Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Endofluke 100 mg/ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance per ml		
Triclabendazole	100	mg

Excipients		
Methyl Parahydroxybenzoate (E218)	2	mg (preservative)
Propyl Parahydroxybenzoate (E216)	0.2	mg (preservative)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral Suspension.

A white to off-white suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle & sheep.

4.2 Indications for use, specifying the target species

For the treatment of adult, immature and early immature stages of liver fluke (*Fasciola hepatica*) susceptible to triclabendazole.

4.3 Contraindications

Do not use in animals known to be hypersensitive to the active substance.

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.
- Under dosing, which may be due to under estimation of bodyweight, 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 triclabendazole has been reported in *Fasciola hepatica* in cattle and sheep. Therefore, the use of this product should be based on local (regional/farm) epidemiological information about susceptibility of the *Fasciola hepatica* and recommendations on how to limit further selection for resistance to anthelmintics.

4.5 Special precautions for use

i) Special precautions for use in animals
Care should be taken when dosing animals to avoid causing injury to the mouth and pharynx.

ii) <u>Special Precautions to be taken by the person administering the product to animals</u>

When using, do not eat, drink or smoke.
Wash splashes from eyes and skin immediately.
Take off immediately any contaminated clothing.
Wash hands and exposed skin before meals and after use.

iii) <u>Other precautions</u>

The use of this product may have harmful effects on fish and aquatic invertebrates. Cattle and sheep must not have any access to the surface water such as streams, ponds or ditches within 7 days after treatment. When spreading manure from treated animals on arable lands, a safety distance of 10m to adjacent surface waters must be kept.

4.6 Adverse reactions (frequency and seriousness)

Occasionally, inflammation of the unpigmented skin, including the udder and the teats may occur after treatment in cattle exposed to intense sunshine.

4.7 Use during pregnancy, lactation or lay

The product is safe for use during pregnancy and lactation. However, the product is not permitted for use during lactation in 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 single oral administration only using properly calibrated dosing equipment. The product is suitable for most types of automatic drenching guns. Shake the container before use.
Use unaltered from original container.
Clean drenching equipment before and after use.

Dosage:
Endofluke 100 mg/ml is given as an oral drench and is suitable for most types of automatic drenching guns.
The recommended dose rate is 12 mg triclabendazole per kg bodyweight in cattle and 10 mg triclabendazole per kg bodyweight in sheep.

Practical Dosage Guide:

Cattle: 6 ml per 50 kg bodyweight:

Animal Weight	**Dose of product**
50 kg	6 ml
100 kg	12 ml
150 kg	18 ml
200 kg	24 ml
250 kg	30 ml
300 kg	36 ml
350 kg	42 ml
400 kg	48 ml
For each additional 50 kg	6 ml

Sheep: 1 ml per 10kg bodyweight

Animal Weight	**Dose of product**
10 kg	1 ml
20 kg	2 ml
30 kg	3 ml
40 kg	4 ml
50 kg	5 ml
60 kg	6 ml
For each additional 10 kg	1 ml

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 overdosing.

The timing for re-treatment should be based on epidemiological risk patterns and should be customised for each individual farm.

To avoid the potential for the accumulation of residues following repeat administration of the product; animals should not be treated with a frequency of less than 10 weeks.

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

A single oral dose of 150-200 mg triclabendazole/kg of live bodyweight may lead to side effects such as unsteady gait, dullness and reduced appetite. These side effects are slight and last 1 to 5 days. An antidote is not known.

4.11 Withdrawal period(s)

Cattle (meat and offal): 56 days

Milk:
Cattle (milk): Milk for human consumption may only be taken from 48 hours after calving. Not intended for use within 45 days of calving. Should a cow calve earlier than 45 days after the last treatment, milk for human consumption may only be taken from 45 days + 48 hours (47 days) after the last treatment.

Sheep (meat & offal): 56 days

Sheep (milk): 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

ATCvet code: QP52AC01
Pharmacotherapeutic group: anthelmintics; benzimidazoles and related substances.

5.1 Pharmacodynamic properties

Triclabendazole differs from other benzimidazoles in that it is a narrow spectrum anthelmintic. The drug accumulates significantly in both immature and adult stages of *Fasciola hepatica* and stimulates the major routes of the parasite's energy generating system, as demonstrated by glucose derived acetate and propionate formation. However, under these conditions the parasite's motility decreased, indicating that the drug is not associated with inhibition of the energy generating pathways. Triclabendazole inhibits colchicine binding to microtubular proteins suggesting interference of the drug with microtubular structure and function. The drug strongly inhibits the release of proteolytic enzymes in immature and adult parasites, a process dependant on microtubular functions. The precise molecular mode of action of this fasciolicidal drug remains to be elucidated.

5.2 Pharmacokinetic particulars

50-75% of the orally administered dose of triclabendazole is absorbed from the gastrointestinal tract. Very rapidly, absorbed triclabendazole is almost completely oxidised to its sulfoxide and sulfone.
In cattle triclabendazole sulfoxide reaches peak concentrations approximately 27 hours after administration of the product and the sulfone reaches peak concentrations 64 to 72 hours after administration.
In sheep triclabendazole sulfoxide reaches peak concentrations approximately 20 hours after administration of the product and the sulfone reaches peak concentrations 30 to 32 hours after administration.
Both metabolites bind strongly to plasma proteins, particularly albumin.
Metabolites are excreted via the bile mainly as conjugates. More than 90%- 95% of the total dose of triclabendazole is excreted in the faeces, about 2% in the urine and less than 1% in the milk. The elimination is virtually complete by 10 days after administration.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xanthan Gum
Methyl Parahydroxybenzoate
Propyl Parahydroxybenzoate
Citric Acid Anhydrous
Sodium Citrate
Polysorbate 80
Silica Colloidal

Anhydrous Simethicone Emulsion
Water, purified

6.2 Major incompatibilities

None Known.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years

6.4 Special precautions for storage

Protect from frost.

6.5 Nature and composition of immediate packaging

1 litre, 2.5 litre, 5 litre, 6L (5 & 1L), 7.5L (5 & 2.5L) and 3 x 5L high-density polyethylene flat bottom backpack containers containing a white to off-white smooth suspension. The closures used for all pack sizes are 38 mm propylene standard caps with an induction heat seal liner. A 38 mm polypropylene spouted cap is also provided with each pack size for dispensing purposes.

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

The product may have toxic effects on fish and aquatic invertebrates. Any unused product or waste material must not enter surface water and should be disposed of in accordance with national requirements.

7 MARKETING AUTHORISATION HOLDER

Bimeda Animal Health Limited
2, 3 & 4 Airton Close
Airton Road
Tallaght
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Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA22033/060/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 August 2002
Date of last renewal: 19 February 2008

10 DATE OF REVISION OF THE TEXT

June 2019