

Annex I

List of the names, pharmaceutical forms, strengths of the veterinary medicinal products, animal species, and marketing authorisation holders in the Member States

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Austria	Chevita Tierarzneimittel GmbH Kaplanstrasse 10 4600 Wels Austria	Chevi-Tyl 200 mg/g Arzneimittel-Vormischung zu Herstellung von Fütterungsarzneimitteln für Schweine, Hühner und Puten	Tylosin tartarate	20 g/100 g powder	Premix for medicated feeding stuff	Pigs, chicken, turkey
Austria	Chevita Tierarzneimittel GmbH Kaplanstrasse 10 4600 Wels Austria	Chevi-Tyl 200 mg/g Pulver zum Eingeben für Schweine, Hühner und Puten	Tylosin tartarate	20 g/100 g powder	Powder for oral solution	Pigs, chicken, turkey
Austria	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 1g/g Granulat zum Eingeben über das Trinkwasser für Schweine, Hühner, Puten und Kälber	Tylosin	1 g tylosin (= 1.1 g tylosin tartate) per 1.1 g of granules	Granules for oral solution	Calves, pigs, chicken, turkey
Austria	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g Arzneimittel-Vormischung zur Herstellung von Fütterungsarzneimitteln für Schweine, Masthühner und Junghennen	Tylosin	100 mg tylosin as tylosin phosphate per g (= 100 000 IU)	Premix for medicated feeding stuff	Pigs, broilers, pullets
Austria	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g Arzneimittel-Vormischung zur Herstellung von Fütterungsarzneimitteln für Schweine, Masthühner und Junghennen	Tylosin	250 mg tylosin as tylosin phosphate per g (= 250 000 IU)	Premix for medicated feeding stuff	Pigs, broilers, pullets
Austria	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g Granulat zum Eingeben für Schweine	Tylosin	20 mg tylosin as tylosin phosphate per g (= 20 000 IU)	Granules for oral solution	Pigs
Austria	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Tylan 20 mg/g - Arzneimittel- Vormischung zur Herstellung von Fütterungsarzneimitteln für Schweine	Tylosin phosphate	20 g/kg	Premix for medicated feeding stuff	Pigs

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Austria	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Tylan soluble - 1 g/g Pulver zur Herstellung einer Lösung zum Eingeben für Schweine, Hühner und Truthühner	Tylosin	110 g tylosin tartate per 110 g powder (= 100 g tylosin-activity)	Powder for oral solution	Pigs, chicken, turkeys
Austria	AniMed Service AG Liebochstrasse 9 8143 Dobl Austria	Tylosin-Phosphat "AniMed Service" 100mg/g - Pulver zum Eingeben für Schweine	Tylosin	100 g tylosin (as tylosin phosphate) per 1000 g powder	Powder for oral solution	Pigs
Austria	Vana GmbH Wolfgang Schmälzlgasse 6 1020 Vienna Austria	Vanatyl-Pulver für Tiere	Tylosin	110 g tylosin tartate per 110 g powder (= 100 g tylosin-base)	Powder for oral solution	Pigs, chicken (broiler), turkeys
Austria	AniMed Service AG Liebochstrasse 9 8143 Dobl Austria	Tylosintartrat PUR "AniMed Service" 1g/g – Pulver zum Eingeben für Tiere	Tylosin	1 g tylosin (as tylosin tartate) per 1 g of powder	Powder for oral solution	Cattle (calve) Chickens Pigs Turkeys
Belgium	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g OG	Tylosin phosphate	20 mg/g (20000 IU)	Granules for oral solution	Pigs
Belgium	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g OG	Tylosin phosphate	250 mg/g (250000 IU)	Granules for oral solution	Pigs
Belgium	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100% w/w	Tylosin tartarate	1 g in 1,1 g granules (1,1 g)	Granules for oral solution	Calves Pigs Chicken Turkey
Belgium	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g Premix	Tylosin phosphate	100 mg/g (100000 IU)	Premix for medicated feeding stuff	Pigs Broilers Pullets

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Belgium	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g Premix	Tylosin phosphate	250 mg/g (250000 IU)	Premix for medicated feeding stuff	Pigs Broilers Pullets
Belgium	Eli Lilly Benelux N.V. Elanco Animal Health Markiesstraat 1 1000 Brussel Belgium	Tylan 20 Granules	Tylosin phosphate	20 mg/g (20000 IU)	Granules for oral solution	Pigs Broilers Pullets
Belgium	Eli Lilly Benelux N.V. Elanco Animal Health Markiesstraat 1 1000 Brussel Belgium	Tylan 100 Granules	Tylosin phosphate	100 mg/g (100000 IU)	Granules for oral solution	Pigs Broilers Pullets
Belgium	Eli Lilly Benelux N.V. Elanco Animal Health Markiesstraat 1 1000 Brussel Belgium	Tylan 20 Vet Premix	Tylosin phosphate	20 mg/g (20000 IU)	Premix for medicated feeding stuff	Pigs Broilers Pullets
Belgium	Eli Lilly Benelux N.V. Elanco Animal Health Markiesstraat 1 1000 Brussel Belgium	Tylan 100 Vet Premix	Tylosin phosphate	100 mg/g (100000 IU)	Premix for medicated feeding stuff	Pigs Broilers Pullets
Belgium	Eli Lilly Benelux N.V. Elanco Animal Health Markiesstraat 1 1000 Brussel Belgium	Tylan 250 Vet Premix	Tylosin phosphate	250 mg/g (250000 IU)	Premix for medicated feeding stuff	Pigs Broilers Pullets
Belgium	Eli Lilly Benelux N.V. Elanco Animal Health Markiesstraat 1 1000 Brussel Belgium	Tylan Soluble	Tylosin tartarate	10 ⁸ (100 g)/lagna 10 ⁹ (1000 g)/saccus (1000 mg/g)	Powder for oral solution	Calves Pigs Chicken Turkey

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Belgium	Kela NV (Kela Laboratoria NV) Sint Lenaartseweg 48 2320 Hoogstraten Belgium	Tylosine 75% Kela	Tylosin tartarate	750 mg/g (750000 IU/g)	Powder for oral solution	Pigs Chicken
Bulgaria	Gabrofam OOD 7002 Russe 16 Aleia Vazrajdane str., ap.42 Bulgaria	ТИЛОЗИН 60 % - БГ Водоразтворим прах	Tylosin	Tylosin tartarate 60 mg/g	Powder for oral solution	Hens and pigs
Bulgaria	Biovet JSC 39 Petar Rakov Str 4550 Peshtera Bulgaria	ТИЛОВЕТ 10% гранули за перорално приложение за свине, прасета, пилета, пуйки, телета за угодяване	Tylosin	Tylosin phosphate 100 mg/g	Granules for oral solution	Swine, pigs, chickens, turkeys, calves for fattening
Bulgaria	Biovet JSC 39 Petar Rakov Str 4550 Peshtera Bulgaria	ТИЛОВЕТ 25% премикс за медикаментозен фураж за свине, прасета, пилета, пуйки, телета за угодяване	Tylosin	Tylosin phosphate 250 mg/g	Premix for medicated feeding stuff	Swine, pigs, chickens, turkeys, calves for fattening
Bulgaria	Biovet JSC 39 Petar Rakov Str 4550 Peshtera Bulgaria	ТИЛОВЕТ 10% премикс за медикаментозен фураж за свине, прасета, пилета, пуйки, телета за угодяване	Tylosin	Tylosin phosphate 100 mg/g	Premix for medicated feeding stuff	Swine, pigs, chickens, turkeys, calves for fattening
Bulgaria	Biovet JSC 39 Petar Rakov Str 4550 Peshtera Bulgaria	ТИЛОВЕТ пулвис водоразтворим прах за пилета, пуйки, прасета и телета	Tylosin	Tylosin tartarate 500 mg/g	Powder for oral solution	Chickens, turkeys, pigs and calves
Bulgaria	Biovet JSC 39 Petar Rakov Str 4550 Peshtera Bulgaria	Тиловет Форте водоразтворими гранули за свине	Tylosin	200 mg/g	Granules for oral solution	Swine
Bulgaria	Pharma SIS 4 San Stefano Str. Dobrich Bulgaria	Оратил 100	Tylosin	108.18 g/110 g	Powder for oral solution	Chicken, turkeys and pigs

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Bulgaria	Pharma SIS 4 San Stefano Str. Dobrich Bulgaria	Тилозин 100 премикс	Tylosin	10 g/100 g	Premix for medicated feeding stuff	Swine
Bulgaria	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g Орални гранули за свине	Tylosin	20 mg/g	Granules for oral solution	Swine
Bulgaria	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g премикс за медикаментозен фураж за свине, бройлери и пилета, отглеждани за носачки	Tylosin	100 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets
Bulgaria	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g премикс за медикаментозен фураж за свине, бройлери и пилета, отглеждани за носачки	Tylosin	250 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets
Bulgaria	Pharma Vet 40 Otec Paisii Str. Shumen Bulgaria	Тилофарм водоразтворим прах	Tylosin	40 000 000 IU (50g)	Powder for oral solution	Hens and pigs
Bulgaria	Zavet JSC 5 Kiril i Metodii Str. Zavet Bulgaria	Тилозин 50% водоразтворим прах	Tylosin	500 000 IU/g	Powder for oral solution	Pigs, swine, broilers, turkeys, chicken and turkey breeders
Croatia	Medical Intertrade d.o.o. Dr. Franje Tuđmana 3 10431, Sveta Nedelja Croatia	Tylan Soluble	Tylosin	bottle: 100 g bag: 1000g	Powder for oral solution	Chickens, turkeys, pigs
Croatia	GENERA d.d. Svetonedeljska 2 Kalinovica, 10436 Rakov Potok Croatia	Tilozin tartarat	Tylosin	Powder, 1 bottle: 70 g	Powder for oral solution	Chickens, turkeys, pigs

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Cyprus	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 100% Κοκκία για χορήγηση με το πόσιμο νερό για μόσχους, χοίρους, ορνίθια και ινδόρνιθες	TYLOSIN	1.1 g of granules contains 1g of tylosin (corresponding to 1.1 g of tylosin tartrate)	Granules for oral solution	Calves, pigs, chickens, turkeys
Cyprus	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	TYLAN G 100 PREMIX 100g/kg Πρόμιγμα για φαρμακούχες ζωοτροφές για χοίρους.	Tylosin phosphate	100.0 g/kg	Premix for medicated feeding stuff	Pigs
Cyprus	DOX-AL ITALIA S.p.a. Via Mascagni 6 20884 Sulbiate (MB) Italy	TYLOSINA BMP Powder Tylosin (from tylosin tartrate) 200 g/Kg Φαρμακούχο πρόμιγμα σε κόκκους για χοίρους και κοτόπουλα κρεωπαραγωγής	Tylosin	200.0 g/kg	Premix for medicated feeding stuff	Swine, broilers
Czech Republic	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100% w/w granules for oral administration in drinking water for oral solution for pigs, chicken, turkey and calves	Tylosin	1g Tylosinum (odpovídající 1.1 g Tylosini tartaras)/1,1 g	Granules for oral solution	Calves, pigs, chicken, turkey
Czech Republic	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g oral granules for pigs	Tylosin	Tylosinum (ut Tylosini phosphas) 20 mg v 1 g (odpovídá 20 000 IU)	Granules for oral solution	Pigs
Czech Republic	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 250 mg/g oral granules for pigs	Tylosin	Tylosinum (ut Tylosini phosphas): 250 mg/g (odpovídá 250 000 IU.)	Granules for oral solution	Pigs

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Czech Republic	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	Tylan powder for oral solution	Tylosin	Tylosinum (ut tylosini tartras) 800 I.U./mg	Powder for oral solution	Chicken broilers, breeding pullets and laying hens, production pullets, turkey, pigs, calves
Czech Republic	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	TYLAN 100 mg/g granules for pigs	Tylosin	Tylosinum (ut phosphas) 100 mg aktivita (odpovídá 100 000 IU)/g	Granules for oral solution	Pigs
Czech Republic	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	TYLAN 100 mg/g medicated pre-mix for pigs	Tylosin	Tylosinum (ut phosphas) 100 mg aktivita (odpovídá 100 000 IU)/g	Premix for medicated feeding stuff	Pigs
Denmark	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan Vet.	Tylosin	100 g/kg	Premix for medicated feeding stuff	Pig
Denmark	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan Vet.	Tylosin	2%	Premix for medicated feeding stuff	Pig
Denmark	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan Vet.	Tylosin	No information available	Powder for oral solution	Pig, poultry

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Denmark	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan Vet.	Tylosin	2%	Powder for oral solution	Pig
Denmark	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan Vet.	Tylosin	10%	Powder for oral solution	Pig
Denmark	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin	Tylosin	20 mg/g	Granules for oral solution	Pig
Denmark	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin	Tylosin	250 mg/g	Granules for oral solution	Pig
Denmark	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin	Tylosin	1 g/g	Granules for oral solution	Calf, pig, poultry
Denmark	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin	Tylosin	100 mg/g	Premix for medicated feeding stuff	Poultry, pig
Denmark	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin	Tylosin	250 mg/g	Premix for medicated feeding stuff	Poultry, pig
Denmark	Ceva Animal Health A/S Ladegårdsvej 2 DK-7100 Vejle Denmark	Tylosin "Ceva" Vet	Tylosin	No information available	Powder for oral solution	Poultry, pig

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Denmark	ScanVet Animal Health A/S Kongevejen 66 DK-3480 Fredensborg Denmark	Tylocure	Tylosin	1 g/g	Granules for oral solution	Pig
Estonia	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 500WSP	Tylosin	500 mg/g	Powder for oral solution	Cattle, pigs, chicken, turkey
Estonia	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 1000 mg/g granules for use in drinking water for pigs, chickens, turkeys and calves	Tylosin	1000 mg/g	Granules for oral solution	Cattle, pigs, chicken, turkey
Finland	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan Premix vet 20 mg/g esisekoite lääkerehua varten	Tylosin phosphate	20 mg/g	Premix for medicated feeding stuff	Pig
Finland	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan vet jauhe oraaliliuosta varten	Tylosin tartarate	1 g oral powder contains 1 g tylosin tartrate resp 800mg tylosin	Powder for oral solution	Pig, poultry
France	SOGEVAL 200 AVENUE DE MAYENNE ZONE INDUSTRIELLE DES TOUCHES 53000 LAVAL France	CONCENTRAT V007 TYLAN 100	Tylosin phosphate	20 000 IU/g	Premix for medicated feeding stuff	Pig Poultry
France	VIRBAC 1ere avenue 2065 m L. I. D. 06516 Carros France	AXENTYL	Tylosin tartarate	80 mg/g	Powder for oral solution	Pig

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France	Lilly France S.A.S. 24 bld Vital Bouhot CS 50004 92521 Neuilly sur Seine cedex France	TYLAN 20 PREMIX	Tylosin phosphate	20 000 IU/g	Premix for medicated feeding stuff	Pig Poultry
France	QALIAN 34 RUE JEAN MONNET ZI D'ETRICHE 49500 SEGRE France	COMPOMIX V T	Tylosin tartarate	92 000 IU/g	Powder for oral solution	Pig
France	QALIAN 34 RUE JEAN MONNET ZI D'ETRICHE 49500 SEGRE France	SANTAMIX TYLO 20	Tylosin phosphate	20 000 IU/g	Premix for medicated feeding stuff	Pig Poultry
France	QALIAN 34 RUE JEAN MONNET ZI D'ETRICHE 49500 SEGRE France	TYLORAL	Tylosin tartarate	100 000 000 IU/sachet or jar	Powder for oral solution	Turkey Pig Cow Poultry
France	QALIAN 34 RUE JEAN MONNET ZI D'ETRICHE 49500 SEGRE	TYLOSINE BUVALE NOE	Tylosin tartarate	100 000 000 IU/sachet	Powder for oral solution	Turkey Pig Cow Poultry
France	LABORATOIRES BIOVE 3 RUE DE LORRAINE 62510 ARQUES France	TYLOLIDE	Tylosin tartarate	100 000 000 IU/jar	Powder for oral solution	Turkey Pig Cow Poultry
France	Lilly France S.A.S. 24 bld Vital Bouhot CS 50004 92521 Neuilly sur Seine cedex France	TYLAN SOLUBLE 100 %	Tylosin tartarate	100 000 000 IU/jar	Powder for oral solution	Pig Cow Poultry

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France	SOGEVAL 200 AVENUE DE MAYENNE ZONE INDUSTRIELLE DES TOUCHES 53000 LAVAL France	SOGETYL 100 MUI POUDRE POUR SO LUTION BUVABLE POUR VEAUX PORCINS ET VOLAILLE	Tylosin tartarate	100 000 000 IU/jar	Powder for oral solution	Pig Cow Poultry
France	QALIAN 34 RUE JEAN MONNET ZI D'ETRICHE 49500 SEGRE France	TYLO 20 PM PORC VOLAILLE	Tylosin phosphate	20 000 IU/g	Premix for medicated feeding stuff	Pig Poultry
France	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 20 G/KG PREMELANGE M EDICAMENTEUX VOLAILLE PORCS	Tylosin phosphate	20 000 IU/g	Premix for medicated feeding stuff	Pig Poultry
France	QALIAN 34 RUE JEAN MONNET ZI D'ETRICHE 49500 SEGRE France	TYLOSOL 9,2	Tylosin tartarate	92 000 IU/g	Powder for oral solution	Pig
France	DELTAVIT ZONE D'ACTIVITES DU BOIS DE TEILLAY 35150 JANZE France	PM 21 TYLOSINE 20 PORC- VOLAILL E	Tylosin phosphate	20 000 IU/g	Premix for medicated feeding stuff	Pig Poultry
France	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	TYLMASIN	Tylosin tartarate	100 000 000 IU/jar	Granules for oral solution	Pig Cow Poultry
France	LABORATORIOS MAYMO VIA AUGUSTA 302 08017 BARCELONA Spain	MAYLOSINE	Tylosin tartarate	No information available	Powder for oral solution	Poultry Pig Cattle

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Germany	aniMedica GmbH Im Südfeld 9 D-48308 Senden-Bösensell Germany	Tylosin G 5% AMV	Tylosin phosphate	50 g/ 1 kg	Premix for medicated feeding stuff	Pig
Germany	aniMedica GmbH Im Südfeld 9 D-48308 Senden-Bösensell Germany	Tylenterol	Tylosin phosphate	20 mg/g	Premix for medicated feeding stuff	Pig
Germany	aniMedica GmbH Im Südfeld 9 D-48308 Senden-Bösensell Germany	TP 10 % AMV	Tylosin phosphate	100.000 IU/g	Premix for medicated feeding stuff	Pig chicken
Germany	aniMedica GmbH Im Südfeld 9 D-48308 Senden-Bösensell Germany	Klato lan	Tylosin tartarate	1000 mg/g	Powder for oral solution	Pig chicken
Germany	bela-pharm GmbH & Co. KG Lohner Str. 19 D-49377 Vechta Germany	Tylosintartrat 100% Kompaktat	Tylosin tartarate	1000 mg/g	Granules for oral solution	Pig chicken
Germany	bela-pharm GmbH & Co. KG Lohner Str. 19 D-49377 Vechta Germany	Tylo-Suscit 100% Kompaktat	Tylosin tartarate	1000 mg/g	Granules for oral solution	Pig chicken turkey
Germany	bela-pharm GmbH & Co. KG Lohner Str. 19 D-49377 Vechta Germany	Tylo-Suscit 25	Tylosin tartarate	250 mg/g	Powder for oral solution	Pig chicken
Germany	bioptivet Tierarzneimittel GmbH & Co. Im Landwehrwinkel 22 D-59073 Hamm Germany	Tylogran WSP, 1000 mg/g	Tylosin tartarate	1000 mg/g	Granules for oral solution	Pig chicken

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Germany	Dopharma Research B.V. Zalmweg 24 NL-4941 VX Raamsdonksveer The Netherlands	TP 25 % Pulver	Tylosin phosphate	250 mg/g	Powder for oral solution	Pig
Germany	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100% w/w Granulat zum Eingeben über das Trinkwasser für Schweine, Hühner, Puten und Kälber	Tylosin tartarate	1,0 g/ 1,1 g	Granules for oral solution	Cattle (calf) pig chicken turkey
Germany	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g Granulat zum Eingeben für Schweine	Tylosin	250 mg/g	Granules for oral solution	Pig
Germany	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g Granulat zum Eingeben für Schweine	Tylosin	20 mg/g	Granules for oral solution	Pig
Germany	KLAT-Chemie GmbH Visbeker Str. 12 D-26197 Ahlhorn Germany	Klato lan feed	Tylosin phosphate	1000 mg/g	Powder for oral solution	Pig chicken
Germany	Kon-Pharma GmbH Senator-Bauer-Str. 34 D-30625 Hannover Germany	Tylosintartrat 100%	Tylosin tartarate	1 g/g	Powder for oral solution	Pig chicken
Germany	Lilly Deutschland GmbH Abt. Elanco Animal Health Werner-Reimers-Straße 2-4 D-61352 Bad Homburg Germany	Tylan Mix 2%	Tylosin phosphate	20 g/kg	Premix for medicated feeding stuff	Pig
Germany	Lilly Deutschland GmbH Abt. Elanco Animal Health Werner-Reimers-Straße 2-4 D-61352 Bad Homburg Germany	Tylan soluble	Tylosin tartarate	100 g/110 g	Powder for oral solution	Cattle(calf) pig chicken turkey

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Germany	Lilly Deutschland GmbH Abt. Elanco Animal Health Werner-Reimers-Straße 2-4 D-61352 Bad Homburg Germany	Tylan G 25%	Tylosin phosphate	250 mg/g	Powder for oral solution	Pig
Germany	bela-pharm GmbH & Co. KG Lohner Str. 19 D-49377 Vechta Germany	Tylo-Suscit 100% Kompaktat	Tylosin tartarate	1 g/g	Granules for oral solution	Pig chicken turkey
Greece	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 2%	Tylosin	20 mg/g	Granules for oral solution	Pigs
Greece	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 100%	Tylosin	1 g	Granules for oral solution	Calves, pigs, chickens, turkeys
Greece	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 10% premix	Tylosin	100 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets
Greece	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMACIN 25% premix	Tylosin	250 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets.
Hungary	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 100 mg/g gyógypremix sertések, broilercsirkék és jércék számára A.U.V.	Tylosin phosphate	100 mg/g	Premix for medicated feeding stuff	Pigs and chickens
Hungary	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 % granulátum ivóvízbe keveréshez sertés, házityúk, pulyka és borjú számára A.U.V.	Tylosin tartarate	100%	Granules for oral solution	Pigs, chickens, turkeys and calves

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Hungary	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g granulátum sertések számára A.U.V.	Tylosin phosphate	20 mg/g	Granules for oral solution	Pigs
Hungary	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 250 mg/g gyógyszermix sertések, broilercsirkék és jércék számára A.U.V.	Tylosin phosphate	250 mg/g	Premix for medicated feeding stuff	Pigs and chickens
Hungary	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	Tylan G 100 gyógyszermix A.U.V.	Tylosin phosphate	100 g/kg	Premix for medicated feeding stuff	Pigs and chickens
Hungary	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	Tylan vízdékony por A.U.V.	Tylosin tartarate	100%	Powder for oral solution	Pigs, chickens, turkeys and calves
Hungary	Kela NV (Kela Laboratoria NV) Sint Lenaartseweg 48 2320 Hoogstraten Belgium	TYLOSIN 75% Kela oral por A.U.V.	Tylosin tartarate	750 mg/g	Powder for oral solution	Pigs and chickens
Ireland	Eli Lilly & Company Ltd Elanco Animal Health Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan G20 Premix for medicated feedingstuff	Tylosin	20 g/kg	Premix for medicated feeding stuff	Pigs
Ireland	Eli Lilly & Company Ltd Elanco Animal Health Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan G100 Premix	Tylosin	100 g/kg	Premix for medicated feeding stuff	Pigs

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Ireland	Eli Lilly & Company Ltd Elanco Animal Health Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan G250 Premix for medicated feedingstuff	Tylosin	250 g/kg	Premix for medicated feeding stuff	Pigs, broilers and pullets
Ireland	Eli Lilly & Company Ltd Elanco Animal Health Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan G50 Premix for medicated feedingstuff	Tylosin phosphate	50 g/kg	Premix for medicated feeding stuff	Pigs
Ireland	Eli Lilly & Company Ltd Elanco Animal Health Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan Soluble Powder for Oral Solution	Tylosin tartarate	100 g	Powder for oral solution	Calves, pigs and poultry
Ireland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g Oral Granules for pigs	Tylosin	20 mg/g	Granules for oral solution	Pigs
Ireland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g Premix for medicated feeding stuff for pigs, broilers and pullets	Tylosin	100 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets
Ireland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g Premix for medicated feeding stuff for pigs, broilers and pullets	Tylosin	250 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets
Ireland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100% W/W Granules for use in Drinking Water for pigs, chickens, turkeys and calves	Tylosin tartarate	100% w/w	Granules for oral solution	Calves, pigs, chickens, turkeys

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Italy	Vetoquinol Italia Via Piana, 265 47032 Bertinoro (FC) Italy	ASCOTYL 200 MP	Tylosin	200 mg/g	Premix for medicated feeding stuff	Pigs, chickens
Italy	LABORATORIO VACCINOGENO PAGNINI SNC Via A. Diaz 147/149 Portici (NA) Italy	BRONCOTYL 100	Tylosin	100 g/kg	Premix for medicated feeding stuff	Cattle, pigs, chickens
Italy	Eli Lilly Italia S.p.A. Via A. Gramsci, 731-733 50019 Sesto Fiorentino (IT) Italy	NEO TYLAN G250 PREMIX	Tylosin phosphate	250 mg/g	Premix for medicated feeding stuff	Chickens, Pigs
Italy	Sintofarm Via P. Togliatti, 5 Guastalla (RE) Italy	PHARMASIN 100	Tylosin	100 g/g	Granules for oral solution	Pigs, Chickens, Turkeys and Calves
Italy	DOX-AL ITALIA S.p.a. Via Mascagni 6 20884 Sulbiate (MB) Italy	PURTYL	Tylosin	1 g/g	Powder for oral solution	Cattle, chickens, turkeys and pigs
Italy	Medilabor Via Cuneo, 17 Cuneo Italy	Tilosina 10%	Tylosin tartarate	100 g/kg	Powder for oral solution	Calves, pigs, chickens
Italy	Filozoo Srl V. del Commercio 28/30 41012 Carpi (MO) Italy	Tilosina 20% Filozoo	Tylosin tartarate	200 g/kg	Powder for oral solution	Calves, chickens, pigs
Italy	Chemifarma S.p.A. Via Don Eugenio Servadei 16 47122 Forlì, Forlì-Cesena Italy	Tilosina 20% Chemifarma	Tylosin tartarate	200 mg/g	Oral solution	Calves, chickens, pigs

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Italy	Neofarma Via Emilia Km.18 1854 - 47020 Longiano (FC) Italy	Tilosina 20% liquida Neofarma	Tylosin tartarate	200 mg/g	Oral solution	Calves, chickens, pigs
Italy	TREI Via Affarosa, 4 42010 Rio Saliceto (RE) Italy	Tilosina 20% liquida TreI	Tylosin tartarate	200 mg/g	Oral solution	Calves, chickens, pigs
Italy	Chemifarma S.p.A. Via Don Eugenio Servadei 16 47122 Forlì, Forlì-Cesena Italy	Tilosina 20% liquida Chemifarma	Tylosin tartarate	200 mg/g	Oral solution	Calves, chickens, pigs
Italy	LABORATORIO VACCINOGENO PAGNINI SNC Via A. Diaz 147/149 Portici (NA) Italy	Tilosina 20% Pagnini	Tylosin tartarate	200 mg/g	Powder for oral solution	Calves, Pigs, Chickens-Broilers (not producing eggs for human consumption)
Italy	TREI Via Affarosa, 4 42010 Rio Saliceto (RE) Italy	Tilosina 20% TreI	Tylosin tartarate	200 g/kg	Powder for oral solution	Calves, Pigs, Chickens-Broilers (not producing eggs for human consumption)
Italy	Vetoquinol Italia Via Piana, 265 47032 Bertinoro (FC) Italy	Tilosina 20% Vetoquinol	Tylosin tartarate	200 mg/g	Powder for oral solution	Pigs, chickens
Italy	Filozoo Srl V. del Commercio 28/30 41012 Carpi (MO) Italy	Tilosina 200 premix	Tylosin	200 g/kg	Premix for medicated feeding stuff	Pigs, chickens

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Italy	Ceva Salute Animale S.p.A. Viale Colleoni, 15 20864 Agrate Brianza (MB) Italy	Tilsol 200 liquido	Tylosin	200 g/kg	Powder for oral solution	Calves, Pigs, Chickens-Broilers, Turkeys (not producing eggs for human consumption)
Italy	Ceva Salute Animale S.p.A. Viale Colleoni, 15 20864 Agrate Brianza (MB) Italy	Tilsol 200 solubile	Tylosin	200 g/kg	Powder for oral solution	Calves, Pigs, Chickens-Broilers (not producing eggs for human consumption)
Italy	Eli Lilly Italia S.p.A. Via A. Gramsci, 731-733 50019 Sesto Fiorentino (IT) Italy	Tylan solubile	Tylosin tartarate	100 g/g	Powder for oral solution	Calves, Pigs, Hens-Broilers, Turkeys
Italy	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin	Tylosin phosphate	250 mg/g	Premix for medicated feeding stuff	Pigs and chickens (not producing eggs for human consumption)
Italy	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin 20mg/g granulato per uso orale per suini	Tylosin phosphate	20 mg/g	Granules for oral solution	Pigs
Italy	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Tylmasin 250mg/g granulato per uso orale per suini	Tylosin phosphate	250 mg/g	Granules for oral solution	Pigs

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Italy	Medilabor Via Cuneo, 17 12030 Cavallermaggiore (CN) Italy	Tylomed 100	Tylosin phosphate	100 g/kg	Premix for medicated feeding stuff	Pigs and chickens (not producing eggs for human consumption)
Italy	DOX-AL ITALIA S.p.a. Via Mascagni 6 20884 Sulbiate (MB) Italy	Tyloplus 200	Tylosin	200 g/kg	Premix for medicated feeding stuff	Pigs and chickens (not producing eggs for human consumption)
Italy	Chemifarma S.p.A. Via Don Eugenio Servadei 16 47122 Forlì, Forlì-Cesena Italy	Tylosin 200 premix	Tylosin	200 g/kg	Premix for medicated feeding stuff	Pigs and chickens (not producing eggs for human consumption)
Italy	TREI Via Affarosa, 4 42010 Rio Saliceto (RE) Italy	Tylox 100 premix	Tylosin phosphate	100 g/kg	Premix for medicated feeding stuff	Pigs and chickens (not producing eggs for human consumption)
Latvia	Magnum Veterinārija SIA Ulbrokas iela 23 Rīga, LV-1021 Latvia	Tylokel 75 MV 750 mg/g šķīdināmais pulveris iekšķīgi lietojama šķīduma pagatavošanai cūkām un mājputniem	Tylosin tartarate	750 mg/g	Powder for oral solution	Pigs and poultry
Latvia	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 500 WSP 500 mg/g ūdenī šķīstošs pulveris iekšķīgai lietošanai cūkām, liellopiem, vistām un tītariem	Tylosin tartarate	500 mg/g	Powder for oral solution	Cattle, pigs, chickens, turkey

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Latvia	Vet Line SIA M. Rāmavas 2 Valdlauči, Ķekavas pag.,LV-1076 Latvia	Macrolan WS pulveris iekšķīgai lietošanai teļiem, kazām, aitām, cūkām un mājputniem	Tylosin tartarate	1000 mg/g	Powder for oral solution	Cattle, goats, sheep, pigs, poultry
Lithuania	bela-pharm GmbH & Co. KG Lohner Str. 19 D-49377 Vechta Germany	TYLO-SUSCIT 100 % Kompaktat, geriamieji milteliai	Tylosin tartarate	1000 mg/g	Powder for oral solution	Pigs and chicken
Lithuania	Chemifarma S.p.A. Via Don Eugenio Servadei 16 47122 Forlì, Forlì-Cesena Italy	TILOSINA 20 % CHEMIFARMA, geriamieji milteliai	Tylosin tartarate	200 mg/g	Powder for oral solution	Non ruminating calves, pigs, poultry
Lithuania	Dopharma Research B.V. Zalmweg 24, 4941 VX Raamsdonksveer, the Netherlands	Tylogran WSP, granulės geriamajam tirpalui	Tylosin tartarate	1000 mg/g	Granules for oral solution	Calves, swine, chicken, turkeys
Lithuania	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 500 mg/g vandenyje tirpūs milteliai kiaulėms, veršeliams, vištoms ir kalakutams	Tylosin tartarate	500 mg/g	Powder for oral solution	Swine, calf, chicken and turkey
Lithuania	DOX-AL ITALIA S.p.a. Via Mascagni 6 20884 Sulbiate (MB) Italy	TILOSINA 20 % LIQUIDA, geriamasis tirpalas	Tylosin	200 g/kg	Oral solution	Calves, swine and broilers.
Lithuania	Franvet, Zone Industrielle d'Etriché, 49500 Segré, France	TYLORAL, geriamieji milteliai	Tylosin tartarate	100 000 000 IU/sachet	Powder for oral solution	Poultry, swine, calves
Lithuania	DOX-AL ITALIA S.p.a. Via Mascagni 6 20884 Sulbiate (MB) Italy	PURTYL, geriamieji milteliai	Tylosin tartarate	1000 mg/g	Powder for oral solution	Chicken, turkeys, swine and calves

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Lithuania	Kela NV (Kela Laboratoria NV) Sint Lenaartseweg 48 2320 Hoogstraten Belgium	TYLOSIN 75 %, geriamieji milteliai	Tylosin tartarate	750 mg/g	Powder for oral solution	Swine, chicken
Malta	Industrial Veterinaria, S.A – INVESA Esmeralda 19 E-08950 Esplugues de Llobregat, Barcelona Spain	TILOSINA 100 GANADEXIL	Tylosin	100 mg/g	Powder for oral solution	Poultry, turkey, swine
The Netherlands	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 20 mg/g Orale Granules voor varkens	Tylosin phosphate	20 mg/g	Granules for oral solution	Pig
The Netherlands	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 100 mg/g premix voor gemedicineerd voer voor varkens, slachtkuikens en opfokleghennen	Tylosin phosphate	100 mg/g	Premix for medicated feeding stuff	Pig, chicken (broilers, future layers/breeders)
The Netherlands	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100% W/W Water Oplosbare Granules	Tylosin tartarate	1 g/1,1 g	Granules for oral solution	Cattle (calves), pig, chicken, turkey
The Netherlands	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g Orale Granules voor varkens	Tylosin phosphate	250 mg/g	Granules for oral solution	Pig
The Netherlands	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 250 mg/g premix voor gemedicineerd voer voor varkens, slachtkuikens en opfokleghennen	Tylosin phosphate	250 mg/g	Premix for medicated feeding stuff	Pig, chicken (broilers, future layers/breeders)

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
The Netherlands	Eli Lilly Nederland B.V. Elanco Animal Health Grootslag 1-5 3991 RA Houten The Netherlands	TYLAN G250 PREMIX 25%	Tylosin phosphate	250 g/kg	Premix for medicated feeding stuff	Pig, chicken (broilers, future layers/breeders)
The Netherlands	Eli Lilly Nederland B.V. Elanco Animal Health Grootslag 1-5 3991 RA Houten The Netherlands	TYLAN W.O., poeder voor oraal gebruik bij kippen, kalkoenen, varkens en kalveren	Tylosin tartarate	Unadulterated	Powder for oral solution	Cattle (calves), pig, chicken, turkey
The Netherlands	Eli Lilly Nederland B.V. Elanco Animal Health Grootslag 1-5 3991 RA Houten The Netherlands	TYLAN 100 PREMIX 10%	Tylosin phosphate	100 g/kg	Premix for medicated feeding stuff	Pig, chicken (broilers, future layers/breeders)
The Netherlands	Eli Lilly Nederland B.V. Elanco Animal Health Grootslag 1-5 3991 RA Houten The Netherlands	TYLAN 2% TOPDRESSING	Tylosin phosphate	20 g/kg	Powder for oral solution	Pig
The Netherlands	Eli Lilly Nederland B.V. Elanco Animal Health Grootslag 1-5 3991 RA Houten The Netherlands	TYLAN 20 PREMIX 2%	Tylosin phosphate	20 g/kg	Premix for medicated feeding stuff	Pig, chicken (broilers, future layers/breeders)
The Netherlands	Dopharma Reasearch B.V. Zalmweg 24 4941 VX Raamsdonkveer The Netherlands	TYLOGRAN WSP	Tylosin tartarate	Unadulterated	Powder for oral solution	Cattle (calves), pig, chicken, turkey
The Netherlands	Eli Lilly Nederland B.V. Elanco Animal Health Grootslag 1-5 3991 RA Houten The Netherlands	Tylosinetartraat 100%	Tylosin tartarate	Unadulterated	Powder for oral solution	Cattle (calves), pig, chicken (broilers, future layers/breeders), turkey

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Poland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g Premiks do sporządzania paszy leczniczej dla świń, brojlerów i młodych kur rzeźnych	Tylosin phosphate	100 mg/g	Premix for medicated feeding stuff	Pigs, Broilers and Pullets
Poland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g granulát doustny dla świń	Tylosin phosphate	20 mg/g	Granules for oral solution	Pigs
Poland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g premiks do sporządzania paszy leczniczej dla świń, brojlerów i młodych kur rzeźnych	Tylosin phosphate	250 mg/g	Premix for medicated feeding stuff	Pigs, Broilers and Pullets
Poland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g granulát doustny dla świń	Tylosin phosphate	250 mg/g	Granules for oral solution	Pigs
Poland	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 1 g/g granulát do podania w wodzie do picia dla świń, cieląt, kur i indyków	Tylosin tartarate	1 g/g	Granules for oral solution	Calves, pigs, chickens, turkeys
Poland	Ceva Salute Animale S.p.A. Viale Colleoni, 15 20864 Agrate Brianza (MB) Italy	Tilsol 200, 200 g/1000g	Tylosin	200 g/1000 g	Powder for oral solution	Chicken, pig
Poland	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	Tylan Soluble Powder	Tylosin	1000 g/kg	Powder for oral solution	Chicken, turkey, pig, cattle

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Poland	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	Tylan G 100 Premix	Tylosin	100 mg/kg	Premix for medicated feeding stuff	Pigs
Poland	P.F.H.U. "Veta" Mariusz Hołownia Kownaty 74 18-421 Kownaty Poland	Tylo-Kel 75 proszek do sporządzania roztworu doustnego dla kur i świń	Tylosin tartarate	750 mg/g	Powder for oral solution	Chicken, pig
Poland	Przedsiębiorstwo Farmaceutyczne Okoniewscy "VETOS FARMA" Sp. z o.o. ul. Dzierżoniowska 21 58-260 Bielawa Poland	FARMATYL, tylozyny winian 1000 g/kg proszek do sporządzania roztworu doustnego dla kur, indyków i świń	Tylosin tartarate	1000 g/kg	Powder for oral solution	Turkey, hen, pig
Poland	Vetoquinol Biowet Sp. z o.o. ul. Kosynierów Gdyńskich 13-14 66-400 Gorzów Wielkopolski Poland	Tylbian, 110 mg/g	Tylosin tartarate	110 mg/g	Granules for oral solution	Hen turkey pig cattle
Portugal	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 g/g Grânulos para administração na água de bebida para suínos, galinhas e frangos, perús e vitelos.	Tylosin	1.1 g of granules contains 1 g of tylosin	Granules for oral solution	Calves, pigs, chickens, turkeys
Portugal	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g Pré-mistura para alimento medicamentoso para suínos, galinhas e frangos de engorda	Tylosin	250 mg per g. (equivalent to 250 000 IU)	Premix for medicated feeding stuff	Pigs, broilers and pullets
Portugal	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g Pré-mistura medicamentosa para alimento medicamentoso para suínos, frangos de engorda e galinhas	Tylosin	100 mg per g. (equivalent to 100 000 IU)	Premix for medicated feeding stuff	Pigs, broilers and pullets

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Portugal	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 20 mg/g Grânulos Oraís para suínos	Tylosin	20 mg per g (equivalent to 20 000 IU)	Granules for oral solution	Pigs
Portugal	REPRESENTAGRO – REPRESENTAÇÕES LDA Estrada da Lapa 1 2665-507 Venda do Pinheiro Portugal	ORATIL 100 P, pó para solução oral para suínos, frangos e perus	Tylosin	1000 mg	Powder for oral solution	Pigs, broilers, turkeys
Portugal	PRODIVET, Comércio de Produtos Químicos, Farmacêuticos e Cosméticos, SA Av. Infante D. Henrique nº 333-H 3º piso Esc. 41 1800-282 Lisboa Portugal	PRODITYL, Pó para solução oral para administração na água de bebida para suínos, frangos e perus	Tylosin	1,1 g	Powder for oral solution	Pigs, broilers, turkeys
Portugal	Ceva Saúde Animal Produtos Farmacêuticos e Imunológicos, Lda. Rua Doutor António Loureiro Borges, 9/9A - 9ºA Miraflores, 1495-131 Algés Portugal	TILPLUS 100 PÓ para solução oral para suínos, frangos e perus	Tylosin	100 g	Powder for oral solution	Pigs, broilers, turkeys
Portugal	Lilly Portugal - Produtos Farmaceuticos, Lda. Torre Occidente Rua Galileu Galilei, n.º 2 Piso 7 fração A/D, 1500-392 Lisboa Portugal	Tylan 100 g/Kg Pré mistura medicamentosa para alimento medicamentoso para suínos e frangos de carne, reprodutoras e poedeiras	Tylosin	100 g/kg	Premix for medicated feeding stuff	Pigs, broilers, chickens

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Portugal	Lilly Portugal - Produtos Farmaceuticos, Lda. Torre Occidente Rua Galileu Galilei, n.º 2 Piso 7 fração A/D, 1500-392 Lisboa Portugal	Tylan 20 g/Kg Pré mistura medicamentosa para alimento medicamentoso para suínos e frangos de carne, reprodutoras e poedeiras	TYLOSIN	20 g/kg	Premix for medicated feeding stuff	Pigs, broilers, chickens
Portugal	Lilly Portugal - Produtos Farmaceuticos, Lda. Torre Occidente Rua Galileu Galilei, n.º 2 Piso 7 fração A/D, 1500-392 Lisboa Portugal	Tylan 250 g/Kg Pré mistura medicamentosa para alimento medicamentoso para Suínos e frangos de carne	TYLOSIN	250 g/kg	Premix for medicated feeding stuff	Pigs, broilers, chickens
Portugal	Lilly Portugal - Produtos Farmaceuticos, Lda. Torre Occidente Rua Galileu Galilei, n.º 2 Piso 7 fração A/D, 1500-392 Lisboa Portugal	TYLAN PÓ SOLÚVEL	TYLOSIN	100 g per bottle	Powder for oral solution	Pigs, broilers, turkeys
Portugal	ZOOPAN Produtos Pecuários S.A. Rua da Liberdade, nº 77 2050-023 Aveiras de Baixo Portugal	TYLOSIN 750 mg/g Pó oral para administração na água de bebida para suínos e frangos	TYLOSIN	750 mg/g	Powder for oral solution	Pigs, broilers
Romania	S.C. PASTEUR -FILIALA FILIPESTI Str. Principala, nr. 944 Filipestii de Padure, Jud. Prahova Romania	Tilozina 100	Tylosin phosphate	10 g/100 g	Premix for medicated feeding stuff	Poultry, pigs

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Romania	S.C. PASTEUR -FILIALA FILIPESTI Str. Principala, nr. 944 Filipestii de Padure, Jud. Prahova Romania	Tilozina	Tylosin tartarate	0,58 g/g	Powder for oral solution	Cattle, pigs, poultry
Romania	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g	Tylosin phosphate	250 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets
Romania	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g	Tylosin phosphate	100 mg/g	Premix for medicated feeding stuff	Pigs, broilers and pullets
Romania	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g	Tylosin phosphate	20 mg/g	Granules for oral solution	Pigs
Romania	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100%	Tylosin tartarate	1 g/g	Granules for oral solution	Calves, pigs, poultry
Romania	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	Tylan G 100g/kg	Tylosin phosphate	100 g/kg	Premix for medicated feeding stuff	Pigs
Romania	Crida Pharm SRL str. Intrarea Vagonetului nr.2, bl.101, ap.47, parter, sector 6 Bucharest Romania	Tylosin 60%	Tylosin tartarate	60 g/100 g	Powder for oral solution	Pigs, broilers

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Romania	SC Delos Impex 96 SRL Str Horia, Closca si Crisan, Otopeni judetul Ilfov Romania	Tilodem 50	Tylosin tartarate	500 mg/g	Powder for oral solution	Pigs, poultry (broilers, breeding broilers, laying hens, replacement pullets)
Romania	SC Delos Impex 96 SRL Str Horia, Closca si Crisan, Otopeni judetul Ilfov Romania	Tilosin 10%	Tylosin tartarate	100 mg/g	Powder for oral solution	Pigs, poultry
Romania	Chemifarma S.p.A. Via Don Eugenio Servadei 16 47122 Forli, Forli-Cesena Italy	Tilosina 20% Chemifarma	Tylosin tartarate	20 g/100 g	Powder for oral solution	Cattle, pigs, poultry (broilers, turkeys)
Romania	Anupco LTd. Crockatt Road Lady Lane Industrial Estate, Hadleigh Ipswich, Suffolk, IP7 6RD United Kingdom	Tylosin 75	Tylosin tartarate	825 mg/g	Powder for oral solution	Pigs, poultry (chicken, turkey)
Romania	Kela NV (Kela Laboratoria NV) Sint Lenaartseweg 48 2320 Hoogstraten Belgium	Tylosin 75% Kela	Tylosin tartarate	750 mg/g	Powder for oral solution	Pigs, poultry
Slovakia	Pharmagal spol. s.r.o. Murgašova 5 949 01 Nitra Slovakia	RESETYL prášok na perorálny roztok	Tylosin tartarate	1000 g/1100 g	Powder for oral solution	Chickens (broilers, pullets, laying hens), turkeys, pigs, calves

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Slovakia	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	TYLAN vodorozpustný prášok	Tylosin tartarate	1000 g/1100 g	Powder for oral solution	Chickens (broilers, pullets, laying hens), turkeys, pigs, calves
Slovakia	Eli Lilly Regional Operations GmbH Elanco Animal Health Kölblgasse 8-10 1030 Vienna Austria	TYLAN 100 mg/g premix	Tylosin phosphate	100 mg/g	Premix for medicated feeding stuff	Pigs
Slovenia	IRIS Mednarodna trgovina d.o.o., Cesta v Gorice 8 1000 Ljubljana Slovenia	TYLAN SOLUBLE prašek za peroralno raztopino za prašiče, kokoši in purane	Tylosin	100 g	Powder for oral solution	Pigs, chicken, turkey
Spain	Elanco Valquímica, S.A. Avda. de la Industria, nº 30 Polígono Industrial de Alcobendas 28108 Alcobendas (Madrid) Spain	TRELACON G 250 PREMEZCLA	Tylosin	250 mg/g	Premix for medicated feeding stuff	Pigs, poultry
Spain	Elanco Valquímica, S.A. Avda. de la Industria, nº 30 Polígono Industrial de Alcobendas 28108 Alcobendas (Madrid) Spain	TRELACON G 50 PREMEZCLA	Tylosin	50 mg/g	Premix for medicated feeding stuff	Pigs, poultry
Spain	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 100 MG/G PREMEZCLA MEDICAMENTOSA PARA PORCINO POLLOS DE ENGORDE	Tylosin	100 mg/g	Premix for medicated feeding stuff	Pigs, broilers, pullets

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Spain	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 250 MG/G PREMEZCLA MEDICAMENTOSA PARA PORCINO POLLOS DE ENGORDE	Tylosin phosphate	250 mg/g	Premix for medicated feeding stuff	Pigs, broilers, pullets
Spain	S.P. VETERINARIA, S.A. CTRA. REUS-VINYOLS, KM.4,1. RIUDOMS (Tarragona) Spain	HIDROTIL POLVO ORAL	Tylosin tartarate	100 g/100 g	Powder for oral solution	Broilers, layer hens and future layer pullets turkeys, pigs and cattle (claves)
Spain	Elanco Valquímica, S.A. Avda. de la Industria, nº 30 Polígono Industrial de Alcobendas 28108 Alcobendas (Madrid) Spain	TRELACON G 20 G/KG PREMEZCLA MEDICAMENTOSA	Tylosin phosphate	20 mg/g	Premix for medicated feeding stuff	Pigs, broilers and replacement pullets
Spain	Elanco Valquímica, S.A. Avda. de la Industria, nº 30 Polígono Industrial de Alcobendas 28108 Alcobendas (Madrid) Spain	TRELACON G 100 G/KG PREMEZCLA MEDICAMENTOSA	Tylosin phosphate	100 mg/g	Premix for medicated feeding stuff	Pigs, broilers and replacement pullets
Spain	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 1G/G GRANULADO PARA ADMINISTRACIÓN EN AGUA DE BEBIDA	Tylosin tartarate	1 g/g	Granules for oral solution	Pigs, calves, chickens, turkeys
Spain	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	PHARMASIN 20 MG/G GRANULADO ORAL PARA PORCINO	Tylosin phosphate	20 mg/g	Granules for oral solution	Pigs

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Spain	Elanco Valquímica, S.A. Avda. de la Industria, nº 30 Polígono Industrial de Alcobendas 28108 Alcobendas (Madrid) Spain	TAILAN	Tylosin	1 g/g	Powder for oral solution	Pigs, poultry (broilers, pullets, layers and turkeys), bovine (pre-ruminants calves).
Spain	S.P. VETERINARIA, S.A. Ctra. Reus-Vinyols, km.4,1. Riudoms (Tarragona) Spain	ORATIL - 100	Tylosin tartarate	1 g/g	Powder for oral solution	Pigs, chickens, turkeys, calves
Spain	INDUSTRIAL VETERINARIA, S.A. Esmeralda 19. 08950 Esplugues de Llobregat (Barcelona) Spain	TILOSINA 100 GANADEXIL	Tylosin tartarate	1 g/g	Powder for oral solution	Pigs, chickens, turkeys
Spain	MEVET, S. A.U. Polígono Industrial El Segre parcela 409-410. 25191 Lérida Spain	TILOVALL PREMEZCLA	Tylosin phosphate	20 mg/g	Premix for medicated feeding stuff	Pigs, poultry and cattle
Spain	LABORATORIOS CALIER, S.A. BARCELONÉS, 26. 08520 Les Franqueses del Valles (Barcelona) Spain	GANAMIX TILOSINA 10% PREMEZCLA	Tylosin phosphate	10 mg/g	Premix for medicated feeding stuff	Pigs, poultry and cattle
Spain	LABORATORIOS HIPRA, S.A. Avda. La Selva, 135. 17170 Amer (Girona) Spain	HIPRAMIX-TIL	Tylosin phosphate	20 mg/g	Premix for medicated feeding stuff	Pigs, poultry and cattle
Spain	ANDRÉS PINTALUBA, S.A. Pol. Industrial Agro-Reus c/ Prudenci Bertrana 5. 43206 Reus (Tarragona) Spain	APSAMIX TILOSINA 10%	Tylosin phosphate	10 mg/g	Premix for medicated feeding stuff	Pigs, poultry and cattle

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
Spain	MEVET, S. A.U. Polígono Industrial El Segre parcela 409-410. 25191 Lérida Spain	TILOVALL POLVO	Tylosin tartarate	1 g/g	Powder for oral solution	Porcine, chickens, calves
Spain	SUPER ´S DIANA, S.L. Ctra. C-17, km 17. 08150 Parets del Valles (Barcelona) Spain	TILOSAN	Tylosin phosphate	20 mg/g	Premix for medicated feeding stuff	Pigs
Sweden	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan vet.	Tylosin	0.83	Powder for oral solution	Pigs and domestic birds
Sweden	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan vet.	Tylosin	0.02	Premix for medicated feeding stuff	Pigs
Sweden	Elanco Animal Health A/S Eli Lilly Danmark A/S Lyskaer 3E, 2 tv. 2730 HERLEV Denmark	Tylan vet.	Tylosin	0.1	Premix for medicated feeding stuff	Pigs
United Kingdom	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100 mg/g Premix for Medicated Feeding Stuff for Pigs, Broilers and Pullets	Tylosin	100 mg/g	Premix for medicated feeding stuff	Pigs Poultry
United Kingdom	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 100% w/w Granules for Use in Drinking Water for Pigs, Chickens, Turkeys and Calves	Tylosin	100% w/w	Granules for oral solution	Cattle Chickens Pigs Turkey

Member State EU/EEA	Applicant/Marketing authorisation holder	Product name	INN	Strength	Pharmaceutical form	Animal species
United Kingdom	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 20 mg/g Oral Granules for Pigs	Tylosin	20 mg/mg	Premix for medicated feeding stuff	Pigs
United Kingdom	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp Belgium	Pharmasin 250 mg/g Premix for Medicated Feeding Stuff for Pigs, Broilers and Pullets	Tylosin	250 mg/g	Premix for medicated feeding stuff	Pigs Poultry
United Kingdom	Eli Lilly & Company Ltd Elanco Animal Health Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan G20 Premix for Medicated Feedingstuff	Tylosin	2.00 % w/w	Premix for medicated feeding stuff	Pigs
United Kingdom	Eli Lilly & Company Ltd Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan G250 Premix for Medicated Feedingstuff	Tylosin	25 % w/w	Premix for medicated feeding stuff	Chickens Pigs
United Kingdom	Eli Lilly & Company Ltd Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan G50 Premix for Medicated Feedingstuff	Tylosin	5.00 % w/w	Premix for medicated feeding stuff	Pigs
United Kingdom	Eli Lilly & Company Ltd Lilly House Priestley Road Basingstoke, RG24 9NL United Kingdom	Tylan Soluble Powder for Oral Solution	Tylosin	10 % w/w	Powder for oral solution	Cattle Chickens Pigs Turkeys

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 tylosin to be administered orally via feed or the drinking water to pigs (see Annex I)

1. Introduction

Tylosin is a macrolide antibiotic which is produced by *Streptomyces fradiae*. It is active mostly against Gram-positive bacteria and mycoplasmas. It is ineffective against *Enterobacteriaceae*. Tylosin and its phosphate and tartrate salts are used in food producing species for the treatment of conditions caused by sensitive organisms. It may be administered by oral or parenteral routes. Tylosin is not used in human medicine.

In the CVMP reflection paper on the use of macrolides, lincosamides and streptogramins (MLS) in food-producing animals in the European Union: development of resistance and impact on human and animal health (EMA/CVMP/SAGAM/741087/2009)¹, the CVMP recommendations on macrolides state that 'there might be a need to review certain SPCs to reduce the approved treatment duration in cases where it is found unnecessarily long in relation to the severity of the disease'. Additionally, recent data show that *in vitro* resistance to macrolides for isolates from the European Union of *Brachyspira hyodysenteriae* (the causative agent of swine dysentery) is very high and tylosin might no longer be effective against this pathogen.

Therefore, on 30 October 2013, Sweden presented to the Agency a referral notification under Article 35 of Directive 2001/82/EC for veterinary medicinal products containing tylosin to be administered orally via feed or the drinking water to pigs. The CVMP was asked to conclude on whether the duration of treatment with veterinary medicinal products containing tylosin beyond three weeks is justified and whether these products are still effective against swine dysentery caused by *B. hyodysenteriae*.

2. Discussion

2.1.1. Treatment durations beyond three weeks

With regard to respiratory disease in pigs, tylosin premix formulations are currently often authorised for treatment using a higher dose for the first two to three weeks of treatment followed by a lower dose (typically 40% of the initial dose) for an extended period of time, often stated as the 'whole risk period'. A similar treatment strategy is recommended for tylosin premix formulation for the treatment of swine dysentery where it is mentioned that treatment can be continued 'until the end of risk', 'as long as necessary' or 'until slaughter'. In contrast, premix formulations authorised for the treatment and prevention of ileitis (caused by *Lawsonia intracellularis*) most often recommend treatment for not longer than up to three weeks. Similarly, with regard to tylosin granules and powders aimed to be mixed in the drinking water for pigs the recommended treatment period is only in exceptional cases extended beyond 3 weeks independent of indication.

It is acknowledged that many oral tylosin formulations for pigs currently available on the EU market have been authorised many years ago, according to posology justification standards regarded acceptable at that time and in the context of what was then regarded as acceptable strategies for the administration of antimicrobials. Thus, it cannot be expected that data concurring with current

¹ Reflection paper on the use of macrolides, lincosamides and streptogramins (MLS) in food-producing animals in the European Union: development of resistance and impact on human and animal health (EMA/CVMP/SAGAM/741087/2009) http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/11/WC500118230.pdf

requirements can be made available, that would provide convincing support for specific dosing strategies for currently accepted indications for oral tylosin formulations for pigs.

Discussion

The knowledge regarding antimicrobial resistance risks has increased over time, and there is also an increasing focus on accommodating dosing strategy to the double aim of administering antimicrobials as long as necessary to obtain sufficient treatment effect, but to avoid unnecessary exposure that would encourage resistance development. The general acceptance of the fact that antimicrobial treatment needs always to be combined with appropriate management and sanitary measures on the farm, to prevent the further spread of any particular microbe and thus reduce the risk for new clinical cases, makes it difficult to defend a need for very long treatment periods. The potential risk for resistance development is evident through the current resistance situation of *B. hyodysenteriae*. To maintain oral tylosin as an efficacious treatment for other currently authorised indications for pigs, unnecessary exposure should be avoided.

Given that, as stated in the above mentioned CVMP reflection paper on the use of macrolides, lincosamides and streptogramins (MLS) in food-producing animals in the European Union: development of resistance and impact on human and animal health (EMA/CVMP/SAGAM/741087/2009), this substance class is critically important for veterinary medicine and for human use and, furthermore, that the development of resistance is reported for veterinary pathogens as well as zoonotic pathogens such as *Campylobacter* spp, extended treatment of pigs beyond what can be regarded medically motivated must be avoided. For similar reasons recommendations to reduce the initial dose for an extended treatment period are not acceptable.

As previously mentioned, most oral tylosin products were authorised in the EU Member States long time ago according to marketing authorisation requirements at that time. Possibly in part due to this, currently for the same indication and the same oral formulation there is significant variation between products regarding the recommended treatment duration for pigs. In this situation it is not to be expected that scientifically well founded justifications for treatment durations can be obtained from the different marketing authorisation holders for different indications for pigs. It is however acknowledged that, regardless of the indication, for most oral tylosin formulations authorised for pigs at present the maximum recommended treatment duration is three weeks, indicating that this has in many cases been concluded to be a sufficient treatment period.

Thus, to state that the administration of oral tylosin for pigs should not exceed three weeks is likely to assure sufficient treatment efficacy for currently authorised indications in pigs and this measure would also satisfy the requirement to avoid unnecessary exposure and thus reduce the risk for resistance development. For products where any specific treatment duration shorter than 3 weeks is recommended this should be maintained in the product information.

2.1.2. Indication for treatment of swine dysentery caused by *Brachyspira hyodysenteriae*

Oral tylosin has had widespread use in pig farming in many EU Member States for decades to treat and prevent disease and before entry into force of Regulation (EC) No 1831/2003, as a growth promoter. The excessive use over time may explain the high proportion of resistance in *B. hyodysenteriae* strains, the cause for swine dysentery, reported from many European countries today. The CVMP reflection paper on the use of macrolides, lincosamides and streptogramins (MLS) in food-producing animals in the European Union: development of resistance and impact on human and animal health

(EMA/CVMP/SAGAM/741087/2009) mentions with support from data from FINRES-Vet (1999)², SVARM (2002-2009)³, Vyt and Hommez (2006)⁴, MARAN (2008)⁵ and Hidalgo *et al.* (2009)⁶, that 90-100% of *Brachyspira* isolates demonstrate *in vitro* resistance. In a study of antimicrobial susceptibility of *B. hyodysenteriae* isolated from 21 Polish farms it was concluded that the lowest antimicrobial activity was demonstrated for tylosin and lincomycin, with inhibition of bacterial growth using concentrations >128 µg/ml and 32 µg/ml, respectively (Zmudzki *et al.* (2012))⁷. A recent report from Spain (Alvarez *et al.* (2013))⁸ confirms this situation by reporting a 100% *in vitro* resistance among 78 isolates from pigs with diarrhoea. Similarly, almost complete *in vitro* resistance was reported among 32 *Brachyspira* isolates from the Czech Republic (Sperling *et al.* (2011))⁹. Although a somewhat lower rate of resistance was noted in Swedish strains collected during 1990-2010, more than 75% of the isolates demonstrate a minimum inhibitory concentration (MIC) far above the proposed epidemiological cut-off value of >16 µg/ml (Pringle *et al.* (2012))¹⁰. In line with these observations, during the 6th international conference on colonic spirochaetal infections in animals and humans in the United Kingdom in September 2013, it was mentioned in a key note that: "tylosin has been rendered totally ineffective through widespread use for in-feed medication over the years" (Thomson (2013))¹¹.

The cause for the high resistance rate can be found in the mechanisms governing the development of non-horizontal transferable resistance. Resistance is caused by point mutations of 23S rDNA. Since for *B. hyodysenteriae* the rRNA operon exists in a single copy one single base mutation is sufficient to achieve macrolide resistant clones (Zuerner and Stanton (1994)¹², Karlsson *et al.* (1999)¹³).

Discussion

The published scientific reports regarding the resistance situation for *B. hyodysenteriae* provide a discouraging picture, where tylosin resistance today is close to complete in many areas of the European Union. Although the resistance situation has not been investigated in every country where tylosin is used against swine dysentery, the awareness that tylosin resistance develops quickly and the bulk of *in vitro* data covering many field isolates from different areas provide sufficient information to conclude that it cannot be expected that the efficacy rate is sufficient to warrant an indication for treatment and prevention of this disease. Given the very high resistance rate it is not regarded a sufficient measure to only include warning or precaution statements indicating that treatment of swine dysentery with tylosin should always be based on susceptibility testing. The risk connected with delaying the initiation of effective treatment by the time required for susceptibility testing is not considered to outweigh the benefit related to the possibility to successfully use tylosin in a few cases.

² FINRES-Vet 1999. Finnish veterinary antimicrobial resistance monitoring and consumption of antimicrobial agents in 1999 (Finnish Ministry of Agriculture and Forestry).

³ SVARM 2002-2009. Swedish Veterinary Antimicrobial Resistance Monitoring (Uppsala, Sweden, The National Veterinary Institute (SVA)).

⁴ Vyt, P., Hommez, J., 2006, Antimicrobial susceptibility of *Brachyspira hyodysenteriae* isolates compared with the clinical effect of treatment. *Flem. Vet. J.* 75, 279-285.

⁵ MARAN 2008. Monitoring of antimicrobial resistance and antimicrobial usage in the Netherlands in 2008.

⁶ Hidalgo, A., Carvajal, A., Garcia-Feliz, C., Osorio, J., Rubio, P., 2009, Antimicrobial susceptibility testing of Spanish field isolates of *Brachyspira hyodysenteriae*. *Res Vet Sci* 87, 7-12.

⁷ Zmudzki, J., Szczotka, A., Nowak, A., Strzelecka, H., Grzesiak, A., Pejsak, Z., 2012. Antimicrobial susceptibility of *Brachyspira hyodysenteriae* isolated from 21 Polish farms. *Pol J Vet Sci* 15, No. 2, 259-265

⁸ Alvarez LF, Martinez-Lobo J, Aller L M, Naharro G, Carvajal A, Rubio P. 2013. Antimicrobial susceptibility of 78 isolates of *Brachyspira hyodysenteriae* recovered from swine dysentery outbreaks in Spain during 2011 & 2012. *Proceeding, Spirochaete Conference, 5-6 September 2013, UK.* P 82.

⁹ Sperling D, Smola J and Cizek A. 2011. Characterisation of multiresistant *Brachyspira hyodysenteriae* isolates from Czech pig farms. *Vet Rec*, 168

¹⁰ Pringle, M., Landén, A., Ericsson Unnerstad, H., Molander, B. and Bengtsson N., 2012, Antimicrobial susceptibility of porcine *Brachyspira hyodysenteriae* and *Brachyspira pilosicoli* isolated in Sweden between 1990 and 2010- *Acta Vet Scand*, 54, 2-6.

¹¹ Thomson J. 2013. Sensitivity and resistance of *Brachyspira* species and consequences for global swine/poultry production. *Proceeding, Spirochaete Conference, 5-6 September 2013, UK.* P 47

¹² Zuerner RL, Stanton TB., 1994, Physical and genetic map of the *Serpulina hyodysenteriae* B78T chromosome. *J Bacteriol.* 176(4):1087-1092.

¹³ Karlsson, M., Fellström, C., Heldtander, M. U., Johansson, K. E., Franklin, A., 1999. Genetic basis of macrolide and lincosamide resistance in *Brachyspira (Serpulina) hyodysenteriae*. *FEMS Microbiol Lett* 172, 255-260.

It is acknowledged that for certain holdings where susceptibility of *B. hyodysenteriae* to tylosin is still evident a removal of this indication would restrict the availability of treatment options. However, effective alternatives are available (e.g. pleuromutilins) and, as there are very few susceptible outbreaks, the risk for inadequate treatment is deemed to outweigh the possible benefit of an additional treatment option in the unlikely event of confirmed susceptibility.

3. Benefit-risk assessment

Benefit assessment

These products are effective medicines for the treatment of several diseases such as respiratory disease and ileitis/porcine intestinal adenopathy (caused by *Lawsonia intracellularis*).

Risk assessment

Extended exposure of tylosin to pigs is related to risk for development of antimicrobial resistance. As macrolides are critically important antimicrobials for pigs, unnecessary exposure leading to further resistance in target animal pathogens would be a serious risk to animal health. In addition, long-term exposure to low doses of tylosin is associated with an increase in the number of resistant *Campylobacter coli* and group medication with antibiotics is a risk factor for spread of methicillin-resistant *Staphylococcus aureus* (MRSA) in pigs.

Risk management or mitigation measures

To limit the selection pressure for bacteria unnecessary use should be avoided. To limit the administration of oral tylosin to pigs to a maximum of three weeks would reduce the risk for selection of resistance without hampering the effective use of these products against currently authorised and justifiable indications.

Evaluation and conclusion on the benefit-risk balance

Oral tylosin is regarded as an effective medicine against several diseases in pigs. Due to resistance development through recent decades, tylosin is however today not considered to provide sufficient efficacy against swine dysentery (*B. hyodysenteriae*), and the substance should thus not be used for this disease. Extended and vaguely defined treatment periods present a risk from resistance perspective and would not be justifiable from a scientific point of view taking into account disease epidemiology as well as current awareness regarding the need to always combine antibiotic use with appropriate sanitary measures.

Provided swine dysentery is excluded from the indications of oral tylosin formulations for pigs and the maximum treatment is restricted to three weeks, the benefit-risk balance of these products could continue to be regarded as positive.

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

Whereas:

- most oral tylosin formulations for pigs are authorised with a recommendation to treat for up to three weeks, the CVMP concluded that this maximum duration of treatment would provide sufficient efficacy. Taking efficacy aspects as well as the risk for resistance emergence into account, a maximum treatment period of three weeks applying the same dose level throughout the treatment period is regarded appropriate independent of disease;

- according to recent published susceptibility data tylosin will not be sufficiently effective against *B. hyodysenteriae* and therefore the CVMP concluded the indication in swine dysentery can no longer be maintained;
- the CVMP considered that the overall benefit-risk balance is positive for veterinary medicinal products containing tylosin to be administered orally via feed or the drinking water to pigs subject to amendments in the product information;

the CVMP recommended variations of the marketing authorisations for veterinary medicinal products containing tylosin to be administered orally via feed or the drinking water to pigs (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.

Annex III

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

Summary of product characteristics

4.2 Indications for use, specifying the target species

Delete, where applicable, the indication 'Swine dysentery caused by *Brachyspira hyodysenteriae*'.

In case the indication(s) for a particular product do not specify swine dysentery, but do not exclude such use, a cross reference to section 4.5 should be added: *For information regarding swine dysentery see section 4.5.*

4.5 Special precautions for use

Special precautions for use in animals

In case the indication(s) for a particular product do not specify swine dysentery, but do not exclude such use, the following sentence should be added to section 4.5: *A high rate of in vitro resistance has been demonstrated in European strains of Brachyspira hyodysenteriae implying that the product will not be sufficiently efficacious against swine dysentery.*

4.9 Amounts to be administered and administration route

Delete, where applicable, any specific dosing recommendation related to swine dysentery caused by *Brachyspira hyodysenteriae*.

Replace, where applicable, treatment recommendations which are extended beyond 3 weeks, or where no treatment duration recommendation is given, with the following statement: *Treatment duration should not exceed 3 weeks.*

Specific treatment recommendations shorter than 3 weeks should be maintained.

Delete, where applicable, any recommendation to reduce the dose after an initial treatment period with a higher dose.

5.1 Pharmacodynamic properties

Delete, where applicable, any references to swine dysentery caused by *Brachyspira hyodysenteriae*.

Labelling:

6. INDICATION(S)

Delete, where applicable, the indication swine dysentery caused by *Brachyspira hyodysenteriae*.

Package leaflet

4. INDICATION(S)

Delete, where applicable, the indication 'Swine dysentery caused by *Brachyspira hyodysenteriae*'.

In case the indication(s) for a particular product do not specify swine dysentery, but do not exclude such use, a cross reference to section 12 should be added: *For information regarding swine dysentery see section 12.*

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Delete, where applicable, any specific dosing recommendation related to swine dysentery caused by *Brachyspira hyodysenteriae*.

Replace, where applicable, treatment recommendations which are extended beyond 3 weeks, or where no treatment duration recommendation is given, with the following statement: *Treatment duration should not exceed 3 weeks.*

Specific treatment recommendations shorter than 3 weeks should be maintained.

Delete, where applicable, any recommendation to reduce the dose after an initial treatment period with a higher dose.

12. SPECIAL WARNING(S)

Special precautions for use in animals

In case the indication(s) for a particular product do not specify swine dysentery, but do not exclude such use, the following sentence should be added to section 12: *A high rate of in vitro resistance has been demonstrated in European strains of Brachyspira hyodysenteriae implying that the product will not be sufficiently efficacious against swine dysentery.*