Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Flukiver Combi 50 mg/ml + 75 mg/ml oral suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Substances:

Closantel (as closantel sodium dihydrate)	50	mg
Mebendazole	75	mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension.
White to faintly cream-coloured suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Sheep and lambs.

4.2 Indications for use, specifying the target species

For the treatment of mixed parasitic infestations where the action of both active substances is required.

Trematodes
Liver flukes:
Fasciola hepatica (adults + 5-8 week-immatures)

Nematodes
Roundworms
Haemonchus contortus (adults, immatures, inhibited stages and BZ-resistant strains)
Bunostomum sp. (adults)
Chabertia ovina (adults + immatures)
Oesophagostomum spp. (adults)
Capillaria spp. (adults)
Cooperia spp. (adults)
Nematodirus spp. (adults + immatures)
Teladorsagia circumcincta (adults + immatures)
Trichostrongylus axei (adults)
Trichostrongylus colubriformis (adults + immatures)
Trichostrongylus vitrinus (adults)

Lungworms
Dictyocaulus filaria (adults + immatures)

Cestodes
Avitellina spp.
Moniezia spp.

Arthropods
Oestrus ovis (nasal bot) 1st, 2nd and 3rd instar

4.3 Contraindications

Do not administer to animals with known hypersensitivity to the active ingredients.

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 underestimation of body weight, misadministration of the product, or lack of calibration of the dosing device (if any).

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 test(s) strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to another pharmacological class and having a different mode of action should be used. Resistance to benzimidazoles has been reported in Teladorsagia, Haemonchus, Cooperia, Chabertia ovina, Nematodirus species and Trichostrongylus species in small ruminants throughout the EU. Resistance to closantel has not been reported in the EU.

Therefore, the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics.
To reduce the risk of anthelmintic resistance, dosing programmes should be discussed with a veterinary surgeon.

4.5 Special precautions for use

Special precautions for use in animals
Flukiver Combi is to be administered carefully with a drenching gun. Care must be taken to avoid causing injury to the mouth or pharynx during dosing.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Avoid any contact with the skin and mucous membranes. Wash splashes from skin immediately.
Avoid contact with the eyes. In case of accidental contact with the eyes, wash the affected eye(s) with copious quantities of water and seek medical advice as necessary.
Wash hands and exposed skin before meals and after work.
Take off immediately any contaminated clothing.

Other
Mebendazole and closantel have potentially toxic effects on dung organisms. In order to limit their impact on dung fauna, systematic mass treatments should be administered only in autumn, after the fly season, or in the early spring. In addition, it is recommended that sheep and lambs should not be turned onto pasture within seven days after treatment.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Flukiver Combi may be administered to pregnant animals. The product may be used during the lactation period but should not be administered to animals producing milk for human consumption.

4.8 Interaction with other medicinal products and other forms of interactions

None known.

4.9 Amounts to be administered and administration route

For oral administration.
Shake well before use. Invert at least 10 times before use.

The recommended dose is 10 mg/kg BW closantel + 15 mg/kg BW mebendazole. This corresponds to 1 ml per 5 kg BW.

Flukiver Combi is to be administered by means of a drenching gun.

To ensure administration of a correct dose, body-weight 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 overdosing.

The veterinary surgeon should give advice regarding appropriate dosing programmes and stock management to achieve adequate parasite control for both fluke- and roundworm infestations.

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

Symptoms of acute closantel overdosage are decreased vision or blindness, anorexia, incoordination and general weakness.

4.11 Withdrawal period(s)

Meat and offal: 65 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

Pharmacotherapeutic group: Anthelmintics
ATC Vet Code: QP52AC59

5.1 Pharmacodynamic properties

Flukiver Combi is a combination of the salicylanilide closantel and the benzimidazole mebendazole. Closantel is highly effective against liver flukes, haematophagous nematodes and larval stages of some arthropods. Mebendazole is highly active against gastro-intestinal nematodes, lungworm and cestodes.

Mode of action:
Closantel is an uncoupler of the mitochondrial oxidative phosphorylation resulting in inhibition of the ATP-synthesis. This induces a dramatic change in the energy metabolism which finally leads to the death of the parasite.
Mebendazole has a selective anthelmintic action through a specific interaction with the microtubular system of the absorptive cells, leading to an irreversible lytic destruction and death of the worm.

5.2 Pharmacokinetic particulars

Closantel is rapidly absorbed into the systemic circulation after oral administration and peak plasma levels are attained at 24 - 48 hours after dosing. In plasma, closantel is bound for more than 99% to albumin. As a result, tissue distribution is very limited. On average, tissue levels are 15 times lower than plasma levels. The elimination half-life from plasma and tissues is 2 to 3 weeks. Metabolism is absent and the main excretion route is the bile. The urinary excretion is negligible.

Mebendazole is poorly soluble in aqueous systems, which results in a low dissolution rate and a low absorption. This is reflected by the high faecal excretion of unchanged parent drug. The very small fraction absorbed is almost completely metabolised by first pass metabolism in the liver, which consists of carbamate hydrolysis and ketone reduction. The degradation products are conjugated to glucuronides and excreted with the bile and urine. The urinary excretion is relatively poor and consists almost exclusively of metabolites.
The kinetics of the active ingredients are not altered when used in combination.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene Glycol
Microcrystalline Cellulose and Sodium Croscarmellose
Hypromellose
Sodium Lauryl Sulphate
Simethicone Emulsion 30%
Water Purified

6.2 Major incompatibilities

None known.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 3 months

6.4 Special precautions for storage

Store in the original package in order to protect from light.

6.5 Nature and composition of immediate packaging

Container: High density polyethylene bottles of 1, 2.5 and 5 litres
Closure: High density polyethylene screw cap

Not all pack sizes may be marketed.

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

Do not contaminate ponds, waterways or ditches with product or used containers.
Dispose of used containers safely.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

To be completed nationally

8 MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 Novembr 2009
Date of last renewal: 15 August 2014

10 DATE OF REVISION OF THE TEXT

July 2021