SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zermex 1% w/v Solution for Injection for Sheep

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Ingredient	
Moxidectin	10 mg

Excipients	
Benzyl Alcohol	40 mg
Butylated Hydroxytoluene	2.5 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A sterile clear to pale yellow aqueous solution

4. CLINICAL PARTICULARS

4.1 Target species

Sheep

4.2 Indications for use, specifying the target species

Indicated for:

Prevention and treatment of Psoroptic mange (*Psoroptes* ovis):

Clinical cure: 2 injections 10 days apart.
Preventive efficacy: 1 injection.

Treatment and control of infestations caused by moxidectin sensitive strains of:

Gastro-intestinal nematodes:

- *Haemonchus contortus*
- *Teladorsagia circumcincta* (including inhibited larvae)
- *Trichostrongylus axei* (adults)
- *Trichostrongylus colubriformis* (adults and L3)
- *Nematodirus spathiger* (adults)
- *Cooperia curticei* (adults)
- *Cooperia punctata* (adults)

- *Gaigeria pachyscelis* (L3)
- *Oesophagostomum columbianum* (L3)
- *Chabertia ovina* (adults)

Respiratory tract nematode:

- *Dictyocaulus filaria* (adults)

Larvae of Diptera:

- Oestrus ovis : L1, L2, L3

Has a persistent effect in preventing infestation or reinfestation for:

- at least 4 weeks against *Psoroptes ovis*
- 5 weeks against *Teladorsagia circumcincta* and *Haemonchus contortus*
- 4 weeks against *Gaigeria pachyscelis* and *Oesophagostomum columbianum*
- 2 weeks against *Trichostrongylus colubriformis*

Trials have shown that the product may be effective against strains of *Haemonchus contortus* resistant to benzimidazoles, ivermectin and doramectin.

4.3 Contraindications

Do not use in animals vaccinated against footrot.

4.4 Special warnings

A single injection will protect against scab for at least 28 days, but contact with infected sheep after this time may result in infestation. All bought-in or returning animals should be treated and isolated for at least 12 days.

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 anthelmintics, an anthelmintics 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

It is important to treat at the recommended dosage and to avoid under-dosing since this will result in spread of sheep scab.

Signs of sheep scab can be confused with chewing louse infestation, against which the product is not effective.

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

Care should be taken to avoid self-injection.
In case of contact with skin and eyes wash affected area with clean water.
Do not smoke, eat or drink while handling the product.
Wash hands after use.
Advice to medical practitioners: In cases of accidental self-injection treat any specific signs symptomatically.

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 more than 4 weeks 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 injectable formulation to sheep, treated animals should not have access to watercourses during the first 11 days after treatment.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Extensive studies in laboratory animals and cattle have shown no adverse effects during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

No known incompatibility with concurrent administration of mineral supplements or fluke treatments.

4.9 Amounts to be administered and administration route

0.1ml/5 kg live bodyweight, equivalent to 0.2mg moxidectin/kg live bodyweight given subcutaneously in the neck using a needle of 18 gauge (1.2mm) diameter or less and 1/2 inch (1.5 cm) length.

When treating groups of animals, use only the ZERMEX Automatic Injector and vented draw-off system. For the treatment of individual sheep a syringe not exceeding 2.5 ml and calibrated in increments of 0.1 ml should 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.

Syringes must be filled from the vial through a dry, sterile draw-off needle that has been placed in the vial stopper. Vial stoppers must not be broached more than 10 times.

For routine prevention of sheep scab, all sheep in the flock must be injected once.

The curative treatment of scab requires two injections 10 days apart.
The two injections must be given on different sides of the neck.

The first dose should be given at around 4-6 weeks of age to lambs to control worms, with a second dose 6 weeks later, if necessary.

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

The symptoms of overdose are consistent with mode of action of moxidectin and generally do not occur at less than 10 times the recommended dose. They are manifested as transient salivation, depression, drowsiness and ataxia 8 and 12 hours post-treatment. No treatment is generally necessary. The symptoms resolve in 24 to 48 hours. There is no specific antidote.

4.11 Withdrawal period(s)

Meat and offal: 70 days from last treatment..
Milk: Not for use in sheep producing milk for human consumption or industrial purposes, including the dry period.

5. PHARMACOLOGICAL PROPERTIES

Moxidectin is a parasiticide active against a wide range of internal and external parasites and is a second generation macrocyclic lactone of the milbemycin family. Its principal mode of action is interference 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 flaccid paralysis and eventual death of parasites exposed to the drug.

Moxidectin is rapidly and completely absorbed following subcutaneous injection with maximum blood concentrations being achieved 8-12 hours post injection. The drug is distributed throughout the body tissues but due to its lipophilicity the target tissue is fat where concentrations are 10-20 times those in other tissues. The depletion half life in fat is 23-28 days.

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

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

EC_{50}: 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
Polysorbate 80
Propylene glycol
Disodium edetate dehydrate
Sodium phosphate anhydrous
Sodium acid phosphate monohydrate
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: 3 years.
Shelf-life after first opening the immediate packaging: 6 months.

6.4 Special precautions for storage

Do not store above 25°C.
Protect from light.
Following withdrawal of the first dose, use the product within 6 months.

6.5 Nature and composition of immediate packaging

Carton containing one high density polyethylene container of 50, 200 or 500 ml content sealed with bromobutylated rubber stopper with an aluminium overseal. 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
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Leatherhead
Surrey
KT22 7LP

8. MARKETING AUTHORISATION NUMBER

Vm 42058/4171

9. DATE OF FIRST AUTHORISATION

07 June 2000

10. DATE OF REVISION OF THE TEXT

November 2020

Approved 06 November 2020