Annex I

List of the names, pharmaceutical form, strengths of the veterinary medicinal product, animal species, route of administration, marketing authorisation holder in the Member States

Member State EU / EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Route of administration	Animal species
Austria	Pfizer Corp. Austria G.m.b.H. Floridsdorfer Hauptstraße 1 A - 1210 Wien Austria	Cydectin TriclaMox 5 mg/ml + 200 mg/ml lösung zum aufgießen für Rinder	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Belgium	Pfizer Animal Health s.a. Rue Laid Burniat 1 1348 Louvain-la-Neuve Belgium	Cydectin TriclaMox 5 mg/ml + 200 mg/ml	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Denmark	Pfizer Oy, Animal Health Tietokuja 4 00330 Helsinki Finland	Cydectin TriclaMox	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
France	Pfizer Holding France 23-25 avenue du Docteur Lannelongue F – 75668 Paris Cedex 14 France	Cydectine TriclaMox 5 mg/ml + 200 mg/ml Solution pour pour-on bovins	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Germany	Pfizer GmbH Linkstraße 10 10785 Berlin Germany	Cydectin® TriclaMox 5 mg/ml + 200 mg/ml Lösung zum Aufgießen für Rinder	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Greece	Pfizer Hellas AE Mesogion Avenue 243 154 51 N. Psychiko Athens Greece	Cydectin TriclaMox	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle

Member State EU / EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Route of administration	Animal species
Ireland	Pfizer Healthcare Ireland Ringaskiddy Co Cork Ireland	Cydectin TriclaMox 5 mg/ml + 200 mg/ml Pour-on Solution for Cattle	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Italy	Pfizer Italia S.r.l. Via Isonzo 71 04100 Latina Italy	Cydectin TriclaMox 5 mg/ml + 200 mg/ml soluzione Pour-on per bovini	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Luxembourg	Pfizer Animal Health s.a. Rue Laid Burniat 1 1348 Louvain-la-Neuve Belgium	Cydectin TriclaMox 5 mg/ml + 200 mg/ml	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Portugal	Laboratórios Pfizer, Lda Lagoas Park – Edíficio 10 2740-271 Porto Salvo Portugal	Cydectin TriclaMox 5 mg/ml + 200 mg/ml solução para unção contínua para bovinos	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Slovenia	Pfizer Luxembourg SARL 51, Avenue J.F.Kennedy L-1855 Luxembourg Luksemburg	Cydectin TriclaMox	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	Cydectin Triclamox 5 mg/ml + 200 mg/ml Solución Pour-on para Bovino	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Route of administration	Animal species
United Kingdom	Pfizer Ltd Ramsgate Road Sandwich CT13 9NJ United Kingdom	Cydectin TriclaMox 5 mg/ml + 200 mg/ml Pour-on Solution for Cattle	Moxidectin Triclabendazole	5.0 mg 200.0 mg	Pour-on solution	Topical – on the back of the animal	Cattle

Annex II

Scientific conclusions and grounds for the variation to the terms of the marketing authorisations

Overall summary of the scientific evaluation of Cydectin TriclaMox (5 mg/ml and 200 mg/ml) pour-on solution for cattle *(see Annex I)*

1. Introduction

Cydectin TriclaMox pour-on solution is a veterinary medicinal product containing 5 mg moxidectin per ml and 200 mg triclabendazole per ml. The product is administered topically on the back of the animal and is indicated for the treatment of mixed nematode and fluke infections in cattle.

Pfizer Animal Health submitted an application for a type II variation to add a new indication against lice species (*Linognatus vituli, Bovicola bovis* and *Solenopotes capillatus*) and reference was made to the monoproduct, Cydectin pour-on containing moxidectin alone and for which the claim against lice was already granted. The application was submitted to France as reference Member State and to Austria, Belgium, Denmark, Germany, Greece, Ireland, Italy, Luxembourg, Portugal, Slovenia, Spain and United Kingdom as concerned Member States. The variation procedure started on 16 May 2012.

During the variation procedure a potential serious risk to animal health was identified by Belgium and in particular that the efficacy against the lice species had been insufficiently substantiated.

This issue remained unsolved and therefore a CMD(v) procedure under Article 13 of Commission Regulation (EC) No 1234/2008 started on 14 January 2013. As the reference and concerned Member States were not able to reach an agreement in respect of the variation, on 3 April 2013, Belgium initiated a referral procedure under Article 13(2) of Commission Regulation (EC) No 1234/2008.

2. Assessment of the data submitted

In order to address the concerns raised by Belgium the MAH provided data to support the non-interference between triclabendazole and moxidectin, a clinical study regarding the efficacy against *Linognatus vituli* and *Bovicola bovis* and literature on the efficacy of moxidectin against lice species.

Pharmacokinetic data

The comparable efficacy of the moxidectin/triclabendazole pour-on combination product (Cydectin TriclaMox) compared to moxidectin alone in the same vehicle was studied in a pharmacokinetics trial. The data did not show any strong signal that any interaction between the active substances that might be present would lead to significantly lower efficacy. In absence of a strong signal, these data can be considered supportive data of the clinical data analysed below.

Efficacy against lice

A confirmatory trial was provided where the efficacy of moxidectin/triclabendazole pour-on combination in cattle was studied at the recommended dose rate of Cydectin TriclaMox (0.5 mg moxidectin/20 mg triclabendazole/kg body weight) against natural infestations of sucking and/or biting lice, with emphasis primarily on *Linognatus vituli* and secondarily on *Bovicola bovis* by comparison with a placebo-treated control group.

The results showed efficacy above 95% except on day 7 (94.5%) and day 28 (87.5%). The latter lower efficacy coincided with an apparent egg hatch on one treated animal where 50 lice were detected. This was not an unusual finding as egg hatch is rapid and can result in a high lice count. For the time point prior to day 28 and the only immediately after that, efficacy was complete for this animal, indicating no apparent lack of efficacy.

Efficacy was also observed in respect to *Bovicola bovis,* however due to the lower infestation inconsistency of findings on some days, the data can only be used as supportive information.

While acknowledging the absence of commingling of the animals which is a worst-case-scenario according to the CVMP guideline on specific efficacy requirements for ectoparasiticides in cattle (EMEA/CVMP/625/03)[1], as a limitation in the study, the CVMP considered the study well conducted.

The CVMP concluded that a second dose confirmatory study for *Linognatus vituli* or the other lice species was deemed not to be necessary based on the data from the confirmatory study and moxidectin's efficacy demonstrated on all other lice species as well as in the literature, even if *Linognatus vituli* is not considered as being the dose-limiting species.

The CVMP based the extrapolation of the efficacy of the product on *Linognatus vituli* to the two other lice species proposed (*Bovicola bovis and Solenopotes capillatus*) on the results of a dose determination study with the monoproduct containing moxidectin as active substance where the three proposed claimed lice species were shown to be controlled (>95 % except for *Solenopotes capillatus* adult before day 21) at half dose for the monoproduct (0.25 mg/kg bw instead of 0.5 mg/kg bw), supported by the pharmacokinetics finding giving no strong signal of interaction between the two active substances in Cydectin TriclaMox.

3. Benefit-risk assessment

Based on (i) the comparable pharmacokinetic profiles for moxidectin when administered as the combination product compared with moxidectin alone in the same vehicle, (ii) the findings of the confirmatory study with *Linognatus vituli* and (iii) the data from the original moxidectin 0.5% pour-on dossier showing that *Linognatus vituli, Bovicola bovis* and *Solenopotes capillatus* were sensitive to moxidectin at half the recommended dose rate (0.25 mg/kg), the CVMP considered that a satisfactory efficacy towards *Linognatus vituli, Bovicola bovis* and *Solenopotes capillatus* can be expected in the field for Cydectin TriclaMox.

The benefit-risk evaluation is deemed to be positive for granting of the variation to the terms of the marketing authorisations for Cydectin TriclaMox concerning treatment of *Linognatus vituli, Bovicola bovis* and *Solenopotes capillatus* infestations caused by moxidectin sensitive strains.

Grounds for the variation to the terms of the marketing authorisations

Whereas

- the CVMP reviewed all available data submitted by the marketing authorisation holder, to support the indication for treatment of lice infestations caused by *Linognatus vituli, Bovicola bovis* and *Solenopotes capillatus*;
- the CVMP on the basis of the available data considered that a satisfactory efficacy towards *Linognatus vituli, Bovicola bovis* and *Solenopotes capillatus* can be expected in the field;

the CVMP recommended the granting of the variation to the terms of the marketing authorisations for the veterinary medicinal products referred to in annex I. The recommended changes in the relevant sections of the product information are set out in annex III.

[1] CVMP guideline on specific efficacy requirements for ectoparasiticides in cattle (EMEA/CVMP/625/03) - http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004643.pdf

Annex III

Amendments in the relevant sections of the summary of product characteristics, labelling and package leaflet

Summary of Product Characteristics

4.2 Indications for use, specifying the target species

In cattle:

Treatment of mixed trematode (fluke) and nematode infections and certain arthropod infestations caused by moxidectin and triclabendazole sensitive strains of:

Parasite	Adult stage		Inhibited stages
NEMATODES		L4	
Gastro-intestinal nematodes:			
Haemonchus placei	●	●	
Ostertagia ostertagi	●	●	●
Trichostrongylus axei	●	●	
Nematodirus helvetianus	●	●	
Cooperia oncophora	●	●	
Cooperia punctata	●		
Oesophagostomum radiatum	●		
Bunostomum phlebotomum	●		
Respiratory tract nematode:			
Dictyocaulus viviparus	●		
TREMATODES			
Liver fluke:		6–8 weeks immatures	
Fasciola hepatica	●	●	
ECTOPARASITES			
Linognathus vituli	●		
Bovicola bovis	●		
Solenopotes capillatus	●		

Labelling:

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

6. INDICATION(S)

In cattle:
Treatment of mixed trematode (fluke) and nematode infections and certain arthropod infestations caused by moxidectin and triclabendazole sensitive strains of:

Parasite	Adult stage		Inhibited stages
NEMATODES		L4	
Gastro-intestinal nematodes:			
Haemonchus placei	●	●	
Ostertagia ostertagi	●	●	●
Trichostrongylus axei	●	●	
Nematodirus helvetianus	●	●	
Cooperia oncophora	●	●	
Cooperia punctata	●		
Oesophagostomum radiatum	●		
Bunostomum phlebotomum	●		
Respiratory tract nematode:			
Dictyocaulus viviparus	●		
TREMATODES			
Liver fluke:		6–8 weeks immatures	
Fasciola hepatica	●	●	
ECTOPARASITES			
Linognathus vituli	●		
Bovicola bovis	●		
Solenopotes capillatus	●		

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING UNITS

6. INDICATION(S)

In cattle:
Treatment of mixed trematode (fluke) and nematode infections and certain arthropod infestations caused by moxidectin and triclabendazole sensitive strains.

Read the package leaflet before use.

Package leaflet:

4. INDICATION(S)

Treatment of mixed trematode (fluke) and nematode infections and certain arthropod infestations caused by moxidectin and triclabendazole sensitive strains of:

Parasite	Adult stage		Inhibited stages
NEMATODES		L4	
Gastro-intestinal nematodes:			
Haemonchus placei	●	●	
Ostertagia ostertagi	●	●	●
Trichostrongylus axei	●	●	
Nematodirus helvetianus	●	●	
Cooperia oncophora	●	●	
Cooperia punctata	●		
Oesophagostomum radiatum	●		
Bunostomum phlebotomum	●		
Respiratory tract nematode:			
Dictyocaulus viviparus	●		
TREMATODES			
Liver fluke:		6–8 weeks immatures	
Fasciola hepatica	●	●	
ECTOPARASITES			
Linognathus vituli	●		
Bovicola bovis	●		
Solenopotes capillatus	●		