Part II
Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Orafluke 5% w/v Oral Suspension.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of suspension contains:

Active Substances

Fenbendazole Ph. Eur.	50.00 mg
Rafoxanide B.P. (Vet)	50.00 mg

Excipients

Quinoline Yellow (E104)	0.09 mg
Propyl Parahydroxybenzoate Ph. Eur. (E216)	0.10 mg
Methyl Parahydroxybenzoate Ph. Eur. (E218)	1.00 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral suspension.
A pale lemon suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle and sheep.

4.2 Indications for use, specifying the target species

Orafluke 5 % oral suspension permits a three-way activity against Fluke, Lungworms and Stomach worms in cattle and sheep. It is a broad spectrum anthelmintic for the treatment of benzimidazole-susceptible mature and immature stages of nematodes and cestodes of the gastrointestinal and respiratory tracts of cattle and sheep.

The product is active against:
Haemonchus sp.
Ostertagia sp.
Trichostrongylus sp.
Cooperia sp.
Nematodirus sp.
Bunostomum sp.
Trichuris sp.
Strongyloides sp.
Oesophagostomum sp.
Dictyocaulus sp.

Moniezia sp.
Immature and mature *Fasciola sp.* over 8 weeks of age.

The product has a good therapeutic effect against type II Ostertagiasis.

4.3 Contraindications

None.

4.4 Special warnings for each target species

As with other anthelmintics, veterinary advice should be sought on appropriate dosing programmes and stock management to achieve adequate parasite control and reduce the likelihood of anthelmintic resistance developing. If the product does not achieve the desired clinical effect, other diseases, nutritional disturbances or anthelmintic resistance may be involved.

4.5 Special precautions for use

Special precautions for use in animals

Where a dosing gun is used to administer the product, care should be taken to avoid causing injury to the mouth and pharynx of animals.

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

Rinse splashes into the eyes with water immediately.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)
None known.

4.7 Use during pregnancy, lactation or lay

Fenbendazole and rafoxanide are safe for use during pregnancy.
See section 4.11.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

For oral administration in cattle and sheep.
For sheep, the recommended therapeutic dose is 7.5mg fenbendazole and 7.5 mg rafoxanide per kilogram bodyweight.
For cattle, the recommended dose is 11.25 mg fenbendazole and 11.25mg rafoxanide per kilogram bodyweight.

Shake well before use.
Estimate bodyweight carefully.
Use only properly calibrated dosing equipment.

Practical dosage recommendations are as follows:

Cattle		Sheep	
50 kg	11.25 ml	10 kg	1.5 ml
100 kg	22.5 ml	15 kg	2.25 ml
150 kg	33.75 ml	20 kg	3.0 ml
200 kg	45 ml	25 kg	3.75 ml
250 kg	56.25 ml	30 kg	4.5 ml

The dose for heavier animals is an additional 11.25 ml per 50 kg for cattle and 1.5 ml per 10 kg for sheep.
At 2 months after housing, when dosing cattle for worms and adult fluke, a lower dose of 7.5 mg/kg can be used i.e. 7.5 ml per 50kg bodyweight, 30 ml per 200kg or 75 ml per 500kg.

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

Orafluke 5 % Oral Suspension is well tolerated in cattle and sheep at three times the recommended dosage.

4.11 Withdrawal Period(s)

Animals must not be slaughtered for human consumption during treatment.
Meat: 60 days
Milk:
Not authorised for use in animals producing milk for human consumption including during the dry period. Do not use during the last trimester of pregnancy in heifers which are intended to produce milk for human consumption. Do not use within 1 year prior to the first lambing in ewes intended to produce milk for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Summary presentation of the active ingredients

Fenbendazole (QP52AC13) is an anthelmintic belonging to the benzimidazole group which acts by blocking fumarate reductase which results in the inhibition of the formation of adenosine triphosphate (involved in mitochondrial energy).

Rafoxanide (QP52AG05) is a salicylanilide anthelmintic and these are known to be potent uncouplers of oxidative phosphorylation in animal tissues.

5.1 Pharmacodynamic properties

Fenbendazole, like many benzimidazoles, blocks fumarate reductase, which results in the inhibition of the formation of adenosine triphosphate (involved in mitochondrial energy). There is also evidence that it inhibits glucose uptake and therefore increases glycogen utilization and depletes the worm's glycogen reserves. The overall effect of this action is
to effectively starve the parasite to death. Furthermore, this action results in the detachment of the parasites, but in the case of intestinal helminths, this detachment does not result in loss of contact with the drug, whereas in the case of the liver fluke, such detachment would reduce such contact. This probably explains its limited effect on the liver fluke and
the good effect on intestinal helminths.

*In vitr*o experiments indicate that salicylanilides, including the commercially used flukicides, oxyclozanide and rafoxanide, uncouple oxidative phosphorylation in *Fasciola hepatica* and other parasites.

5.2 Pharmacokinetic properties

Fenbendazole

Fenbendazole is absorbed poorly from the gastro-intestinal tract leading to low plasma levels of fenbendazole, oxfendazole and sulphone. It is mainly excreted in the faeces though some of the metabolites that have been identified are excreted in the urine and bile. The active and its metabolites are mainly found in the plasma.

Rafoxanide

Kinetic studies of rafoxanide in cattle have shown that it is absorbed into the blood with a mean peak concentration of circa 23 microg.ml-1 achieved in 2 to 3 days. Plasma levels are considerably higher than those in tissues. Only one metabolite has been identified (3,5-di-iodosalicylic acid) and this was found in blood tissues and milk. There is little known or reported on the excretion of rafoxanide though it is apparently excreted in the bile.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xanthan Gum
Quinoline Yellow
Simethicone Emulsion
Propyl Parahydroxybenzoate (E216)
Methyl Parahydroxybenzoate (E218)
Tween 80
Sodium citrate (E331)
Sodium metabisulphite (E223)
Citric acid monohydrate
Purified water

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale in white HDPE containers: Three years

6.4 Special precautions for storage

Do not store above 25°C.
Protect from freezing and light.

6.5 Nature and composition of immediate packaging

1L (jerrican and flexipack), 2.5L (jerrican and backpack) or 5L (jerrican) HDPE white containers closed with a polypropylene screw cap with an induction heat seal liner.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

7 MARKETING AUTHORISATION HOLDER

Interchem (Ireland) Ltd.,
29 Cookstown Industrial Estate,
Dublin 24.

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10555/003/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

5th June 2006

10 DATE OF REVISION OF THE TEXT