United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

TermaWorm Cat Tablets 230/20 mg

Date Created: July 2016

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	TermaWorm Cat Tablets 230/20 mg
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd. Loughrea Co. Galway Ireland
Active substance	Pyrantel Embonate Praziquantel
ATC Vetcode	QP25AA51
Target species	Cats
Indication for use	For the treatment of mixed infections caused by the following gastrointestinal roundworms and tapeworms: **Roundworms:** *Toxocara cati, Toxascaris leonina,* **Tapeworms:** *Dipylidium caninum, Taenia taeniaeformis, Echinococcus multilocularis*

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.

I. SCIENTIFIC OVERVIEW

The product has been developed as a generic hybrid of Drontal Cat Film-coated Tablets. The reference product has been authorised in the UK since August 1994. The application is for a generic hybrid, as bioequivalence could not be demonstrated for the proposed product. The product contains pyrantel embonate and praziquantel to be administered orally at a dose of 20 mg/kg pyrantel (as 57.5 mg/kg pyrantel embonate), and 5 mg/kg respectively. This equates to 230 mg pyrantel embonate and 20 mg praziquantel per tablet. The products are indicated for the treatment of mixed infections of gastrointestinal roundworms and tapeworms.

The products are 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 products can be safely used in the target species, any reactions observed are indicated in the SPC.[1]

The products are 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 products was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

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

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTIUENTS

II.A. Composition

The product contains pyrantel embonate and praziquantel as active substances. The excipients that are used for the tablet are maize starch, microcrystalline cellulose, crospovidone, magnesium stearate and colloidal anhydrous silica. The coating of the tablet is made from grilled meat flavour and Opadry 03F28415 White.

The product is presented in either:

Individual blisters made up of a PVC/PE/PCTFE white opaque copolymer and a 20µm heatseal lacquer/aluminium containing 2, 4, 6, 8, 10, 12, 14, 16, 18 or 20 tablets.

or

Individual blisters made up of 45µm PVC/aluminium/orientated polyamide and a 20µm heatseal lacquer/aluminium containing 2 or 8 tablets.

The blisters are packed into cartons containing either: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 24, 28, 30, 32, 36, 40, 42, 44, 48, 50, 52, 56, 60, 64, 68, 70, 72, 76, 80, 84, 88, 92, 96, 98, 100, 104, 106, 108, 112, 116, 120, 128, 136, 140, 144, 150, 152, 160, 168, 176, 180, 184, 192, 200, 204, 206, 208, 216, 224, 232, 240, 248, 250, 280, 300, 500 or 1000 tablets

These are packaged into an outer carton providing between 2 and 1,000 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.

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 product is manufactured by mixing the active substances and maize starch with crospovidone in purified water to form a granulate. The remaining excipients are added, mixed and subsequently tableted. To form the tablet coating a suspension is made from the excipients using water. Once coated the tablets are packaged into blisters. Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substances are pyrantel embonate and praziquantel, established active substances described in the European Pharmacopoeia (Ph. Eur.). The

active substances are 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 excipients are manufactured in accordance with the relevant Ph. Eur. monographs. The grilled meat flavour and Opadry 03F28415 White are not described in a pharmacopeia. Suitable in-house specifications were provided.

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. The tests include those for identification and assay of the active substances, identification of impurities, appearance, dissolution and microbiological quality

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.

II.F. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. For one manufacturer, stability data were provided permitting a re-test period of 36 months when stored in double polythene bags inside an iron drum. For the second manufacturer, a re-test period of 60 months was agreed acceptable on the basis of data provided.

For the finished product, tests were performed under appropriate VICH[3] guidelines, which included analyses of both presentations of the product for 36 months and 6 months at 25°C/60% RH and 40°C/75% RH. Moisture content and degradation products were analysed.

[3] VICH – Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.

G. Other Information

- Shelf life of the finished product as packaged for sale is 5 years.
- This product does not require any special temperature conditions.
- Discard unused half tablets.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (3), and bioequivalence with a reference product has been established, results of pharmacological tests are not required.

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

Pharmacological Studies

As this is a generic hybrid application, no pharmacological data has been submitted.

Toxicological Studies

As this is a generic hybrid application, no toxicological data has been submitted.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the product is not expected to pose a risk for the user when used as recommended.

Toxicity on the active substance:

Praziquantel
Praziquantel has been used to treat up to 25,000 humans using single dosing schemes. In humans, doses of up to 50mg/kg bw of praziquantel were well tolerated with no clinically relevant changes.

Pyrantel
Pyrantel (as the embonate salt) has been used in human medicine for more than 20 years. It is normally administered orally at a dose rate of 10 to 20 mg/kg bw per day for 1 to 3 days. In case of overdose, adverse effects in humans have been reported to include gastro-intestinal disturbances, CNS[4] effects and skin reactions.

[4] Central nervous system

Excipients
The excipients are widely used as pharmaceutical excipients and are generally regarded as non-toxic, non-irritant or non-hazardous.

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

Environmental Safety

The applicant provided a Phase I environmental risk assessment in compliance with VICH and CVMP guidelines and showed that no further assessment is required. The assessment concluded that the product will be administered for individual treatment of companion animals and the risk of environmental exposure is minimal. No environmental warnings or information are therefore required as the product is safe for the environment when used as directed.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Pharmacodynamics
As this is a generic hybrid application, no data for pharmacodynamics has been submitted as bioequivalence with the reference product was accepted.

Pharmacokinetics
The applicant conducted an *in vivo* bioequivalence study in cats that contributed to the overall opinion that the products are efficacious. The GLP[5] compliant study was carried out on 24 cats aged 1-6 years. Each cat received the same dose (either 1 or 1 ½ tablets) of the test or reference product, during both of the two periods. Appropriate observations and clinical measurements were made at suitable time points. Results showed that bioequivalence for praziquantel can be accepted, and although the results were inconclusive for pyrantel, bioequivalence was accepted as the results for pyrantel were of limited clinical significance as pyrantel is poorly absorbed following oral administration, with a high proportion remaining in the gastro-intestinal tract to act 'locally'.
A validation study was conducted in accordance with GLP and the validation method is accepted as adequate for the determination of praziquantel, hydroxy-praziquantel and pyrantel in cat plasma. The applicant also submitted a comparative dissolution study and bioequivalence was accepted.

Tolerance in the Target Species

As this is a generic hybrid application, no data for target species tolerance has been submitted as bioequivalence with the reference product was accepted.

[5] GLP – Good Laboratory Practice.

Resistance

As this is a generic hybrid application, no resistance data has been submitted as bioequivalence with the reference product was accepted.

IV.II. Clinical Documentation

As this is a generic hybrid application, submitted according to Article 13 (3) of Directive 2001/82/EC as amended, no clinical documentation data has been submitted as bioequivalence with the reference products was accepted. Sufficient data was submitted to conclude the proposed and reference products are bioequivalent. Bioequivalence of praziquantel was accepted based on *in vivo* data submitted and further support for bioequivalence of pyrantel was 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.

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