Agencia Española de Medicamentos y Productos Sanitarios

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28022 – Madrid
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PROCEDURE ES/V/0160/001/DC

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0160/001/DC
Name, strength and pharmaceutical form	KELAPROFEN 100 mg/ml solution for injection for cattle, horses and pigs.
Applicant	KELA N.V., St. Lenaartseweg 48, 2320 Hoogstraten, Belgium.
Active substance(s)	Ketoprofen
ATC Vet code	QM01AE03
Target species	Cattle, horses and pigs
Indication for use	Horse - the alleviation of inflammation and pain associated with musculoskeletal disorders; - the alleviation of visceral pain associated with colic. Cattle - the supportive treatment of parturient paresis associated with calving; - reducing the pyrexia and distress associated with bacterial respiratory disease when used in conjunction with antimicrobial therapy as appropriate; - improving the recovery rate in acute clinical mastitis, including acute endotoxin mastitis, caused by gram negative micro-organisms, in conjunction with antimicrobial therapy; - reducing oedema of the udder associated with calving. Pigs - reducing the pyrexia and respiratory rate associated with bacterial or viral respiratory disease when used in conjunction with antimicrobial therapy as appropriate; - the supportive treatment of Mastitis Metritis Agalactia Syndrome in sows, in conjunction with antimicrobial therapy as appropriate.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (http://www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 44 of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	29/08/2011
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	BE, CY, CZ, DE, EE, FR, HU, IE, LT, LU, NL, PL, RO, UK

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.
It has been shown that the product can be safely used in the target species; the slight reactions observed are indicated in the SPC.
The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

For applications based on informed consent to another authorisation:

The quality / safety / efficacy aspects of this product is/are identical to original product. The initial application for original product was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

II. QUALITY ASPECTS

A. Composition

The product contains 100 mg of ketoprofen and L arginine, benzyl alcohol (E1519), citric acid monohydrate (E330) and water for injections as excipients.

The product is packed in 50, 100 ml or 250 ml amber glass vials type II. For closing the vial, a rubber closure type I is used, specifically a bromobutyl stopper, over which, for sealing the set, an aluminium capsule is placed. The aluminium overseals are not in contact with the product and follow in house specifications. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the presence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is ketoprofen an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

A copy of the European Pharmacopoeia Certificate of Suitability has been provided.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

F. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

G. Stability

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

The claim of 28 days stability after broaching is based on the demonstration of stability for a batch broached and stored 28 days at 25°C.

III. SAFETY AND RESIDUES ASSESSMENT

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with a reference product has been demonstrated, results of safety and residue tests are not required, except for species that the product is administered intramuscularly which a residue tests was submitted.

The aspects of safety of this product are identical to the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing

Pharmacological Studies

The applicant has not submitted results of safety test since the application was presented according to Article 13 (1) of Directive 2001/82/EC, as amended.

Toxicological Studies

The applicant has not submitted results of safety test since the application was presented according to Article 13 (1) of Directive 2001/82/EC, as amended.

User Safety

The applicant submitted a user safety assessment in compliance with the relevant guideline which showed that no further assessment is required.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

Bioequivalence with the reference product was demonstrated. However, differences at the injection site could occur and thus residue depletion studies were conducted in cattle and pig using the final formulation by intramuscular route.

Concentrations of ketoprofen and its metabolite (RP69400) in target tissues of each animal were quantitated in order to calculate the percent residue with pharmacological activity with respect to the ADI.

The analytical method was LCMS/MS. The method was fully validated.

MRLs

Ketoprofen is mentioned in Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin and no MRL is required.

Withdrawal Periods

Based on the data provided the following withdrawal periods were established:

Cattle:
Meat and offal:
- IV: 1 day
- IM: 2 days

Milk: zero hours

Horses:
Meat and offal: 1 day
Milk: Not authorised for use in lactating animals producing milk for human consumption

Pigs:

Meat and offal: 2 days

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

The applicant has submitted two bioequivalence studies performed between the products: Ketofen 10% RTU and Kelaprofen 10% for target species: cattle and pig.
A single intramuscular injection was administered to an appropriate number of animals. The pivotal parameters to demonstrate bioequivalence are the Area Under the concentration/time Curve (AUC) and Cmax (peak concentration).

In pigs, confidence intervals calculated from Cmax and AUC were within the stipulated range of 80-125%, bioequivalence was therefore established.

In cattle, the confidence intervals calculated were within the equivalence bounds: from AUC 80-125% and from Cmax 70-143%

Tolerance in the Target Species of Animals

Local and systemic tolerance was monitored after intramuscular administration during the bioequivalence studies. Separate tolerance animal studies were not done.

IV.B Clinical Studies

The applicant has not submitted results of clinical studies since the application was presented according to Article 13 (1) of Directive 2001/82/EC, as amended

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the veterinary Heads of Agencies website (www.hma.eu).

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

None