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 DOLOVET

BACKGROUND INFORMATION

Dolovet vet 2.4g oral powder is a powder presented in sachets of 15g, each containing 2.4g ketoprofen and is authorised for the treatment of fever and inflammation in cattle.

A Mutual Recognition Procedure (MRP) started on 22 September 2005 with Finland acting as Reference Member State and twelve Concerned Member States.

Belgium and Norway could not agree with granting a marketing authorisation. They considered the product to present a potential serious risk 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 (CVMP).

Belgium and Norway considered that this medicinal product could present a potential serious risk to animal health on the grounds that the efficacy had not been sufficiently substantiated in the dossier.

The CVMP during its meeting of 14-16 March 2006 started a referral procedure under Article 33(4) of Directive 2001/82/EC, as amended. The Marketing Authorisation Holder (MAH) was requested to substantiate the efficacy of the product.

A dose confirmation study was submitted with the response. The experimental design of the study mimicked acute toxic mastitis. The statistical report indicated that the number of animals used did not allow equivalence to be established (nor non-inferiority) between Dolovet containing ketoprofen administered orally at the dose of 4 mg/kg bodyweight and Ketofen containing ketoprofen administered intramuscularly at the dose of 3 mg/kg.

However, given that the pharmacokinetic data allowed the optimisation of the dose (keeping overall exposure comparable between the two products), it was concluded that a bridge existed allowing well established use to apply to Dolovet. Even though equivalence has not been formally shown, the two products perform similarly when compared to placebo in regards to a number of critical parameters, both clinical and otherwise (thromboxane B2 levels in plasma). If one accepts that a bridge exists, then the clinical indications that exist for Ketofen, as evidenced in the literature, should apply in large part to Dolovet. For example, in generic applications, a preclinical bridge is made that allows extrapolation to the field situation. For generic applications bioequivalence must be demonstrated. For well-established use dossiers the bridge can be constructed more tentatively.

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To restrict the indications of Dolovet to only those that were tested (endotoxemic mastitis control) would be inappropriate.

Reducing of pyrexia or fever and alleviation of inflammation are considered important clinical claims that should be retained as they have been sufficiently well demonstrated.

Considering the data provided and the well-established use of ketoprofen, the CVMP was of the opinion that the claim “Alleviation of inflammation and reduction of fever in individual animals” had been substantiated.

The CVMP Opinion was adopted on 9 November 2006 and the subsequent Commission Decision on 17 April 2007.
