Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Anthelmin 230 mg/20 mg film-coated tablets for cats

Date: 28 April 2017

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0160/001/DC
Name, strength and pharmaceutical form	Anthelmin 230 mg/20 mg film-coated tablets for cats
Applicant	KRKA d.d., Novo mesto, Šmarješka cesta 6 8501 Novo mesto Slovenia
Active substance(s)	Pyrantel embonate Praziquantel
ATC Vetcode	QP52AA51
Target species	Cats
Indication for use	For the treatment of mixed infestations with roundworms and tapeworms in cats, caused by: - adult stages of ascarids: *Toxocara cati (syn. mystax)* - adult stages of hookworms: *Ancylostoma tubaeforme, Ancylostoma braziliense* - tapeworms*: Echinococcus multilocularis, Dipylidium caninum, Hydatigera (Taenia) taeniaeformis, Mesocestoides spp., Joyeuxiella pasqualei.*

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised procedure	25 January 2017
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure	AT, BE, BG, CZ, EE, ES, FI, FR, HR, HU, IE, IT, LT, LV, NL, PL, PT, RO, SI, SK, UK

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.

The safety and efficacy aspects of this product are identical to the reference product. The initial application for the reference product was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains Pyrantel embonate 230.0 mg, Praziquantel 20 mg and the excipients Maize starch, Povidone K25, Cellulose Microcrystalline, Silica Colloidal Anhydrous, Magnesium stearate, Hypromellose, Polyethylene glycol 4000, Titanium dioxide E171.

The container/closure system consists of a blister pack made of a laminated oPA/Al/PVC foil and an aluminium lidding foil.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

The active substances are Pyrantel Embonate, and Praziquantel established substances described in the European Pharmacopoeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with this specifications have been provided.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

D. Control on intermediate products

Not applicable.

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.

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.

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.

G. Other Information

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13.1, and the *in-vitro* dissolution profiles of praziquantel and pyrantel embonate proved to be similar for Anthelmin/Dehinel and its reference product Drontal, results of safety tests are not required.

The pharmacological and toxicological aspects of this product are identical to the reference product.

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

Environmental Risk Assessment

Phase I

The environmental risk assessment can stop in Phase I because the product is only used for administration in cats.

Conclusion

Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT (EFFICACY)

This application is made in accordance with Article 13 (1) of the Directive 2001/82/EC, as amended. The product is intended for the treatment of mixed infestations with adult stages of roundworms (ascarids *[Toxocara cati syn. Mystax]),* hookworms (*Ancylostoma tubaeforme, Ancylostoma braziliense),* and tapeworms (*Echinococcus multilocularis, Dipylidium caninum, Hydatigera (Taenia) taeniaeformis, Mesocestoides spp., Joyeuxiella pasqualei)* in cats. The reference

veterinary medicinal product is Drontal 230/20 mg film-coated tablets for cats (hereafter named Drontal), authorised in Germany since 1995 (authorisation number: 15584.00.01). The generic product Anthelmin/Dehinel is comparable to the reference product Drontal both in terms of the pharmaceutical form and qualitative and quantitative composition of the active substances. The excipients are qualitatively comparable but not quantitatively. However, the differences in the amount of some excipients in the generic product are negligible.

An experimental bioequivalence study was performed for praziquantel in cats. The *in-vitro* dissolution profiles of praziquantel and pyrantel embonate proved to be similar for both products. In addition, the efficacy of a single oral dose of the intended formulation Anthelmin/Dehinel against zoonotic *Echinococcus multilocularis* in experimentally infected cats has been demonstrated.

Based on these data, the safety and efficacy aspects of Anthelmin/Dehinel are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

An *in-vivo* bioequivalence study has been performed comparing praziquantel plasma levels of the test product Anthelmin/Dehinel with the reference product Drontal. The study was designed and conducted according to the guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2; 2011).
Bioequivalence of Anthelmin/Dehinel and Drontal could not be decisively demonstrated for praziquantel because C_{max} was not within the pre-defined range, and AUC_{last} was inside the acceptance range.

Consequently, a dose confirmation study with the zoonotic tapeworm *Echinococcus multilocularis* was conducted in cats with 100% efficacy.

In addition, the applicant conducted *in-vitro* dissolution studies comparing the test and reference product. The *in-vitro* dissolution studies were performed according to the guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2; 2011). All dissolution profiles of pyrantel embonate and praziquantel from the test and reference product proved to be similar under all conditions tested. The *f*2 values were between 50 and 100.

Tolerance in the Target Species of Animals

Due to the generic application according to Article 13 (1) of Directive 2001/82/EC as amended, target animal safety studies are not required. In the *in-vivo* bioequivalence

study both products were well tolerated and no treatment related adverse reactions were observed..

No adverse effects were seen in the dose confirmation study in cats experimentally infected with *Echinococcus multilocularis* and some of the cats were dosed in excess of the minimum recommended dose.

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

Due to the generic application according to Article 13 (1) of Directive 2001/82/EC as amended, resistance data are not required. However, adequate warnings and precautions are included in the product literature.

IV.B Clinical Studies

A dose confirmation study with the intended product Anthelmin/Dehinel and the zoonotic tapeworm *Echinococcus multilocularis* was conducted in experimentally infected cats.
The study was well-designed, performed and documented according to VICH Topic GL9 (Guideline on good clinical practices, CVMP/VICH/595/98-Final, 4 July 2000), to VICH Topic GL 7 (efficacy requirements for anthelmintics: overall guidelines, CVMP/VICH/832/99-corr, 7 December 2000), and to VICH Topic GL 20 (Efficacy of anthelmintics: specific recommendations for feline, CVMP/VICH/545/00-Final, 30 July 2001). The included suitable number of parasite-naive were appropriate for the purpose of this study. Animals received either treatment with a single oral administration of the intended veterinary product or no treatment at all. The measure of effectiveness was the worm counts at necropsy on day 5 post application. The number of worms were summarised using descriptive statistics. For the calculation of percent of effectiveness geometric means were considered primary. Efficacy based on arithmetic means were also presented. The adequacy of infection with *Echinococcus multilocularis* was confirmed in untreated controls. Efficacy of Anthelmin/Dehinel based on both geometric and arithmetic mean was 100 %. No adverse effects were observed.
Taking into account the results of the *in-vitro* studies, equivalence of this product to the reference product Drontal was demonstrated.

Laboratory Trials

No data needed.

Field Trials

No data needed.

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 risk benefit 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 Heads of Veterinary Medicinal Agencies website (www.hma.eu).

This section 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.

Quality changes

Summary of change	Section updated in Module 3	Approval date
Change in the shelf-life of the finished product (DE/V/0160/001/IB/005)	N/A	05/02/2020