[Version 9.1,11/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZIPYRAN XL 175 mg / 175 mg / 525 mg tablets for dogs [AT, BE, DE, FR, NL and UK]
ZIPYRAN 175 mg / 175 mg / 525 mg tablets for dogs XL [IT]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:
Praziquantel.....175 mg
Pyrantel.....175 mg
(equivalent to 504.43 mg of pyrantel embonate)
Febantel.....525 mg

Excipients:

Qualitative composition of excipients and other constituents
Povidone
Cellulose, microcrystalline
Silica, colloidal anhydrous
Sodium laurilsulfate
Crospovidone
Saccharin sodium
Magnesium stearate
Maize starch
Beef flavour

Yellowish oblong scored tablet, divisible into two equal parts.
Beef flavoured tablets.

3. CLINICAL PARTICULARS

3.1 Target species

Dogs

3.2 Indications for use for each 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

3.3 Contraindications

See section ”Use during pregnancy, lactation or lay”.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

3.4 Special warnings

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.

3.5 Special precautions for use

Special precautions for safe use in the target species:
In debilitated or heavily infested animals, the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal 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.

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):	Anorexia Lethargy Gastrointestinal disturbances (diarrhoea and vomiting) Hyperactivity

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 its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Teratogenic effects attributed to high doses of febantel administered during early pregnancy have been reported in rats, sheep and dogs.

The safety of the veterinary medicinal product has not been investigated during the 1st and 2nd half of pregnancy.
Do not use in pregnant bitches during the first four weeks of gestation.
The veterinary medicinal product may be used during lactation.

3.8 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.

3.9 Administration routes and dosage

Oral use.

Dosage: the recommended dose is 5 mg of Praziquantel, 5 mg of Pyrantel (embonate) and 15 mg of Febantel per kg of body weight (equivalent to one tablet/35 kg bw) in accordance with the following table:

Animal Body weight (kg)	Nº of tablets
17.5	½
> 17.5 - 35	1
> 35 – 52.5	1 ½
> 52.5 – 70	2

To ensure a correct dosage, body weight should be determined as accurately as possible.
For single oral treatment only.
The tablets are administered by placing whole and/or divided tablets at the back of the tongue for forced swallowing.
In cases of confirmed single infestation by cestodes or nematodes, a monovalent veterinary medicinal product containing a cestocide or a nematocide alone should be used.

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

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

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: QP52AA51

4.2 Pharmacodynamics

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

4.3 Pharmacokinetics

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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 36 months.
Shelf life of the divided tablet after first opening the immediate packaging: any divided tablet portion should be immediately discarded and not stored

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

Blisters of PVC and aluminium in a cardboard box.

Pack sizes:
Cardboard box with 1 blister of 2 tablets
Cardboard box with 2 blisters of 2 tablets
Cardboard box with 5 blisters of 2 tablets
Cardboard box with 12 blisters of 2 tablets
Cardboard box with 16 blisters of 2 tablets
Cardboard box with 24 blisters of 2 tablets
Cardboard box with 30 blisters of 2 tablets

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

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

LABORATORIOS CALIER, S.A.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

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 III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZIPYRAN XL 175 mg / 175 mg / 525 mg tablets [AT, BE, DE, FR, NL and UK]
ZIPYRAN 175 mg / 175 mg / 525 mg tablets XL [IT]

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:

Active ingredients:
Praziquantel.....175 mg
Pyrantel.....175 mg
(equivalent to 504.43 mg of pyrantel embonate)
Febantel.....525 mg

3. PACKAGE SIZE

1 x 2 tablets
2 x 2 tablets
5 x 2 tablets
12 x 2 tablets
16 x 2 tablets
24 x 2 tablets
30 x 2 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Any divided tablet portion should be immediately discarded and not stored.

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

LABORATORIOS CALIER, S.A.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister of PVC and aluminium

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZIPYRAN XL [AT, BE, DE, FR, NL and UK]
ZIPYRAN XL [IT]

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Each tablet contains:

Praziquantel ……. 175 mg
Pyrantel …… 175 mg
(equivalent to 504.43 mg of pyrantel embonate)
Febantel …… 525 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

ZIPYRAN XL 175 mg / 175 mg / 525 mg tablets for dogs [AT, BE, DE, FR, NL and UK]
ZIPYRAN 175 mg / 175 mg / 525 mg tablets for dogs XL [IT]

2. Composition

Each tablet contains:

Active ingredients:

Praziquantel …… 175 mg
Pyrantel ……... 175 mg
(equivalent to 504.43 mg of pyrantel embonate)
Febantel ……. 525 mg

Yellowish oblong scored tablet, divisible into two equal parts.
Beef flavoured tablets.

3. Target species

Dogs.

4. Indications for use

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

5. Contraindications

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

6. Special warnings

Special warnings:
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.

Special precautions for safe use in the target species:
In debilitated or heavily infested animals, the veterinary medicinal 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.
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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.

Pregnancy and lactation:
Teratogenic effects attributed to high doses of febantel administered during early pregnancy have been reported in rats, sheep and dogs.
The safety of the veterinary medicinal product has not been investigated during the 1st and 2nd third of pregnancy.
Do not use in pregnant bitches during the first four weeks of gestation.
The veterinary medicinal product may be used during lactation.

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.

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

7. Adverse events

Dogs:

Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Anorexia Lethargy Gastrointestinal disturbances (diarrhoea and vomiting) Hyperactivity

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 its local representative or the national competent authority via the national reporting system.

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

Oral use.

Dosage: the recommended dose is 5 mg of Praziquantel, 5 mg of Pyrantel (embonate) and 15 mg of Febantel per kg of body weight (equivalent to one tablet/35 kg bw) in accordance with the following table:

Animal Body weight (kg)	Nº of tablets
17.5	½
> 17.5 - 35	1
> 35 – 52.5	1 ½
> 52.5 – 70	2

To ensure a correct dosage, body weight should be determined as accurately as possible.
For single oral treatment only.
The tablets are administered by placing whole and/or divided tablets at the back of the tongue for forced swallowing.

9. Advice on correct administration

The tablets are administered by placing whole and/or half tablets at the back of the tongue for forced swallowing.
To ensure administration of a correct dose, body weight should be determined as accurately as possible.
In cases of confirmed single infestation by cestodes or nematodes, a monovalent veterinary medicinal product containing a cestocide or a nematocide alone should be used.

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 stated on the carton after Exp. The expiry date refers to the last day of that month.

Shelf life of the divided tablet after first opening the immediate packaging: any divided tablet portion should be immediately discarded and not stored

12. Special precautions for disposal

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

Pack sizes:
Cardboard box with 1 blister of 2 tablets
Cardboard box with 2 blisters of 2 tablets
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Cardboard box with 12 blisters of 2 tablets
Cardboard box with 16 blisters of 2 tablets
Cardboard box with 24 blisters of 2 tablets
Cardboard box with 30 blisters of 2 tablets

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 manufacturer responsible for batch release and <contact details to report suspected adverse events>:
[To be completed nationally]

<Local representatives <and contact details to report suspected adverse events>:>
[To be completed nationally]

<For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.>