1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Endofluke 100 mg/ml Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Triclabendazole 100 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Xanthan Gum	
Methyl Parahydroxybenzoate (E218)	2 mg
Propyl Parahydroxybenzoate (E216)	0.2 mg
Citric Acid Anhydrous	
Sodium Citrate	
Polysorbate 80	
Silica Colloidal	
Anhydrous Simethicone Emulsion	
Water, purified	

A white to off-white suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and sheep.

3.2 Indications for use for each target species

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

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

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 veterinary medicinal 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 veterinary medicinal 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.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Care should be taken when dosing animals to avoid causing injury to the mouth and pharynx.

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

Special precautions for the protection of the environment:
The use of this veterinary medicinal 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 10 metres to adjacent surface waters must be kept.

3.6 Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data):	Skin inflammation[1]

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

Sheep: None known.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder <or its local representative> or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Can be used during pregnancy and lactation. However, the veterinary medicinal product is not permitted for use during lactation in animals producing milk for human consumption.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Oral use.
For single oral administration only
The use of suitably calibrated dosing equipment is recommended.
The veterinary medicinal 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:
Cattle: The recommended dose rate is 12 mg triclabendazole per kg bodyweight.
Sheep: The recommended dose rate is 10 mg triclabendazole per kg bodyweight.

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 10 kg 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

Underdosing could result in ineffective use and may favour resistance development.

To ensure a correct dosage, body weight should be determined as accurately as possible.

Accuracy of the dosing device should be thoroughly 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.

For infestations with *Fasciola hepatica*, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifecycle.

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

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Cattle:
Meat and offal: 56 days
Milk: Not authorised for use in lactating animals producing milk for human consumption.
When used during the dry period in dairy cows, 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 and offal: 56 days
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.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP52AC01

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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 veterinary medicinal 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 veterinary medicinal 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

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

5.3 Special precautions for storage

Protect from frost.

5.4 Nature and composition of immediate packaging

High-density polyethylene flat bottom backpack sealed with 38 mm polypropylene standard caps with an induction heat seal liner. A 38 mm polypropylene spouted cap is also provided with each pack size for dispensing purposes.

Pack size:
1L
2.5L
5L
Carton box containing 1 backpack containing 1L of product.
Carton box containing 1 backpack containing 1L of product and 1 backpack containing 5L of product.
Carton box containing 1 backpack containing 2.5L of product and 1 backpack containing 5L of product.
Carton box containing 3 backpacks containing 5L of product.

Not all pack sizes may be marketed.

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

The veterinary medicinal 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.

Medicines should not be disposed of via wastewater <or household waste>.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

7. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

8. DATE OF FIRST AUTHORISATION

[To be completed nationally]

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{Carton – 1L, 6L (5 &1L), 7.5L (5 & 2.5L), 15L (3 x 5L)}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Endofluke 100 mg/ml Oral Suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Triclabendazole: 100 mg/ml

3. PACKAGE SIZE

1L
6L (5L & 1L)
7.5L (5L & 2.5L)
15L (3 x 5L)

4. TARGET SPECIES

Cattle and sheep.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

Withdrawal period:

Cattle:
Meat and offal: 56 days
Milk: Not authorised for use in lactating animals producing milk for human consumption.
When used during the dry period in dairy cows, 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 and offal: 56 days
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.

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Protect from frost.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

14. MARKETING AUTHORISATION NUMBERS

[To be completed nationally]

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{Label – 1L}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Endofluke 100 mg/ml Oral Suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Triclabendazole: 100 mg/ml

3. TARGET SPECIES

Cattle and sheep.

4. ROUTES OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:
Meat and offal: 56 days
Milk: Not authorised for use in lactating animals producing milk for human consumption.
When used during the dry period in dairy cows, 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 and offal: 56 days
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.

6. EXPIRY DATE

Exp. {mm/yyyy}

7. SPECIAL STORAGE PRECAUTIONS

Protect from frost.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

9. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{Label: 2.5L and 5L Label}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Endofluke 100 mg/ml Oral Suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Triclabendazole: 100 mg/ml

3. TARGET SPECIES

Cattle and sheep.

4. ROUTES OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:
Meat and offal: 56 days
Milk: Not authorised for use in lactating animals producing milk for human consumption.
When used during the dry period in dairy cows, 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 and offal: 56 days
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.

6. EXPIRY DATE

Exp. {mm/yyyy}

7. SPECIAL STORAGE PRECAUTIONS

Protect from frost.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Endofluke 100 mg/ml Oral Suspension

2. Composition

Each ml contains:

Active substances:
Triclabendazole 100 mg

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

A white to off-white suspension.

3. Target species

Cattle and sheep.

4. Indications for use

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

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special warnings:
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 an under-estimation of bodyweight, misadministration of the veterinary medicinal 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 these 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 veterinary medicinal product should be based on local (regional/farm) epidemiological information about susceptibility of *Fasciola hepatica* and recommendations on how to limit further selection for resistance to anthelmintics.

Only use for liver fluke strains susceptible to triclabendazole.
If inefficacy is suspected, seek veterinary advice.

Special precautions for safe use in the target species:
Care should be taken when dosing animals to avoid causing injury to the mouth and pharynx.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands and exposed skin before meals and after use.
When using, do not eat, drink or smoke.
Wash splashes from eyes and skin immediately.
Take off immediately any contaminated clothing.

Special precautions for the protection of the environment:
The use of this veterinary medicinal 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.

Pregnancy and lactation:
Can be used during pregnancy and lactation. However, the veterinary medicinal product is not permitted for use during lactation in animals producing milk for human consumption.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose:
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.

Major incompatibilities:
None known.

7. Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data)	Skin inflammation[1]

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

Sheep: None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder <or the local representative of the marketing authorisation holder> using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

Oral use.
For single oral administration only
The use of suitably calibrated dosing equipment is recommended.
The veterinary medicinal product 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.
Sheep: The recommended dose rate is 10mg triclabendazole per kg bodyweight.

Practical Dosage Guide:

CATTLE **6 ml per 50 kg bodyweight**		**SHEEP** **1 ml per 10 kg bodyweight**	
Animal Weight	**Dose of product**	**Animal Weight**	**Dose of product**
50 kg	6 ml	10 kg	1 ml
100 kg	12 ml	20 kg	2 ml
150 kg	18 ml	30 kg	3 ml
200 kg	24 ml	40 kg	4 ml
250 kg	30 ml	50 kg	5 ml
300 kg	36 ml	60 kg	6 ml
350 kg	42 ml	For each additional 10 kg	1 ml
400 kg	48 ml		
For each additional 50 kg	6 ml		

Underdosing could result in ineffective use and may favour resistance development.

To ensure a correct dosage, body weight should be determined as accurately as possible.

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.

Accuracy of the dosing device should be thoroughly checked.

For infestations with *Fasciola hepatica*, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifecycle.

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

9. Advice on correct administration

Shake container well before use.
Use unaltered from the original container.
Clean drenching equipment before and after use.

10. Withdrawal periods

Cattle:
Meat and offal: 56 days
Milk: Not authorised for use in lactating animals producing milk for human consumption.

When used during the dry period in dairy cows, 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 and offal: 56 days
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.

11. Special storage precautions

Keep out of the sight and reach of children.
Protect from frost.
Do not use this veterinary medicinal product after the expiry date which is stated on the label or carton after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

The veterinary medicinal 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.

Medicines should not be disposed of via wastewater <or household waste>.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

[To be completed nationally]
Pack size:
1L
2.5L
5L
Carton box containing 1 backpack containing 1L of product.
Carton box containing 1 backpack containing 1L of product and 1 backpack containing 5L of product.
Carton box containing 1 backpack containing 2.5L of product and 1 backpack containing 5L of product.
Carton box containing 3 backpacks containing 5L of product.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder [IE, UK(NI)]:
Bimeda Animal Health Limited
2/3/4 Airton Close
Tallaght
Dublin 24
Ireland

Marketing authorisation holder [DE]:
aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell

Manufacturer responsible for batch release:
Bimeda Animal Health Limited
2/3/4 Airton Close
Tallaght
Dublin 24
Ireland

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information