22 August 2016
EMA/462762/2016
Veterinary Medicines Division

Questions and answers on veterinary medicinal products containing a combination of lincomycin and spectinomycin to be administered orally to pigs and/or poultry

Outcome of a referral procedure under Article 35 of Directive 2001/82/EC (EMEA/V/A/110)

On 19 May 2016, the European Medicines Agency (the Agency) completed a review of the safety and effectiveness of, and antimicrobial resistance to, veterinary medicinal products containing a combination of lincomycin and spectinomycin to be administered orally to pigs and/or poultry. The Agency's Committee for Medicinal Products for Veterinary Use (CVMP) concluded 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, as the use of these products at the recommended dosing regimens entails a high risk of resistance selection and development due to exposure to low antimicrobial levels for prolonged periods. The CVMP recommended that all marketing authorisations for premixes for medicated feeding stuff and powders to be administered with the feed containing a combination of lincomycin and spectinomycin be withdrawn throughout the European Union (EU).

The CVMP also concluded that the overall benefit-risk balance for powders for use in the drinking water containing a combination of lincomycin and spectinomycin is positive and recommended harmonised indications, dosing regimens and warning sentences on prudent use.

What are lincomycin and spectinomycin?

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 the drinking water.

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Why were veterinary medicinal products containing a combination of lincomycin and spectinomycin reviewed?

In September 2012 Belgium initiated a referral procedure under Article 34 of Directive 2001/82/EC for Linco-Spectin 100, powder for use in the drinking water for pigs and chickens (EMEA/V/A/088). The procedure was concluded and on 11 July 2014 the European Commission adopted a Decision[1].

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 EU to promote effective and rational use of the lincomycin-spectinomycin combination in orally administered veterinary medicinal products, and thereby limit the risk of the development of resistance. 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.

The CVMP was requested to assess the available data and to review the indications, dosage regimens and withdrawal periods for pigs and poultry in order to ensure consumer safety, efficacious treatment in pigs, chickens and other poultry species, as well as a lower risk of the development of antimicrobial resistance to lincomycin and spectinomycin.

Which data has the CVMP reviewed?

Proprietary data and scientific references on efficacy and residue depletion were provided by the marketing authorisation holders in this Article 35 referral procedure.

What are the conclusions of the CVMP?

Based on the evaluation of the currently available data, the CVMP concluded that the overall benefit-risk balance for premixes for medicated feeding stuff and powders containing a combination of lincomycin and spectinomycin, to be administered with the feed, is negative, as the use of these products at the recommended dosing regimens entails a high risk of resistance selection and development due to exposure to low antimicrobial levels for prolonged periods. The CVMP recommended the withdrawal of the marketing authorisations for premixes for medicated feeding stuff and powders containing a combination of lincomycin and spectinomycin to be administered with feed.

The CVMP further concluded that the overall benefit-risk balance for powders for use in the drinking water containing a combination of lincomycin and spectinomycin is positive and agreed harmonised indications, dosing regimens and warning sentences on prudent use. The CVMP recommended that the marketing authorisations for powders containing a combination of lincomycin and spectinomycin for use in the drinking water should be varied in order to amend the product information accordingly. No amendments to the currently approved withdrawal periods for pigs and chicken for the aforementioned powders for use in the drinking water were considered necessary.

The full changes made to the product information for powders for use in the drinking water are detailed in Annex III of the CVMP opinion on the 'All documents' tab.

The European Commission issued a decision on 22 August 2016.

[1] Commission Decision concerning, in the framework of Article 34 of Directive 2001/82/EC of the European Parliament and of the Council, the marketing authorisations for “Linco-Spectin 100 and its associated names”, veterinary medicinal products which contain the active substances “Lincomycin and spectinomycin” ((2014)5053 of 11/07/2014) http://ec.europa.eu/health/documents/community-register/html/vo25233.htm