ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cestem F XL tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

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

Excipients:

Qualitative composition of excipients and other constituents
Liver powder flavour
Tablet grade inactive yeast
Sodium laurilsulfate
Croscarmellose sodium
Povidone K30
Anhydrous colloidal silica
Cellulose microcrystalline
Magnesium stearate
Maize starch

Yellow brown, oval tablet with a score line on one side.
The tablets can be divided into equal halves

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each the target species

Treatment of mixed infections by 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* species, *(E. Granulosus, E. Multilocularis), Taenia* species (T. hydatigena, T. pisiformis, T. taeniformis), *Dipylidium caninum* (adult and immature forms).

3.3 Contraindications

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

See section 3.7 below.

3.4 Special warnings

Dogs kept together or in kennels should be treated at the same time.
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.

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 according to a benefit/risk assessment by the responsible veterinarian.
To minimise the risk of reinfestation and new infestation, excreta should be collected and properly disposed of for 24 hours following treatment.

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.

Special precautions for the protection of the environment:
Not applicable

Other precautions:
Since it contains praziquantel, the veterinary medicinal product is effective against *Echinococcus spp*. which does 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.

3.6 Adverse events

Dogs :

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Vomiting, Diarrhoea Lethargy

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

Lactation:
The veterinary medicinal product may be used during lactation. (see Section 3.9 below).

3.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with piperazine or levamisole, as the anthelmintic effects of pyrantel 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

For dogs over 17.5 kg.
Oral use.
The recommended dose rates are: 15 mg febantel/kg bodyweight, 5 mg pyrantel (as embonate)/kg bodyweight and 5 mg praziquantel /kg bodyweight. This is equivalent to 1 tablet per 35 kg bodyweight, in a single 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 are flavoured and consequently taken by most dogs voluntarily.
The tablets can be given to the dog with or without food. No starvation is needed before or after treatment.
To ensure a correct dosage, body weight should be determined as accurately as possible.

If there is a risk for re-infestation, the advice of a veterinarian should be sought regarding the need for and the frequency of repeat administration.
In case of confirmed single infestation by cestode or by nematode, 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 and antidotes)

In safety studies, single doses of 5 times the recommended dose or greater gave rise to occasional vomiting.

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 period(s)

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP52AA51.

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

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

Half-tablets should be discarded.

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

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.

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 THE MARKETING AUTHORISATION HOLDER

7. MARKETING AUTHORISATION NUMBER(S)

8.. DATE OF FIRST AUTHORISATION

Date of first authorization: {DD/MM/YYYY}

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).

ANNEXE III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
Cardboard box containing 2 to 48 tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cestem F XL

2. STATEMENT OF ACTIVE SUBSTANCES

One tablet contains:
525 mg of febantel / 175 mg of pyrantel / 175 mg of praziquantel

3. PACKAGE SIZE

2 tablets (1 blister)
4 tablets (2 blisters)
8 tablets (2 blisters)
48 tablets (12 blisters)
48 tablets (24 blisters)

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

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

14. MARKETING AUTHORISATION NUMBER(S)

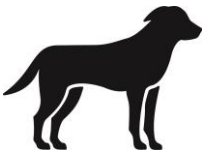
15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cestem F XL



2. QUANTITATIVE PATICULARS Y OF THE ACTIVE SUBSTANCES

525 mg of febantel /175 mg of pyrantel /175 mg of praziquantel

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR

1. Name of the veterinary medicinal product

Cestem F XL tablets for dogs

2. Composition

Each tablet contains:
525 mg of febantel / 175 mg of pyrantel /175 mg of praziquantel

Excipients include liver flavouring.

Yellow brown, oval, divisible tablets.

3. Target species

Dogs.

4. Indications for use

Treatment of mixed infections by 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* species, *(E. granulosus, E. multilocularis), Taenia* species (*T. hydatigena, T. pisiformis, T. taeniformis*), *Dipylidium caninum* (adult and immature forms).

5. Contraindications

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

6. Special warnings

Special warnings :
Dogs kept together or in kennels should be treated at the same time.
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.

Special precautions for safe use in the target species:
The veterinary medicinal product is not recommended for use in puppies of less than 3 kg bodyweight.

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

User warnings:
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 veterinary medicinal 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.

Use during pregnancy or lactation:
Do not use in pregnant bitches during the first 4 weeks of pregnancy.
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 or levamisole, as the anthelmintic effects of pyrantel 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:
In safety studies single doses of 5 times the recommended dose or greater gave rise to occasional vomiting.

7. Adverse events

Dogs :

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Vomiting, Diarrhoea Lethargy

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 or its local representative using the contact details at the end of this leaflet, or via your national reporting system.

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

Oral use.

- 1 tablet per 10 kg bodyweight, in a single administration (for medium and small dogs).
- 1 tablet per 35 kg bodyweight, in a single administration (for large dogs).

This is equivalent to 15 mg febantel/kg bodyweight, 5 mg pyrantel (as embonate)/kg bodyweight and 5 mg praziquantel/kg bodyweight.

Dosages are as follows:

Bodyweight (kg)	Cestem F XL tablets for dogs For dogs and large breed puppies over 17.5 kg.
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.

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

If there is a risk for re-infestation, the advice of a veterinarian should be sought regarding the need for and the frequency of repeat administration**.**
In case of confirmed single infestation by cestode or by nematode, a monovalent veterinary medicinal product containing a cestocide or a nematocide alone should be used.

9. Advice on correct administration

The tablets can be given to the dog with or without food. No starvation is needed before or after treatment.

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 carton after Exp.
Half-tablets should be discarded.

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 authorization numbers and pack sizes

(MA)

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.

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:
(Name and address to be completed nationally)
Tel: +800 35 22 11 51
Email: pharmacovigilance@ceva.com

Manufacturer for the batch release:
Ceva Santé Animale, Z.I. Très le Bois, 22600 Loudéac, France
Ceva Santé Animale – Boulevard de la communication – Zone autoroutière – 53950 Louverné, France

17. Other information

The tablets are flavoured and consequently taken by most dogs voluntarily.