Institute for State Control of Veterinary Biologicals and Medicines
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621 00 Brno
Czech Republic
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Rivalgin 500 mg/ml solution for injection
(BE, BG, CZ, ES, HR, HU, IT, LT, PT)

Rivalgin vet. 500 mg/ml solution for injection
(DK, IS, NO)

MODULE 1

PRODUCT SUMMARY

EU Procedure number	CZ/V/0152/001/DC
Name, strength and pharmaceutical form	Rivalgin 500 mg/ml solution for injection (BE, BG, CZ, ES, HR, HU, IT, LT, PT) Rivalgin vet. 500 mg/ml solution for injection (DK, IS, NO)
Applicant	Richter Pharma AG, Feldgasse 19, 4600 Wels, Austria
Active substance(s)	Metamizole sodium monohydrate
ATCvet code	QN02BB02
Target species	Horses, cattle, pigs, dogs.
Indication for use	Diseases of horses, cattle, pigs and dogs where a positive effect of the central analgesic, spasmolytic, antipyretic or low anti-inflammatory effects of the product can be expected, such as: General pain relief to suppress nervousness and defensive reactions caused by pain. Attenuation of pain in colic conditions of varying origins or spastic states of the internal organs in horses and cattle. Occlusion of the oesophagus with foreign bodies in horses, cattle and pigs. Feverish illnesses such as severe mastitis, MMA syndrome, swine flu. Lumbago, tetanus (in combination with tetanus antiserum). Acute and chronic arthritis, rheumatic states of muscles and joints, nerve inflammation, neuralgia, tendovaginitis.

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.
Date of completion of the original decentralised procedure	03/07/2019
Date product first authorised in the Reference Member State (MRP only)	NA
Concerned Member States for original procedure	BE, BG, DK, ES, HR, HU, IS, IT, LT, NO, PT

I. SCIENTIFIC OVERVIEW

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.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 500 mg/ml of metamizole sodium monohydrate (which is equivalent to 443.1 mg/ml of metamizole) and the excipients benzyl alcohol and water for injections.

The container-closure system is 100ml clear glass vial type II with bromobutyl rubber stopper and aluminium pull-off or aluminium/plastic flip-off cap.

The choice of the presence of preservative is 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 at 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 metamizole sodium monohydrate, 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.

Scientific data and a certificate of suitability issued by the EDQM 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

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 has been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substance has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

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 shelf-life after first opening is supported by adequate in-use stability data.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

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 tests are not required. The formulation of this product is identical to the reference product.

III.A Safety Testing

Observations in Humans

Metamizole is used in human medicine and the effects in humans are well documented. The applicant has provided bibliographical data which show the side effects of metamizole treatment in humans. The main adverse reactions are agranulocytosis, anaphylactic shock and skin disorders. The therapeutic dose recommended for humans can be reached even in case of accidental self-injection of a small volume (2 ml) of the product and therefore appropriate safety warnings are necessary to be included in the SPC.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that risks for the user listed in the SmPC are acceptable. Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to users.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will be used to treat a small number of animals in a flock or herd. Warnings and precautions as listed on the product literature are adequate to ensure safety to environment of the product.

III.B Residues documentation

Residue Studies

The applicant has submitted the generic application in accordance with Article 13(1) of Directive 2001/82/EC, as amended. No residue depletion studies were required at this case.

MRLs

According to the Annex I of Commission Regulation (EU) No. 37/2010 – following MRLs have been established for the active substance:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
Active substance					
Metamizole	4-Methylaminoantipyrin	Bovine, porcine, *Equidae*	100 µg/kg 100 µg/kg 100 µg/kg 100 µg/kg	Muscle Fat Liver Kidney	For porcine species the fat MRL relates to 'skin and fat in natural

			50 µg/kg	Milk	proportions'

Withdrawal Periods

Based on information above, the following withdrawal periods were approved:

Withdrawal period(s):

Horses: Meat and offal (intravenous application): 5 days
Cattle: Meat and offal: 12 days
Milk: 48 hours
Pigs: Meat and offal: 12 days
Not authorised for use in mares producing milk for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, 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.

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

None