United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Bimeprazol 370 mg/g Oral Paste for Horses

Date Created: October 2020

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Bimeprazol 370 mg/g Oral Paste for Horses
Applicant	Bimeda Animal Health Limited 2/ 3/ 4 Airton Close Tallaght Dublin 24 Ireland
Active substance	Omeprazole
ATC Vetcode	QA02BC01
Target species	Horses
Indication for use	For treatment and prevention of gastric ulcers in horses.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

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 conclusion of the procedure	18/08/2019

I. SCIENTIFIC OVERVIEW

Bimeprazol 370 mg/g Oral Paste for Horses contains 370 mg/g omeprazole and the proposed indication is for the treatment and prevention of gastric ulcers. The dosage regimen for the treatment of gastric ulcers is 4 mg omeprazole/kg bodyweight for 28 consecutive days followed by 1 mg omeprazole/kg bodyweight for a further 28 consecutive days. The dosage regimen for the prevention of gastric ulcers is 1 mg omeprazole/kg bodyweight.

The application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended, via the national route. The reference product is GastroGard 370 mg/g oral paste, marketed by Boehringer Ingelheim Animal Health UK Ltd, which has been authorised in the UK since 9th January 2003.

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, any reactions observed are indicated in the SPC.[1] The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [2] of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains omeprazole and the excipients butylhydroxytoluene, calcium stearate, hydrogenated castor oil, triglycerides, momoethanolamine, potassium sorbate, sesame oil, sodium stearate, ferric oxide and apple flavour.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

The container/closure system consists of white HDPE syringe fitted with a HPDE plunger and LDPE cap. The plunger is sub-divided into five increments of 100 kg body weight with an additional 75 kg increment up to a total of 575 kg.
The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence of preservative are justified.

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

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of a continuous mixing process.

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

II.C. Control of Starting Materials

The active substance is omeprazole 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.

The appropriate valid CEP (certificate of Suitability) has been provided.

All the excipients, with the exception of ferric oxide, monoethanolamine and apple flavour, are tested against the relevant monographs in the current European Pharmacopoeia.
Ferric oxide (E172) does not feature in the European Pharmacopoeia and as such is controlled in accordance with the current USPNF monograph. It also conforms to the specifications in Commission Regulation 2008/128 concerning colours for use in foodstuffs.
A residual solvent statement was provided from the suppliers of each of the excipients confirming the absence of any residual solvents.

As per the CEP, the active omeprazole is packed into double polyethylene bags (outer black) placed in a polyethylene drum with a silica gel sachet in between.
The finished product is presented in a white, high density polyethylene (HDPE) syringe with a low-density polyethylene (LDPE) cap/seal.

II.C.4. Substances of Biological Origin

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

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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. Control tests on the finished product are those for appearance, Omeprazole assay, identification by HPLC, degradation microbiological purity.

II.F. Stability

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

G. Other Information

The product has a shelf life of 2 years with the storage condition of store below 30°C.The proposed 28 day in-use shelf life is considered acceptable.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore, the following applicant's user recommendations are appropriate:

- Do not smoke or eat while handling the product.
- Wash hands after use.

- Keep out of the sight and reach of children.
- For animal treatment only.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.
The applicant followed the VICH decision tree and stopped at question 5. It is claimed that the proposed product will be used to treat a small number of animals in a flock or herd. It is noted that the CVMP MRL Summary report for omeprazole (EMEA/MRL/841/02-FINAL) states in the conclusion and recommendations:
'Omeprazole is used in a small number of animals for infrequent or non-regular treatments.'.
This is consistent with suggested target species being performance horses such as racehorses (i.e. not reared specifically for human consumption) which, due to their husbandry and training are highly susceptible to the indication (Bell et al., 2007). Risk factors for performance horses include:
- High energy feed
- Confinement in stalls
- Intermittent feeding
- Intense exercise including racing

The horse is a grazing animal; it is postulated that the constant flow of saliva and feed material into the stomach, during grazing, acts as a buffer which protects against excessive gastric acidity. When horses are put into training they are stabled for prolonged periods and often have no access to grazing. Therefore, the husbandry, training and racing of these performance horses are predisposing factors for the development of gastric ulcers in this sub-group of animals, treatment of non-performance horses is therefore considered negligible. As a result, the applicant ends the exposure assessment at this question.
No Phase II assessment was required. The disposal advice on the SPC and product literature was considered acceptable.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Due to the nature of the application, no pharmacodynamic or pharmacokinetic studies were required.

Tolerance in the Target Species

Tolerance studies were not required because of the nature of the application.
Adverse reactions are as cited in the SPC.

IV.II. Clinical Documentation

The application is submitted according to Article 13(1) of Directive 2001/82/EC, as amended, therefore this data was not required.
An *in vivo* bioequivalence study was conducted to compare the proposed product, Bimeprazol 370 mg/g Oral Paste for Horses, to the reference product, GastroGard 370 mg/g Oral Paste. The study was well conducted and the 90% confidence intervals for the ratio of means (test/reference) for Cmax and AUCt fell within the acceptance limits of 80 - 125%. Bioequivalence of the test and reference products can be accepted.

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 benefit/risk profile of the product is favourable.

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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