Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

RidaWorm 100mg Film-Coated Tablets for Small Dogs
RidaWorm 500mg Film-Coated Tablets for Adult Dogs
Armitage Worm Away 100mg Film-Coated Tablets for Small Dogs
Armitage Worm Away 500mg Film-Coated Tablets for Adult Dogs

Date Created: May 2019

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	RidaWorm 100mg Film-Coated Tablets for Small Dogs RidaWorm 500mg Film-Coated Tablets for Adult Dogs Armitage Worm Away 100mg Film-Coated Tablets for Small Dogs Armitage Worm Away 500mg Film-Coated Tablets for Adult Dogs
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd
Active substance	Nitroscanate
ATC Vetcode	QP52AX01
Target species	Dogs
Indication for use	Treatment of the following cestodes (tapeworms) and intestinal nematodes (roundworms): Nematodes: Ascarids: *Toxocara canis* (adult parasite stage) Hookworms: *Ancylostoma caninum* (adult parasite stages) Cestodes Taenia species (*T. hydatigena, T. pisiformis, T. ovis*) (adult and immature parasite stages) and *Dipylidium caninum* (adult parasite stage).

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	These were full bibliographic applications submitted in accordance with Article 13 (a) of Directive 2001/82/EC, as amended by 2004/28/EC ('well established use' applications).
Date of conclusion of the procedure	Armitage products 22nd March 2019 RidaWorm products 30th May 2019

These were national applications for full bibliographic applications submitted in accordance with Article 13 (a) of Directive 2001/82/EC, as amended by 2004/28/EC ('well established use' applications). Both the 100 mg and 500 mg tablets are identical to Beaphar One Dose Dog Wormer Nitroscanate Film Coated Tablets (100 mg or 500 mg), previously Troscan Film-coated Tablets, (100 mg or 500 mg), authorised in the UK since 1994. Nitroscanate is currently marketed in the UK by Novartis as 'Beaphar One Dose Wormer' and 'Johnson's One Dose Easy Wormer' as 'Bob Martin Clear Wormer' and 'Troscan', as 'Wilko One Dose Worming Tablet'. These products are copycats of the Troscan products or the expired Novartis product 'Lopatol' (expired in 2008). Troscan 100 mg and 500 mg Film-coated Tablets authorised in the UK in 1994 were authorised on the basis of the same dossier that has been presented for this current application.

The products are indicated for use in dogs for treatment of the following cestodes (tapeworms) and intestinal nematodes (roundworms): nematodes: ascarids: *Toxocara canis* (adult parasite stage), hookworms: *Ancylostoma caninum* (adult parasite stages), cestodes *Taenia* species (*T. hydatigena, T. pisiformis, T. ovis*) (adult and immature parasite stages) and *Dipylidium caninum* (adult parasite stage).

The dose of the product is 50 mg nitroscanate/kg bodyweight, which is equivalent to 1 x 100 mg tablet per 2 kg (4.4 lb) bodyweight for the 100 mg product. For the 500 mg product the dose is also 50 mg nitroscanate/kg bodyweight, which is equivalent to 1 x 500 mg tablet per 10 kg (22 lb) bodyweight. To ensure precise dosing, the 500 mg product may be used in combination with the 100 mg product. The product should be administered together with about one-fifth of the daily food ration in the morning when the dog's stomach is empty. The remaining food ration should be administered in the evening. The tablets should be given whole.

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.[1] 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 [2] 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. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains nitroscanate 100 mg or 500 mg per tablet. The excipients are maize starch, microcrystalline cellulose, sodium starch cellulose, sodium laurilsulfate, magnesium stearate and purified water. (The purified water is not present in the finished product) The container/closure system is made of aluminium foil, low density polyethylene strips in an outer carton containing 4, 6 or 100 tablets for the 100 mg products, and 1, 4, 60 or 100 tablets for the 500 mg products. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence of preservative are 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 manufacturing method consists of: mixing, preparation of maize starch paste, granulation, drying, sizing/milling, lubrication/blending, compression, film coating, strip packaging and final packaging.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is an established active substance described in an active substance Masterfile and produced to the applicant's specification. The active

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

substance is 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.

All excipients are described in the European Pharmacopoeia. The components coating the tablets are not described in a pharmacopoeia. An applicant's specification was 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. 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. Control tests on the finished product are those for: appearance, identification and assay of the active substance, disintegration of tablet, uniformity of mass and microbial purity. Suitable dissolution data were provided.

II.F. Stability

Stability data on the active substance, finished product and product packaged for sale have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 5 years.
Store in a dry place.
Do not store above 25°C.
Keep blister strip in outer carton.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Sufficient bibliographical data were provided to support the safety aspects of the products.

Pharmacodynamics

The mode of action of nitroscanate is not well established, however, there is evidence that nitroscanate decreases the ATP/ADP ratio affecting energy producing pathways within the target parasites, leading to the death of the parasite.

Pharmacokinetics

Pharmacokinetic data from dogs are not available. In other species (mice and sheep), the drug is only partly absorbed from the gastrointestinal tract when administered orally, with the majority of the dose being eliminated in the faeces. The remainder of the dose is metabolised and excreted in the urine.

Toxicological Studies

The applicant provided bibliographical data.

- Single Dose Toxicity

A supporting study noted that nitroscanate was mildly irritating to the eye of the rabbit, and a moderate irritant to the skin. However, contact to the user is unlikely as the active substance is contained within the product.

- Repeated Dose Toxicity

A supporting study provided showed that elevated live enzymes were only significant after x 5 the recommended dose was provided to dogs. A NOAEL[3] of 150 mg/mg bodyweight in this species was accepted.

- Reproductive Toxicity, including Teratogenicity

[3] NOAEL – No observed adverse effect level.

Although toxicity data for active substance are sparse as regards reproductive parameters, the data requirements for toxicity data in this respect as regards non-food producing species permitted that no further data were required.

- Mutagenicity/Carcinogenicity

A large amount of references referring to mutagenicity tests satisfactorily concluded that the active substance is not a genetic carcinogen. Further studies were not required for non-food producing animals.

Studies of Other Effects

The applicant provided bibliographical data.

Observations in Humans

The active substance is not authorised for use in humans.

Studies on Metabolites, Impurities, Other Substances and Formulation

A brief summary was provided for the excipients and the components of the film-coating for the tablets. All components are of established use, and do not pose a threat to health when the product is used as recommended.

User Safety

A user risk assessment was provided in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. The following applicant's user recommendations are appropriate:

- Tablets are film coated and should not be broken or divided to avoid skin and eye irritation.
- This product may cause hypersensitivity (allergy). Avoid contact with this product if you know you are sensitised.
- Accidental ingestion may cause gastro intestinal disturbances. If symptoms persist, seek medical advice and show the package leaflet or the label to the physician.
- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

IV. CLINICAL DOCUMENTATION

IV.I Pre-Clinical Studies

Pharmacology

Details of the pharmacodynamic and pharmacokinetic properties of the active substance were provided in Section III.

Tolerance in the Target Species

The applicant submitted a laboratory study and literature references. The references showed that vomiting may rarely occur 4-16 hours after administration. Other rare adverse reactions include hypersalivation, diarrhoea, and blood in vomit or diarrhoea have been reported. The treatment should not be repeated if vomiting occurs shortly after dosing. Treat symptomatically. Neurological disorders (convulsions/epileptic seizures, ataxia, muscle tremors and collapse), may occur in very rare cases.

Resistance

There are no current data to suggest that there is resistance among the target parasite species to nitroscanate.

IV.II. Clinical Documentation

An historical dose-determination study and numerous references supported the efficacy of the product in laboratory trials. The product should not be administered to puppies less than six months of age because of the requirement to restrict food intake at the time of administration.

The applicant submitted data in relation to five original studies and a series of references.

Based on the data provided, it was determined that efficacy was established for the target parasite species as defined in the SPC.

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 of the products is favourable.

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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