SUMMARY OF PRODUCTS CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Avicas, febantel 15 mg, tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingrediants	Per tablet
Febantel	15.0 mg

For full list of excipients: see section 6.1.

3. PHARMACEUTICAL FORM

Tablet
White, round biconvex tablets, diameter 7 mm, odourless.

4. CLINICAL PARTICULARS

4.1 Target species

Racing pigeons

4.2 Indications for use, specifying the target species

Prevention and treatment of worm infections in racing pigeons, caused by *Ascaridia columbae* (roundworm) and *Capillaria* spp. (hairworm).

4.3 Contra-indications

Do not administer AVICAS during the moulting period or to parents which are feeding nestlings.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i. Special precautions for use in target animals

In the case of clinical infections, treat all the pigeons in the loft at the same time. Following treatment, disinfect the pigeon-loft in order to avoid reinfections.

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

The wearing of gloves is recommended whilst administering this product.
Wash hands after use.

iii. Other precautions

None.

4.6 Adverse reactions (frequency and seriousness)

None.

4.7 Use during pregnancy, lactation or lay

Do not administer AVICAS during the moulting period or to parents which are feeding nestlings.
From the limited information available on the effects of febantel on reproduction, it is not expected that Avicas will have adverse effects on breeding birds.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on possible interactions with other products.

4.9 Amount(s) to be administered and administration route

The recommended dose rate is 30 mg febantel per kg bodyweight, or 1 tablet per pigeon, to be administered orally.

Curative treatment
For the treatment of clinical worm infections 1 tablet should be given and the same dose repeated after 8 days. In the case of heavy *Capillaria* infection, 1 tablet should be given on two consecutive days and this two day treatment repeated one week later.

Preventive treatment
For routine prophylactic treatment 1 tablet should be given 1 month before the breeding season, and again 1 month before the racing season.

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

Benzimidazoles have a wide margin of safety.

4.11 Withdrawal period(s)

Avicas must not be used in pigeons intended for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:

anthelminticum, benzimidazole

ATC Vet Code:

QP52AC05

5.1 Pharmacodynamic properties

The anthelmintic activity of febantel is principally due to its metabolites: fenbendazole, oxfendazole and febantel sulphoxide.
Fenbendazole and oxfendazole have been used as anthelmintics for many years. Since they are the main metabolites of febantel, their mode of action is discussed below.

Benzimidazoles interfere with the energy-generating metabolism, whilst mebendazole is an inhibitor of the glucose transport, others such as albendazole, cambendazole, fenbendazole, oxibendazole, parbendazole and thiabendazole are inhibitors of mitochondrial reactions. If glucose is transported into the worm, and is metabolized through glycolysis, it may enter the mitochondria for further reactions and electron transport-associated energy generation. The benzimidazole anthelmintics inhibit the fumarate reductase step, thereby block mitochondrial function and inhibit energy generation (Prichard, R.K., 1970).

Sharma and Abuzar (1983) described a more recent theory of mode of action of benzimidazole anthelmintics, based on their binding affinity *in vitro* and *in vivo* with tubulin, an important component of the cytoskeleton of all living cells. The authors further reported that *in vitro* experiments with bovine and sheep brain tubulin indicate that thiabendazole, cambendazole, oxibendazole, parbendazole and fenbendazole all bind with tubulin and inhibit its polymerization (assembly) to microtubules.

Dorny et al. (1987) reported morphological changes in *Capillaria obsignata* eggs after treatment with cambendazole. According to the authors, it appears that benzimidazoles have a pronounced ovicidal activity in female trichostrongylids, whereas in Trichuroidae (*Trichuris*, *Capillaria*), eggs are often viable but abnormal in size, shape, and colour. The authors suggested that the drug acts on the ovary during treatment.

5.2 Pharmacokinetic particulars

Absorption

A combined pharmacokinetics-efficacy study was performed by Baert et al. (1992). These authors found that febantel was rapidly cleared from the circulation and highly metabolised. Plasma concentration profiles following intravenous and oral administration of 15 mg febantel were compared. After oral administration, in only two pigeons out of six febantel was detected. The Cp^{max} (µg/ml) values were 0.18 and 0.46, with a t^{max} (min.) value of 150 min. and 90 min., respectively. The AUC_{0-72h} (µg.min./ml) values were 13.58 and 35.81, respectively.

Oxfendazole, febantelsulfoxide and febendazole were measured in plasma after intravenous and oral administration in all pigeons. The AUC_{0-72h} for oxfendazole was significantly higher ($p \leq 0.05$) after oral administration than after intravenous administration. This might suggest that additional metabolites are formed out of fenbendazole and febantelsulfoxide without forming oxfendazole. This phenomenon was also described in other species (Delatour et al., 1982; Montessissa et al., 1989).

No significant difference was observed in AUC_{0-72h} after intravenous and oral administration for fenbendazole ($p > 0.05$) and febantelsulfoxide ($p > 0.05$).

No significant difference was observed in Cp^{max} after intravenous and oral administration for the three different metabolites ($p > 0.05$). After intravenous administration, the t^{max} for fenbendazole was significantly lower ($p \leq 0.05$) than the t^{max} for febantel sulfoxide, which was significantly lower ($p \leq 0.05$) than the t^{max} of oxfendazole. After oral administration only the t^{max} of febantelsulfoxide was significantly lower ($p \leq 0.05$) than the t^{max} of oxfendazole.

After oral administration of 15 mg febantel (30 mg/kg) to heavily or lightly infected pigeons no significant difference was observed in Cp^{max} (µg/ml), t^{max} (min.) and AUC_{0-72h} (µg.min./ml) ($p > 0.05$) for febantel and its three metabolites except for the Cp^{max} of fenbendazole which was significantly higher for the heavily infected pigeons ($p < 0.05$) in comparison to the lightly infected pigeons.

Distribution

Febantel was quickly cleared from the circulation as indicated by a very short plasma elimination half-life of about 10 minutes. Febantel showed a very large distribution volume (67 litres/kg) which might be explained by a high tissue affinity and its pronounced lipophylic character (Baert et al., 1992).

Biotransformation

Febantel

Febantel is a prodrug of benzimidazoles (probenzimidazole), metabolically converted into active moieties with identical chemical structure to fenbendazole/oxfendazole. Chemically, febantel is a phenylguanidine, which is hydrolyzed by removal of a methoxyacetylgroup and then cyclized to fenbendazole (McKellar and Scott, 1990). The major metabolites reported in sheep are febantel sulfoxide, fenbendazole and oxfendazole. These three metabolites were also detected in pigeons. No data are available about the anthelmintic activity of febantel sulfoxide (Baert et al., 1992).

Excretion

Fenbendazole

A comparative elimination study of fenbendazole in chickens, turkeys and ducks revealed the following: hydroxyfenbendazole was the major metabolite excreted by all three species. Total metabolite excretion was highest for the chicken, and lowest for the turkey.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose microcrystalline
Sodium starch glycollate
Polysorbate 80
Povidone K30
Silicon dioxide
Magnesium stearate
Lactose Monohydrate

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal products as packaged for sale: 5 years.

6.4 Special precautions for storage

1. Do not store above 25°C.
2. Store in dry place.
3. Protect from light.

6.5 Nature and composition of immediate packaging

i. Pack size:2 x 20 tablets per carton
ii. Container:Clear polyvinyl chloride blister
iii. Closure:Aluminium foil

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products, if appropriate

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

Oropharma n.v.
70 Kapellestraat
BE-9800 Deinze

8. MARKETING AUTHORISATION NUMBER(S)

Vm 13058/4000

9. DATE OF FIRST AUTHORISATION

Date: 19th may 1994

10. DATE OF REVISION OF THE TEXT

Date: 22nd October 2008