United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Butazocare Flavour 1g Oral Powder for Horses and Ponies

Date Created: May 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0651/001/DC
Name, strength and pharmaceutical form	Butazocare Flavour 1g Granules in Sachet for Horses and Ponies
Applicant	Animalcare Ltd, 10 Great North Way, York Business Park, Nether Poppleton, York, Yorkshire, YO26 6RB
Active substance(s)	Phenylbutazone
ATC Vetcode	QM01AA01
Target species	Horses
Indication for use	For the treatment of musculoskeletal disorders in horses and ponies where the anti-inflammatory and analgesic properties of phenylbutazone can offer relief. Examples of conditions normally considered suitable for treatment with phenylbutazone include lameness associated with osteoarthritic conditions, acute and chronic laminitis, bursitis and carpitis, and in the reduction of post-surgical soft tissue reaction.

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 decentralised procedure	13/03/2019
Concerned Member States for original procedure	Austria and Germany

I. SCIENTIFIC OVERVIEW

This is an oral powder and contains 1 g phenylbutazone per 2 g single-dose sachet. The indications in horses and ponies are as follows:
'For the treatment of musculoskeletal disorders in horses and ponies where the anti-inflammatory and analgesic properties of phenylbutazone can offer relief. Examples of conditions normally considered suitable for treatment with phenylbutazone include lameness associated with osteoarthritic conditions, acute and chronic laminitis, bursitis and carpitis and in the reduction of post-surgical soft tissue reaction.'
The dosage is as follows:

Horses: 450 kg (1000 lb) body weight: the contents of two sachets to be administered twice on day 1 of treatment (equivalent to 8.8 mg/kg/day) followed by the contents of one sachet twice daily for four days (4.4 mg/kg/day), then one sachet daily, or on alternate days, sufficient to keep the horse comfortable (2.2 mg/kg/day).

Ponies: 225 kg (500lb) body weight, one sachet (4.4 mg/kg) on alternate days.

The application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended by 2004/28/EC. The reference product is Equipalazone 1 g Oral Powder, marketed by Dechra Ltd., which has been authorised in the UK since August 1994.

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 the active phenylbutazone 1000 mg/sachet and the excipients cellulose microcrystalline, hypromellose, ethylcellulose, magnesium stearate, sucrose and peppermint flavour.

The container/closure system consists of a sachet with a paper/polyethylene outer layer and an aluminium/polyethylene inner layer. Each sachet contains 2 g Butazocare powder. 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 granulation of phenylbutazone and cellulose microcrystalline using a solution of hypromellose in purified water. The granules are then coated using ethylcellulose, hypromellose and magnesium stearate in ethanol and purified water. The granules are then blended with sucrose and peppermint flavour.

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

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

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 satisfactory, valid certificate of suitability has been provided.

The excipients microcrystalline cellulose, hyromellose (pharmacoat 606 & 603), ethylcellulose, magnesium stearate and sucrose meet the requirements of the current monographs in the European Pharmacopeia.
Purified water and ethanol 96% are used in the coating process and meet the requirements of the current monographs in the European Pharmacopeia.
Peppermint flavour is compliant with Regulation (EC) 1334/2008 on the use of flavourings in or on foods and food additives.

The active substance is packaged in double polyethylene bags and placed into cardboard drums. The bulk granules are transported in containers, consisting of double polyethylene bags stored in high density polyethylene drums with a high density polyethylene screw lid. The finished product is packaged in four-layer laminate sachets made of paper, low density polyethylene and aluminium foil.

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

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

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 sites have been provided demonstrating compliance with the specification. Control tests on the finished product include those for appearance, identity of phenylbutazone, assay of phenylbutazone, related substances, uniformity of dosage units, dissolution and microbiological quality.

II.F. Stability

The retest period of the active substance is 3 years and is covered by the relevant certificate of suitability.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.

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

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

The application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended. Due to the legal basis of the application pharmacological data are not required.

Toxicological Studies

The application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended. Due to the legal basis of the application toxicological data are not required.

User Safety

The applicant did not provide any data relating to the user safety of the product, the risk to the user is identical to that of the reference product.
The user warnings are the same as for the reference product but have been updated in line with the format described in the CVMP Guideline on user safety (EMA/CVMP/543/03-Rev.1). The user warnings are as follows:

- This product may cause hypersensitivity (allergic) reactions in those sensitised to phenylbutazone, either via skin contact or accidental inhalation.
- People with known hypersensitivity to phenylbutazone 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 eyes. Avoid contact with the eyes. In case of accidental eye contact, irrigate eyes with plenty of clean water. If irritation persist seek medical advice. Wash 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 Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
The applicant provided a Phase I decision tree and correctly concluded that the ERA should end at Phase I as the product is intended for use in non-food horses and as a result environmental exposure will be low. A Phase II ERA was not required.

IV.I. Pre-Clinical Studies

Pharmacology

Pharmacodynamics

As the application was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended, data were not required.

Pharmacokinetics

One *in-vivo* study was submitted, to investigate the bioequivalence between Phenylbutazone Granules for horses and Equipalazone 1 g oral powder in clinically healthy horses following a single oral administration. Bioequivalence was demonstrated.

Tolerance in the Target Species

As the application was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended, tolerance studies were not required.

Resistance

As the application was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended, resistance studies were not required.

IV.II. Clinical Documentation

As the application was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended, data were not required.

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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