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Veterinary Medicines and Product Data Management

EPAR Scientific Discussion post-authorisation update for Rheumocam extension X/006

Scope of extension: addition of 15 mg/ml oral suspension for horses

Rheumocam 15 mg/ml Oral Suspension for Horses

An application for an extension of the Community marketing authorisation for Rheumocam to include a 15 mg/ml oral suspension for horses was submitted to the European Medicines Agency on 26 October 2009 by Chanelle Pharmaceuticals Manufacturing Limited in accordance with article 2(a) of Commission Regulation (EC) No 1085/2003 and annex II thereof.

Rheumocam 15 mg/ml oral suspension for horses is indicated for the alleviation of inflammation and relief of pain in both acute and chronic musculo-skeletal disorders in horses. The route of administration is oral. The target species is horses.

Part 1 – Administrative particulars

The description of Chanelle Pharmaceuticals Manufacturing Limited's pharmacovigilance system globally fulfils the current legal requirements. Relevant details were provided on the manufacturing sites.

Part 2 - Quality

Composition

Rheumocam 15 mg/ml oral suspension for horses contains 15 mg/ml of meloxicam as active ingredient. Various excipients are present in the formulation including a preservative and a honey flavour.

Container

The product Rheumocam 15 mg/ml oral suspension for horses is presented in HDPE bottles of 100 and 250 ml with a measuring syringe. The applicant has demonstrated that a reproducible and accurate dose of the product is delivered with the measuring syringe under testing conditions which take due account of the range of the proposed dosage regimen.

Development pharmaceutics

Rheumocam 15 mg/ml oral suspension for horses has been formulated to be bioequivalent to the reference product Metacam 15 mg/ml oral suspension for horses.

The anti-microbial preservative efficacy testing has been performed according to the European Pharmacopoeia (Ph.Eur.) and shows a satisfactory antimicrobial efficacy of the sodium benzoate in the finished product at the low limit.

Method of manufacture

The finished product is manufactured according to a standard process in which the in-process controls guarantee the reproducibility of the manufacture. The validation of the manufacturing process has been satisfactorily demonstrated.

Control of starting materials

Active substance

The active substance, meloxicam, is described in the Ph.Eur. and data were submitted in an Active Substance Master File which has been assessed for the previous applications for Rheumocam 1.5 mg/ml oral suspension for dogs and Rheumocam chewable tablets for dogs.

Excipients

The excipients are described in the Ph.Eur. except the honey flavour for which supplier's data are provided. This excipient is also used in Rheumocam 1.5 mg/ml oral suspension for dogs.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

No input materials used for the production of the finished product fall within the scope of the guidance document "Note for guidance on minimising the risk of Transmitting Animal Spongiform Encephalopathy agents via Human and Veterinary Medicinal Products" (EMEA/410/01).

Control tests during production

The in-process controls described in the dossier are satisfactory.

Control tests on the finished product

The release specifications of the finished product are considered acceptable for this type of dosage form. The control methods used in the control of the finished product at release are well validated.

Stability

The proposed retest period for the active substance was described and considered acceptable. Results from storage of batches of the substance for up to 60 months at 25°C/ 60% RH[1], at 30°C/ 70% RH and for 6 months at 40°C/ 75% RH are available. No relevant changes were observed.

Results from storage of the finished product were also presented. Batches have been stored for 18 months at 25°C/ 60% RH and for 6 months at 40°C/ 75% RH. Based on the current results, the proposed shelf-life of 36 months is accepted.

The applicant has provided an in-use stability study at 3 months. Based on the available results, the 3-month in-use shelf-life is accepted.

Overall conclusions on quality

The quality of the product as described in the dossier is acceptable.

Part 3 – Safety

As this application is made in accordance with Article 13.1(a) (iii) of Directive 2001/82/EC, as amended (i.e. a generic product), the toxicological profile of meloxicam does not need to be reassessed. The applicant has provided a user risk assessment that was conducted in accordance with the current guideline on user safety for pharmaceutical veterinary medicinal products (EMEA/CVMP/543/03-FINAL). Based on the fact that bioequivalence is claimed with Metacam oral suspension for horses, that the excipients included in the formulations are considered safe[2] and that the posology and indications are identical to those of the reference product Metacam, it can be accepted that the potential hazard to the user posed by Rheumocam oral suspension for horses will not be any greater than that posed by the reference product. The proposed user safety statements are considered appropriate.

The product is intended to be used in horses for the alleviation of inflammation and pain in both acute and chronic musculo-skeletal disorders.

Based on the Phase I decision tree, as the product is intended for the treatment of individual animals, the environmental risk assessment can end at Phase I and no further data on environmental risk assessment are deemed necessary.

This is a generic application for a product administered by the oral route. As bioequivalence is correctly demonstrated between the new product, Rheumocam 15 mg/ml oral suspension for horses, and the reference product, Metacam 15 mg/ml oral suspension for horses, it is not necessary to perform residue depletion studies with the new product. The established withdrawal period of the reference product will be applied for the new product, i.e. 3 days. From a consumer safety perspective, all excipients were considered safe as used in the product.

In the SPC, in section 4.11, the following labelling has been added for the withdrawal period of milk "Not authorised for use in lactating animals producing milk for human consumption."

[1] RH: Relative Humidity
[2] The excipients listed in section 6.1 of the SPC are either allowed substances for which table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or are considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this product.

Part 4 – Efficacy

A GLP bioequivalence study was performed in horses between Metacam and Rheumocam 15 mg/ml oral suspension for horses following single oral administration of meloxicam at 0.6 mg/kg bodyweight. This study was correctly performed (design, target species, treatment). The analytical method used to assay meloxicam in plasma samples was correctly validated. From the data, the bioequivalence of two products is demonstrated, i.e. Rheumocam 15 mg/ml oral suspension for horses is bioequivalent with Metacam 15 mg/ml oral suspension for horses. From this study, it was also shown that, at the claimed dose, the product is well tolerated. Section 5 of the SPC of Rheumocan 15 mg/ml oral suspension for horses is identical to the SPC of Metacam 15 mg/ml oral suspension for horses.

As bioequivalence has been demonstrated, the expected efficacy and tolerance profile in the field is the same as that of the reference product.

Part 5 – Benefit Risk Assessment

The application for Rheumocam 15 mg/ml oral suspension for horses is a generic application. The product was developed in such a way as to closely resemble the formulation of the originator product, Metacam 15 mg/ml oral suspension for horses.

The active substance, meloxicam, is a well known non-steroidal anti-inflammatory drug in veterinary medicine. It has been included in other formulations of Rheumocam which have already been authorised (oral suspension for dogs, chewable tablets for dogs). The primary mode of action of meloxicam is inhibition of cyclo-oxygenases in the arachidonic acid inflammatory pathway. It is beneficial in the alleviation of inflammation and pain in both acute and chronic musculoskeletal disorders, including in horses.

Since bioequivalence was demonstrated *in vivo* between the two products, Rheumocam 15 mg/ml oral suspension for horses is expected to be as safe and efficacious as Metacam 15 mg/ml oral suspension for horses.

The product is presented as an oral suspension with honey flavour for easy administration to horses. The risks identified for this product are strictly the same as those that exist for the reference product. No negative impact on the environment is anticipated. The SPC and product literature are identical to those of the reference product.

Following authorisation by the Commission, periodic safety update reports for Rheumocam will be required at 6-monthly intervals for the first two years, yearly for the next two years and thereafter at 3-yearly intervals. This was considered necessary to ensure more frequent pharmacovigilance monitoring in view of the extension of the indications to a new target species (horses).

The overall benefit risk balance is deemed positive. Based on the original and complementary data presented, it is concluded that the quality, safety, and efficacy of Rheumocam 15 mg/ml Oral Suspension for Horses were considered to be in accordance with the requirements of Directive 2001/82/EC, as amended.