European Medicines Agency
*Veterinary Medicines and Inspections*

London, 30 April 2009
EMEA/681319/2008

# COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

## OPINION FOLLOWING AN ARTICLE 78[1] PROCEDURE FOR

**Veterinary medicinal products containing**

**Alpha2-adrenoreceptor agonists[2]**

(International Non-Proprietary Name (INN): Xylazine, Medetomidine, Detomidine, Romifidine)

## BACKGROUND INFORMATION

Alpha2-adrenoreceptor agonists are pharmaceutically active substances that are commonly used to induce effects such as sedation, analgesia and muscle relaxation. Xylazine, detomidine, medetomidine and romifidine are alpha2-adrenoreceptor agonists.

The College Ter Beoordeling van Geneesmiddelen (Medicines Evaluation Board, The Netherlands), in accordance with Article 78(1) of Directive 2001/82/EC, as amended by Directive 2004/28/EC, informed the EMEA by a letter dated 25 August 2006 of its intention to vary the marketing authorisation and to add a new precautionary measure for 21 veterinary medicinal products containing alpha2-adrenoreceptor agonists authorised in The Netherlands.

The basis for the notification was a suspected adverse reaction report received in The Netherlands after a veterinarian accidentally injected himself with the product Sedivet, which contains romifidine as the active ingredient. The veterinarian experienced cardiovascular and central nervous system effects over a period of 3 days. The extrapolation of the proposed warnings for one alpha2-adrenoreceptor agonist to other alpha2-adrenoreceptor agonists was considered justified, since the pharmacological mode of action is the same and because several of the substances have shown similar effects in humans.

In accordance with Article 78(3) of Directive 2001/82/EC, as amended, the Committee for Medicinal Products for Veterinary Use (CVMP) is to give its opinion on the conclusions and intended risk management measures presented by the notifying Authority which in this procedure was the Dutch Medicines Evaluation Board.

On 13 September 2006 the procedure was initiated by adoption of a list of questions to be put to the concerned Marketing Authorisation Holders. Dr Anja Holm was appointed as Rapporteur and Dr Peter Ekström as Co-Rapporteur. Written explanations were provided by the Marketing Authorisation Holders on 13 October 2006.

[1] Article 78 of Directive 2001/82/EC, as amended
[2] See Annex I for the complete list of concerned products

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 84 47
E-mail: mail@emea.europa.eu http://www.emea.europa.eu
© European Medicines Agency, 2009. Reproduction is authorised provided the source is acknowledged.

During its December 2006 meeting, the CVMP, in light of the overall data submitted, additional data from the public domain and the scientific discussion within the Committee, adopted by consensus an opinion concerning the 21 veterinary medicinal products as authorised in the Netherlands. The extrapolation of the proposed warnings for one alpha2-adrenoreceptor agonist to other alpha2-adrenoreceptor agonists was considered justified, since the pharmacological mode of action is the same and because several of the substances have shown similar effects in humans. The concerned Marketing Authorisation Holders were informed accordingly by a letter dated 13 December 2006. The assessment report and the opinion were transferred to the European Commission for decision.

Following further communication with the European Commission in years 2007 and 2008 on the opinion and the scope of the procedure, the CVMP in the July 2008 plenary meeting agreed to complete the procedure under Article 78 of Directive 2001/82/EC, as amended, for all marketing authorisations held in the EU for the 21 products containing alpha2-adrenoreceptor agonists initially notified and to revise the initial opinion accordingly. Member States identified and informed the Agency of the concerned marketing authorisations in their respective territories. A revised list of questions addressed to the concerned Marketing Authorisation Holders was adopted on 16 July 2008. The Committee reconfirmed Dr A. Holm as Rapporteur and Dr P. Ekström as Co-Rapporteur for the procedure. Written responses were received by Marketing Authorisation Holders for 81 of the 108 notified authorisations held by a total of 66 Marketing Authorisation Holders by 16 September 2008. No new substantial data was provided by any of the responding Marketing Authorisation Holders and therefore the assessment remains based on the data considered in 2006.

The CVMP concluded that, on the basis of the available data, there is at present a potential risk to human health posed by the use of products containing alpha2-adrenoreceptor agonists, and issued a revised opinion on 12 November 2008.

The Committee considered that specific precautionary measures should be reflected in the product literature of concerned products containing alpha2-agonists.

Additionally, the CVMP concluded that the need for updating the product literature to reflect the matters above is not urgent.

The list of product names concerned is given in the Annex I. The scientific conclusions are provided in the Annex II.

The final opinion was converted into a Decision by the European Commission on 30 April 2009.