IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

DV8WORM 50 mg/144 mg/200 mg Tablets for dogs

PRODUCT SUMMARY

Name, strength and pharmaceutical form	DV8WORM 50 mg/144 mg/200 mg Tablets for dogs
Active substance(s)	Praziquantel, pyrantel embonate, fenbendazole
Applicant	Duggan Veterinary Supplies Limited Unit 9 Stradavoher Business Park Thurles Tipperary Ireland
Legal basis of application	Well-established use application (Article 13a of Directive No 2001/82/EC)
Date of completion of procedure	27/05/2022
Target species	Dogs
Indication for use	Treatment of mixed infections by nematodes and cestodes of the following species and life stages of parasite: <u>Nematodes</u>: Ascarids: *Toxocara canis, Toxascaris leonina* (L5 and adults) Hookworms: *Ancylostoma caninum, Uncinaria stenocephala* (adults) Whipworms: *Trichuris vulpis* (adults) <u>Cestodes</u>: Tapeworms: *Dipylidium caninum, Taenia hydatigena, Taenia pisiformis*, *Echinococcus granulosus (adult and late immature forms)* The veterinary medicinal product is exclusively indicated when use against gastrointestinal nematodes and cestodes is indicated at the same time.
ATC vet code	QP52AA51

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (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; any 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. Qualitative and Quantitative Particulars
The product contains 50 mg of praziquantel, 144 mg of pyrantel embonate and 200 mg of fenbendazole as active substances. The excipients in the formulation are maize starch, microcrystalline cellulose, lactose monohydrate, povidone K30, sodium starch glycolate (Type A), talc, magnesium stearate and colloidal anhydrous silica. The container closure system is a PVC/Alu blister or polyethylene container. The choice of the formulation has been justified. The product is an established pharmaceutical form and its development is adequately described in the 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 praziquantel, pyrantel embonate, and fenbendazole are established substances described in the European Pharmacopoeia. All 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 material. 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 (pharmaceuticals)
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.

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 marketing authorisation application was submitted in accordance with Article 13a (well-established use) of Directive 2001/82/EC, as amended. The product contains praziquantel, pyrantel embonate and fenbendazole. The product is to be administered at a dose of 5 mg praziquantel/kg, 14.4 mg pyrantel embonate/kg and 20 mg fenbendazole/kg by the oral route.

III. SAFETY ASSESSMENT

Pharmacological Studies
The pharmacodynamic and pharmacokinetic properties of praziquantel, pyrantel embonate and fenbendazole have been well characterised using published literature.

The published literature also demonstrate synergy of the combination of pyrantel and fenbendazole at the proposed dosage against *Toxocara canis*.
Based upon the legal basis of this application and given the well-established use of the active ingredients within the Community for a period in excess of ten years the combination of praziquantel, pyrantel embonate and fenbendazole can be accepted.

Toxicological Studies
No toxicity studies have been provided; however, extensive literature examining the toxicological effects of praziquantel, pyrantel embonate and fenbendazole have been provided and were considered satisfactory.

User Safety
The applicant has provided a user safety assessment in compliance with the relevant guideline. Estimated exposure following accidental ingestion of tablets has been compared with the NOAELs of praziquantel, pyrantel embonate and fenbendazole from the published literature giving an unacceptable margin of exposure for children and adults and consequently, risk mitigation measures have been introduced. Dermal absorption is considered negligible due to the pharmaceutical form when following basic hygienic measures. Literature indicates that hypersensitivity can occur; therefore, appropriate warnings have been included in the SPC. Warnings and precautions as listed on the product literature are considered adequate to ensure safety to users of the product.

Environmental Safety
An environmental risk assessment was provided. It was accepted that the assessment can end at Phase I and that the product will not present an unacceptable risk for the environment when handled, used, stored and disposed of in accordance with the recommendations included in the SPC.

IV. CLINICAL ASSESSMENT

IV.I. Pre-Clinical Studies
Tolerance in the Target Species
Results of a proprietary target animal safety study were provided along with a number of literature references in which the safety of praziquantel, pyrantel embonate and fenbendazole has been investigated. Based on the findings from this study and the studies cited in the published literature, the SPC includes appropriate information on the potential adverse reactions that may occur following administration of the product. Gastrointestinal disorders (vomiting and diarrhoea) and nonspecific signs such as lethargy, anorexia or hyperactivity were reported very rarely. As no data supporting safety of use during early pregnancy were provided, the product should not be used in pregnant animals during the first and second trimesters of pregnancy.

Resistance
No significant resistance data were located for these active substances in a published literature search. The SPC includes prudent warnings relating to the potential for resistance emergence.

Dose confirmation studies
The results of numerous literature references which evaluated very similar formulations to the proposed formulation were provided in support of the proposed dose of the product. These data provide sufficient evidence to conclude that the proposed doses of praziquantel, pyrantel embonate and fenbendazole for the claims proposed in dogs are well-established. Based on the data provided, it was accepted that the indications for this product have been adequately supported.

IV.II. Clinical Documentation
The results of one proprietary field study and numerous literature references which evaluated very similar formulations to the proposed formulation were provided in support of efficacy of the product under field conditions of use. These data provide sufficient evidence to conclude that the proposed use of praziquantel, pyrantel embonate and fenbendazole for the claims proposed in dog is well-established.
Based on the data provided, it was accepted that the indications for this product have been adequately supported.

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, safety and efficacy of the product is acceptable.

VI. POST-AUTHORISATION ASSESSMENTS

Not applicable.