SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cydectin TriclaMox 1mg/ml + 50 mg/ml Oral Solution for Sheep

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances

Moxidectin	1.0 mg
Triclabendazole	50.0 mg

Excipients

Benzyl alcohol (E1519)	40.0 mg
Butylhydroxytoluene (E321)	1.0 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Oral solution
A clear yellow to brown liquid

4. CLINICAL PARTICULARS

4.1 Target Species

Sheep

4.2 Indications for use, specifying the target species

For the treatment of mixed nematode and fluke infections, caused by moxidectin and triclabendazole sensitive strains of:
The product has a persistent efficacy and protects sheep against infection or re-infection with the following parasites for the period indicated:

The product has a persistent efficacy and protects sheep against infection or re-infection with the following parasites for the period indicated:

Parasite	Adult stage	L4	Inhibited stages
NEMATODES			
Gastro-intestinal nematodes:			
Haemonchus contortus	•	•	•
Teladorsagia circumcincta	•	•	•
Ostertagia trifurcata	•	•	
Trichostrongylus axei	•	•	•
Trichostrongylus colubriformis	•	•	
Trichostrongylus vitrinus	•	•	
Nematodirus battus	•	•	
Nematodirus spathiger	•	•	
Nematodirus filicolis	•		
Strongyloides papillosus		•	
Cooperia curticei	•		
Cooperia oncophora	•	•	
Oesophagostomum columbianum	•	•	
Oesophagostomum venulosum	•		
Chabertia ovina	•	•	
Trichuris ovis	•		
Respiratory tract nematode:			
Dictyocaulus filaria	•		
TREMATODES			
Liver fluke:	**Adult stage**	**Early Immature stages**	**Late Immature stages**
Fasciola hepatica	•	•	•

The product has a persistent efficacy and protects sheep against infection or re-infection with the following parasites for the period indicated:

Species	Protection period (days)
Teladorsagia circumcincta	35
Haemonchus contortus	35

Clinical trials, after experimental and natural infection, have shown that the product is effective against certain benzimidazole resistant strains of:
. *Haemonchus contortus*
. *Teladorsagia circumcincta*
. *Trichostrongylus colubriformis*
. *Cooperia curticei*

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance(s) or to any of the excipient(s).

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 macrocyclic lactones has been reported in *Teladorsagia* in sheep in a number of countries. In 2008, throughout Europe, moxidectin resistance is very rare. Resistance to triclabendazole has been reported in *Fasciola hepatica* in sheep in some European countries. Therefore the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of parasites, local history of treatments and recommendations on how to use the product under sustainable conditions to limit further selection for resistance to antiparasitic compounds. These precautions are especially important when moxidectin is being used to control resistant strains.

4.5 Special precautions for use

Special precautions for use in animals

This product should not be used for the treatment of single infections.

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

Avoid direct contact with skin and eyes.
Wash hands after use.
Do not smoke, drink or eat when using this product.
Wear impermeable rubber gloves during use.

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

This product is safe for use in breeding animals. See also Section 4.11.

4.8 Interactions 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 bodyweight, equivalent to 0.2 mg moxidectin/kg bodyweight and 10 mg triclabendazole/kg bodyweight, using any standard drenching equipment.
To ensure a correct dosage, 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 body weight and dosed accordingly, in order to avoid under- or overdosing.

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

Signs of overdoses have not been seen at 3 and 5 times the recommended dose. However, if they do occur they should be consistent with the mode of action of moxidectin and/or triclabendazole and would be manifested as transient salivation, depression, drowsiness, ataxia and reduced food intake 8 to 12 hours post-treatment. Treatment is not generally necessary and recovery is generally complete within 1 to 5 days. There is no specific antidote.

4.11 Withdrawal period(s)

Meat and offal: 31 days
Milk:not authorized for use in ewes producing milk intended 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 PROPERTIES

Pharmacotherapeutic group: antiparasitic product, endectocide
ATC vet code: QP54AB52, moxidectin combination

5.1 Pharmacodynamic properties

Moxidectin is an endectocide 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 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, and binds to the glutamate-gated chloride channels. 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.
Triclabendazole is a flukicide belonging to the benzimidazole group of anthelmintics. It is well established that benzimidazole anthelmintics selectively bind to β-tubulin, thus causing the depolymerisation of microtubules and the subsequent disruption of microtubule-based processes in helminths.

5.2 Pharmacokinetic particulars

Moxidectin is distributed throughout the body tissues but due to its lipophilicity the highest drug concentrations are obtained in fat tissue. Moxidectin undergoes biotransformation by hydroxylation. The only significant route of excretion is the faeces. The main pharmacokinetic parameters of moxidectin when administered in the final formulation were the following: AUC_{tot} 58 ng.day.mL^{-1}, C_{max} 12 ng.mL^{-1} , T max : 6 hours and plasma half-life 3.5 days.

The majority of the oral dose of triclabendazole in rats, sheep, goats and rabbits is eliminated in faeces after 6-10 days, as unchanged drug or products of biliary excretion. Urinary excretion is minimal. Sulphone, sulphoxide, ketone and 4-hydroxy triclabendazole derivatives are the main metabolites identified in plasma. The main pharmacokinetic parameters of the active metabolite triclabendazole sulfoxide when triclabendazone was administered in the final combined formulation were: AUC_{tot} 608 µg.h.mL^{-1}, C_{max} 10 µg.mL^{-1}, T_{max} 21 h and plasma half-life 20 h.

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	EC50	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 (E1519)
Butylhydroxytoluene (E321)
Polysorbate 80
Sorbitan oleate
Propylene glycol, dicaprylocaprate

6.2 Major 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

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

6.5 Nature and composition of immediate packaging

1 litre, 2.5 litre and 5 litre polyethylene containers with polypropylene screw-cap.

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 as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

Vm 42058/4030

9. DATE OF FIRST AUTHORISATION

18 December 2009

10. DATE OF REVISION OF THE TEXT

November 2021

Approved: 10/11/21

D Austin