26 June 2017
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Veterinary Medicines Division

Questions and answers on veterinary medicinal products containing zinc oxide to be administered orally to food-producing species

Outcome of a referral procedure under Article 35 of Directive 2001/82/EC (EMEA/V/A/118)

On 16 March 2017, the European Medicines Agency (the Agency) completed a review of the safety and effectiveness of veterinary medicinal products containing zinc oxide to be administered orally to food-producing species. The Agency's Committee for Medicinal Products for Veterinary Use (CVMP) concluded that the overall benefit-risk balance for veterinary medicinal products containing zinc oxide to be administered orally to pigs is negative, as the benefits of zinc oxide for the prevention of diarrhoea in pigs do not outweigh the risks for the environment. The CVMP recommended the refusal of the granting of the marketing authorisations and the withdrawal of the existing marketing authorisations for veterinary medicinal products containing zinc oxide.

What is zinc oxide?

Zinc oxide is an inorganic compound and is known to be relatively poorly absorbed. Veterinary medicinal products containing zinc oxide are used for the treatment and/or prevention and control of post-weaning diarrhoea in piglets. Different indications and dosages are currently recommended, but zinc oxide is mainly used in the feed at a dosage of 100 mg per kg body weight per day for 14 consecutive days, which equates to 2500 ppm zinc in feed.

Why were orally-administered veterinary medicinal products containing zinc oxide reviewed?

In May 2015, following a referral procedure (EMEA/V/A/108) under Article 33(4) of Directive 2001/82/EC for Gutal 1000 g/kg premix for medicated feeding stuff for piglets[1], the CVMP identified a risk to the environment due to accumulation of zinc. The CVMP considered that there is some uncertainty associated with the calculated risks for some environmental compartments and recommended various risk mitigation measures, which were anticipated to reduce the accumulation of zinc in the environment.

[1] CVMP opinion on Article 33(4) referral for Gutal 1000 g/kg premix for medicated feeding stuff for piglets (Procedure no. EMEA/V/A/108) - link

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Nevertheless, in February 2016, due to remaining concerns related to the risk to the environment and the potential increase of prevalence of antibiotic resistant bacteria from the use of products containing zinc oxide, the Netherlands and France initiated a referral procedure under Article 35 of Directive 2001/82/EC for all orally-administered veterinary medicinal products containing zinc oxide and requested the CVMP to review all available data and to evaluate the overall benefit-risk balance of the products concerned.

Which data has the CVMP reviewed?

The applicants and marketing authorisation holders concerned by the referral procedure submitted proprietary data and scientific references on efficacy, antimicrobial resistance and environmental risk.

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 veterinary medicinal products containing zinc oxide to be administered orally to pigs is negative, as the benefits of zinc oxide for the prevention of diarrhoea in pigs do not outweigh the risks for the environment. The CVMP acknowledged that there is a risk of co-selection for resistance (the selection of multiple antimicrobial resistance genes by an antimicrobial) associated with the use of zinc oxide but that, at the present time, such risk is not quantifiable. Effective measures to manage the accumulation of zinc in the environment were not identified and, as a result, the CVMP recommended the refusal of the granting of the marketing authorisations and the withdrawal of the existing marketing authorisations for veterinary medicinal products containing zinc oxide.

The European Commission issued a decision on 26 June 2017 and Member States may defer the withdrawal of the marketing authorisations for up to five years from this date, if they consider that immediate action may have adverse impact in their territory given the lack of availability of alternatives and the change required in pig farming practices.