ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cydectin TriclaMox 1 mg/ml + 50 mg/ml oral solution for sheep

Cydectin TriclaMox 1 mg/ml + 50 mg/ml orale Lösung für Schafe (Austria, Germany)
Cydectine TriclaMox 1 mg/ml + 50 mg/ml solution orale pour ovins (Belgium, France, Luxembourg)
Cydectin TriclaMox 1 mg/ml + 50 mg/ml Πόσιμο διάλυμα για πρόβατα (Greece)
Cydectin TriclaMox 1 mg/ml + 50 mg/ml mixtúra, lausn handa sauðfé (Iceland)
Cydectin TriclaMox 1 mg/ml + 50 mg/ml soluzione orale per pecore (Italy)
Cydectin TriclaMox 1 mg/ml + 50 mg/ml oral solution for sheep (Ireland, UK)
Cydectin TriclaMox 1 mg/ml + 50 mg/ml orale oplossing voor schapen (The Netherlands)
Cydectin TriclaMox 1 mg/ml + 50 mg/ml solução oral para ovinos (Portugal)
Cydectin TriclaMox 1 mg/ml + 50 mg/ml solución oral para ovino (Spain)
TriclaMox vet. 1 mg/ml + 50 mg/ml, oral lösning till får (Sweden)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Moxidectin	1.0 mg
Triclabendazole	50.0 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	40.0 mg
Butylhydroxytoluene (E321)	1.0 mg
Polysorbate 80	
Sorbitan oleate	
Propylene glycol, dicaprylocaprate	

A clear yellow to brown liquid.

3. CLINICAL INFORMATION

3.1 Target species

Sheep.

3.2 Indications for use for each target species

For the treatment of mixed nematode and fluke infections, caused by moxidectin and triclabendazole sensitive strains of:

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*

3.3 Contraindications

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

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.
- 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.

3.5 Special precautions for use

Special precautions for safe use in the target species:
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:
People with known hypersensitivity to the active substance should avoid contact with the veterinary medicinal product.
Avoid direct contact with skin and eyes.
Wash hands after use.
Do not smoke, drink or eat when using this product.
Personal protective equipment consisting of impermeable gloves should be worn when handling the veterinary medicinal product.

Special precautions for the protection of 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.

3.6 Adverse events

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 also the section "Contact Details" of the package leaflet.

3.7 Use during pregnancy, lactation or lay

Fertility:
Can be used in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Oral use.
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.

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

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.

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

Meat and offal: 31 days.
Milk: not authorised 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.

4. PHARMACOLOGICALINFORMATION

4.1 ATCvet code: QP54AB52

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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.

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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 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.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

1 L HDPE and 2.5L and 5L fluorinated HDPE bottles with polypropylene screw cap with induction seal.

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

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. The veterinary medicinal product should not enter water courses as moxidectin may be dangerous for fish and other aquatic organisms.

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

To be completed nationally.

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*).