Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Fenylbutazon 1 g Oral Powder for Horses and Ponies (UK)

Equipalazone 1 g Oral Powder for Horses and Ponies [AT, BE, PL, PT, SK]

Fenylbutazon Dechra Vet 1 g oral powder for horses and ponies [NO]

Date Created: July 2017

PuAR correct as of 18/03/2019 when RMS was transferred to BE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0627/001/DC
Name, strength and pharmaceutical form	Fenylbutazon 1 g Oral Powder for Horses and Ponies
Applicant	Dechra Limited Snaygill Industrial Estate Keighley Road Skipton North Yorkshire BD23 2RW UK
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 hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedure	15th June 2017
Concerned Member States for original procedure	Austria, Belgium, Norway, Poland, Portugal and Slovakia

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

The application was for an MA submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended by 2004/28/EC (a 'hybrid' application). The reference product is Equipalazone 1 g Oral Powder, marketed by Dechra, which has been authorised in the UK since August 1994. The candidate product is an auto-generic of the reference product; however, a 'hybrid' application. For this reason, a palatability study was submitted, resulting in the omission of statements present on the reference product SPC and product literature regarding the necessity to administer the product in dry feed. The application was accepted on the basis of identicality of the proposed product to the reference product, under the Guideline on the conduct for bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2). Section 7.1(d)

The product is indicated 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 proposed dosage and duration of treatment is as follows:

"The dosage should be adjusted according to the individual animal's response, but the following may be taken as a guide:

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

Discontinue treatment if no response is evident after four to five days treatment.

The product is administered orally and for ease the sachet(s) can be mixed with a small quantity of feed.

The legal category in the UK will be a POM-V, the same as for the reference 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 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 acacia, gelatin and silicon dioxide.

The container/closure system consists of a sachet with a paper/polyethylene outer layer and aluminium/polyethylene inner layer. 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.

[1] SPC – Summary of Product Characteristics.

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 the encapsulation process of the active substance before it is filtered, dried, sieved and shipped to the UK site for filling.

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.

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 Certificate of Suitability from was provided for the active Phenylbutazone.

The excipients acacia, gelatin and purified water comply with the European Pharmacopoeia; Silicon Dioxide complies with the United States National Formulary and glutaraldehyde with the British Veterinary Pharmacopoeia.

The primary packing is a sachet manufactured from a four-layer laminate consisting of a paper/polyethylene outer layer and aluminium/polyethylene inner layer.

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 micro-encapsulated powder that is shipped from Italy is classified as an intermediate product and appropriate specification is applied by the UK filling site, including testing for identity, assay, particle size and appearance.

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 HPLC Assay of phenylbutazone and Degradation products in Equipalazone Powder.

II.F. Stability

Phenylbutazone is a well-established active substance and complies with the requirements of the monograph of the European Pharmacopoeia and is supplied under a Certificate of Suitability. The active substance is packaged and stored in a sealed double layer polyethylene bag placed in a cardboard drum. The active substance is subject to a 36 month re-test period. 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 shelf-life of four years is recommended when the product is stored below 25°C and when stored in a cool place.

Equipalazone Powder is presented in unit-dose sachets. The powder is not reconstituted prior to use; it is mixed with a portion of the feed ration. It is not necessary, therefore, to establish a shelf-life after reconstitution or opening.

G. Other Information

Do not store above 25°C.
Store in a dry place.
Shelf life of veterinary medicinal product as packaged for sale: 4 years.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

For generics, insert in the relevant sections as appropriate:

III.A Safety Documentation

Pharmacological Studies

As this is a generic hybrid application submitted according to Article 13(3) of Directive 2001/82/EC, as amended and bioequivalence with the reference product has been determined on the basis of identicality, the results of pharmacological studies are not required. Acacia, gelatin and silicon dioxide are the excipients in the formulation and are regarded as standard pharmaceutical constituents, and will pose no risk to the safety of the product.

Toxicological Studies

As this is a generic hybrid application submitted according to Article 13(3) of Directive 2001/82/EC, as amended and bioequivalence with the reference product has been determined on the basis of identicality, the results of toxicological studies are not required. Acacia, gelatin and silicon dioxide are the

excipients in the formulation and are regarded as standard pharmaceutical constituents, and will pose no risk to the safety of the product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the main routes of exposure for the user are inhalation exposure due to the dust given off by the product, dermal exposure due to spillage and also ocular exposure may occur. In addition, hypersensitivity reactions may be apparent. The likelihood that the user will encounter oral exposure due to hand mouth contact is considered negligible as it can be expected that the owner will adhere to the principles of elementary personal hygiene practices as explained by the veterinarian. The product is expected to be only be handled by veterinary surgeons and the horse owner.

Warnings and precautions as listed on the SPC and product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- The 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 eyes. Avoid contact with the eyes.
- In case of accidental eye contact, rinse eyes with plenty of 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.
- The safety of phenylbutazone I pregnancy has not been established. The product should not be administered by pregnant women or women attempting to conceive.

Environmental Safety

The applicant provided a Phase I Environmental Risk Assessment (ERA) which was carried out in accordance with VICH and CVMP guidelines.
The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required. 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.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

As this is a generic hybrid application submitted according to Article 13(3) of Directive 2001/82/EC, as amended and bioequivalence with the reference product was accepted on the basis of identicality, results of toxicological, pharmacological or clinical tests are not required.

Tolerance in the Target Species

As this is a generic hybrid application submitted according to Article 13(3) of Directive 2001/82/EC, as amended and bioequivalence with the reference product was accepted on the basis of identicality, the results of tolerance studies are not required.

IV.II. Clinical Documentation

Laboratory Trials

As this is a generic hybrid application submitted according to Article 13(3) of Directive 2001/82/EC, as amended and bioequivalence with the reference product has been determined on the basis of identicality, the results of laboratory trials are not required.

Clinical Trials

As this is a generic hybrid application submitted according to Article 13(3) of Directive 2001/82/EC, as amended and bioequivalence with the reference product was accepted on the basis of identicality, the results of clinical trials are 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 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 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.

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