Annex I

List of the names, pharmaceutical forms, strengths of the veterinary medicinal products, animal species, routes of administration, applicants / marketing authorisation holders in the Member States

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Austria	Continental Farmaceutica SPRL Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIMOXECTIN 18,92 mg/g, Gel zum Eingeben für Pferde und Ponys	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	EQUEST PRAMOX 19,5 mg/g + 121,7 mg/g Gel zum Eingeben für Pferde	Moxidectin, praziquatel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	EQUEST 18,92 mg/g, Gel zum Eingeben für Pferde und Ponys	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	Cydectin TriclaMox 1 mg/ml + 50 mg/ml Lösung zum Eingeben für Schafe	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	Cydectin 1 mg/ml - Lösung zum Eingeben für Schafe	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Austria	Continental Farmaceutica SPRL Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox 19,5 mg/g +121,7 mg/g Gel zum Eingeben für Pferde	Moxidectin, praziquatel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	Cydectin TriclaMox 5 mg/ml + 200 mg/ml Lösung zum Aufgießen für Rinder	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	CYDECTIN 5 mg/ml POUR-ON - Lösung zum Übergießen für Rinder	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 1% m/v	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 0,1%	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 0,5%	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 10% LA	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin Triclamox 1 mg/ml+50 mg/ml solution orale pour ovins	Moxidectin triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin TriclaMox 5 mg/ml + 200 mg/ml solution pour-on pour bovins	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest Gel Oral	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest Pramox gel oral	Moxidectin praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Belgium	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equimoxectin gel oral	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Belgium	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox gel oral	Moxidectin praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Belgium	Zoetis Belgium SA Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equest oral gel	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Czech Republic	Zoetis Česká republika s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	Equest 18,92 mg/g perorální gel	Moxidectin	Oral gel	18,92 mg	Horse and pony	Oral
Czech Republic	Zoetis Česká republika s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	Equest Pramox perorální gel	Moxidectin praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU / EEA	Applicant / Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Czech Republic	Zoetis Česká republika s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	Equipramox perorální gel	Moxidectin praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Denmark	Zoetis Finland OY Tietokuja 4 00330 Helsinki Finland	Cydectin Pour-On Vet.	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Denmark	Zoetis Finland OY Tietokuja 4 00330 Helsinki Finland	Cydectin TriclaMox	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Denmark	Zoetis Finland OY Tietokuja 4 00330 Helsinki Finland	Cydectin TriclaMox	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
Denmark	Zoetis Finland OY Tietokuja 4 00330 Helsinki Finland	Cydectin Vet.	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Denmark	Zoetis Finland OY Tietokuja 4 00330 Helsinki Finland	Cydectin Vet.	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Denmark	Zoetis Finland OY Tietokuja 4 00330 Helsinki Finland	Equest Pramox Vet.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Denmark	Zoetis Finland OY Tietokuja 4 00330 Helsinki Finland	Equest Vet.	Moxidectin	Oral gel	18,92 mg	Horse and pony	Oral
Denmark	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equimoxectin	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Denmark	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Estonia	Zoetis Belgium S.A. Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest 2% Oral Gel for Horses	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Estonia	Zoetis Belgium S.A. Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest Pramox Oral Gel	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Estonia	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Finland	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Cydectin Pour-On vet	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Finland	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Equest Pramox	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Finland	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Equest vet	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Finland	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equimoxectin vet	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Finland	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox vet	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
France	ZOETIS France 23-25 Avenue du Docteur Lannelongue 75014 Paris France	EQUEST GEL ORAL	Moxidectin	Oral gel	18,92 mg / g	Horse and pony	Oral
France	ZOETIS France 23-25 Avenue du Docteur Lannelongue 75014 Paris France	EQUEST PRAMOX	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
France	ZOETIS France 23-25 Avenue du Docteur Lannelongue 75014 Paris France	MOXIQUEST GEL ORAL	Moxidectin	Gel oral	18,92 mg/g	Horse and pony	Oral
France	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIMOXECTIN 18,92 MG/G GEL ORAL POUR CHEVAUX ET PONEYS	Moxidectin	Gel oral	18,92 mg/g	Horse and pony	Oral
France	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIPRAMOX 19,5 MG/G + 121,7 MG/G GEL ORAL	Moxidectin, Praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE 1 % SOLUTION INJECTABLE POUR BOVINS	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE 0,1 % SOLUTION ORALE POUR OVINS	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE 0,5 % SOLUTION POUR-ON POUR BOVINS	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE 1 % SOLUTION INJECTABLE POUR OVINS	Moxidectin	Solution for injection	10 mg/ml	Sheep	Subcutaneous
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE 10 % LA POUR BOVINS	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE LA 20 MG/ML SOLUTION INJECTABLE POUR OVINS	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE TRICLAMOX 1 MG/ML + 50 MG/ML SOLUTION BUVABLE POUR OVINS	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ ml	Sheep	Oral
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	ZERMEX 2% LA SOLUTION INJECTABLE POUR OVINS	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	ZERMEX 10 % LA SOLUTION INJECTABLE POUR BOVINS	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
France	ZOETIS FRANCE 23-25 Avenue du Docteur Lannelongue 75014 Paris France	CYDECTINE TRICLAMOX 5 MG/ML + 200 MG/ML SOLUTION POUR POUR-ON POUR BOVINS	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
France	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	ZERMEX 5 MG/ML SOLUTION POUR-ON POUR BOVINS	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
France	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	ZERMEX 1 MG/ML SOLUTION ORALE POUR OVINS	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Germany	CC-Pharma GmbH In den Feldern 2 D-54570 Densborn Germany	Equest Pramox 19,5 mg/g + 121,7 mg/g	Moxidectin praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Germany	Continental Farmaceutica s.p.r. Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox 19,5 mg/g + 121,7 mg/g	Moxidectin praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Germany	Continental Farmaceutica s.p.r. Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equimoxectin 18,92 mg/g	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Germany	Zoetis Deutschland GmbH Schellingstr. 1 D-10785 Berlin Germany	Cydectin 1% Injektionslösung	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Equest Orales Gel	Moxidectin	Oral gel	18,92 mg/g	Horse	Oral
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Cydectin 0.1% orale Lösung für Schafe	Moxidectin	Oral suspension	1 mg/ml	Sheep	Oral
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Cydectin 10% LA für Rinder	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Cydectin TriclaMox 1 mg/ml + 50 mg/ml Lösung zum Eingeben für Schafe	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Equest Pramox 19,5 mg/g + 121,7 mg/g	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Zermex 1 mg/ml	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Cydectin TriclaMox 5 mg/ml + 200 mg/ml Lösung zum Aufgießen für Rinder	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
Germany	Zoetis Deutschland GmbH Schellingstraße 1 D-10785 Berlin Germany	Cydectin 0,5% Pour-on	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN cattle	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN oral sheep	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN pour on cattle	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN 1%	Moxidectin	Solution for injection	10 mg/ml	Sheep	Subcutaneous
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN LA Cattle	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN 2% sheep	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN TRICLAMOX SHEEP	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	CYDECTIN TRICLAMOX CATTLE	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	EQUEST ORAL GEL	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Greece	ZOETIS HELLAS Mesogeion 243 154 51 Neo Psixiko Athens Greece	EQUEST PRAMOX	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Hungary	Zoetis Hungary Kft. 1123 Budapest Alkotás u. 53. Hungary	Cydectin 1% oldatos injekció juhok részére A.U.V.	Moxidectin	Solution for injection	10 mg/ml	Sheep	Subcutaneous
Hungary	Zoetis Hungary Kft. 1123 Budapest Alkotás u. 53. Hungary	Equest oral gél A.U.V.	Moxidectin	Oral gel	18,92 mg/g	Horse	Oral
Hungary	Zoetis Hungary Kft. 1123 Budapest Alkotás u. 53. Hungary	Equest Pramox 19,5 mg/g + 121,7 mg/g oral gél A.U.V.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Hungary	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox 19,5 mg/g + 121,7 mg/g oral gél A.U.V.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Iceland	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Cydectin TriclaMox	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Iceland	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Equest Pramox vet.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Iceland	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox vet.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Cydectin 0.1% w/v oral solution for sheep.	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	CYDECTIN 0.5% w/v Pour-On for cattle.	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Cydectin 1% w/v Injectable Solution for Sheep	Moxidectin	Solution for injection	10 mg/ml	Sheep	Subcutaneous
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	CYDECTIN 1% w/v Solution for Injection for cattle.	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Cydectin 10% LA Solution for Injection for Cattle.	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	CYDECTIN 20 mg/ml LA Solution for Injection for Sheep	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Cydectin TriclaMox 1mg/ml + 50 mg/ml Oral Solution for sheep.	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Cydectin TriclaMox 5 mg/ml + 200 mg/ml Pour-on Solution for cattle.	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	EQUEST ORAL GEL, 18.92 mg/g, oral gel for horses and ponies	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Equest Pramox Oral Gel.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Ireland	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIMOXECTIN 18.92 mg/g, oral gel for horses and ponies.	Moxidectin	Oral gel	18.92 mg/g	Horse and pony	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Ireland	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox 19.5 mg/g + 121.7 mg/g oral gel.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Ireland	Chanelle Pharmaceuticals Manufacturing Ltd. Loughrea, Co. Galway Ireland	Moxodectin 1 mg/ml oral solution for sheep	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Ireland	Chanelle Pharmaceuticals Manufacturing Ltd. Loughrea, Co. Galway Ireland	Symec 1 mg/ml oral solution for sheep	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	MOXIGRO 1 mg/ml Oral Solution for Sheep.	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	MOXIGRO 5 mg/ml Pour-on Solution for Cattle	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Ireland	Norbrook Laboratories Limited Station Works Newry Co. Down, BT35 6JP Northern Ireland	Tauramox 5 mg/ml Pour-on Solution for Cattle	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Italy	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIPRAMOX	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Italy	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIMOXECTIN	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN 0,1% SOLUZIONE ORALE PER PECORE	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN 1% INIETTABILE BOVINI	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	EQUEST GEL ORALE	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN TRICLAMOX SOLUZIONE ORALE PER PECORE	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN 0,5% POUR-ON	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN 1% SOLUZIONE INIETTABILE PER OVINI	Moxidectin	Solution for injection	10 mg/ml	Sheep	Subcutaneous

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	EQUEST PRAMOX GEL ORALE	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN 2% LA PER OVINI	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN 10% LA	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	CYDECTIN TRICLAMOX POUR-ON PER BOVINI	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
Latvia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest Pramox	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Latvia	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Lithuania	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIPRAMOX 19,5 mg/g + 121,7 mg/g, geriamasis gelis	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Lithuania	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	EQUEST PRAMOX, geriamasis gelis	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Lithuania	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	EQUEST, 18,92 mg/g, geriamasis gelis arkliams	Moxidectin	Oral gel	18,92 mg/g	Horse	Oral
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 0.1% sol orale ovins	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 0.5% pour-on bovins	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 1%	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin 10% LA	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin Triclamox bovins	Moxidectin, triclabendazole	Transcutaneous solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin triclamox ovins	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest 18.92 mg/g gel oral chevaux, poneys	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Luxemburg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest pramox gel oral	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Norway	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Equest Pramox vet	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Norway	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	EQUEST VET	Moxidectine	Oral gel	18,92 mg/g	Horse	Oral
Norway	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox vet	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Poland	Zoetis Polska Sp. z o. o. ul. Postępu 17 B 02-676 Warszawa Poland	Equest Pramox 19,5 mg/g + 121,7 mg/g oral gel	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Portugal	Zoetis Portugal, Lda. Lagoas Park Edifício 10 2740-271 Porto Salvo Portugal	Cydectin 0,5% Solução para unção contínua para bovinos	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Portugal	Zoetis Portugal, Lda. Lagoas Park Edifício 10 2740-271 Porto Salvo Portugal	Cydectin 1% Solução Injectável para bovinos	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Portugal	Zoetis Portugal, Lda. Lagoas Park Edifício 10 2740-271 Porto Salvo Portugal	Cydectin TriclaMox 1 mg/ml + 50 mg/ml Solução Oral para Ovinos	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Portugal	Zoetis Portugal, Lda. Lagoas Park Edifício 10 2740-271 Porto Salvo Portugal	Cydectin TriclaMox 5 mg/ml + 200 mg/ml solução para unção contínua para bovinos	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
Portugal	Zoetis Portugal, Lda. Lagoas Park Edifício 10 2740-271 Porto Salvo Portugal	EQUEST GEL ORAL, 18,92 mg/g, gel oral para cavalos e póneis	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Portugal	Zoetis Portugal, Lda. Lagoas Park Edifício 10 2740-271 Porto Salvo Portugal	Equest Pramox 19,5 mg/g + 121,7 mg/g Gel oral para cavalos	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Romania	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	EQUEST GEL ORAL 18,92 mg/g	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Slovakia	Zoetis Česká republika, s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	Equest 18,92 mg gél na perorálne použitie	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Slovakia	Zoetis Česká republika, s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	EQUEST PRAMOX perorálny gél	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Slovakia	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox perorálny gél	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Slovenia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	CYDECTIN 0,5 % POUR ON kožni poliv, raztopina za govedo	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Slovenia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Cydectin TriclaMox 5 mg/ml + 200 mg/ml kožni poliv, raztopina za govedo	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
Slovenia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	EQUEST 18,92 mg/g peroralni gel za konje in ponije	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Slovenia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Equest Pramox 19,5 mg/g + 121,7 mg/g peroralni gel	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Slovenia	Continental Farmaceutica, Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox 19,5 mg/g + 121,7 mg/g peroralni gel	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	CYDECTIN SOLUCIÓN INYECTABLE AL 1% PARA GANADO VACUNO	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	CYDECTIN SOLUCIÓN ORAL AL 0,1% PESO/VOLUMEN PARA GANADO OVINO	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	CYDECTIN POUR-ON AL 0,5% P/V PARA GANADO VACUNO	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	CYDECTIN SOLUCIÓN INYECTABLE AL 1% PARA GANADO OVINO	Moxidectin	Solution for injection	10 mg/ml	Sheep	Subcutaneous

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	EQUEST GEL ORAL 18,92 mg/g, gel oral para caballos y ponis	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	CYDECTIN 10% L.A. PARA GANADO VACUNO	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	EQUEST PRA-MOX	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	CYDECTIN LARGA ACCION 20 mg/ml PARA OVINO	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	CYDECTIN TRICLAMOX 1 mg/ml +50 mg/ml SOLUCION ORAL PARA OVINO	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
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	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
Spain	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIMOXECTIN 18,92 mg/g gel oral para equino y ponis	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
Spain	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	EQUIPRA-MOX 19,5 mg/g + 121,7 mg/g gel oral	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Spain	Zoetis Spain, S.L. Avda. de Europa 20 B Parque Empresarial La Moraleja 28108 Alcobendas (Madrid) Spain	BIODECTIN	Moxidectin, *Clostridium septicum, Clostridium perfringens D, Clostridium tetani, Clostridium novyi, Clostridium chauvoei, Corynebacterium pseudotuberculosis*	Solution for injection	5 mg/ml; 2,5 IU; 5, 0 IU; 2,5 IU; 3,5 IU; 9/10 % protection, 0,05 EIAU	Sheep	Subcutaneous

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
Sweden	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Cydectin vet.	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
Sweden	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Triclamox vet.	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
Sweden	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Cydectin® vet	Moxidectin	Oral gel	18,92 mg/g	Horse	Oral
Sweden	Zoetis Finland Oy Tietokuja 4 00330 Helsinki Finland	Cydectin comp vet.	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
Sweden	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equimoxectin vet	Moxidectin	Oral gel	18,92 mg/g	Horse	Oral
Sweden	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox vet	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
The Netherlands	Zoetis B.V. Rivium Westlaan 74 2909 LD Capelle a/d Ijssel The Netherlands	Cydectin 0,1% w/v orale oplossing voor schapen	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
The Netherlands	Zoetis B.V. Rivium Westlaan 74 2909 LD Capelle a/d Ijssel The Netherlands	CYDECTIN 0,5% W/V POUR-ON, oplossing voor runderen	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
The Netherlands	Zoetis B.V. Rivium Westlaan 74 2909 LD Capelle a/d Ijssel The Netherlands	Equest orale gel, 18,92 mg/g, orale gel voor paarden en pony's	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
The Netherlands	Zoetis B.V. Rivium Westlaan 74 2909 LD Capelle a/d Ijssel The Netherlands	EQUEST PRAMOX 19,5 mg/g en 121,7 mg/g orale gel	Moxidectin, praziquantel	Oral gel	19,5 mg/g	Horse	Oral
The Netherlands	Wirtz Farma B.V. Europaweg 26 9636HT Zuidbroek The Netherlands	CYDECTIN 0,5% W/V POUR-ON VOOR RUNDVEE	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
The Netherlands	Zoetis B.V. Rivium Westlaan 74 2909 LD Capelle a/d Ijssel The Netherlands	CYDECTIN TRICLAMOX 1 mg/ml + 50 mg/ml orale oplossing voor schapen	Moxidectin, triclabendazole	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
The Netherlands	Wirtz Farma B.V. Europaweg 26 9636HT Zuidbroek The Netherlands	Cydectin 0,1%, orale oplossing voor schapen	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
The Netherlands	Holland Animal Care B.V. Rijssensestraat 158 7642NN Wierden The Netherlands	CYDECTIN 0,5% W/V POUR-ON VOOR RUNDVEE	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
The Netherlands	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equimoxectin 18,92 mg/g orale gel voor paarden en ponies	Moxidectin	Oral gel	18,92 mg/g	Horse and pony	Oral
The Netherlands	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox 19.5 mg/g + 121.7 mg/g orale gel	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin 0.1% w/v Oral Solution for Sheep	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin 0.5% w/v Pour-On for Cattle	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin 1% w/v Solution for Injection for Cattle	Moxidectin	Solution for injection	10 mg/ml	Cattle	Subcutaneous
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin 1% w/v Solution for Injection for Sheep	Moxidectin	Solution for Injection	10 mg/ml	Sheep	Subcutaneous

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin 10% LA Solution for Injection for Cattle	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin 20 mg/ml LA Solution for Injection for Sheep	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin TriclaMox 1 mg/ml + 50 mg/ml Oral Solution for Sheep	Moxidectin	Oral solution	1 mg/ml 50 mg/ml	Sheep	Oral
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Cydectin TriclaMox 5 mg/ml + 200 mg/ml Pour-on Solution for Cattle	Moxidectin, triclabendazole	Pour-on solution	5 mg/ml 200 mg/ml	Cattle	Topical – on the back of the animal
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Equest Oral Gel 18.92 mg/g Oral Gel for Horses and Ponies	Moxidectin	Oral gel	18,92 mg/g	Horse and Pony	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Equest Pramox 19.5 mg/g + 121.7 mg/g Oral Gel	Moxidectin	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
United Kingdom	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equimoxectin 18.92 mg/g, Oral Gel for Horses and Ponies	Moxidectin	Oral gel	18.92 mg/g	Horse and Pony	Oral
United Kingdom	Continental Farmaceutica Rue Laid Burniat 1, 1348 Louvain-la-Neuve Belgium	Equipramox 19.5 mg/g + 121.7 mg/g Oral Gel	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse	Oral
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Moxigro 1 mg/ml Oral Solution for Sheep	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Moxigro 5 mg/ml Pour-On Solution for Cattle	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Moxiquest 18.92 mg/g Oral Gel for Horses & Ponies	Moxidectin	Oral gel	18.92 mg/g	Horse and Pony	Oral

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Pramoxiquest Oral Gel for Horses and Ponies	Moxidectin, praziquantel	Oral gel	19,5 mg/g 121,7 mg/g	Horse and Pony	Oral
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Zermex 0.1% w/v Oral Solution for Sheep	Moxidectin	Oral solution	1 mg/ml	Sheep	Oral
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Zermex 0.5% w/v Pour-on Solution for Cattle	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Zermex 1% w/v Solution for Injection for Sheep	Moxidectin	Solution for injection	10 mg/ml	Sheep	Subcutaneous
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Zermex 100 mg/ml LA Solution for Injection for Cattle	Moxidectin	Solution for injection	100 mg/ml	Cattle	Subcutaneous

Member State EU/EEA	Applicant/Marketing authorisation holder	Name	INN	Pharmaceutical form	Strength	Animal species	Route of administration
United Kingdom	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE United Kingdom	Zermex 20 mg/ml LA Solution for Injection for Sheep	Moxidectin	Solution for injection	20 mg/ml	Sheep	Subcutaneous
United Kingdom	Norbrook Laboratories Limited Station Works Camlough Road Newry, Co. Down BT35 6JP Northern Ireland	Tauramox 5 mg/ml Pour-On Solution for Cattle	Moxidectin	Pour-on solution	5 mg/ml	Cattle	Topical – on the back of the animal

Annex II

Scientific conclusions and grounds for amendment of the summaries of product characteristics, labelling and package leaflets

Overall summary of the scientific evaluation of veterinary medicinal products containing moxidectin to be administered orally, topically or subcutaneously to cattle, sheep and horses (see Annex I)

1. Introduction

Moxidectin is an anthelmintic macrocyclic lactone endectocide that is widely used in veterinary medicine. Veterinary medicinal products containing moxidectin as a sole active substance or in combination with another antiparasitic active substance(s) (e.g. triclabendazole or praziquatel) are widely used for the treatment and prevention of internal and external parasitic infections in food-producing animals and companion animals.

In the context of marketing authorisation applications submitted to the German national competent authority, Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, under Article 13 of Directive 2001/82/EC as amended, i.e., a generic application, for veterinary medicinal products containing moxidectin, as pour-on solution for cattle, a study on bioaccumulation was provided. Based on the available information, Germany considered that the active substance moxidectin may have persistent, bioaccumulative and toxic (PBT) properties in accordance with the CVMP guideline on the assessment of PBT or very persistent and very bioaccumulative (vPvB) substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012)[1]. Germany was of the opinion that a potential serious risk to the environment may arise from the use of veterinary medicinal products containing moxidectin and consequently, action should be taken at EU level since veterinary medicinal products containing moxidectin are authorised in the majority of the EU/EEA Member States.

Therefore, on 22 October 2015, Germany initiated a referral procedure under Article 35 of Directive 2001/82/EC, for veterinary medicinal products containing moxidectin to be administered orally, topically or subcutaneously to cattle, sheep and horses. The Committee for Medicinal Products for Veterinary Use (CVMP) was requested to consider whether moxidectin meets the criteria to be classified as a PBT substance and if necessary to provide a recommendation on appropriate measures to prevent emission of moxidectin into the environment. The Committee was also asked to recommend whether the marketing authorisations for the aforementioned veterinary medicinal products should be maintained, varied, suspended or withdrawn.

2. Discussion of data available

PBT Assessment

Persistence

For the assessment of persistence, two Good Laboratory Practice (GLP) compliant laboratory studies were provided.

The first study on transformation in soil was performed in accordance with OECD guideline no. 307[2]. The degradation of [^{3}H]-moxidectin was investigated under aerobic conditions at 20±2 ºC for 120 days in the dark, following application at a nominal rate of 0.01 mg/kg soil to four different types of soil (i.e. sandy loam, sand, clay loam and loam with organic carbon content of 1.0%, 0.4%, 2.0% and 4.5%,

[1] CVMP guideline on the assessment of PBT or very persistent and very bioaccumulative (vPvB) substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012) – link
[2] Organisation for Economic Co-operation and Development (OECD) guideline for the testing of chemicals no. 307: Aerobic and Anaerobic Transformation in Soil - link

respectively, and a moisture content adjusted to 50% of the maximum water holding capacity). Material balance, calculated as the percent of applied radioactivity, was maintained within guideline specification (90-110% of applied radioactivity) for all four soils. The mean evolved tritiated water at day 120 (% of applied radioactivity) was 6.48%, 3.22%, 7.6% and 5.10% for the soils sandy loam, sand, clay loam and loam, respectively. Mean non-extractable residues at day 120 (% of applied radioactivity) were 7.22%, 5.23%, 10.15% and 5.38% for the soils sandy loam, sand, clay loam and loam, respectively. One major degradation product (>10% of applied radioactivity) was observed in all four soils which reached mean maximum levels of 37.81%, 29.12%, 42.97% and 31.14% of applied radioactivity, respectively. The following dissipation half-lives (DT_{50}) at 20 °C were calculated using the best fit kinetic model i.e. simple first-order: 78.6, 139.0, 78.7 and 133.6 days for the soils sandy loam, sand, clay loam and loam, respectively. The worst-case DT_{50} was 296.6 days at 12 °C, extrapolated from 139 days at 20 °C in sandy soil. The mean DT_{50} value was 104 days at 20 °C and 222 days normalised to 12 °C.

The second biodegradation study with moxidectin was performed in three different soils (i.e. sandy loam, loam and silt loam with an organic carbon content of 0.58%, 1.39%, and 1.8%, respectively, and a moisture content maintained at 70% of the field capacity) at 25 °C under aerobic conditions for 63 days in the dark. No guideline was given. Mineralisation (evolution of $^{14}CO_2$) accounted for up to 5% of the applied radioactivity. Levels of radioactivity recovered in the organic soil extracts at the end of the study at day 63 ranged between 74-82%. Non-extractable residues accounted for 4-10% of the radioactivity applied to the soil. As the mean recovery of moxidectin at the end of the study (63 days) was less than 50%, a value of 63 days is used as half-life value of moxidectin. It was concluded that moxidectin degrades in soil with a dissipation half-life (DT_{50}) of approximately 2 months and slowly mineralises. This study was considered as being not valid, because: the reliability of the study cannot be evaluated; the study design and test requirements did not comply with the OECD guideline no. 307; the test substance concentrations were determined on one sample point only at day 63, consequently dissipation kinetics are not available and a sound DT_{50} cannot be derived; and, the reported DT_{50} of approximately 63 days is only a very rough estimation. Nevertheless, the results of this study supported the conclusion on persistence from the first study.

The CVMP considered the experimental laboratory study on [^{3}H]-moxidectin transformation in soils in accordance with OECD guideline no. 307 the most reliable and appropriate reference for assessing the persistence of moxidectin in different soil types and determining the DT_{50} for the substance. Based on the results, a DT_{50} of 296.6 days normalised to 12 °C (DT_{50} 139.0 days at 20 °C) as recommended in the CVMP guideline on the assessment of PBT/vPvB substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012), is used to confirm that moxidectin fulfils the vP (very persistent) criterion (i.e. the DT_{50} in soil is higher than 180 days). This is supported by the non-standard degradation study in soil with an estimated DT_{50} of 63 days at 25 °C (= DT_{50} of 216.6 days normalised to 12 °C).

Bioaccumulation

For the assessment of the potential for bioaccumulation, one GLP compliant laboratory study was provided.

The bioaccumulation study in fish was performed in accordance with the OECD guideline no. 305[3] via aqueous exposure under flow-through conditions with continuous renewal of the test media at nominal [^{3}H]-moxidectin concentrations of 0.00055 and 0.0011 µg/l (based on an acute LC_{50} (the concentration of a test substance which results in a 50% mortality of the test species) value of 0.11 µg/l). The duration of the uptake (exposure) and depuration phases were 28 and 49 days, respectively. The test

[3] OECD guideline for the testing of chemicals no. 305: Bioaccumulation in Fish: Aqueous and Dietary Exposure - link

organism were in total sixty (60) rainbow trout (*Oncorhynchus mykiss*) with a mean total length of 5.6 cm and a mean wet weight of 1.738 g at the start of the test. The bioconcentration factors (BCFs) at the various time intervals were calculated by dividing the fish [^{3}H]-residue concentration (parent equivalents in mg/kg), by the nominal concentration (parent equivalents in mg/l) of [^{3}H]-residues in the test medium. The bioconcentration factor was also calculated as the ratio between uptake rate constant (k1) and depuration rate constant (k2). The uptake rate constant (k1) and depuration rate constant (k2) were estimated to be 194.7108 and 0.0739, respectively, for the low dose and 165.1532 and 0.0534, respectively, for the high dose. The bioconcentration factors were also determined as a function of lipid content of the fish following normalisation for a lipid content of 5%.

Based on the [^{3}H]-residues as [^{3}H]-moxidectin in the test media, the bioconcentration factors for whole fish tissue were as follows:

Concentration	BCF_S (l/kg)	BCF_{SL} (l/kg)	BCF_K (l/kg)	BCF_{KL} (l/kg)
Low	2033	1672	2635	2162
High	2124	1745	3093	2543

BCF_S = bioconcentration factor at steady state

BCF_{SL} = bioconcentration factor at steady state corrected for 5% lipid content

BCF_K = kinetic bioconcentration factor

BCF_{KL} = kinetic bioconcentration factor corrected for 5% lipid content

The CVMP considered the study as reliable and concluded that moxidectin fulfils the B criterion for bioaccumulation (BCF_{KL} 2543 l/kg) as specified in CVMP guideline on the assessment of PBT/vPvB substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012), i.e. the bioconcentration factor in aquatic species is higher than 2000.

Additionally, a bioconcentration factor of 2244 l/kg was calculated using the following equation in a quantitative structure–activity relationship (QSAR) model: log BCF_{fish} = 0.85 x logK_{ow} -0.70, based on an experimentally derived logK_{ow} of 4.766.

While the BCF for moxidectin exceeds the established threshold for classification as a bioaccumulative substance, marketing authorisation holders argued that the metabolism studies in the target animals showed no indication of bioaccumulation, based on a steady decline of moxidectin levels in fat after treatment with half-lives of 9 days for muscle to 12-14 days for fat tissues. Further, a full secondary poisoning assessment was performed for moxidectin by dividing the Predicted Environmental $Concentration_{oral\_predator}$ by the Predicted No Effect $Concentration_{oral}$. The respective risk quotient for moxidectin is 0.01 which is below the trigger value of 1. It can be concluded that there is a negligible risk for secondary poisoning from moxidectin.

The CVMP considered the experimental study on bioaccumulation in fish in accordance with OECD guideline no. 305 the most appropriate and reliable reference for assessing the bioaccumulation potential of moxidectin. The experimental bioconcentration factor of 2543 l/kg is supported by the QSAR modelled bioconcentration factor of 2244 l/kg. However, it has to be noted that the use of QSAR values as a substitute for experimental data for pharmaceuticals is not supported as no validated models are available for pharmaceuticals. With regards to the metabolism in the target animal, the lack of accumulation in mammals does not automatically exclude the potential for accumulation in fish; in general the activity of enzymes involved in the transformation of xenobiotics decrease at lower trophic levels as stated in the CVMP guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38 (EMEA/CVMP/ERA/418282/2005-

Rev.1)[4]. The CVMP considered that assessment of secondary poisoning can only be used as supportive information but is not part of the PBT assessment.

Toxicity

A number of GLP compliant laboratory studies on toxicity in aquatic invertebrates, fish, green algae, sediment invertebrates and dung insects were provided.

Algae

Two GLP compliant studies on algae were performed in accordance with OECD guideline no. 201[5].

A study with *Pseudokirchneriella subcapitata* was performed over 72 hours as limit test with 0.5 mg/l corresponding to a mean measured concentration of 0.11 mg/l. The EC_{50} (the concentration of a test substance which results in 50% of the test animals being adversely affected, i.e., both mortality and sub-lethal effects) of moxidectin was therefore concluded to be >0.11 mg/l; the No Observed Effect Concentration (NOEC) was determined as ≥ 0.11 mg/l based on geometric mean of measured test concentrations.

In a second study with *Raphidocelis subcapitata* over 72 hours, no inhibition in the growth was noted at 86.9 µg/l, the highest concentration tested. The EC_{50} and the NOEC were established as >86.9 µg/l and 86.9 µg/l.

Daphnids

Two GLP compliant studies on acute toxicity to daphnids were provided. The first study was performed in accordance with OECD guideline no. 202[6]. An EC_{50} for immobilisation was established as 26 ng/l based on geometric mean of measured test concentrations. The second study was performed in accordance with the US FDA Environmental Assessment Technical Assistance Document no. 4.08[7] which is comparable to the current OECD methods. Under the conditions of the study, the 48-hour EC_{50} value for immobilisation was established as 30.2 ng/l.

Two GLP compliant studies on the effects on daphnid reproduction in accordance with OECD guideline no. 211[8] were submitted. The first study was conducted with [^{3}H]-moxidectin and resulted in a NOEC and lowest observed effect concentration (LOEC) for reproduction as well as for parental growth at 0.0031 µg/l and 0.025 µg/l, respectively. The 21-day LC_{50} for parental mortality (based on immobilisation) was determined to be 0.028 µg/l, with complete mortality observed at the highest mean measured test concentration of 0.14 µg/l. In the second study no effects on *D. magna* survival and reproduction were seen at a concentration of 10 ng/l over the test period. The NOEC of moxidectin for reproduction in *D. magna* was therefore concluded to be >10 ng/l.

Fish

Three GLP compliant studies on acute toxicity in fish were provided. The first study with the common carp (*Cyprinus carpio*), was performed in accordance with OECD guideline no. 203[9] and a LC_{50} value for moxidectin was established as 0.11 µg/l based on geometric mean of measured test concentrations. The second study in rainbow trout (*Oncorhynchus mykiss*), was performed in accordance with US FDA Environmental Assessment Technical Assistance Document no. 4.11[10]. Under

[4] CVMP guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38 - EMA/CVMP/ERA/418282/2005-Rev.1- Corr. - link
[5] OECD guideline for the testing of chemicals no. 201: Freshwater Alga and Cyanobacteria, Growth Inhibition Test - link
[6] OECD guideline for the testing of chemicals no. 202: *Daphnia* sp. Acute Immobilisation Test - link
[7] US FDA Environmental Assessment Technical Handbook. Technical Assistance Document no. 4.08 Daphnia Acute Toxicity
[8] OECD guideline for the testing of chemicals no. 211: *Daphnia magna* Reproduction Test - link
[9] OECD guideline for the testing of chemicals no. 203: Fish, Acute Toxicity Test - link
[10] US FDA Environmental Assessment Technical Handbook. Technical Assistance Document no. 4.11 Freshwater Fish Acute Toxicity

the conditions of the study, the LC_{50} value for moxidectin was established as 0.16 µg/l. The third acute study following the same procedures was conducted in bluegill (*Lepomis macrochirus*). A LC_{50} value of 0.62 µg/l was calculated based on measured concentrations.

The effect of prolonged exposure of moxidectin on the early life stages of the fathead minnow, (*Pimephales promelas)*, was investigated in a GLP compliant study according to OECD guideline no. 210[11]. The study was conducted over a 28-day post-hatch period under continuous flow conditions. The NOEC for fry survival, the most sensitive study endpoint, was established as 3.2 ng/l.

Sediment dwelling organisms

Two GLP compliant studies were provided on toxicity to sediment dwelling organisms in accordance with OECD guideline 218[12]. Both studies were performed with *Chironomus riparius* exposed via spiked sediment. The NOECs for emergence ratio, the most sensitive study endpoint, were 235 µg/kg dry weight based on nominal sediment concentrations and 111 µg moxidectin equivalents/kg dry weight, respectively.

Dung fauna

A comprehensive risk assessment for moxidectin and dung fauna has been provided. A tiered approach was applied considering the CVMP draft guideline on the higher tier testing of veterinary medicinal products to dung fauna (EMA/CVMP/ERA/409350/2010)[13]. Data were provided for laboratory (Tier A), extended laboratory with incurred residues (Tier B) and field studies (Tier C). These have been discussed by target species (cattle, sheep, and horses) and by route of administration (pour-on, injectable, oral). The Tier A studies have been performed according to OECD standard guidelines. The Predicted No Effect Concentrations (PNECs) derived by dividing the most sensitive endpoints (LC_{50}/EC_{50}) for the most sensitive standard organism by an assessment factor of 100 amount to 4.7 and 10 µg/kg dry weight for the dung fly (*Musca autumnalis*) and the dung beetle (*Aphodius constans*), respectively. However, the data provided for Tier B and C assessment do not comply with current standards. Most of these laboratory studies and field studies using incurred residues examined the duration after treatment that did impact dung fauna, rather than attempting to derive effect concentrations. Residues in dung were toxic to dung flies for more than 7 days or for more than 28 days after treatment, depending on study duration, species and formulation.

Dung flies were shown to be the most sensitive species as demonstrated in laboratory tests and in field studies. An impact on dung flies was shown for all target species (cattle, sheep, and horses) and all routes of administration (pour-on, injectable, oral).

The non-standard field studies indicated that the risk derived from laboratory tests may not fully reflect what is observed under field conditions of use; differences were shown in sensitivity of dung beetle and dung fly and additionally a lower toxicity of moxidectin compared to other avermectins. However, on the basis of these studies it was not possible to conclude that abundance and diversity of dung insect populations (flies and beetles) will not be significantly affected by frequent and repeated use of moxidectin containing products over the years.

As no valid and reliable higher Tier studies were provided, the PNECs derived from the Tier A standard laboratory studies with spiked cattle manure are used for further risk assessment for all target species.

Taking into account all the information provided it can be concluded that moxidectin is highly toxic to dung fauna with dung fly being the most sensitive species.

[11] OECD guideline for the testing of chemicals no. 210: Fish, Early-life Stage Toxicity Test - link
[12] OECD guideline for the testing of chemicals no. 218: Sediment-Water Chironomid Toxicity Using Spiked Sediment - link
[13] CVMP draft guideline on the higher tier testing of veterinary medicinal products to dung fauna (EMA/CVMP/ERA/409350/2010) - link

Earthworms

Two GLP compliant studies were provided on toxicity to earthworms. The subacute toxicity was investigated in a GLP compliant study according to US FDA Environmental Assessment Technical Assistance Document no. 4.12[14]. Earthworms were exposed to moxidectin-treated cow manure in artificial soil over a 28-day exposure period. The LC_{50} for mortality was established as 37.2 mg/kg; the corresponding NOEC was 20 mg/kg. The NOEC for bodyweight change, the most sensitive study endpoint, was established as 1 mg/kg. The effect on the reproduction of *Eisenia foetida* was investigated in a GLP compliant study according to OECD guideline 222[15]. Earthworms were exposed to moxidectin in artificial soil over a 28-day exposure period, followed by an additional test period of four weeks where the number of offspring hatched from the cocoons was determined. The NOEC for reproduction was determined as 0.84 mg/kg dry soil based on nominal concentrations.

Plants

A terrestrial plant study with 12 weed species was also provided which was considered not relevant for the current assessment.

Overall the CVMP considered that moxidectin fulfils the T criterion based on the high toxicity of moxidectin to aquatic organisms, i.e. a NOEC of 3.1 ng/l for *Daphnia magna* and a NOEC of 3.2 ng/l for fish (*Pimephales promelas*). The threshold specified in the CVMP guideline on the assessment of PBT/vPvB substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012) is NOEC or EC_{10} for marine or freshwater organisms less than 0.01 mg/l.

Conclusion on the PBT assessment

The CVMP considered that moxidectin fulfils the criteria for persistence (P), bioaccumulation (B) and toxicity (T) according to the results of the laboratory studies and consequently, has to be classified as a PBT substance.

Qualitative PBT risk assessment

The CVMP guideline on the assessment of PBT/vPvB substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012) suggests that the standard approach used to determine the risk to the environment associated with veterinary medicinal products (risk quotient approach, where a risk is characterised by calculating the Predicted Environmental Concentration (PEC)/Predicted No Effect Concentration (PNEC) ratio) is not appropriate for substances classified as PBT. Therefore, a qualitative risk assessment, i.e. the likelihood of persistence, bioaccumulation and toxicity to occur under realistic conditions, has been performed by the marketing authorisation holders, taking into account a weight of evidence approach.

Concerning the assessment of persistence, the high adsorption of moxidectin onto solid particles, its metabolism and biotransformation and abiotic degradation via photolysis were considered, as well as the appropriateness of the transformation studies in soil. The marketing authorisation holders considered that degradation rates at 12 °C are overly conservative and do not reflect likely degradation rates under normal conditions of use. That is, the marketing authorisation holders argued that mean land surface temperatures during spring/summer in predominant agricultural regions in Europe are likely to be higher leading to a faster degradation. However, it has to be noted that other factors such as low moisture content also lead to reduced degradation. Considering that degradation mechanisms in soil are in place, together with the high immobility of moxidectin in soil, the marketing

[14] US FDA Environmental Assessment Technical Handbook. Technical Assistance Document no. 4.12 Earthworm Subacute Toxicity
[15] OECD guideline for the testing of chemicals no. 222: Earthworm Reproduction Test (*Eisenia fetida/Eisenia andrei*) - link

authorisation holders concluded that exposure of surface water to moxidectin is unlikely or extremely low. Furthermore, the marketing authorisation holders argued that bioaccumulation tested under laboratory conditions, i.e. continuous exposure under flow-through conditions, is not reflecting realistic exposure in the field. Altogether, the marketing authorisation holders concluded that the likelihood of moxidectin to bioaccumulate in fish is rather low. So far, no criteria for bioaccumulation assessment in sediment or soil organisms have been established and the classification is based on the standard bioaccumulation study in fish. Regarding the inherent toxicity of moxidectin to aquatic organisms, the marketing authorisation holders considered that acute effects as in the acute toxicity test with *D. magna*, i.e. effects after 48 hours under continuous exposure, are not transferable to the field situation. The marketing authorisation holders argued that under realistic conditions, aquatic exposure to moxidectin will be either unlikely or extremely low due to strong adsorption of moxidectin onto soil or will not be maintained longer than 24 hours due to rapid partitioning into sediment. As exposure of aquatic organism is unlikely to occur, the toxicity will be reduced significantly.

The CVMP acknowledged that aquatic exposure might be low due to immobility of moxidectin in soil and rapid partitioning into sediment and consequently might reduce toxicity to aquatic organisms. However, toxicity to sediment-dwelling organisms is still very likely. When considering persistence under field conditions, the Committee acknowledged that degradation mechanisms exist and that a soil temperature of 12 °C might not be representative for all European regions. However, when considering PBT status, the established criteria are based on evaluation of persistence at a soil temperature of 12 °C and this is accepted as mean European temperature. Transformation of moxidectin in soil will indeed be faster at higher temperatures but even at 20 °C, as in the laboratory degradation study in soil, moxidectin was shown to be persistent in sandy soil. However, it should be noted that temperatures can also be lower, resulting in slower degradation rates and degradation may also be impaired by low moisture content.

The marketing authorisation holders' conclusion that the likelihood of persistence, bioaccumulation and toxicity occurring under realistic conditions is low, is based on theoretical considerations, as outlined above. Data on the fate and behaviour of moxidectin in the environment under real conditions to verify the proposed low likelihood of environmental impact are not available. Thus, to verify the weight of evidence approach as proposed by the marketing authorisation holders, and to assess whether the theoretical hazards translate into environmental impacts, the CVMP considered that data on fate and behaviour of moxidectin in the environment under actual use conditions should be generated. A targeted sampling in the environment following the use of veterinary medicinal products as a pour-on solution containing 5 mg moxidectin per ml or as a solution for injection containing 100 mg moxidectin per ml in beef cattle in pasture animals for three consecutive years was considered necessary in order to obtain a better understanding of the actual environmental exposure.

Emission and risk assessment

The PBT hazard assessment clearly identifies moxidectin as a PBT substance based on the laboratory data provided. As previously noted, and as outlined in the CVMP guideline on the assessment of PBT/vPvB substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012), a quantitative risk assessment is not appropriate for the PBT hazard assessment. However, any consideration of risk to the environment must take into account knowledge on the aspects of the specific product and its use that contribute to the actual emission in the environment, e.g. route of administration (pour-on, injectable, oral), husbandry conditions (indoor/outdoor/confined), terrestrial/aquaculture, closed/open water systems, individual animal treatment/flock treatment, control of environmental release, waste management, metabolism in the target animal, etc.

In order to address the emissions of veterinary medicinal products containing moxidectin into the environment worst-case scenarios have been calculated for all product types (pour-on, injectable, oral)

in cattle, sheep and horses, taking into account the specific pattern of use in each target species and the maximum number of treatments that might be applied within one year.

Comprehensive PEC calculations have been submitted for the relevant compartments (soil, surface water, sediment, and groundwater) covering cattle, sheep and horses, including the entry pathways run-off from pasture and direct entry to surface waters via excretion for pasture animals. Because of the PBT status of moxidectin, emission scenarios have also been presented for stabled animals covering the spreading of manure onto soil.

The maximum $PEC_{soil\_initial}$ equals 4.18 µg/kg dry weight for cattle after subcutaneous route of administration (injectable products) using a dose of 0.5 mg/kg bodyweight and the respective default values. Considering a DT_{50_soil} of 222 days for 12 °C the $PEC_{soil\_plateau}$ has been calculated to 6.15 µg/kg dry weight for the bi-annual application. Taking into account a default $DT_{50\_sediment}$ of 1000 days (as a water/sediment study was not available) one marketing authorisation holder calculated the $PEC_{sediment\_plateau}$ to be 55.8 µg/kg dry weight.

For cattle, the highest PECs for surface water were 0.436 ng/l for run-off after subcutaneous route of administration (injectable products) and 0.219 ng/l for direct excretion into surface waters after topical (cutaneous) route of administration (pour-on products). For sheep, the subcutaneous route of administration (injectable products) resulted in a $PEC_{surfacewater}$ of 0.122 ng/l for run-off. For horses, the oral use resulted in a PEC of 0.3 ng/l for run-off.

Further PEC refinements were performed by the marketing authorisation holders for each concerned product and for all target animal species and routes of administration by application of the FOCUS models. Additionally, data on faecal excretion were considered by the marketing authorisation holders for the justification of the proposed risk mitigation measures and warnings, respectively. During the refinement steps, processes such as sorption onto soil or partitioning into sediment were also taken into account.

Considering further PEC-refinement (FOCUS SW – calculations and excretion pattern evaluation for risk mitigation measures) the maximum PEC values for the relevant environmental compartments are summarised as follows:

	Pasture Scenarios	Stable Scenarios
$PEC_{soil\ plateau}$ (ng/kg)	3690 (cattle, solution for injection containing 100 mg moxidectin per ml)	6100 (horse, oral)
$PEC_{surfacewater\ run\text{-}off}$ (ng/l)	0.239 (cattle, solution for injection containing 100 mg moxidectin per ml)	0.025 (cattle, pour-on)
$PEC_{surfacewater\ direct}$ (ng/l)	0.058 (cattle, solution for injection containing 10 mg moxidectin per ml)	---
$PEC_{sediment\ run\text{-}off}$ (ng/kg)	325 (cattle, pour-on solution containing 5 mg moxidectin per ml)	53 (cattle, pour-on)
$PEC_{sediment\ direct}$ (ng/kg)*	35 (sheep, solution for injection containing 20 mg moxidectin per ml)	---

*-PEC calculation for direct excretion by sheep is not necessary as per CVMP guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38 (EMEA/CVMP/ERA/418282/2005-Rev.1) but was calculated by a marketing authorisation holder to cover every possible scenario.

The CVMP considered the results acceptable for use in the derivation of risk mitigation measures for the aquatic and sediment compartment.

3. Benefit-risk assessment

Benefit assessment

Direct therapeutic benefits

In cattle, topical administration of the pour-on monoproducts (moxidectin only) is intended for the treatment of gastro-intestinal nematodes, respiratory tract nematodes, warble grubs, lice, mange mites and horn flies.

In cattle, topical administration of the pour-on combination products (moxidectin in combination with triclabendazole) is intended for the treatment of gastro-intestinal nematodes, respiratory tract nematodes, trematode (fluke) and certain arthropod infestations.

In cattle, subcutaneous administration of the injectable products is intended for the treatment and prevention of gastro-intestinal nematodes, respiratory tract nematodes, warble grubs, lice and mange mites.

In sheep, subcutaneous administration of the injectable products is intended for the treatment and prevention of gastro-intestinal nematodes, respiratory tract nematodes, larvae of bot fly and mange mites.

In sheep, oral administration of the monoproducts is intended for the treatment and prevention of gastro-intestinal nematodes and respiratory tract nematodes.

In sheep, oral administration of the combination products is intended for the treatment of gastro-intestinal nematodes, respiratory tract nematodes and trematode (fluke) infestations.

In horses and ponies, oral administration of the monoproducts is intended for the treatment of large and small strongyles, ascarids and other parasites e.g. pinworm, throat bot.

In horses and ponies, oral administration of the combination products (moxidectin in combination with praziquantel) is intended for the treatment of large and small strongyles, ascarids, tapeworm and other parasites e.g. pinworm, throat bot.

The aforementioned internal and external parasites are recognised as causing significant loss of production and negatively impacting on animal welfare.

Although the efficacy of veterinary medicinal products containing moxidectin has not been re-assessed specifically in this referral procedure, these pour-on, injectable and oral products are considered effective veterinary medicines in the treatment of the abovementioned internal and external parasites in cattle, sheep and horses.

Additional benefits

Given the limited number of different classes of end-/ectoparasiticides and the responsible use principle requiring the use of substances of different classes of antiparasitics for the control of parasitoses in order to reduce the risk of resistance development, veterinary medicinal products containing moxidectin are considered an important therapeutic option.

Risk assessment

Quality, target animal safety, user safety, consumer safety and efficacy were not assessed in this referral procedure.

Risk to the environment

The CVMP considered that moxidectin fulfils the criteria for persistence (P), bioaccumulation (B) and toxicity (T) according to the results of the laboratory studies and consequently, has to be classified as

PBT substance. PBT substances pose a hazard where the fate and behaviour in the environment and its toxicity in the long-term cannot be predicted. Thus, the standard risk assessment approach where the risk is characterised by calculating the PEC/PNEC ratio is not appropriate for PBT substances as outlined in the CVMP guideline on the assessment of PBT/vPvB substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012). Consequently, risk mitigation measures tempering a quantitative risk are considered suitable neither to eliminate the hazard nor to prevent emission into the environment.

A qualitative risk assessment based on a weight of evidence discussion was provided and this considered the likelihood of persistence, bioaccumulation and toxicity to occur under real environmental conditions. It was argued that laboratory conditions, as used for the determination of the PBT properties, may not reflect the real world situation. It was considered that degradation in soil might be faster under higher temperatures, that aquatic toxicity and bioaccumulation might be reduced due to intermittent rather than continuous exposure, and that moxidectin would adsorb rapidly to sediment. The assumption that the likelihood of persistence, bioaccumulation and toxicity occurring under real-world environmental conditions is low is based on theoretical considerations, as outlined above. Data on the fate and behaviour of moxidectin in the environment to verify the proposed low likelihood under real conditions are not available. Thus, to verify the weight of evidence approach as proposed by the marketing authorisation holders, and to assess whether the theoretical hazards translate into environmental impacts, the CVMP considered that data on fate and behaviour of moxidectin in the environment under actual use conditions should be generated.

Based on the available data high toxicity of moxidectin to aquatic and sediment organisms has been identified, i.e. a NOEC of 3.1 ng/l for *Daphnia magna*, a NOEC of 3.2 ng/l for fish and a NOEC of 111 µg/kg dry weight for chironomids. A comprehensive risk assessment for dung organisms was also provided, resulting in risk quotients (PEC/PNEC) of >5000 and >1000 for dung flies and dung beetles, respectively, indicating a risk for dung fauna.

Environmental profile of alternatives

The environmental profile of therapeutic alternatives including the group of macrocyclic lactones (ivermectin, abamectin, eprinomectin, and doramectin) and other groups of parasiticides such as organophosphates, synthetic pyrethroids and insect growth regulators has been considered based on available data. It appeared that the therapeutic alternatives to moxidectin do not necessarily have more favourable environmental profiles, in particular in terms of toxicity to aquatic and dung insects.

Risk management or mitigation measures

The CVMP recommended risk mitigation measures to be included in the product information for all concerned products in order to mitigate the risk to aquatic and sediment organisms, including exclusion times for limited access to water courses for each target species. These exclusion times are based on refined risk quotients with refined PEC values.

Risk mitigation measures for dung insects fulfilling the criteria of the CVMP reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products (EMA/CVMP/ERAWP/409328/2010)[16] could not be established. Thus, the Committee recommended warning sentences to be added to the product information, taking account of the risk of toxic residues in dung to dung fauna.

In addition, the Committee noted that in the product information of some pour-on products there is a warning advising that risk to dung fauna may be reduced by avoiding treatment periods that coincide

[16] CVMP reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products (EMA/CVMP/ERAWP/409328/2010) – link

with periods of local high activity of dung beetles. The CVMP considered that such warning is not in line with good agricultural practice and therefore should be deleted from the product information.

Additionally, the Committee recommended that the product information for the concerned products should include information on the hazard posed by moxidectin due to its PBT properties and advice to administer these products only when infestation is confirmed.

It is noted that according to the CVMP reflection paper on the authorisation of VMPs containing PBT or vPvB substances (EMA/CVMP/448211/2015)[17] further measures intended to ensure responsible use of antiparasitic veterinary medicinal products, for example, targeted selective treatment of individual animals on farm level, are considered to limit environmental exposure. It may be considered appropriate that such additional measures are applied in the future in the light of any new information.

Evaluation and conclusions on the benefit-risk assessment

From a clinical point of view avermectins are considered the most suitable treatment alternative to moxidectin, given the similar spectrum of activity against internal and external parasitic species in cattle, sheep and horses. Apart from macrocyclic lactones, established classes of antiparasitics in cattle, sheep and horses include benzimidazoles, tetrahydropyrimidines (pyrantel), imidazothiazoles (levamisole), amino-acetonitril derivates (monepantel), spiroindoles (derquantel). Avermectins have a very similar broad spectrum of activity, but partly achieved through different mode of action on glutamate-gated chloride channel receptors in nematode and arthropod cells, and efflux pathways at molecular levels. On the other hand, there is evidence from literature (Prichard *et al.*, 2012)[18] that the resistance against avermectins and moxidectin is not always genetically identical, which implies that avermectin resistant parasite strains can be successfully treated with moxidectin. In conclusion, withdrawal of veterinary medicinal products containing moxidectin from the European market would limit the number of adequate therapeutic alternatives which is not considered desirable from a resistance perspective. Consequently, given the limited number of different classes of end-/ectoparasiticides, veterinary medicinal products containing moxidectin are an important therapeutic alternative to other veterinary medicinal products containing macrocyclic lactones. At this time it is considered important to maintain the marketing authorisations for veterinary medicinal products containing moxidectin on the European market for the treatment and control of parasitoses in cattle, sheep and horses to reduce the risk of development of resistance in line with responsible use principles.

A risk to the environment has been identified which can be partially mitigated by appropriate risk mitigation measures. More importantly, moxidectin poses a hazard due to its PBT properties that can neither be eliminated by risk mitigation measures nor can the emission into the environment be prevented. Data on the fate and behaviour of moxidectin in the environment to verify the proposed low likelihood under real conditions are not available. Thus, to verify the weight of evidence approach as proposed by the marketing authorisation holders, and to assess whether the theoretical hazards translate into environmental impacts, the Committee considered that a targeted sampling in the environment following the use of veterinary medicinal products as a pour-on solution containing 5 mg moxidectin per ml or as a solution for injection containing 100 mg moxidectin per ml in beef cattle in pasture animals is necessary to obtain a better understanding of the actual environmental exposure.

[17] CVMP reflection paper on the authorisation of veterinary medicinal products containing (potential) persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) substances (EMA/CVMP/448211/2015) – link

[18] Prichard, R., Ménez, C., Lespine, A., 2012. Moxidectin and the avermectins: Consanguinity but not identity. International Journal for Parasitology: Drugs Drug Resistance 2:134-53.

The overall benefit-risk balance for veterinary medicinal products containing moxidectin to be administered to cattle, sheep and horses as pour-on, injectable and oral formulations (see Annex I) is deemed positive subject to the recommended changes in the product information (see Annex III). Moreover, in view of the need for a targeted field study to generate data on the fate and behaviour of moxidectin in different environmental compartments under actual use conditions and to verify that the likelihood of persistence, bioaccumulation and toxicity to occur in the environment is low, it is considered that conditions affecting the marketing authorisations should be imposed (see Annex IV).

The subsequent evaluation of data generated further to the fulfilment of these conditions should be undertaken by the CVMP due to the complexity of the data thus generated and in the interest of maintaining the harmonised EU approach achieved by this referral procedure.

The data generated further to the fulfilment of these conditions, along with any other relevant information which might become available, will form the basis of a subsequent assessment by the CVMP of its conclusions on the benefit-risk balance for veterinary medicinal products containing moxidectin to be administered to cattle, sheep and horses as pour-on, injectable and oral formulations.

Grounds for amendment of the summaries of product characteristics, labelling and package leaflets

Whereas

- the CVMP considered that based on the available data moxidectin fulfils the criteria for persistence, bioaccumulation and toxicity according to the results of the laboratory studies and consequently, has to be classified as a persistent, bioaccumulative and toxic (PBT) substance;
- the CVMP considered that veterinary medicinal products containing moxidectin to be administered to cattle, sheep and horses as pour-on, injectable and oral formulations are effective veterinary medicines in the treatment of the internal and external parasites in cattle, sheep and horses;
- the CVMP considered that veterinary medicinal products containing moxidectin to be administered to cattle, sheep and horses as pour-on, injectable and oral formulations are an important therapeutic alternative, given the limited number of different classes of end-/ectoparasiticides and the responsible use principle requiring the use of substances of different classes of antiparasitics for the control of parasitoses in order to reduce the risk of resistance development;
- the CVMP considered that based on the available data high toxicity of moxidectin to aquatic and sediment organisms and a risk for dung fauna have been identified;
- the CVMP considered that in order to reduce the identified risks for aquatic and sediment organisms, risk mitigation measures should be included in the product information. No appropriate risk mitigation measures can be established for dung fauna, hence, warning sentences should be included in the product information. Furthermore, the PBT status of moxidectin should be communicated in the product information;
- the CVMP considered that a targeted sampling in the environment following the use of veterinary medicinal products as a pour-on solution containing 5 mg moxidectin per ml or as a solution for injection containing 100 mg moxidectin per ml in beef cattle in pasture animals is necessary to obtain a better understanding of the actual environmental exposure;
- the CVMP considered that based on the currently available data the overall benefit-risk balance is positive for the veterinary medicinal products containing moxidectin to be administered to cattle, sheep and horses as pour-on, injectable and oral formulations (see Annex I), subject to amendments in the product information and conditions on the marketing authorisations;

- the CVMP considered that the data generated further to the fulfilment of these conditions, along with any other relevant information which might become available, will form the basis of a subsequent assessment by the CVMP of its conclusions on the benefit-risk balance for veterinary medicinal products containing moxidectin to be administered to cattle, sheep and horses as pour-on, injectable and oral formulations;

the CVMP has recommended the variation of the marketing authorisations for veterinary medicinal products containing moxidectin to be administered orally, topically or subcutaneously to cattle, sheep and horses (see Annex I) in order to amend the summaries of product characteristics, labelling and package leaflets in line with recommended changes in the product information as set out in Annex III.

The conditions imposed on the marketing authorisations are described in Annex IV.

Annex III

Amendments in the relevant sections of the summaries of product characteristics, labelling and package leaflets

A. For veterinary medicinal products listed in Annex I as pour-on solution and administered to cattle containing 5 mg moxidectin per ml or 5 mg moxidectin and 200 mg triclabendazole per ml

Summary of product characteristics

Add, to all products:

4.5 Special precautions for 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 cattle with the product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period more than 2 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, field studies 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 pour-on formulation, treated animals should not have access to watercourses during the first week after treatment.

Delete, where applicable, the following sentence: '*Risk to dung fauna may be reduced by avoiding treatment that coincides with periods of local high activity of dung beetles.*'.

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.

6.6 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.

Labelling:

Add, to all products:

9. SPECIAL WARNING(S), IF NECESSARY

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 cattle with the product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period of more than 2 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, field studies 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. 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, the product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the pour-on formulation, treated animals should not have access to watercourses during the first week after treatment.

Delete, where applicable, the following sentence: '*Risk to dung fauna may be reduced by avoiding treatment that coincides with periods of local high activity of dung beetles.*'.

In case of insufficient space on the label:

9. SPECIAL WARNING(S), IF NECESSARY

Environmental risks have been identified for this product and special precautions apply. Read the package leaflet before use.

Package leaflet:

Add, to all products:

12. SPECIAL WARNING(S)

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, in particular aquatic organisms and dung fauna.

- Faeces containing moxidectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of cattle with the product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period of more than 2 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, field studies 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. 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, the product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the pour-on formulation, treated animals should not have access to watercourses during the first week after treatment.

Delete, where applicable, the following sentence: '*Risk to dung fauna may be reduced by avoiding treatment that coincides with periods of local high activity of dung beetles.*'.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

B. For veterinary medicinal products listed in Annex I as solution for injection and administered to cattle containing 10 mg moxidectin per ml or 100 mg moxidectin per ml

Summary of product characteristics

Add, to all products:

4.5 Special precautions for 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 cattle with the product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period 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, field studies 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, treated animals should not have access to watercourses during the 10 days after treatment.

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.

Add, to all products:

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.

Labelling:

Add, to all products:

9.	SPECIAL WARNING(S), IF NECESSARY

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 cattle 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, field studies 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. 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, the product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the injectable formulation, treated animals should not have access to watercourses during the first 10 days after treatment.

In case of insufficient space on the label:

9.	SPECIAL WARNING(S), IF NECESSARY

Environmental risks have been identified for this product and special precautions apply. Read the package leaflet before use.

Package leaflet:

Add, to all products:

12. SPECIAL WARNING(S)

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, in particular aquatic organisms and dung fauna.

- Faeces containing moxidectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of cattle 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, field studies 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. 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, the product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the injectable formulation, treated animals should not have access to watercourses during the first 10 days after treatment.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

C. For veterinary medicinal products listed in Annex I as oral solution and administered to sheep containing 1 mg moxidectin per ml or 1 mg moxidectin and 50 mg triclabendazole per ml

Summary of product characteristics

Add, to all products:

4.5 Special precautions for 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.

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.

6.6 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.

Labelling:

Add, to all products:

9.	SPECIAL WARNING(S), IF NECESSARY

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.

In case of insufficient space on the label:

9.	SPECIAL WARNING(S), IF NECESSARY

Environmental risks have been identified for this product and special precautions apply. Read the package leaflet before use.

Package leaflet:

Add, to all products:

12. SPECIAL WARNING(S)

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, in particular aquatic organisms and dung fauna.

- 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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

D. For veterinary medicinal products listed in Annex I as solution for injection and administered to sheep containing 10 mg moxidectin per ml or 20 mg moxidectin per ml

Summary of product characteristics

Add, to all products:

4.5 Special precautions for 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.

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- 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.

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:

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	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.

6.6 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.

Labelling:

Add, to all products:

9.	SPECIAL WARNING(S), IF NECESSARY

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.

In case of insufficient space on the label:

9.	SPECIAL WARNING(S), IF NECESSARY

Environmental risks have been identified for this product and special precautions apply. Read the package leaflet before use.

Package leaflet:

Add, to all products:

12. SPECIAL WARNING(S)

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, in particular aquatic organisms and dung fauna.

- 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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

E. For veterinary medicinal products listed in Annex I as oral gel and administered to horses and ponies containing 18.92 mg moxidectin per gram or 19.5 mg moxidectin and 121.7 praziquantel per gram

Summary of product characteristics

Add, to all products:

4.5 Special precautions for 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. In order to reduce the emission of moxidectin to surface water and based on the excretion profile of moxidectin when administered as the oral formulation to horses, treated animals should not have access to watercourses during the first week after treatment.

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 horses with the product, levels of moxidectin that are potentially toxic to dung beetles and flies may be excreted over a period of more than 1 week and may decrease dung fauna abundance.
- Moxidectin is inherently toxic to aquatic organisms including fish. The product should be used only according to the label instructions.

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.

6.6 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.

Labelling:

Add, to all products:

9.	SPECIAL WARNING(S), IF NECESSARY

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. In order to reduce the emission of moxidectin to surface water and based on the excretion profile of moxidectin when administered as the oral formulation to horses, treated animals should not have access to watercourses during the first week after treatment.

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 horses with the product, levels of moxidectin that are potentially toxic to dung beetles and flies may be excreted over a period of more than 1 week and may decrease dung fauna abundance.
- Moxidectin is inherently toxic to aquatic organisms including fish. The product should be used only according to the label instructions.

In case of insufficient space on the label:

9.	SPECIAL WARNING(S), IF NECESSARY

Environmental risks have been identified for this product and special precautions apply. Read the package leaflet before use.

Package leaflet:

Add, to all products:

12. SPECIAL WARNING(S)

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. In order to reduce the emission of moxidectin to surface water and based on the excretion profile of moxidectin when administered as the oral formulation to horses, treated animals should not have access to watercourses during the first week after treatment.

Like other macrocyclic lactones, moxidectin has the potential to adversely affect non-target organisms, in particular aquatic organisms and dung fauna.

- Faeces containing moxidectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of horses with the product, levels of moxidectin that are potentially toxic to dung beetles and flies may be excreted over a period of more than 1 week and may decrease dung fauna abundance.
- Moxidectin is inherently toxic to aquatic organisms including fish. The product should be used only according to the label instructions.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

Annex IV

Conditions of the marketing authorisations

The following conditions should be fulfilled by all marketing authorisation holders:

Conditions	Date
A field study should be conducted to generate data on the fate and behaviour of moxidectin in different environmental matrices under actual conditions of use of veterinary medicinal products administered to pasture animals for the prevention/treatment of parasite infestation. The field study should fulfil the following criteria: • A pour-on solution containing 5 mg moxidectin per ml or a solution for injection containing 100 mg moxidectin per ml in beef cattle on pasture should be used as this represents a realistic worst case emission scenario. • The duration of the study should be three consecutive years in order to consider seasonal and annual variations. • The study should be performed in one or more European geographical regions, representing worst case climatic and epidemiological conditions and adjacent to small water bodies. If the study is conducted in one geographical region, the marketing authorisation holders should justify that this is truly the worst case. • Different target matrices that should be considered for the occurrence of moxidectin such as dung, surface water/suspended particles, sediment and soil. The following findings should be reported: • Concentrations of moxidectin in the different target matrices. • Indication for seasonal variation of the moxidectin concentrations due to different temperature, humidity, soil properties and, if applicable, for regional variation as well. • Evidence of a trend i.e. increasing/decreasing concentrations or plateau.	Within 60 months of Commission Decision for this procedure
Detailed information on the field study design (protocol), including proposals for timelines for the provision of interim reports, should be submitted to the CVMP.	Within 12 months of Commission Decision for this procedure
The final study report should be submitted to the CVMP for assessment.	Within 60 months of Commission Decision for this procedure

The abovementioned data should be provided to the CVMP for assessment not later than 5 years after the Commission Decision on this referral procedure.