Bundesamt für Sicherheit
im Gesundheitswesen

BASG - Federal Office for Safety in Health Care

AGES - Austrian Agency for Health and Food Safety
Traisengasse 5, A-1200 Vienna
www.basg.gv.at

Company:
Richter Pharma AG

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Rifen 100 mg/ml - Injektionslösung für Pferde, Rinder und Schweine

AT/V/0002/001/MR

Last update: 14.08.2018

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH l Austrian Agency for Health and Food Safety Traisengasse 5 l 1200 Vienna l AUSTRIA l www.ages.at
DVR: 0014541 l Registration court: Vienna Commercial Court l Commercial register: FN 223056z l VAT No.: ATU 54088605

Modules 1-3 reflect the scientific discussion for the approval of Rifen 100 mg/ml - Injektionslösung für Pferde, Rinder und Schweine. The procedure was finalised on 21/12/2007. For information on changes after this date please refer to module 4.

MODULE 1

PRODUCT SUMMARY

EU procedure number	AT/V/0002/001/MR
Name, strength and pharmaceutical form	Rifen 100 mg/ml - Injektionslösung für Pferde, Rinder und Schweine
Applicant	Richter Pharma AG Feldgasse 19 4600 Wels / Austria
Active substance(s)	KETOPROFEN
ATCvet code	QM01AE03
Target species	Horse, cattle, swine
Indication for use	Horses: For treatment of diseases affecting the osteoarticular and muscular-skeletal system associated with acute pain and inflammation (lameness of traumatic origin, arthritis, osteitis, spavin, tendinitis, bursitis, naviculitis, laminitis, myositis). Ketoprofen is also indicated for postsurgical inflammation, symptomatic therapy of colic and fever. Cattle: For treatment of diseases associated with inflammation, pain or fever (respiratory diseases, mastitis, osteoarticular and muscular-skeletal disorders such as lameness, arthritis and to ease uprise post parturition, Injuries) Swine: For treatment of diseases associated with inflammation, pain or fever (MMA – Syndrome, respiratory tract infections, symptomatic treatment of fever). For the short-term relief of postoperative pain associated with minor soft tissue surgery such as castration in piglets.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Reference medicinal product	Romefen 10% - Injektionslösung für Tiere (Solution for injection for animals)
Date of completion of the original mutual recognition procedure	21/12/2007
Date product first authorised in the Reference Member State (MRP only)	02/03/2007
Concerned Member States for original procedure	CZ, ES, FI, HU, IT, SE, SK
Concerned Member States for RUP 1st wave	DE, EL, FR, IE, LV, NL, PT, UK
Concerned Member States for RUP 2nd wave	BE, DK, PL

I. SCIENTIFIC OVERVIEW

Rifen 100 mg/ml solution for injection for horses, cattle and swine contains the active substance Ketoprofen. The product is indicated for use in diseases associated with inflammation, pain or fever in cattle and swine and for the short-term relief of post-operative pain associated with minor soft tissue surgery such as castration in piglets. In horses the product is indicated for use in diseases affecting the osteoarticular and muscular-skeletal system associated with acute pain and inflammation and for postsurgical inflammation, symptomatic therapy of colic and fever.

In horses the dose rate is 2.2 mg Ketoprofen per kg body weight and day intravenously once daily for up to 3 to 5 consecutive days, i.e. 1 ml per 45 kg body weight. In order to treat colic one injection is normally sufficient. A second administration of Ketoprofen requires a reassessment of the patient's clinical status. In cattle the dose rate is 3 mg Ketoprofen per kg body weight and day intravenously or deep intramuscularly once daily for up to 3 consecutive days, i.e. 3 ml per 100 kg body weight. In swine the dose rate is 3 mg Ketoprofen per kg body weight as a single deep intramuscular injection, i.e. 3 ml per 100 kg body weight. For reduction of post-operative pain in swine the product should be injected 10 - 30 minutes before surgical intervention. Particular care should be taken with regard to the accuracy of dosing including the use of an appropriate dosing device (i.e.: low dose syringe) and proper determination of body weight.

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 (see 4.6 "adverse reactions").

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.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains:

Active substance Ketoprofen 100 mg and the excipient(s) Benzyl alcohol, Arginine, Citric acid monohydrate and water for injection.

The container/closure systems are 50 ml or 100 ml amber glass vials type II, with bromobutyl rubber stopper type I and aluminium caps.

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 at a licensed manufacturing site.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

The active substance is Ketoprofen. 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.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

D. Control on intermediate products (pharmaceuticals)

Not applicable.

E. 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.

F. 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 stability after opening the immediate packaging is acceptable, for details see section 6.3 of SPC.

G. Other Information

Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years

Shelf-life after first opening the immediate packaging: 28 days

Special precautions for storage

Keep the glass vial in the outer carton in order to protect from light.

After first opening the immediate packaging do not store above 25 °C.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, data on pharmacodynamics and pharmacokinetics are not required as it has already been presented for the reference product.

Toxicological Studies

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, this information is not required as it has already been presented for the reference product.

User Safety

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, a detailed user safety is not required.

Nevertheless the applicant provided a satisfactory user risk assessment, identifying the risk to the users of the product and the potential routes of exposure. This showed that the most likely route of exposure to the product would be via accidental self-injection. As Ketoprofen has been described as a substance with low toxicity in humans even in acute overdose it is considered that Ketoprofen does not present any risk for the consumer.
Warnings and precautions as listed on the SPC and product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The environmental risk assessment demonstrated that use of Rifen would not result in extensive environmental exposure.
Warnings and precautions as listed on the SPC and product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, no residue depletion studies were conducted. The residue depletion profile is deemed as essentially similar to the reference medicinal product.

Withdrawal Periods

The withdrawal period(s) for the proposed product is/are the same as those of the reference product, as follows:

Meat and offal: 4 days

Milk (cattle): Zero hours

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, this information is not required as it has already been presented for the reference product.

Tolerance in the Target Species of Animals

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, this information is not required as it has already been presented for the reference product.

IV.B Clinical Studies

Laboratory Trials

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, this information is not required as it has already been presented for the reference product.

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 Heads of Veterinary Medicines 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.

Significant changes

Summary of change **(Application number)**	**Approval date**
AT/V/0002/001/E/001 This marketing authorization was extended to other MS and therefore reassessed.	13/08/2009
AT/V/0002/001/II/007 Addition of a new therapeutic indication	14/12/2011
AT/V/0002/001/E/002 This marketing authorization was extended to other MS and therefore reassessed.	08/05/2012
AT/V/0002/001/R/001 This marketing authorization was renewed unlimited.	15/11/2012
AT/V/0002/001/IB/010 Change in the invented name of the medicinal product in FR, IE, NL, UK	27/04/2013