IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Drontal Dog Tasty Bone 150/144/50 mg tablets

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PRODUCT SUMMARY

EU Procedure number	IE/V/0335/001/DC
Name, strength and pharmaceutical form	Drontal Dog Tasty Bone 150/144/50 mg tablets
Active substance(s)	Febantel/Pyrantel Embonate/Praziquantel
Applicant	Bayer Ltd.
Legal basis of application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended
Date of Authorisation	23/07/2014
Target species	Dogs
Indication for use	Treatment of mixed infections by nematodes and cestodes of the following species: Roundworms: Ascarids (adult and late immature forms): *Toxocara canis, Toxascaris leonina* Hookworms (adults): *Uncinaria stenocephala, Ancylostoma caninum* Whipworms (adults): *Trichuris vulpis* Tapeworms (adult and immature forms): *Echinococcus granulosus, Echinococcus multilocularis, Dipylidium caninum, Taenia spp.*
ATCvet code	QP52AA51
Concerned Member States	AT, DE, DK, FI, FR, IS, IT, NL, NO, SE, UK

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

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 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.

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II QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains 150 mg febantel, 144 mg pyrantel embonate (equivalent to 50 mg pyrantel) and 50 mg praziquantel per tablet and the excipients maize starch, lactose monohydrate, microcrystalline cellulose, povidone K25, magnesium stearate, sodium laurilsulfate, colloidal anhydrous silica, croscarmellose sodium and meat flavour.
The product is presented in blisters formed from PA/Alu/PE foil and sealed with Alu/PE foil. Cartons contain 2, 4, 6, 24, 102 or 312 tablets.

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 at a licensed manufacturing site.

Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substances are febantel, pyrantel embonate and praziquantel which are established active 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 these specifications have been provided.

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

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 has been provided.
Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

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F. Stability

Stability data on the active substances has 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 has 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

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This is a 'generic' type application via the decentralised procedure submitted by Bayer Ltd. in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The reference product for this procedure is Drontal Plus Flavour BoneShaped Tablets (VPA 10021/014/004; Bayer Ltd.).

III.A Safety Testing

The candidate formulation is the same as the reference product in terms of pharmaceutical form (tablet), qualitative and quantitative composition of active ingredients and majority of excipients. The only difference in composition between products is a change in type and amount of flavouring agent and the inclusion of croscarmellose sodium in the candidate product.

Pharmacological Studies

For the product under consideration, the applicant argued that bioequivalence can be accepted in the absence of an *in vivo* bioequivalence study.

Dissolution tests were performed at three difference pH (1, 4.5 and 6.8). Batches of the test and reference product were sampled at ≥5 time points up to 60 minutes. Typically, 12 replicates were sampled at each time point. From the results, it is noted that:

At pH 1, greater than 85% dissolution was achieved for all three actives by 15 minutes.

At pH 4.5 greater than 85% dissolution was achieved for praziquantel and febantel by 15 and 20 minutes, respectively. For pyrantel, greater than 85% dissolution was not achieved within the 60 minute test period. However, it is noted that tablets from both batches of both product behave similarly.

At pH 6.8, greater than 85% dissolution was achieved for praziquantel and pyrantel by 15 minutes and for febantel by 20 minutes.

For those pH/substance combinations where greater than 85% dissolution is not achieved by 15 minutes, the applicant compares dissolution profiles using the 'f2 statistic'. Where used, the applicant concludes that similar dissolution profiles were confirmed.

Given:

The similarity in formulations between the test and reference products: o The candidate formulation is the same as the reference product in terms of pharmaceutical form (tablet), qualitative and quantitative composition of active ingredients and majority of excipients. The only difference in composition between products is a change in type and amount of flavouring agent and the inclusion of croscarmellose sodium in the candidate product.

- o the specifications and test methods of the active ingredient and common excipients are identical and the sources of the active ingredient and common excipients are identical;

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The fact that the differences between products in terms of excipients are unlikely to impact on bioavailability; and

The conclusions of the *in vitro* dissolution studies confirming similar dissolution profiles under the conditions tested,

It is accepted that the products will behave similarly once ingested and that an exemption from the conduct of an *in vivo* bioequivalence study is justified.

In conclusion, bioequivalence is accepted and cross reference to the safety and efficacy of the reference product is justified. The results of pharmacological and toxicological studies are not required.

Toxicological Studies

Bioequivalence is accepted and cross reference to the safety and efficacy of the reference product is justified. The results of pharmacological and toxicological studies are not required.

User Safety

A user risk assessment has not been provided by the applicant. Given that: the test product is identical to the reference product in terms of active substances and the majority of excipients, and, the excipients new to the candidate formulation (pork liver flavour and croscarmellose sodium) do not pose a risk to the user, it is accepted that the candidate product does not pose any greater risk to the user than the reference product. Therefore, the user safety statements agreed for the reference product can be applied to the test product.

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

Ecotoxicity

An environmental risk assessment was provided by the applicant. Based on the information provided, it is accepted that the assessment can end at Phase I.

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 (EFFICACY)

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

Product specific target animal safety data have not been presented. Given that: the test product is identical to the reference product in terms of active substances and the majority of excipients, and,

the excipients new to the candidate formulation (pork liver flavour and croscarmellose sodium) do not pose a risk to the target animal,

it is accepted that the candidate product does not pose any greater risk to the target animal than the reference product. Therefore, the text agreed for sections 4.6 and 4.10 of the authorised reference product can be applied to the test product.

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

Resistance

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

Efficacy data have not been presented.

Based on the information provided, it can be accepted that the test and reference products are bioequivalent; therefore, an equivalent efficacy profile can be assumed.

A palatability study was conducted to evaluate the acceptance/palatability of a flavoured Drontal Plus tablet when presented to privately owned dogs in households. Based on the findings of the study as reported, it is accepted that the product can be considered palatable.

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.

VI 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 HPRA website.

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.

Changes:
None.

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