

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zermex 0.1% w/v Oral Solution for Sheep

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Moxidectin 1 mg

Excipients:

Benzyl Alcohol 40 mg

Butylated Hydroxytoluene 2.5 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Solution

A pale, yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Sheep

4.2 Indications for use, specifying the target species

Infestations of sheep with parasites sensitive to moxidectin.

For the treatment and prevention of infestations caused by:

- Adult and immature (L4) gastro-intestinal nematodes:

. *Haemonchus contortus* (including inhibited larvae)

. *Teladorsagia circumcincta* (including inhibited larvae)

. *Ostertagia trifurcata*

. *Trichostrongylus axei* (including inhibited larvae)

. *Trichostrongylus colubriformis*

. *Trichostrongylus vitrinus*

. *Nematodirus battus*

. *Nematodirus spathiger*

. *Nematodirus filicolis* (adults only)

. *Strongyloides papillosus* (larval stages only)

- . *Cooperia curticei* (adults only)
- . *Cooperia oncophora*
- . *Oesophagostomum columbianum*
- . *Oesophagostomum venulosum* (adults only)
- . *Chabertia ovina*
- . *Trichuris ovis* (adults only)

- Adult respiratory tract nematode
- . *Dictyocaulus filaria*

The product has a persistent effect in preventing reinfestation:

- for 5 weeks by *Teladorsagia circumcincta* and *Haemonchus contortus*
- for 4 weeks by *Oesophagostomum columbianum*.

Clinical trials, after experimental and natural infestation, have shown that it is effective against certain benzimidazole resistant strains of:

- *Haemonchus contortus*
- *Teladorsagia circumcincta*
- *Trichostrongylus colubriformis*
- *Cooperia curticei*

4.3 Contraindications

Do not mix with other products.

4.4 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.
- Underdosing, which may be due to underestimation 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 macrocyclic lactones has been reported in *Teladorsagia* in sheep in a number of countries. In 2008, throughout Europe, moxidectin resistance is

very rare; it has been reported in a single case involving a levamisole-, benzimidazole and ivermectin-resistant strain of *Teladorsagia circumcincta*. Therefore the use of moxidectin should be based on local (regional, farm) epidemiological information about susceptibility of nematodes, local history of treatments and recommendations on how to use the product under sustainable conditions to limit further selection for resistance to anthelmintics. These precautions are especially important when moxidectin is being used to control resistant strains.

4.5 Special precautions for use

i. Special precautions for use in animals

None known.

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

Wear protective impermeable gloves during use.

Avoid direct contact with skin and eyes.

In case of contact with skin and eyes wash affected area with clean water.

Seek medical advice if irritation persists.

Do not smoke, drink or eat while handling the veterinary medicinal product.

Wash hands after use.

iii. Other precautions regarding impact on the environment

Moxidectin fulfils the criteria for a (very) persistent, bioaccumulative and toxic (PBT) substance; therefore, exposure of the environment to moxidectin must be limited to the extent possible. Treatments should be administered only when necessary and should be based on faecal egg counts or evaluation of the risk of infestation at the animal and/or herd level.

Like other macrocyclic lactones, moxidectin has the potential to adversely affect non-target organisms:

- Faeces containing moxidectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of sheep with the product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period of 4 days and may decrease dung fly abundance during that period. It has been established in laboratory tests that moxidectin may temporarily affect dung beetle reproduction; however, studies with incurred residues indicate no long-term effects. Nevertheless, in case of repeated treatments with moxidectin (as with products of the same anthelmintic class) it is advisable not to treat animals every time on the same pasture to allow dung fauna populations to recover.

- Moxidectin is inherently toxic to aquatic organisms including fish. The product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the oral formulation to sheep, treated animals should not have access to watercourses during the first 3 days after treatment.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Should be given as a single oral drench of 1 ml/5 kg live bodyweight, equivalent to 200 µg moxidectin/kg live bodyweight, using any standard drenching equipment.

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.

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

Symptoms generally do not occur at less than 5 times the recommended dose. They are manifested as transient salivation, depression, drowsiness and ataxia 8 to 12 hours post-treatment. Treatment is not generally necessary and recovery is generally complete within 24 to 48 hours. There is no specific antidote.

4.11 Withdrawal period(s)

Meat & offal: 14 days.

Milk: 5 days.

5. PHARMACOLOGICAL PROPERTIES

ATC Vet Code: QP 54 AB 02

Moxidectin is a parasiticide active against a wide range of economically important internal and external parasites and is a second generation macrocyclic lactone of the milbemycin family. Its principal mode of action is interfering with neuromuscular transmission of the GABA (gamma amino butyric acid)-gated or glutamate-gated chloride channels.

Moxidectin stimulates the release of GABA and increases its binding to the postsynaptic receptors. The net effect is to open the chloride channels on the postsynaptic junction to allow the inflow of chloride ions and induce an irreversible resting state. This results in flacid paralysis and eventual death of parasites exposed to the drug.

Moxidectin is 22% absorbed following oral dosing with maximum blood concentrations being achieved 9 hours post treatment. The drug is distributed throughout the body tissues but due to its lipophilicity the target tissue is fat where concentrations are 10 to 20 times higher than those found in other tissues. The depletion half life in fat is 23-28 days.

Moxidectin undergoes limited biotransformation by hydroxylation. The only significant route of excretion is the faeces.

5.3 Environmental properties

Moxidectin fulfils the criteria for a (very) persistent, bioaccumulative and toxic (PBT) substance. In particular, in acute and chronic toxicity studies with algae, crustaceans and fish, moxidectin showed toxicity to these organisms, yielding the following endpoints:

Organism		EC ₅₀	NOEC
Algae	<i>S. capricornutum</i>	>86.9 µg/l	86.9 µg/l
Crustaceans (Water fleas)	<i>Daphnia magna</i> (acute)	0.0302 µg/l	0.011 µg/l
	<i>Daphnia magna</i> (reproduction)	0.0031 µg/l	0.010 µg/l
Fish	<i>O. mykiss</i>	0.160 µg/l	Not determined
	<i>L. macrochirus</i>	0.620 µg/l	0.52 µg/l
	<i>P. promelas</i> (early life stages)	Not applicable	0.0032 µg/l
	<i>Cyprinus carpio</i>	0.11 µg/l	Not determined

EC₅₀: the concentration which results in 50% of the test species individuals being adversely affected, i.e. both mortality and sub-lethal effects.

NOEC: the concentration in the study at which no effects are observed.

This implies that when allowing moxidectin to enter water bodies, this may have a severe and lasting impact on aquatic life. To mitigate this risk, all precautions for use and disposal must be adhered to.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
Butylated Hydroxytoluene
Disodium Edetate
Polysorbate 80
Propylene Glycol
Sodium Phosphate Dodecahydrate
Sodium Acid Phosphate Monohydrate
Phosphoric Acid and/or Sodium Hydroxide (For pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years
Shelf-life after first opening the immediate packaging: 6 months

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Carton containing one high-density polyethylene container of 1 litre, 2.5 litres or 5 litres, with a moulded handle and a polypropylene cap (screw fit).
Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste material derived from such veterinary medicinal products should be disposed of in accordance with local requirements. Do not contaminate watercourses with the product.
Dangerous to fish and aquatic life.

7. MARKETING AUTHORISATION HOLDER

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

8. MARKETING AUTHORISATION NUMBER

Vm 42058/4169

9. DATE OF FIRST AUTHORISATION

02 February 2000

10. DATE OF REVISION OF THE TEXT

November 2020

A handwritten signature in black ink, consisting of several vertical strokes followed by a long, sweeping horizontal stroke that curves upwards at the end.

Approved 06 November 2020