SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CESTEM Flavoured tablets for large dogs [UK, IT, DE, AT, BE, NL, LU, ES, PL, BG, CY, CZ, EE, EL, HU, LT, LV, PT, RO, SK, SI]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:
Febantel .....525 mg
Pyrantel (as embonate) .....175 mg
Praziquantel .....175 mg

Excipients

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.
Yellow brown, oval, divisible tablet, with liver flavouring.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs (over 17.5 kg).

4.2 Indications for use, specifying the target species

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

Nematodes:
Ascarids: *Toxocara canis*, *Toxascaris leonina* (adult and late immature forms).
Hookworms: *Uncinaria stenocephala*, *Ancylostoma caninum* (adults).
Whipworms: *Trichuris vulpis* (adults).

Cestodes:
Tapeworms: *Echinococcus* spp., *Taenia* spp., *Dipylidium caninum* (adult and immature forms).

4.3 Contraindications

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 for one common type of tapeworm – *Dipylidium caninum*. Tapeworm infestation may reoccur unless control of intermediate hosts such as fleas, mice etc is undertaken.

4.5 Special precautions for use

Special precautions for use in animals
Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Wash hands after administration to the animal.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
People with known hypersensitivity to any of the ingredients should avoid contact with the veterinary medicinal product.

Other precautions
Since it contains praziquantel, the product is effective against Echinococcus spp. which do not occur in all EU member states but are becoming more common in some. Echinococcosis represents a hazard for humans. As Echinococcosis is a notifiable disease to the World Organisation for Animal Health (OIE), specific guidelines on the treatment and follow-up, and on the safeguard of persons, need to be obtained from the relevant competent authority.

4.6 Adverse reactions (frequency and seriousness)

Gastro-intestinal signs (vomiting, diarrhoea), possibly associated with lethargy, have been observed very rarely in spontaneous reports.
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

Pregnancy:
Do not use in pregnant bitches during the first 4 weeks of pregnancy.

Lactation:
The product may be used during lactation (see Section 4.9 below).

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

For dogs and large breed puppies over 17.5 kg.
Oral use.

15 mg/kg bodyweight febantel, 5 mg/kg pyrantel (as embonate) and 5 mg/kg praziquantel. This is equivalent to 1 tablet per 35 kg bodyweight, in one administration.

Dosages are as follows:

Body weight (kg)	Tablet quantity
17.5	½
>17.5 – 35	1
>35 – 52.5	1 ½
>52.5 – 70	2

The smaller tablet size should be used to achieve accurate dosing in dogs weighing less than 17.5 kg.
The tablets can be given to the dog with or without food. No starvation is needed before or after treatment.
To ensure administration of a correct dose, body weight should be determined as accurately as possible.

The dosing program should be established by the veterinary surgeon.
As a general rule, puppies should be treated at 2 weeks of age and every 2 weeks until 12 weeks of age. Thereafter they should be treated at 3 month intervals. It is advisable to treat the bitch at the same time as the puppies.
For the control of *Toxocara canis*, nursing bitches should be dosed 2 weeks after giving birth and every two weeks until weaning.
For routine worm control adult dogs should be treated every 3 months.
In case of confirmed single infestation by cestode or by nematode, a monovalent product containing a cestocide or a nematocide alone should be preferred.

For routine treatment a single dose is recommended.
In the event of heavy roundworm infestation a repeat dose should be given after 14 days.

If an infestation caused by Echinococcus (*E.granulosus*) is detected in dogs, a repetition of the treatment is recommended for safety purpose.

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

In safety studies, single doses of 5 times (4 times in very young puppies) the recommended dose or greater gave rise to occasional vomiting.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: anthelmintics.
ATCvet code: QP52AA51.

5.1 Pharmacodynamic properties

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

The spectrum of activity of praziquantel covers all important cestode species in dogs, in particular *Taenia* spp, *Dipylidium caninum, Echinococcus granulosus* and *Echinococcus multilocularis*. Praziquantel acts against all adult and immature forms of these parasites.

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 oral administration to dogs, praziquantel is extensively and quickly absorbed from the gastro-intestinal tract. Maximum plasma concentration of 752 µg/L is obtained in less than 2 hours. It is rapidly and extensively metabolised in the liver into hydroxylated derivatives of the parent compound, then rapidly eliminated, mainly in urine.

After oral administration to dogs, febantel is moderately absorbed from the gastro-intestinal tract. Febantel is rapidly metabolised in the liver into fenbendazole and its hydroxy and oxidative derivatives like oxfendazole. Maximum plasma concentration of fenbendazole (173 µg/L) is obtained after about 5 hours. Maximum plasma concentration of oxfendazole (147 µg/L) is obtained after about 7 hours. The excretion occurs mainly in the faeces.

After oral administration to dogs, pyrantel embonate is poorly absorbed. Maximum plasma concentration of 79 µg/L is obtained after about 2 hours. It is rapidly and extensively metabolised in the liver, then rapidly excreted, mainly in the faeces (the unchanged form) and in urine (the metabolites).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Liver powder flavour
Tablet grade inactive yeast
Sodium laurilsulfate
Croscarmellose sodium
Povidone K30
Anhydrous colloidal silica
Cellulose microcrystalline
Magnesium stearate
Maize starch

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the blister: 7 days

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Return any halved tablet to the opened blister pack and use within 7 days.

6.5 Nature and composition of immediate packaging

Nature of immediate packaging:
Polyamide-aluminium-PVC / aluminium blister packs.

Pack sizes:
Box containing 1 blister of 2 tablets
Box containing 2 blisters of 2 tablets
Box containing 2 blisters of 4 tablets
Box containing 12 blisters of 4 tablets
Box containing 24 blisters of 2 tablets

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLYAND/OR USE