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Veterinary Medicines Division

Questions and answers on Closamectin Pour-On Solution and associated names

Outcome of a procedure under Article 78 of Directive 2001/82/EC

On 8 October 2015, the European Medicines Agency (the Agency) completed a review of the animal safety of Closamectin Pour-On Solution and associated names. The Agency's Committee for Medicinal Products for Veterinary Use (CVMP) concluded that the benefits of Closamectin Pour-On Solution and associated names continue to outweigh their risks subject to variation of the marketing authorisations to include new adverse reactions and precautionary measures and conditions concerning risk mitigation and surveillance measures.

What is Closamectin Pour-On Solution and associated names?

Closamectin Pour-On Solution and associated names contain closantel and ivermectin and are authorised in several European Union (EU) Member States[1] via decentralised and national procedures. The products are effective for use in beef cattle for the treatment of mixed trematode (fluke) and nematode or arthropod infestations due to roundworms, lungworms, eyeworms, warbles, mites and lice.

Why were Closamectin Pour-On Solution and associated names reviewed?

Between 25 May 2011 and 31 May 2015 the French medicines regulatory agency (Agence Nationale du Médicament Vétérinaire (ANMV)) received a total of 123 adverse event reports involving CLOSAMECTIN POUR-ON POUR BOVINS in which 401 animals were affected and 121 died. The adverse events principally related to neurological signs (ataxia, recumbency, paresis/paralysis and blindness) and/or gastrointestinal disorders (diarrhoea, anorexia etc.) some of which had a fatal outcome. The nature of the reported clinical signs was considered by ANMV to be indicative of the clinical signs associated with overdose toxicity of closantel. Although the overall incidence of adverse events was considered to be within acceptable limits (0.006% in the last annual periodic safety update report) the continued occurrence of serious adverse events and the severity of subsequent losses on farms in France were considered significant, which led to the suspension of the marketing authorisation in France on 6 July 2015. The product was also recalled at veterinary clinic and wholesale level.

[1] Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, Poland, Portugal, Romania, Spain, Sweden, Slovenia, Slovakia and the United Kingdom

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On 19 June 2015, France triggered a procedure under Article 78 of Directive 2001/82/EC for Closamectin Pour-On Solution and associated names following evaluation of pharmacovigilance data indicating serious concerns for animal safety and subsequent suspension of the marketing authorisation for the product. Accordingly, the CVMP was requested to give its opinion on the matter concerning animal safety.

Which data has the CVMP reviewed?

To investigate the potential relation between the adverse events observed and Closamectin Pour-On Solution and associated names, the CVMP considered the data provided by the marketing authorisation holder (MAH). This included a review of scientific literature regarding the pharmacology and toxicology of ivermectin and closantel, cumulative pharmacovigilance experience following use of the products in the EU since 2009, a comparison with ivermectin-based products and with ivermectin/closantel injectable formulations held by the MAH, investigations carried out by the MAH to identify possible factors involved in reported adverse events and proposals for risk mitigation measures and actions.

What are the conclusions of the CVMP?

Based on the evaluation of the currently available data and the scientific discussion within the Committee, the CVMP concluded that the benefits of Closamectin Pour-On Solution and associated names continue to outweigh their risks subject to:

- variation of the marketing authorisations for Closamectin Pour-On Solution and associated names to amend the summary of product characteristics and package leaflet to include new precautionary measures and adverse reactions; and
- conditions of the marketing authorisations concerning risk mitigation and surveillance measures.

It was also recommended that the suspension of the marketing authorisation for CLOSAMECTIN POUR-ON SOLUTION POUR BOVINS in France be lifted.

The European Commission issued a decision on 22 March 2016.