Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Chanazone 1 g, Oral Powder for Horses

Chanazone (DK)

Chanbute 1 g, Oral Powder for Horses (AU, DE)

Date Created: May 2016

PuAR correct as of 14/03/2019 when RMS was transferred to AT. Please contact the RMS for future updates

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0571/001/DC
Name, strength and pharmaceutical form	Chanazone 1 g, Oral Powder for Horses
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd Loughrea, Co. Galway Ireland
Active substance	Phenylbutazone
ATC Vetcode	QMA01AA01
Target species	Horses
Indication for use	The product is indicated for the treatment of musculoskeletal conditions in the horse where relief from pain and a reduction in the associated inflammation is required, e.g. in lameness associated with osteoarthritic conditions, bursitis, laminitis and soft tissue inflammation, particularly where continued mobility is considered desirable. It is also of value in limiting post-surgical inflammation, myositis and other soft tissue inflammation. Phenlybutazone powder can be used as an anti-pyretic where this is considered advisable e.g. in viral respiratory infections.

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 completion of the original decentralised procedure	27 January 2016
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Belgium, Czech Republic, Denmark, Estonia, Germany, Latvia, Lithuania, Poland, Spain

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, submitted in accordance with Article 13 (1) of Directive 2001/82/EC as amended. The reference product was Pro Dynam Oral Powder 1 g Phenylbutazone Per Sachet, authorised in the UK since 1994.

The proposed product is indicated for the treatment of musculo-skeletal conditions in horses, in association with osteoarthritic conditions, bursitis, laminitis and soft tissue inflammation. The product is also of value in limiting post-surgical inflammation, myositis and other soft tissue inflammation. Phenylbutazone powder can be used as an anti-pyretic, e.g. in viral respiratory infections. The recommended dose is 4.4 – 8.8 mg/kg per day, and for each 450 kg of bodyweight the dose is recommended as follows for individual response: Day 1 4.4 mg phenylbutazone/kg of bodyweight twice daily, (equivalent to two sachets or 10 g of the product twice daily). Day 2-4, 2.2 mg phenylbutazone /kg of bodyweight is given twice daily, (equivalent to one sachet or 5 g of the product twice daily), followed by 2.2 mg phenylbutazone /kg of bodyweight daily, (equivalent to one sachet or 5 g of the product daily), or on alternate days as required.

If there is no response after 4-5 days, discontinue the treatment. Hay may delay the absorption of phenylbutazone, thus affecting the onset of a clinical effect. It is advisable not to administer hay immediately prior to, or during the administration of the product.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto 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 phenylbutazone and the excipients glucose monohydrate, povidone, apple flavour, xantham gum and crospovidone.

The container/closure system consists of paper and foil sachets (Paper/LDPE/Foil/LDPE), holding 5g of powder per sachet, contained in a pack size of 16 or 100 sachets. 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 wet granulation processing method.

II.C. Control of Starting Materials

The active substance is phenlybutazone, an established active substance described in the European Pharmacopoeia (Ph. Eur). 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. Appropriate Certificates of Suitability were provided. All excipients apart from the apple flavour are monographed in the Ph. Eur. The apple flavour is prepared to an approved specification.

II.C.4. Substances of Biological Origin

The applicant has also declared that no substances of animal origin are used for the manufacture of the product and has provided a satisfactory declaration.

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

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 include those for appearance, packaging integrity, moisture, identification of key elements, average weight, uniformity of mass and dosage units, and microbial purity.

II.F. Stability

The retest period on the active substance is 3 years. 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. A stability commitment was provided.

G. Other Information

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

This veterinary medicinal product does not require any special storage conditions.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological data were not required. A bioequivalence study was provided to confirm bioequivalence.

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 and the environment.

III.A Safety Documentation

Studies of Other Effects - User Safety

A user risk assessment was provided in compliance with the relevant guideline. The applicant also provided additional bibliographical data which show that the product may be irritating to the eyes and skin. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

The SPC carries suitable warnings:

- This product may cause hypersensitivity (allergic) reactions in those sensitized to phenylbutazone, either via skin contact or accidental inhalation.
- People with known hypersensitivity to phenylbutazone, or any of the excipients, should avoid contact with this product.
- If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes, or difficulty breathing, are more serious symptoms and require urgent medical attention.
- This product can be irritating to the skin and the eyes. Avoid contact with the eyes. In case of accidental eye contact, irrigate eyes with plenty of clean water. If irritation persists seek medical advice. Wash any exposed skin and hands after use.
- Care should be taken to avoid ingesting the powder. In the event of accidental ingestion, seek medical advice and show the product packaging to the physician

Environmental Safety

The applicant provided a Phase I Environmental Risk Assessment. This product will be used in a small number of food producing animals, and therefore is not expected pose an undue risk the environment when used as directed.

Withdrawal Periods

- Not for use in horses intended for human consumption.

- Treated horses may never be slaughtered for human consumption.
- The horse must have been declared as not intended for human consumption under national horse passport legislation.

IV CLINICAL DOCUMENTATION

As this is a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, further efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.I. Pre-Clinical Studies

Pharmacology

Pharmacokinetics

Bioequivalence Study

A single-dose, two-period, two-sequence, cross-over bioequivalence study with a 14 day wash-put period was performed. The study was performed to GLP[3] standards, on 24 clinically healthy horses formally declared as excluded from the human food chain. Animals had received no clinically inappropriate treatment up to one month before the trial. Two sampling groups were created, with Group A given the proposed product first and Group B administered the reference product first. After the first treatment and the following 14 day wash-out period, the treatments were changed to that of the alternate product. Feed was removed from the animals 12 hours before administration of the products, and a single dose was administered, Doses were given based on body-weight, and given at 4.4 mg/kg body-weight.

Blood samples were taken at a variety of time points, in order to detect phenlybutazone and oxyphenylbutazone. Samples were frozen and then tested appropriately. Pivotal parameters assessed were AUC[4] and C_{max}[5] for the presence of phenlybutazone. The acceptable limits for AUC were 80%-125% and widened C_{max} parameters were permitted (70% - 143%), as the products were administered orally, and maximum plasma concentration of phenlybutazone was not expected to impact the efficacy or safety of the products. Other parameters analysed provided supportive data. Statistical analysis was performed using ANOVA, ln-transformed data. All tested parameters produced results within the expected confidence limits, and bioequivalence was therefore demonstrated. As bioequivalence was confirmed, there was no requirement to submit pharmacodynamic, target species tolerance, or other clinical data.

[3] GLP – Good Laboratory Practice.
[4] AUC – Area under the curve.
[5] C_{max} – Maximum plasma concentration.

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(s) is favourable

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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.

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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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