IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Phenoleptil 100 mg Tablets for dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0635/004 (formerly UK/V/0336/004)
Name, strength and pharmaceutical form	Phenoleptil 100 mg Tablets for dogs
Active substances(s)	Phenobarbital
Applicant	Dechra Regulatory B.V. Handelsweg 25 5531 AE Bladel Netherlands
Legal basis of application	Hybrid application (Article 13(3) of Directive No 2001/82/EC)
Date of Authorisation	24 October 2012 (UK) 15 February 2013 (IE)
Target species	Dogs
Indication for use	Prevention of seizures due to generalised epilepsy in dogs.
ATCvet code	QN03AA02
Concerned Member States	AT, BE, CZ, DE, DK, EL, ES, FI, FR, HR, HU, IS, IT, LU, NO, PL PT, SE, SI, SK, UK(NI)

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

This was a line extension application to existing marketing authorisations for Phenoleptil 12.5 mg Tablets for Dogs and Phenoleptil 50 mg Tablets for Dogs, in order to add 25 mg and 100 mg products to the range. Bioequivalence was assured by means of suitable dissolution studies. Phenoleptil 25 mg Tablets for Dogs and Phenoleptil 100 mg Tablets for dogs are authorised for use in dogs for the prevention of seizures due to generalised epilepsy. Each tablet contains 25 mg or 100 mg of phenobarbital as an active substance. The dosage rate of phenobarbital is 2.5 mg per kg body weight twice daily. However, due to differences in phenobarbital excretion and differences in sensitivity among patients the active doses may vary considerably, ranging from 1 mg to 15 mg per kg bodyweight twice daily. Do not use in dogs weighing less than 5 kg bodyweight. Refer to the SPC for information on the adjustment of dose for animals of varying size.

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, 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. QUALITY ASPECTS

A. Composition

The product contains phenobarbital as an active substance and lactose monohydrate, microcrystalline cellulose, chicken flavour, dried yeast from *Saccharomyces*, sodium starch glycolate (Type A), silica colloidal anhydrous and magnesium stearate as excipients.

The product is packaged in aluminium/PVC blister strips or in aluminium/PVC/PE/PVdC blister strips. The products consist of 100 tablets in a cardboard carton containing 10 blister strips, each strip with 10 tablets, or 500 tablets in a cardboard carton containing 50 blister strips each strip with 10 tablets.

The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation 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 from 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 supporting data for phenobarbital have been provided in the form of an EDQM[1] Certificate of Suitability. It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies
Magnesium stearate is a material that may be sourced from either animal or non-animal sources. A declaration has been provided certifying that the raw materials, ingredients and additives used to produce magnesium stearate are exclusively of synthetic and vegetable origin.

E. Control on intermediate products
Not applicable.

F. 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.

G. Stability
Stability data on the active substance have been provided for eight batches of phenobarbital. Based on the data provided, a retest interval of three years was justified.

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. The shelf-life of the veterinary medicinal product as packaged for sale is 3 years.

H. Genetically Modified Organisms
Not applicable.

J.Other Information
The shelf-life of the veterinary medicinal product as packaged for sale is 3 years. Do not store above 30°C. Keep the container in the outer package in order to protect from light. Divided tablets should be stored in the open blister pack.
[1] The European Directorate for the Quality of Medicines & HealthCare.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As these were extension applications, and all four tablet types can be considered homothetic, the results of additional pharmacological or toxicological tests were not required.

III.A Safety Testing

User Safety

The applicant provided a user risk assessment (URA) in compliance with the relevant guideline, based on the original URAs which reflected those of the original products. Additional data were provided to support the approval of the 100 mg product.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:-

- Warnings and precautions as listed on the product literature are the same as those of the products from which the new products were derived and are adequate to ensure safety of the product to users and the environment.
- People with known hypersensitivity to barbiturates should avoid contact with the veterinary medicinal product. Wash hands after use.
- Take utmost care that children do not come into contact with the product.
- Children are particularly at risk of intoxication which may prove fatal.
- In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. If possible, the physician should be informed about the time and amount of ingestion, as this information may help to ensure that appropriate treatment is given.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. The assessment reflected those already approved for the original products. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV. CLINICAL ASSESSMENT

Dissolution studies were required to ensure bioequivalence between four homothetic products. Products used for studies were the 25 mg, 50 mg and 100 mg products. No other data were required.

IV.A Pre-Clinical Studies

Pharmacology

The analysis of dissolution profiles for the 25 mg, 50 mg and 100 mg products were considered suitable to ensure extrapolation of results to *in vivo* situations. Dissolution profiles were studies at three pH conditions: 2.0, 4.5 and 8.0. All products were subjected to a standard study in which relevant variants were controlled. Experiments were performed on a specified number of tablets, in replicate. After suitable analysis of the results, it was concluded that bioequivalence could be confirmed.

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.