Annex I

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

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	Linco–Spectin 22 / 22 mg/g - Arzneimittelvormischung zur Herstellung von Fütterungsarzneimitteln für Schweine	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Premix for medicated feeding stuff	Pigs	Oral
Austria	Zoetis Österreich GmbH Floridsdorfer Hauptstrasse 1 1210 Wien Austria	Linco-Spectin 222 mg/g + 444,7 mg/g - Pulver zum Eingeben über das Trinkwasser für Schweine und Hühner	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Austria	Animed Service AG Liebochstrasse 9 8143 Dobl Austria	Lincomycin-Spectinomycin 1,1% "Animed Service" - Pulver zum Eingeben für Schweine	Lincomycin and Spectinomycin	5,5 g/kg 5,5 g/kg	Powder to be administered with the feed	Pigs	Oral
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 100	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 22 + 22	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Belgium	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 44	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Powder to be administered with the feed	Pigs	Oral
Belgium	KELA N.V. Sint Lenaartseweg 48 2320 Hoogstraten Belgium	Spectoliphen 100	Lincomycin and Spectinomycin	222 mg/g 444 mg/g	Powder for use in drinking water	Pigs, poultry	Oral
Belgium	V.M.D. nv Hoge Mauw 900 2370 Arendonk Belgium	Lincomycine-Spectinomycine VMD Pulvis	Lincomycin and Spectinomycin	33,3 g/150 g 66,6 g/150 g	Powder for use in drinking water	Pigs	Oral
Bulgaria	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 100, powder for oral solution	Lincomycin and Spectinomycin	33.3 g/150 g 66.7 g/150 g	Powder for use in drinking water	Pigs, chickens, turkeys	Oral
Bulgaria	Kepro B.V. Maagdenburgstraat 17 7421 ZE Deventer The Netherlands	L.S.POWDER WSP	Lincomycin and Spectinomycin	222 mg/g 444 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Bulgaria	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linko-spectin 44 premix	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs, chickens	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Bulgaria	Zavet AD Ul. Kiril I Metodiy No. 5 Zavet Bulgaria	Lincomycin 222 Spectinomycin 444 WSP	Lincomycin and Spectinomycin	222 mg 444 mg	Powder for use in drinking water	Pigs, chickens	Oral
Croatia	Zoetis Netherlands Holdings B.V. Podružnica Zagreb za promidžbu Petra Hektorovića 2 10000 Zagreb Croatia	LINCO-SPECTIN 100	Lincomycin and Spectinomycin	33.3 g/150 g 66.7 g/150 g	Powder for use in drinking water	Pigs, chickens	Oral
Croatia	Zoetis Netherlands Holdings B.V. Podružnica Zagreb za promidžbu Petra Hektorovića 2 10000 Zagreb Croatia	LINCO-SPECTIN 44	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Croatia	Vet Consulting d.o.o. Matije Gupca 42 43500 Daruvar Croatia	L-SPEC 100 S	Lincomycin and Spectinomycin	33.3 g/150 g 66.6 g/150 g	Powder for use in drinking water	Pigs	Oral
Cyprus	Zoetis Hellas SA 253-255 Messogeion Ave 15451 Neo Psychiko Athens Greece	Linco-Spectin 100 SP 66.7g Spectinomycin, 33.3g Lincomycin Σκόνη για χορήγηση μέσω διαλύματος από το στόμα για ορνίθια	Lincomycin and Spectinomycin	33.3 g/150 g 66.7 g/150 g	Powder for use in drinking water	Chickens	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Cyprus	Zoetis Hellas SA 253-255 Messogeion Ave 15451 Neo Psychiko Athens Greece	LINCO-SPECTIN 44 PREMIX POWDER, πρόμιγμα για φαρμακούχο ζωοτροφή	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Czech Republic	Zoetis Česká republika s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	LINCO – SPECTIN 22/22 mg/g premix pro medikaci krmiva	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Premix for medicated feeding stuff	Pigs	Oral
Czech Republic	Zoetis Česká republika s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	Linco-spectin 222/444,7 mg/g prášek pro podání v pitné vodě pro prasata a kura domácího	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Czech Republic	FATRO S.p.A. Via Emilia, 285 40064 Ozzano Emilia (BO) Italy	MICOSPECTONE plv. sol.	Lincomycin and Spectinomycin	166,5 mg/g 333,5 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Denmark	Pfizer Oy Animal Health Tietokuja 4 FI-003300 Helsinki Finland	Linco-spectin Vet	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Powder to be administered with the feed	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Denmark	Pfizer Oy Animal Health Tietokuja 4 FI-003300 Helsinki Finland	Linco-spectin Vet	Lincomycin and Spectinomycin	220 mg/g 440 mg/g	Powder for use in drinking water	Pigs, poultry	Oral
Estonia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 100	Lincomycin and Spectinomycin	222 mg/g 444.7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Estonia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 44 Premix	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Premix for medicated feeding stuff	Pigs	Oral
France	Zoetis France 23-25 Avenue du Docteur Lannelongue 75014 Paris France	LINCO-SPECTIN 100, 222/444, 7 MG/G POUDRE POUR ADMINISTRATION DANS L'EAU DE BOISSON POUR PORCINS ET POULETS	Lincomycin and Spectinomycin	222 mg/g 444.7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
France	Deltavit Zone D'Activites Du Bois De Teillay 35150 Janze France	PM 27 LINCOMYCINE 4.4 SPECTINOMYCINE 4.4 PORC	Lincomycin and Spectinomycin	4,4 mg/g 4,4 mg/g	Premix for medicated feeding stuff	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
France	Sogeval 200 Avenue de Mayenne Zone Industrielle des Touches 53000 Laval France	CONCENTRAT V061 LINCOMYCINE 4.4 SPECTINOMYCINE 4.4 PORC	Lincomycin and Spectinomycin	4,4 mg/g 4,4 mg/g	Premix for medicated feeding stuff	Pigs	Oral
France	Qalian 34 rue Jean Monnet ZI d'Etriche 49500 SEGRE France	LINCOMYCINE 4.4 SPECTINOMYCINE 4.4 PORC FRANVET	Lincomycin and Spectinomycin	4,4 mg/g 4,4 mg/g	Premix for medicated feeding stuff	Pigs	Oral
Germany	Zoetis Deutschland GmbH Schellingstrasse 1 D-10785 Berlin Germany	Lincospectin Top	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Powder to be administered with the feed	Pigs	Oral
Germany	Zoetis Deutschland GmbH Schellingstrasse 1 D-10785 Berlin Germany	Lincospectin Pulver	Lincomycin and Spectinomycin	222 mg/g 445 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Germany	Bela-Pharm GmbH & Co.KG Lohner Str. 19 49377 Vechta Germany	Pyanosid Pulver	Lincomycin and Spectinomycin	227 mg/g 455 mg/g	Powder for use in drinking water	Pigs, chickens	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Germany	Kon-Pharma GmbH Senator-Bauer-Str. 34 D-30625 Hannover Germany	Lincomycin-Spectinomycin Pulver	Lincomycin and Spectinomycin	227 mg/g 455 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Germany	Pharmacia GmbH Linkstr. 10 D-10785 Berlin Germany	Lincospectin 44 Premix	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Premix for medicated feeding stuff	Pigs	Oral
Greece	PROVET AE 19300, Aspropyrgos Attikis Greece	LINCOVET-S	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Greece	PROVET AE 19300, Aspropyrgos Attikis Greece	LINCOVET-S WSP	Lincomycin and Spectinomycin	33,3 g/150 g 66,7 g/150 g	Powder for use in drinking water	Chickens (broilers)	Oral
Greece	Zoetis Hellas SA 253-255 Messogeion Ave 15451 Neo Psychiko Athens Greece	LINCO-SPECTIN	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Greece	Zoetis Hellas SA 253-255 Messogeion Ave 15451 Neo Psychiko Athens Greece	LINCO-SPECTIN	Lincomycin and Spectinomycin	33,3 g/150 g 66,7 g/150 g	Powder for use in drinking water	Chickens (broilers)	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Greece	AVICO AE 2 Km Paiania-Spata Av 1902 Paiania Attiki Greece	MICOSPECTONE	Lincomycin and Spectinomycin	16,65 g/100 g 33,35 g/100 g	Powder for use in drinking water	Pigs, chickens (broilers)	Oral
Hungary	Zoetis Hungary Kft. 1123 Budapest Alkotás u. 53. Hungary	LincoSpectin SolPO 222/444,7 mg/g por ivóvízbe keveréshez sertések és házityúkok számára A.U.V.	Lincomycin and Spectinomycin	222 mg/g 444.7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Hungary	Zoetis Hungary Kft. 1123 Budapest Alkotás u. 53. Hungary	Linco-Spectin 44 gyógypremix A.U.V.	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Linco-Spectin 100, 222/444.7 mg/g Powder for use in drinking water for pigs and chickens	Lincomycin and Spectinomycin	222 mg/g 444.7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Ireland	Zoetis Ireland Limited 25/28 North Wall Quay Dublin 1 Ireland	Linco-Spectin Premix for medicated feed.	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Premix for medicated feed	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	Lincospectin 222/444,7 mg/g	Lincomycin and Spectinomycin	222 mg 444,7 mg	Powder for use in drinking water	Pigs, chickens	Oral
Italy	Zoetis Italia S.r.l. Via Andrea Doria, 41 M 00192 Roma Italy	Lincospectin 44 mg/g	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Italy	FATRO S.p.A. Via Emilia, 285 40064 Ozzano Emilia (BO) Italy	MICOSPECTONE 166,5 mg/g + 333,5 mg/g polvere per soluzione orale per vitelli, suinetti e polli.	Lincomycin and Spectinomycin	166,5 mg/g 333,5 mg/g	Powder for use in drinking water or milk	Calves, piglets, chickens	Oral
Latvia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 44 Premix	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Latvia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 100	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Lithuania	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	LINCO-SPECTIN 44 vaistinis premiksas	Lincomycin and Spectinomycin	22 g/kg 22 g/kg,	Premix for medicated feeding stuff	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Lithuania	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 100, 222/444,7 mg/g milteliai, skirti naudoti su geriamuoju vandeniu kiaulėms ir vištoms	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, poultry	Oral
Lithuania	Bela-Pharm GmbH & Co.KG Lohner Str. 19 49377 Vechta Germany	PYANOSID, geriamieji milteliai	Lincomycin and Spectinomycin	33,3 g/146,36 g 66,7 g/146,36 g	Powder for use in drinking water	Pigs, poultry (broiler, pullet) and turkey	Oral
Luxembourg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	LINCO-SPECTIN 100	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, poultry	Oral
Luxembourg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	LINCO-SPECTIN 22 + 22 premix	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Luxembourg	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	LINCO-SPECTIN 44	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Powder to be administered with the feed	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Malta	FATRO S.p.A. Via Emilia, 285 40064 Ozzano Emilia (BO) Italy	Micospectone	Lincomycin and Spectinomycin	166.5 mg/g 333.5 mg/g	Powder for use in drinking water	Piglets, calves, chickens	Oral
Malta	V.M.D. nv Hoge Mauw 900 2370 Arendonk Belgium	Lincomycin-spectinomycin VMD Pulvis	Lincomycin and Spectinomycin	33.3 g/150 g 66.6 g/150 g	Powder for use in drinking water	Pigs	Oral
The Netherlands	Zoetis B.V. Rivium Westlaan 74 2909 LD Capelle a/d Ijssel The Netherlands	LINCO-SPECTIN 100, 222 mg/g + 444,7 mg/g poeder voor gebruik in drinkwater voor varkens en kippen, REG NL 9916	Lincomycin and Spectinomycin	222 mg/g 444.7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
The Netherlands	Zoetis B.V. Rivium Westlaan 74 2909 LD Capelle a/d Ijssel The Netherlands	LINCO-SPECTIN PREMIX voor varkens, REG NL 9708	Lincomycin and Spectinomycin	22 mg/g 22 mg/g	Premix for medicated feeding stuff	Pigs	Oral
Poland	Zoetis Polska Sp. z o.o. ul. Postępu 17 B 02-676 Warszawa Poland	Linco-Spectin 100	Lincomycin and Spectinomycin	222 g/kg 444 g/kg	Powder for use in drinking water	Pigs, hens pigeons, ducks, turkeys	Oral
Poland	Zoetis Polska Sp. z o.o. ul. Postępu 17 B 02-676 Warszawa Poland	Linco-Spectin Premix	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Portugal	Zoetis Portugal Lda. Lagoas Park, Edifício 10 2740-271 Porto Salvo Portugal	LINCO-SPECTIN 44 pré-mistura medicamentosa para Suínos	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Portugal	Zoetis Portugal Lda. Lagoas Park, Edifício 10 2740-271 Porto Salvo Portugal	Linco-Spectin 100, 222 + 444,7 mg/g pó para administração na água de bebida para suínos e galinhas	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Portugal	Laboratorios Maymó, S.A. Via Augusta, 302 08017 Barcelona Spain	Lismay Premix, Pré-mistura medicamentosa para alimento medicamentoso	Lincomycin and Spectinomycin	440 g/1.5 kg 440 g/1.5 kg	Premix for medicated feeding stuff	Pigs	Oral
Romania	Pfizer Animal Health MA EEIG Ramsgate Road Sandwich, Kent CT13 9NJ United Kingdom	Linco-Spectin 44	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Romania	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco-Spectin 880	Lincomycin and Spectinomycin	293,3 g/kg 293,3 g/kg	Premix for medicated feeding stuff	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Romania	Pfizer Animal Health MA EEIG Ramsgate Road Sandwich, Kent CT13 9NJ United Kingdom	Linco-Spectin 100	Lincomycin and Spectinomycin	33,3 g/150g 66,7 g/150g	Powder for use in drinking water	Pigs, chickens, turkeys	Oral
Slovakia	Zoetis Česká republika s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	Linco-Spectin 44 g/kg premix na medikáciu krmiva	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Slovakia	Zoetis Česká republika s.r.o. Stroupežnického 17 150 00 Praha 5 Czech Republic	Linco-Spectin 100 prášok na perorálny roztok	Lincomycin and Spectinomycin	33,3 g/150 g 66,7 g/150 g	Powder for use in drinking water	Pigs, poultry	Oral
Slovakia	FATRO S.p.A. Via Emilia, 285 40064 Ozzano Emilia (BO) Italy	MICOSPECTONE 166,5 mg + 333,5 mg prášok na perorálny roztok	Lincomycin and Spectinomycin	166,50 mg/g 333,50 mg/g	Powder for use in drinking water	Piglets, chickens	Oral
Slovenia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco Spectin 100 prašek za peroralno raztopino za prašiče in perutnino	Lincomycin and Spectinomycin	33,3 g/150 g 66,7 g/150 g	Powder for use in drinking water	Pigs, poultry	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Slovenia	Zoetis Belgium SA Rue Laid Burniat, 1 1348 Louvain-la-Neuve Belgium	Linco Spectin 44 predmešanica za zdravilno krmno mešanico za prašiče	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Spain	Laboratorios Ovejero S.A. Ctra. León-Vilecha, 30 24192 León Spain	HEMOENTEROL PREMEZCLA MEDICAMENTOSA	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Spain	SUPER´S DIANA, S.L Ctra. C-17, km 17 Parets del Valles 08150 Barcelona Spain	LINCOTRIMEX-PREMIX	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral
Spain	Laboratorios Maymó, S.A. Via Augusta, 302 08017 Barcelona Spain	LISMAY PREMIX	Lincomycin and Spectinomycin	440 g/1.5 kg 440 g/1.5 kg	Premix for medicated feeding stuff	Pigs	Oral
Spain	Zoetis Spain, S.L. Avda. de Europa, 20B Parque Empresarial La Moraleja Alcobendas 28108 Spain	*LINCO-SPECTIN 22/22 mg/g premezcla medicamentosa para porcino*	Lincomycin and Spectinomycin	22 g/kg 22 g/kg	Premix for medicated feeding stuff	Pigs	Oral

Member State EU/EEA	Marketing authorisation holder	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Spain	Zoetis Spain, S.L. Avda. de Europa, 20B Parque Empresarial La Moraleja Alcobendas 28108 Spain	LINCO-SPECTIN 100	Lincomycin and Spectinomycin	222 mg/g 444,7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
Spain	MEVET, S.A. Poligono Industrial El Segre Parc. 409-410 25191 Lérida Spain	*LINESVALL 22 g/Kg PREMEZCLA MEDICAMENTOSA*	Lincomycin and Spectinomycin	11 g/kg 11 g/kg	Premix for medicated feeding stuff	Pigs	Oral
United Kingdom	Zoetis UK Limited 5th Floor, 6 St. Andrew Street London, EC4A 3AE United Kingdom	Linco-Spectin 100, 222/444.7 mg/g Powder for Use in Drinking Water for Pigs and Chickens	Lincomycin and Spectinomycin	222 mg/g 444.7 mg/g	Powder for use in drinking water	Pigs, chickens	Oral
United Kingdom	Zoetis UK Limited 5th Floor, 6 St. Andrew Street London, EC4A 3AE United Kingdom	Linco-Spectin Premix for Medicated Feed	Lincomycin and Spectinomycin	2.2 % w/w 2.2 % w/w	Premix for medicated feeding stuff	Pigs	Oral
United Kingdom	Zoetis UK Limited 5th Floor, 6 St. Andrew Street London, EC4A 3AE United Kingdom	Linco-Spectin SP 222 mg/g + 444.7 mg/g powder for use in drinking water for pigs and chickens	Lincomycin and Spectinomycin	22.2 % w/w 44.4 % w/w	Powder for use in drinking water	Pigs, chickens	Oral

Annex II

Scientific conclusions

Overall summary of the scientific evaluation of veterinary medicinal products containing a combination of lincomycin and spectinomycin to be administered orally to pigs and/or poultry (see Annex I)

1. Introduction

Lincomycin is a lincosamide antibiotic derived from *Streptomyces lincolnensis* which inhibits protein synthesis. The lincosamides are considered to be bacteriostatic agents. Lincomycin is active against gram-positive bacteria, some anaerobic gram-negative bacteria and *Mycoplasma* spp.

Spectinomycin is an aminocyclitol antibiotic derived from *Streptomyces spectabilis;* it has bacteriostatic activity and is active against some aerobic gram-negative bacteria, gram-positive cocci and *Mycoplasma* spp.

For pigs and poultry three pharmaceutical forms for oral administration exist with a combination of lincomycin and spectinomycin - premixes for medicated feeding stuff, powders to be administered with the feed and powders for use in drinking water.

Following a referral procedure (EMEA/V/A/088)[1] under Article 34 of Directive 2001/82/EC, the product information was harmonised for Linco-Spectin 100, powder for use in drinking water for pigs and chickens, containing 222 mg lincomycin/g and 444.7 mg spectinomycin/g. The Commission Decision C(2014)5053 was issued on 11 July 2014.

Subsequent to the outcome of the aforementioned Article 34 referral procedure for Linco-Spectin 100, Belgium considered that it is in the interest of the Union to promote effective and rational use of the lincomycin-spectinomycin combination in orally administered veterinary medicinal products, and thereby limit the risk of resistance development. Therefore, on 5 May 2015, Belgium initiated a procedure under Article 35 of Directive 2001/82/EC for veterinary medicinal products containing a combination of lincomycin and spectinomycin to be administered orally to pigs and/or poultry.

2. Discussion of data available

Indications, dosages and residue data in pigs

Extensive data are available in relation to the treatment of swine dysentery caused by *Brachyspira hyodysenteriae* and associated enteric pathogens, and for the treatment of porcine proliferative enteropathy caused by *Lawsonia intracellularis*.

From the data provided, it appears that within the lincomycin-spectinomycin combination only lincomycin is active against the primary causal agent of swine dysentery, the anaerobic spirochete *B. hyodysenteriae*, which is intrinsically resistant to spectinomycin. Overall there is no significant evidence of a synergistic interaction *in vitro* between lincomycin and spectinomycin in *B. hyodysenteriae*, and most authors consider that the benefit of the combination with spectinomycin in the treatment of swine dysentery lies rather in the extension of the spectrum to a broader range of organisms, i.e. spectinomycin would act against concurrent pathogens or on enteric bacteria establishing conditions in the gut favourable to the development of swine dysentery.

When considering lincomycin *in vitro* susceptibility data against *B. hyodysenteriae*, even if differences occur between geographical areas, and variability arises from the absence of standardised testing methodology, it appears clearly that the minimum inhibitory concentration (MIC) range is broad and

[1] http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/veterinary/referrals/Linco-Spectin_100_and_associated_names/vet_referral_000097.jsp&mid=WC0b01ac05805c5170

that most of the isolates show an increased MIC in a bacterial population where the wild-type is reduced (or even absent). The data available do not allow the establishment of a clear time pattern for the evolution of MICs. However, some attempts were made to establish relationships between MIC values and the clinical outcome, using limited clinical and/or PK (colonic content concentration) data. Those data indicate that strains with some level of MIC increase might nevertheless be effectively treated, leading to a favourable clinical outcome. It appears however that this represents a minority of strains; also, this is based on sparse data and on several estimations, and no firm clinical breakpoint has been established up until now.

Several pig enteric pathogens can be associated with *B. hyodysenteriae* infections and constitute possible targets for spectinomycin. These include notably, *Escherichia coli*, *Salmonella spp.,* and *Campylobacter spp.* In *E. coli* and *Salmonella*, based on *in vitro* data, spectinomycin resistance rates of about 30-50% can be expected. Some of the strains might be naturally resistant. In *Campylobacter,* variable but possibly high resistance rates were shown against lincomycin; however the situation could be more complex because those bacteria are also considered susceptible to spectinomycin, for which few data are available.

The available clinical data show that the combination, administered in the drinking water at a dose of 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw/day for 7 days (i.e. the harmonised dose for Linco-Spectin 100), is clinically effective in treating mixed infections involving *B. hyodysenteriae* and other enteric pathogens targeted by spectinomycin, and that in those situations it is superior to the individual substances. The associated aetiology of *B. hyodysenteriae* and its role in pathogenesis is however not fully clear and no bacteriological follow-up has been performed in those studies. Most importantly, these studies are very old (they were conducted in the context of the development and marketing of the combination more than 40 years ago) and the *in vitro* susceptibility of the *B. hyodysenteriae* strains is unknown. Therefore, most available clinical data do not take into account the current status of *in vitro* susceptibility/resistance of the concerned bacterial species.

Only one study with premixes for medicated feeding stuff containing the combination lincomycin-spectinomycin against swine dysentery was submitted. The results are favourable but the treatment was metaphylactic. Some sparse literature data relating to in-feed administration of lincomycin alone, show a majority of treatment failures or relapses. The treatment durations were unclear but were probably of several weeks. More generally, treatment with premixes for medicated feeding stuff and oral powders to be administered with the feed to pigs containing the combination lincomycin-spectinomycin as currently recommended exposes the target pathogens and other bacteria to low doses for prolonged periods, which increases risk of resistance selection.

Therefore, when considering the high *in vitro* resistance rate in *B. hyodysenteriae*, and to a lesser extent in possible associated pathogens, together with the limitations of the available clinical data, it appears that in the current situation the combination may remain effective only in a minority of field situations, and no well-established interpretive criterion or standardised test method exists which allows the user to predict efficacy against *B. hyodysenteriae*. This major uncertainty cannot be addressed until new clinical studies are conducted, under well controlled conditions including proper diagnoses and follow-up of the bacterial pathogens involved and determination of their *in vitro* susceptibility.

For similar reasons, i.e. because of high *in vitro* resistance rates, in 2014, in the context of a referral procedure (EMEA/V/A/100)[2] 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 recommended the indication 'swine dysentery caused by *B. hyodysenteriae'* to be deleted from the

[2] http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/veterinary/referrals/Veterinary_medicinal_products_containing_tylosin_to_be_administered_orally_via_feed_or_the_drinking_water_to_pigs/vet_referral_000098.jsp&mid=WC0b01ac05805c5170

product information. The macrolide tylosin is closely related to lincosamides and binds to an overlapping ribosomal site. It was concluded that most *Brachyspira* isolates demonstrated *in vitro* resistance and that it could not be expected that oral tylosin would be sufficiently efficacious for the treatment of swine dysentery. It is generally considered that the resistance status against tylosin closely follows that for lincomycin because of cross-resistance (see e.g. the CVMP reflection paper (EMA/CVMP/SAGAM/741087/2009))[3], although the two situations are not directly comparable since the MIC values for tylosin are, overall, higher, and the doses used and pharmacokinetics may also differ. This CVMP decision should also be taken into account in the present referral procedure.

It appears that currently pleuromutilins still constitute an effective alternative for the treatment of the disease, although MIC increases, deemed as alarming, have been detected in several surveys (see CVMP reflection paper (EMA/CVMP/AWP/119489/2012))[4]. Pleuromutilins also share with lincosamides overlapping binding sites at the ribosomal peptidyl transferase center, and multi-resistant strains (to pleuromutilins, macrolides and lincosamides) have arisen. In addition, some mutations in that area can confer increased MICs to both pleuromutilins and lincosamides. It follows that, while concerns could be expressed if pleuromutilins would remain the sole antimicrobial class indicated in swine dysentery, on the other hand the use of lincomycin against strains of intermediate susceptibility, might possibly contribute to pleuromutilin resistance development through co-selection.

The CVMP considers that the obvious increase in MIC values in European *B. hyodysenteriae* isolates with regard to wild-type strains, impacts the benefit-risk assessment for the group of products under assessment since this is not taken into account in most available clinical efficacy studies which were conducted at the time of product development. No firm clinical breakpoint could be proposed which would allow the prediction of clinical efficacy in the presence of poorly susceptible isolates, which currently represent the majority of isolates. It is considered that indications relating to swine dysentery caused by *B. hyodyenteriae*, and associated pathogens, are not sufficiently supported and that the use of the products in such conditions entails a risk of treatment failure, which, in addition, is linked to a risk of further resistance selection and co-selection.

Despite the poor *in vitro* activity of the active substances against *L. intracellularis*, which appears from the scarce data available, the results of a relatively recent, multicentric field study support efficacy of the lincomycin-spectinomycin combination at a dose of 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw/day for 7 days in drinking water. There is only weak evidence that the effect on *L. intracellularis* infection would be superior to the single substances, and the respective roles of lincomycin and spectinomycin in the context of pig ileitis have not been well established. It is possible that the substances are synergistic, act at different locations (intra- and extracellularly), or act by influencing the concurrent gut flora conditions. Data from a pilot challenge study suggest efficacy in case of proliferative enteropathy associated with a colibacillosis outbreak, although the study was not formally designed to investigate efficacy against *E. coli*.

Therefore, based on the activity spectrum of the combination, on general considerations of the pathogenesis of porcine proliferative enteropathy and on the available clinical data, it is considered that the indication for the treatment and prevention of porcine proliferative enteropathy (ileitis) caused by *L. intracellularis*, and associated enteric pathogens (*E. coli*) at a dose of 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw/day for 7 days in drinking water, approved during the Article 34 referral procedure (EMEA/V/A/088) for Linco-Spectin 100, is justified.

[3] 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) - http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/11/WC500118230.pdf

[4] CVMP reflection paper on use of pleuromutilins in food-producing animals in the European Union: development of resistance and impact on human and animal health (EMA/CVMP/AWP/119489/2012) - http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/11/WC500154734.pdf

One monocentric study concerning in-feed use is presented, which shows a beneficial effect in case of porcine proliferative enteropathy, but this uses lincomycin alone at a high dose in comparison to those used in the combination.

No appropriate efficacy data or no data at all have been presented regarding the other indications currently approved for the group of products under assessment.

Most available clinical efficacy data relate to administration of the combination as powder for use in drinking water; those from the basis for the harmonised dosing regimen of 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw/day for 7 days for Linco-Spectin 100, as approved during the Article 34 referral procedure (EMEA/V/A/088).

Very limited data or no data were provided to support the use of premixes for medicated feeding stuff and oral powders to be administered with the feed containing lincomycin and spectinomycin. The administration of the lincomycin and spectinomycin combination with the animal feed is currently recommended at relatively low doses and for prolonged periods (approximately 1 to 2.5 mg combined actives per kg bw (which is between 10% and 25% of the daily dose for powders for use in drinking water) for a relatively long period of 21 days). This low dose for a long period entails a high risk of antimicrobial resistance selection in pathogenic and commensal bacteria and treatment failure.

The residue data presented for powders for use in drinking water do not call into question the withdrawal periods approved for each product individually at the dose of 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw/day, for 7 days. Also pharmacovigilance data do not indicate a risk of MRL violation. Therefore, the Committee considers that there is no need to amend the currently approved withdrawal periods for pigs meat and offal for the products concerned by the procedure.

Indications, dosages and residue data in chickens

The available *in vitro* susceptibility data indicate that spectinomycin and lincomycin can act synergistically in avian mycoplasmas such as *M. gallisepticum*. In those bacterial species there is no evidence of an important resistant population or of an evolving resistance status. Spectinomycin is active against avian *E. coli*, with observed rates of *in vitro* resistance of less than 20%. Spectinomycin is also active against *Salmonella* spp., and both compounds are active against *Campylobacter* spp.

A series of old studies using challenge models show efficacy of the combination, administered in the drinking water, in chickens infected by *M. gallisepticum* and/or *E. coli*, or by *M. synoviae*. Although doses are only expressed as levels in water, it can be estimated that the optimal doses range from 75 to 300 mg combined actives/kg bw. In those studies the superiority of the combination over spectinomycin alone is not clearly established.

A series of old field studies, which investigated the impact of a systematic treatment on the zootechnical performances of flocks in comparison to a positive control, are also presented. In those trials, it seems that the treatment is used for prevention in a non-specific manner, maybe even as a growth promoter. The typical dosing regimen in these studies comprises a first phase at about 150 mg combined actives/kg bw/day and a second phase at about 50 mg combined actives/kg bw/day. It is likely that at the beginning, the product was developed and used in the same manner as a growth promoter and to prevent mortality and performance loss.

In a GCP-compliant randomised, blinded and negatively controlled challenge study, chickens were treated with powder for use in drinking water containing a combination of lincomycin and spectinomycin against induced *E. coli*, *M. gallisepticum* and combined *E. coli* plus *M. gallisepticum* infection. This study showed that, overall, the lincomycin-spectinomycin combination significantly improved the tested clinical, pathological and bacteriological endpoints in an experimental model of aerosol infection, at a dose of 16.65 mg lincomycin and 33.35 mg spectinomycin/kg bw (50 mg combined actives/kg bw) per day for 7 days. Bacteria were frequently re-isolated in the treated

animals and in the case of *E. coli*, the reduction in the percentage of positive animals is not statistically significant. This is however difficult to interpret in terms of field efficacy since this study was based on an experimental infection model. In addition, in the study the induced clinical signs can only be considered only as moderate, since no mortality occurred and clinical scores were rather low.

Based primarily on the latter experimental study, it is considered that the indication relating to chicken chronic respiratory disease (CRD) caused by *M. gallisepticum* and *E. coli* and associated with a low mortality rate, and the associated dosing regimen of 16.65 mg lincomycin and 33.35 mg spectinomycin/kg bw (50 mg combined actives/kg bw) per day for 7 days, as approved during the Article 34 referral procedure (EMEA/V/A/088) for Linco-Spectin 100, are justified as the only validated indication and dosage in chickens. From the available information it appears that the resistance rates in the target bacteria are relatively low, and there is no indication of an evolving status. Deletion of target species chickens from the concerned products could increase the use of antimicrobial substances currently considered as even more critical in terms of the consequences of selection of resistance and relevance for public health, such as fluoroquinolones.

It is known from the PK properties of spectinomycin that only negligible amounts are absorbed from the gut and that in any case, blood levels do not reach MIC levels. In addition, spectinomycin is polar and does not readily cross membranes to distribute into the intracellular compartment. Nonetheless, there are indications (from laboratory clinical studies) of clinical efficacy against *E. coli* located in and acquired via the respiratory tract, and against mycoplasmas, which are intracellular infections. On the basis of *in vitro* tests, some have hypothesised that a metabolite or degradation product of spectinomycin was produced in the gut and was able to reach the infection site and interfere with *E. coli* adherence to the respiratory mucosa. However this has not been validated and it has not been shown that spectinomycin undergoes any metabolism in any species and it appears from PK data that most of the therapeutic dose can be recovered from faeces and urine. A likely explanation to the mechanism of action of spectinomycin against respiratory *E. coli* is rather an indirect effect on the gut flora, leading to a reduction of the shedding into the environment. Therefore, although overall the combination of lincomycin and spectinomycin showed to be clinically effective against *E. coli* in chickens, appropriate sentence should be included in SPC section 5.1 Pharmacodynamic properties to reflect the lack of absorption of spectinomycin in the gut.

All indications and dosing instructions corresponding to systematic prevention in healthy animals or to fixed antimicrobial levels in the drinking water relate to variable and uncontrolled antimicrobial exposures, should be deleted from the product literature.

No data were provided to support the use of a premix for medicated feeding stuff in chickens.

The residue data presented for powders for use in drinking water do not call into question the withdrawal periods approved for each product individually at the dose of 16.65 mg lincomycin and 33.35 mg spectinomycin/kg bw/day, for 7 days. Also, pharmacovigilance data do not indicate a risk of MRL violation. Therefore there is no need to change the currently approved withdrawal periods for the products under assessment.

Indications, dosages and residue data in poultry species other than chickens

During the Article 34 referral procedure (EMA/V/A/088) for Linco-Spectin 100, the limited efficacy data that were provided and the lack of residue data did not lead to the approval of any harmonised indications in poultry species other than chickens. No further data have been presented in the framework of this referral to support any indications in poultry species other than chickens.

3. Benefit-risk assessment

In view of the available *in vitro* susceptibility and clinical data in pigs, it appears that the combination is justified on theoretical grounds by its extended spectrum of activity, in the case of swine dysentery caused by *B. hyodysenteriae* and associated enteric pathogens susceptible to spectinomycin. Its added value above the single substances in that context has been demonstrated in old clinical studies, although with limitations at the level of bacteriological inclusion criteria and bacteriological follow-up. Nevertheless, the available *in vitro* susceptibility data suggest that the expected benefit is now considerably reduced due to a rapid and widespread MIC increase in *B. hyodysenteriae.* Although that some disease outbreaks would still be treated with sufficient efficacy in the current field situation, the risks of treatment failure and delay of effective therapy by pleuromutilins, due to the high *in vitro* resistance rates and high uncertainty regarding the associated clinical outcome, are considered to outweigh the clinical benefit in a minority of field outbreaks. Moreover, product use in such conditions is associated with a risk of further resistance selection or co-selection. SPC warnings informing the user about that resistance status are not considered sufficient to mitigate that risk, notably because of the absence of interpretive criteria and standardised methods for susceptibility testing. Therefore, the benefit-risk balance in relation to the use of the concerned class of products against swine dysentery caused by *B. hyodysenteriae*, is considered to be negative due to development of acquired resistance and high uncertainty about its impact in terms of *in vivo* efficacy. The indication against swine dysentery caused by *B. hyodysenteriae*, can no longer be maintained and should be removed.

Concerning powders for use in drinking water containing a combination of lincomycin and spectinomycin to be administered orally to pigs at a dose of 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw (10 mg combined actives/kg bw) per day for 7 days is considered effective in cases of porcine proliferative enteropathy caused by *L. intracellularis*, and possible associated pathogens among which is *E. coli*. The risk for possible *in vitro* resistant strains should be included in the product information.

In chickens, powders for use in drinking water containing a combination of lincomycin and spectinomycin at a dose of 16.65 mg lincomycin and 33.35 mg spectinomycin/kg bw (50 mg combined actives/kg bw) per day for 7 days is considered effective in cases of CRD caused by *M. gallisepticum* and *E. coli,* and associated with a low mortality rate. Deletion of target species chickens from the concerned products could increase the use of antimicrobial substances currently considered as even more critical in terms of the consequences of selection of resistance and relevance for public health, such as fluoroquinolones.

The use of premixes for medicated feeding stuff or powders to be administered with the feed containing a combination of lincomycin and spectinomycin is currently recommended at relatively low doses and for prolonged periods, which infers use for growth promotion. Such use has not been associated with substantial evidence of efficacy of treatment or associated metaphylaxis; therefore, this also entails a high risk of resistance selection and treatment failure. Considering that formulations for administration in the drinking water are available, which are recommended for shorter treatment courses based on sufficient efficacy data, it is considered that the overall benefit-risk balance for premixes for medicated feeding stuff and powders to be administered with the feed containing a combination of lincomycin and spectinomycin is negative and consequently the marketing authorisations for these products should be withdrawn.

Any other product use than powders for use in drinking water entails a risk of treatment failure and of resistance development in pathogenic and commensal bacteria through unnecessary or inadequate exposure to the antimicrobial agents, and is not counterbalanced by a demonstrated benefit.

Therefore the overall benefit-risk balance for veterinary medicinal products containing a combination of lincomycin and spectinomycin as powders for use in drinking water, remains positive and the product information should be amended in line with the recommended changes in Annex III.

Grounds for withdrawal of the marketing authorisations for premixes for medicated feeding stuff and powders to be administered with the feed containing a combination of lincomycin and spectinomycin and variation of the marketing authorisations for powders for use in drinking water containing a combination of lincomycin and spectinomycin

Whereas

- the CVMP considered that the use of premixes for medicated feeding stuff containing a combination of lincomycin and spectinomycin is supported by inadequate clinical data and the currently recommended dosing regimens entails a higher risk of selection and development of resistance due to exposition to low antimicrobial levels for prolonged periods. Thus the overall benefit-risk balance for such product formulations is considered negative.
- the CVMP considered that the use of powders to be administered with the feed containing a combination of lincomycin and spectinomycin is not supported by data and the currently recommended dosing regimens entails a higher risk of selection and development of resistance due to exposition to low antimicrobial levels for prolonged periods. Thus the overall benefit-risk balance for such product formulations is considered negative.
- the CVMP considered that on the basis of the available data for powders for use in drinking water containing a combination of lincomycin and spectinomycin, the overall benefit-risk balance is positive and the product information should be amended as provided in Annex III.

the CVMP has recommended the withdrawal of the marketing authorisations for premixes for medicated feeding stuff and powders to be administered with the feed to pigs and/or chickens containing a combination of lincomycin and spectinomycin as referred in Annex I.

Furthermore the CVMP recommended variations of the marketing authorisations for powders for use in drinking water containing a combination of lincomycin and spectinomycin to be administered orally to pigs and/or chickens (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 for all powders for use in drinking water containing a combination of lincomycin and spectinomycin to be administered orally to pigs and/or chickens

Summary of product characteristics

4.1 Target species

Delete, where applicable, any references to any poultry species other than chickens.

Where the following target species have already been approved, the wording below relating to the relevant species should be used:

4.2 Indications for use, specifying the target species

Pigs

For the treatment and metaphylaxis of porcine proliferative enteropathy (ileitis) caused by *Lawsonia intracellularis*, and associated enteric pathogens (*Escherichia coli*) susceptible to lincomycin and spectinomycin.
The presence of the disease in the group must be established before the product is used.

Chickens

For the treatment and metaphylaxis of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* and *Escherichia coli* susceptible to lincomycin and spectinomycin, and associated with a low mortality rate.
The presence of the disease in the flock must be established before the product is used.

Add, to all products:

4.4 Special warnings for each target species

In *E. coli,* a significant part of the strains show high MIC values (minimum inhibitory concentrations) against the lincomycin-spectinomycin combination and may be clinically resistant, although no breakpoint is defined.

Due to technical constraints the susceptibility of *L. intracellularis is* difficult to test *in vitro*, and data about the lincomycin-spectinomycin resistance status in that species are lacking.

Where the following target species have already been approved, the wording below relating to the relevant species should be used:

4.9 Amounts to be administered and administration route

Delete, where applicable, any references to systematic/prophylactic use.

For use in drinking water.

The recommended dosage rates are:

Pigs: 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw/day, for 7 days.

Chickens: 16.65 mg lincomycin and 33.35 mg spectinomycin/kg bw/day, for 7 days.

Where the following target species have already been approved, the following withdrawal periods apply:

4.11 Withdrawal period(s)

Pigs: *To be completed nationally.*

Chickens: *To be completed nationally.*

Not authorised for use in birds producing eggs for human consumption, including replacement chicks which are intended to produce eggs for human consumption.

Animals must not be slaughtered for human consumption during treatment.

Add, to all products and delete the existing text:

5.1 Pharmacodynamic properties

Delete, where applicable, any references to swine dysentery caused by *Brachyspira hyodysenteriae*, or to other bacterial species than those specified in the indications.

Lincomycin is active against gram-positive bacteria, some anaerobic gram-negative bacteria and mycoplasmas. It has little or no action against gram-negative bacteria such as *Escherichia coli*.

Spectinomycin is an aminocyclitol antibiotic derived from *Streptomyces spectabilis*, it has bacteriostatic activity and is active against *Mycoplasma* spp. and against some gram-negative bacteria such as *E. coli*.

The mechanism by which spectinomycin administered orally acts on pathogens at the systemic level despite a poor absorption is not fully elucidated, and might rely partly on indirect effects on the gut flora.

In *E. coli* the MIC distribution appears to be bimodal, with a significant number of strains showing high MIC values; this could partly correspond to natural (intrinsic) resistance.

In vitro studies as well as clinical efficacy data show that the lincomycin-spectinomycin combination is active against *Lawsonia intracellularis.*

Due to technical constraints the susceptibility of *Lawsonia intracellularis* is difficult to test *in vitro*, and data about the resistance status in that species are lacking.

Labelling:

5. TARGET SPECIES

Delete, where applicable, any references to any poultry species other than chickens.

Package leaflet

Where the following target species have already been approved, the wording below relating to the relevant species should be used:

4. INDICATION(S)

Pigs

For the treatment and metaphylaxis of porcine proliferative enteropathy (ileitis) caused by *Lawsonia intracellularis*, and associated enteric pathogens (*Escherichia coli*) susceptible to lincomycin and spectinomycin.
The presence of the disease in the group must be established before the product is used.

Chickens

For the treatment and metaphylaxis of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* and *Escherichia coli* susceptible to lincomycin and spectinomycin, and associated with a low mortality rate.
The presence of the disease in the flock must be established before the product is used.

7. TARGET SPECIES

Delete, where applicable, any references to any poultry species other than chickens.

Where the following target species have already been approved, the wording below relating to the relevant species should be used:

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

Delete, where applicable, any references to systematic/prophylactic use.

For use in drinking water.

The recommended dosage rates are:

Pigs: 3.33 mg lincomycin and 6.67 mg spectinomycin/kg bw/day, for 7 days.

Chickens: 16.65 mg lincomycin and 33.35 mg spectinomycin/kg bw/day, for 7 days.

Where the following target species have already been approved, the following withdrawal periods apply:

10. WITHDRAWAL PERIOD

Pigs: *To be completed nationally.*

Chickens: *To be completed nationally.*

Not authorised for use in birds producing eggs for human consumption, including replacement chicks which are intended to produce eggs for human consumption.

Animals must not be slaughtered for human consumption during treatment.

Add, to all products:

12. SPECIAL WARNING(S)

Special warnings for each target species:

In *E. coli,* a significant part of the strains show high MIC values (minimum inhibitory concentrations) against the lincomycin-spectinomycin combination and may be clinically resistant, although no breakpoint is defined.

Due to technical constraints the susceptibility of *L. intracellularis is* difficult to test *in vitro*, and data about the lincomycin-spectinomycin resistance status in that species are lacking.

…