The active substances are not known to cause particular adverse effects in young animals. Nevertheless the safety of the formulation has not been established in dogs less than 5 months of age.

Roundworm and hookworm infections: In some animals, *Ancylostoma caninum* and *Toxocara canis* may not be eradicated by the treatment, resulting in a continued risk of egg shedding into the environment. Follow-up examinations of the faeces are advisable and according to the results of these examinations, treatment with a nematocidal product may be carried out, if necessary.

To minimise the risk of re-infestation and new infestation, excreta should be collected and properly disposed out of for 24 hours following treatment.

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

In case of accidental ingestion, seek medical advice and show the package leaflet to the physician.

In case of accidental contact wash hands thoroughly

People with known hypersensitivity to any of the ingredients should avoid contact with the veterinary medicinal product

Wash hands after use

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Teratogenic effects attributed to high doses of febantel administered during early pregnancy have been reported in rats, sheep and dogs.
The safety of the product has not been investigated during pregnancy.
Do not use in pregnant bitches during the first four weeks of gestation.

The product may be used during lactation

4.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with piperazine, as the anthelmintic effects of pyrantel and piperazine may be antagonized.

Plasma concentrations of praziquantel may be decreased by concomitant administration with drugs that increase the activity of cytochrome P-450 enzymes (e.g. dexamethasone, phenobarbital).

Concurrent use with other cholinergic compounds can lead to toxicity.

4.9 Amounts to be administered and administration route

To ensure administration of a correct dose, body weight should be determined as accurately as possible.

For single oral treatment only.

The recommended dose is 5 mg of Praziquantel, 5 mg of Pyrantel (as embonate) and 15 mg of Febantel per kg of body weight (equivalent to one tablet/10 kg bw) in accordance with the following table:

Animal Body weight (kg)	Nº of tablets
2.5 – 5	½
5 – 10	1
10 – 15	1 ½
15 – 20	2
20 - 25	2 ½
25 - 30	3

The tablets are administered by placing whole and/or divided tablets at the back of the tongue for forced swallowing.
To further improve accuracy of dosing, tablets may be quartered.

In cases of confirmed single infestation by cestodes or nematodes, a monovalent product containing a cestocide or a nematocide alone should be used.

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

Doses higher than 3 times the recommended dose can cause digestive disorders (vomiting and diarrhea)

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anthelmintics, quinoline derivatives and related substances, praziquantel combinations.
ATCvet code: QP52AA51

5.1 Pharmacodynamic properties

In this fixed combination pyrantel and febantel act against nematodes (ascarids, hookworms) in dogs. In particular the activity spectrum covers Toxocara canis, Toxascaris leonina, Uncinaria stenocephala and Ancylostoma caninum. This combination shows synergistic activity in the case of hookworms.

Praziquantel is effective against a number of cestodes. Activity of praziquantel against adult and immature forms of these parasites has been described in literature.

Praziquantel is very rapidly absorbed through the parasite's surface and distributed throughout the parasite. Both in vitro and in vivo studies have shown that praziquantel causes severe damage to the parasite integument, resulting in the contraction and paralysis of the parasites. There is an almost instantaneous tetanic contraction of the parasite musculature and a rapid vacuolisation of the syncytial tegument. This rapid contraction has been explained by changes in divalent cation fluxes, especially calcium.

Pyrantel acts as a cholinergic agonist. Its mode of action is to stimulate nicotinic cholinergic receptors of the parasite, induce spastic paralysis of the nematodes and thereby allow removal from the gastro- intestinal (GI) system by peristalsis.

Within the mammalian system febantel undergoes ring closure forming fenbendazole and oxfendazole. It is these chemical entities which exert the anthelmintic effect by inhibition of tubulin polymerisation. Formation of microtubules is thereby prevented, resulting in disruption of structures vital to the normal functioning of the helminth. Glucose uptake, in particular is affected, leading to a depletion in cell ATP. The parasite dies upon exhaustion of its energy reserves, which occurs 2-3 days later

5.2 Pharmacokinetic particulars

After the oral administration praziquantel is nearly completely absorbed in the digestive tract. The maximum concentration is reached approximately 60 minutes after the administration.
Praziquantel is widely metabolized in the liver. Praziquantel is found in the urine as metabolites (40% after 8 hours).

After oral administration, the maximum plasmatic concentrations of Febantel are reached approximately after 3 hours. Febantel is metabolized as Fenbendazole and its derivates oxides and hydroxides. Febantel traces are found in faeces and as metabolites in the urine.
The embonate salt of Pyrantel has low aqueous solubility and is poorly absorbed from the intestinal tract in dogs. It is found as active substance in the faeces (50 to 60%). Following absorption, pyrantel embonate is quickly and almost completely metabolized into inactive components which are rapidly excreted in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone

Cellulose, microcrystalline

Silica, colloidal anhydrous

Sodium laurilsulfate

Crospovidone

Saccharin sodium

Magnesium stearate

Maize starch

Beef flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

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

Any divided tablet portion should be immediately discarded and not stored

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

Blisters of PVC and aluminium

Pack sizes:

Cardboard box containing 1 blister of 2 tablets

Cardboard box containing 2 blisters of 2 tablets

Cardboard box containing 1 blister of 4 tablets

Cardboard box containing 3 blisters of 2 tablets

Cardboard box containing 4 blisters of 2 tablets

Cardboard box containing 1 blister of 10 tablets.

Cardboard box containing 25 blisters of 10 tablets

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 products should be disposed of in accordance with local requirements

7. MARKETING AUTHORISATION HOLDER

Laboratorios Calier, SA
C/ Barcelonès 26 (Plà del Ramassar)
08520 Les Franqueses del Valles (Barcelona)
Spain

8. MARKETING AUTHORISATION NUMBER

Vm 20634/4004

9. DATE OF FIRST AUTHORISATION

28 July 2011

10 DATE OF REVISION OF THE TEXT

May 2017

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