European Medicines Agency
Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

OPINION FOLLOWING AN ARTICLE 33 (4) REFERRAL

FOR ENURACE 50

BACKGROUND INFORMATION

Enurace 50 is a tablet formulation containing ephedrine as active ingredient and is indicated for treatment of urinary incontinence caused by urethral sphincter mechanism incompetence in ovario-hysterectomised dogs.

In June 2006 a Mutual Recognition Procedure started with The Netherlands as Reference Member State and six Concerned Member States.

France and Italy could not agree to the granting of a marketing authorisation as they considered there were potentially serious risks for animal health. The matter was referred to the Co-ordination Group for Mutual Recognition and Decentralised Procedures CMD(v) and subsequently to the Committee for Medicinal Products for Veterinary Use.

France considered the benefit/risk analysis unfavourable for the animal when the adverse effects were weighed against the potential benefits of effective treatment of incontinence. Italy could have accepted the application but with revised wording in the SPC.

The CVMP during its meeting of December 2006 started a referral procedure under Article 33(4) of Directive 2001/82/EC as amended for Enurace 50. The Marketing Authorisation Holder was requested to provide all supporting data to justify a positive benefit/risk ratio for the treated animal.

In response to the questions related to toxicity, the applicant argued that due to the pharmacologic effect of ephedrine and the individual variation in receptor density no safety margin could be determined and increasing doses will be associated to increased intensity and frequency of well known adverse effects. This conclusion was accepted. Although toxicity data for the target animal may be scarce, the adverse effects connected to ephedrine treatment are well known from human use, and the applicant had provided some post-marketing information regarding the use in dogs. At the recommended dose level, which according to the suggested SPC should be individually adjusted, safety is ensured to a reasonable level.

With regard to the related to cardiovascular diseases, the SPC is to be modified under section 4.5 to include the sentence “the dog’s cardiovascular functionality should be carefully assessed before the start of the treatment with Enurace 50 and it should be periodically monitored during the treatment”. Efficacy data are connected to several shortcomings and the amount of data available is sparse. However, the study where Enurace 50 is compared to Propaline (ACE129802) is convincing although a non-inferiority analysis has not been performed. The raw outcome shows good effect in both test and control groups, an effect that might be somewhat higher in treatment naïve animals.

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These results were convincing when compared to the 20 % placebo treated animals that became continent in study ACE129801.

The CVMP, therefore, concluded that the benefit/risk for this product was favourable.

The CVMP Opinion was adopted on 18 April 2007 and the subsequent Commission Decision on 10 July 2007.
