Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Parafend Plus Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances

Oxfendazole	2.5% w/v	[25 mg/ml]
Closantel	5.0% w/v	[50 mg/ml]

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral suspension.
An off white suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Sheep.

4.2 Indications for use, specifying the target species

For the treatment of mixed infections of mature and developing immature gastrointestinal roundworms, lungworms, tapeworms and fluke or sheep nasal fly in sheep and lambs. It is ovicidal against nematode eggs and delays egg laying in trematodes (fluke).

The product is recommended for the treatment of mixed infections including:

Gastrointestinal roundworms:
Ostertagia spp (adult, arrested and inhibited larvae)
Haemonchuscontortus (adult, arrested and inhibited larvae)
Nematodirus spp (including *N.battus*) (adult and immature)
Cooperia spp (adult and immature)
Trichostrongylus spp (adult and immature)
Oesophagostomum spp (adult and immature)
Chabertia spp (adult and immature)

Lungworms:
Dictyocaulusfilaria (adult)

Tapeworms:
Moniezia spp

Sheep nasal fly:
Oestrus ovis (larvae)

Flukes:
Chronic and sub-acute fasciolosis due to *Fasciola hepatica* (mature and late immature flukes).

4.3 Contraindications

Do not use in animals with known hypersensitivity to the active ingredients.

Do not use in cases where infections with benzimidazole resistant species are suspected. In this case an appropriate narrow spectrum product should be used.
The use of this product is contra-indicated in cases of known hypersensitivity to other benzimadazoles.
(See sections 4.7 and 4.11)

4.4 Special warnings for each target species

Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:
- Too frequent and repeated use of anthelmintics from the same class over an extended period of time
- Underdosing which may be due to under-estimation of bodyweight, mis-administration of the product, or lack of calibration of the dosing device.
Suspected clinical cases of resistance to anthelmintics should be further investigated using appropriate tests (e.g. faecal egg count reduction test). Where the results of the tests strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to another pharmacological class and having a different mode of action should be used.

4.5 Special precautions for use

Special precautions for use in animals
To be administered by the oral route only.
Do not exceed the recommended dose.
The bodyweight should be assessed as accurately as possible before calculating the dosage.
As with any husbandry procedure, care should be taken when handling the animals especially when inserting the dosing gun nozzle into the animal's mouth. Unnecessary force should not be used as this may cause damage to the mouth and pharyngeal region.

Special precautions to be taken by the person administering the veterinary medicinal product to the animals:
Direct contact with the skin should be kept to a minimum.
Do not eat, drink or smoke while handling the product.
Suitable protective clothing, including impervious rubber gloves should be worn.
In case of accidental ingestion, consult your doctor immediately. In humans, temporary blindness, nausea and vomiting may occur.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Oxfendazole has been shown to have an embryotoxic and teratogenic effect when administered at four times the recommended dose during the first third of pregnancy.
Do not use during pregnancy and lactation.
(See section 4.11).

4.8 Interaction with other medicinal products and other forms of interactions

No data available.

4.9 Amounts to be administered and administration route

The dosage rate is 5 mg oxfendazole per kg and 10 mg closantel per kg bodyweight by single oral administration (1 ml per 5 kg).
The suspension must be thoroughly shaken before administration to ensure even dispersal of the active ingredients. Clean, properly calibrated drenching equipment must be used.
To ensure administration of a correct dose, bodyweight should be determined as accurately as possible; accuracy of the dosing device should be checked.
If animals are to be treated collectively rather than individually, they should be grouped according to their bodyweight and dosed accordingly, in order to avoid under- or over-dosing.

The following table gives an indication of dosing requirements.

Bodyweight (kg)	**Dose**
5 kg	1 ml
10 kg	2 ml
15 kg	3 ml
20 kg	4 ml
25 kg	5 ml
30 kg	6 ml
40 kg	8 ml
50 kg	10 ml
60 kg	12 ml
70 kg	14 ml
80 kg	16 ml

Dosing Schedule:
The timing for treatment should be based on epidemiological factors and should be customised for each individual farm. Veterinary advice should be sought on appropriate dosing programmes and stock management to achieve adequate parasite control, and to reduce the likelihood of anthelmintic resistance developing. Veterinary advice should also be sought if the product does not achieve the desired clinical effect, as other diseases, nutritional disturbances or anthelmintic resistance might be involved.

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

Oxfendazole has been administered to lambs at a dose of up to 7.5 mg/kg with no adverse effects.

The lethal dose 50% for closantel in sheep has been calculated as being greater than 40 mg/kg. In the case of 3-fold overdose animals may exhibit inappetance and be slightly depressed. Blindness, hypotonia and quadriplegia and death may occur from a 3-fold overdose.

The product administered to sheep and lambs at up to 3 times the recommended dose has been shown to be well tolerated.

4.11 Withdrawal period(s)

Meat and offal: 42 days.
Not authorised for use in ewes producing milk for human consumption including during the dry period. 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

ATC Vet Code: QP52AQC02
Pharmacotherapeutic Group: Oxfendazole, combinations

5.1 Pharmacodynamic properties

Oxfendazole belongs to a class of compounds, the benzimidazoles. The benzimidazoles possess anti-mitotic properties, related to their capacity to bind to tubulin leading to inhibition of formation of microtubules. This in turn leads to disruption of cell division. Eventually cell lysis and disintegration occur. Oxfendazole may concentrate preferentially in intestinal cells of parasites to exert its toxic effects principally at this site. Similar effects do not occur in host cells, possibly because of differential binding characteristics. The disruption of parasite metabolic processes and the effects of oxfendazole on enzymes of helminth parasites involves inhibition of glucose and sodium uptake, reduced muscle glycogen content, uncoupling of oxidative phosphorylation and inhibition of malate dehydrogenase and fumarate reductase.

Oxfendazole is a sulphoxide identical to the sulphoxide metabolite of fenbendazole, both are known to be anthelmintically active and metabolically interconvertible. Reduction of oxfendazole to fenbendazole occurs in the ruminal fluid while oxidation of fenbendazole to oxfendazole is carried out by hepatic microsomal enzymes in the liver. Much of fenbendazole's anthelmintic activity is attributed to oxfendazole, the latter being much more potent.

Oxfendazole has been shown to be effective against gastrointestinal roundworms, lungworms and tapeworms, including inhibited/arrested larvae of *Haemonchus* and *Ostertagia* spp.

Closantel is a member of the salicylanilide class of anthelmintics. Salicylanilides are hydrogen (proton) ionophores (referred to as oxidative phosphorylase uncouplers).

The chemical structure of salicylanilides illustrate the possession of a detachable proton. This type of molecule is lipophilic and is known to shuttle protons across membranes, in particular the inner mitochondrial membrane. Closantel acts by uncoupling oxidative phosphorylation.

Closantel is effective against late immature and adult *F. hepatica, O. ovis* and immature and adult *H. contortus*, including benzimidazole resistant strains.

5.2 Pharmacokinetic particulars

Oxfendazole and related compounds are absorbed to a limited extent, but following absorption they recycle across the gut wall between the blood and the GIT. Extensive metabolism occurs following oral administration and the primary metabolites appear to deplete from tissues relatively rapidly via urine and bile. Metabolites are generally more water-soluble than the parent drug and are thus more readily excreted.

Absorption of closantel may be influenced by feed intake. Closantel is highly and possibly irreversibly bound to plasma protein. Tissue concentrations are well below plasma concentrations. Closantel is usually found unmetabolised in urine and faecal extracts. Elimination half-life in sheep is 2-3 weeks.

After oral administration of the recommended dose of the product to sheep (5 mg oxfendazole and 10 mg closantel per kg bodyweight), the following parameters were observed:

Oxfendazole: Cmax 0.529 µg/ml; AUC 18.11 µg/ml.h; Tmax 15.43 hours, T½ elimination 18 hours.
Closantel: Cmax 43.9 µg/ml; AUC 21350 µg/ml.h; Tmax 65.3 hours, T½ elimination 273.8 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene Glycol: E1520
Sodium Lauryl Sulphate
Microcrystalline Cellulose: E460
Carmellose Sodium: E466
Hypromellose
Simethacone Emulsion
Citric Acid: E330
Purified Water

6.2 Major incompatibilities

None known.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 18 months. Following withdrawal of the first dose use the product within 3 months.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and composition of immediate packaging

White low-density polyethylene backpacks of 1L, 2.5 L, 5.0 L and 2 x 5L and a 10L jerry-can.

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

DANGEROUS to fish and aquatic life.
Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with national requirements.

Do not contaminate ponds, waterways or ditches with the product or used container.

7 MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA22664/070/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30 June 2003
Date of last renewal: 28 October 2008

10 DATE OF REVISION OF THE TEXT

February 2019