Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dectomax 5 mg/ml Pour-on Solution for Cattle

Date Created: October 2023

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Dorimec 5 mg/ml Pour-on Solution for Cattle, Pour-on solution
Applicant	C&H Generics Ltd, c/o Michael McEvoy and Co, Seville House,, New Dock Street, Galway, Ireland
Active substance	Doramectin
ATC Vetcode	QP54AA03
Target species	Cattle
Indication for use	For treatment of infestations of gastrointestinal roundworms, lungworms, eyeworms, warbles, sucking and biting lice, mange mites and hornfly in cattle. Gastrointestinal roundworms (adults and fourth stage larvae) *Ostertagia ostertagi (inc. inhibited larvae)* *O. lyrata*[1] *Haemonchus placei* *Trichostrongylus axei* *T. colubriformis* *Cooperia oncophora* *C. punctata*[1] *C. surnabada*[1] *(syn. mcmasteri)* *Bunostomum phlebotomum*[1] *Oesophagostomum radiatum* *Trichuris* spp.[1] [1] adults Lungworms (adults and fourth stage larvae) *Dictyocaulus viviparus* Eyeworms (adults) *Thelazia* spp. Warbles (parasitic stages) *Hypoderma bovis, H. lineatum*

	Biting lice *Damalinia (Bovicola) bovis* Sucking lice *Haematopinus eurystemus,* *Linognathus vituli,* *Solenopotes capillatus* Mange mites *Psoroptes bovis,* *Sarcoptes scabiei,* *Chorioptes bovis* Horn fly *Haematobia irritans* The product also controls horn flies (*Haematobia irritans*) for at least 42 days after treatment.

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 application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	24/8/23

I. SCIENTIFIC OVERVIEW

The quality / safety / efficacy aspects of this product are identical to Dectomax 5 mg/ml marketed by Elanco Europe and Zearl 5 mg/ml marketed by Elanco GmbH. The initial applications for these products were assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains doramectin and the excipients cetearyl octanoate, triethanolamine and isopropyl alcohol.

The container/closure system consists of high-density polyethylene (HDPE) bottles sealed with a polypropylene cap. 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 and dilution.

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 doramectin, an established active substance. The active 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.

An ASMF has been provided.

Triethanolamine and isopropyl alcohol comply with the relevant pharmacopoeial standards, and a Certificate of Analysis has been provided for ceterayl octanoate.

CoAs have been provided for the packaging components.

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 of the active substance and of PDA, related impurities, uniformity of fill and microbial purity.

II.F. Stability

Stability data on the active substance 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

Shelf life of the veterinary medicinal product as packaged for sale: 5 years
Shelf life after first opening the immediate packaging: 1 year

Do not refrigerate.
Protect from light.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Not applicable due to the legal basis of the application. Bioequivalence has been established to the reference product.

Toxicological Studies

Not required.

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. Therefore the following applicant's user recommendations are appropriate:,

People with known hypersensitivity to the doramectin should avoid contact with the product. Do not smoke or eat while handling the product. Wash hands after use. The product may be irritating to human skin and eyes and users should be careful not to apply it to themselves or to other people. Operators should wear impermeable rubber gloves and boots with a waterproof coat when applying the product. Protective clothing should be washed after every use. If accidental skin contact occurs, wash the affected area immediately with soap and water. If irritation persists, seek medical attention. If accidental eye exposure occurs, flush the eyes immediately with clean water and seek medical attention immediately. Avoid accidental inhalation of this product, as this may cause drowsiness and dizziness. Use only in well-ventilated areas or outdoors.

Highly Flammable - Keep away from heat, sparks, open flame or other sources of ignition.

Environmental Safety

A Phase I and II environmental risk assessment (ERA) in accordance with current guidance were provided. The environment will be exposed via spreading of manure from treated animals onto land and via direct excretion onto pasture and into surface waters. Despite the $PEC_{soil\ initial}$ being less than the trigger value (100 µg/kg), a Phase II ERA was required as the product is an ecto- and endo-parasiticide.

The applicant submitted numerous proprietary, GLP-compliant studies in Phase II of the ERA, together with several references from the published literature.

Proprietary study data relating to each of the required physicochemical properties of the active substance; doramectin, were provided, except for information on molecular weight which has been sourced from published literature. These data were considered satisfactory for use in the ERA.

In respect of environmental behaviour, proprietary degradation and adsorption/desorption studies in soil were provided. The results of these studies indicate that doramectin is moderately persistent (DT_{50} = 30.7 days) and slightly immobile (K_{OC} = 46 215 ml/g) in soil. Additionally, metabolism data from the published literature were cited and indicate that the majority of the active substance or its metabolites are excreted in faeces, with approximately 43% of the excreted residues comprising unchanged parent product and the major metabolite, 3”-O-desmethyl-doramectin.

Proprietary ecotoxicological effects studies were submitted in Tier A of the Phase II assessment. These studies were conducted in accordance with the appropriate OECD guidelines and are acceptable for use in the ERA. In accordance with current guidance no data on the toxicity of doramectin to terrestrial plants and microorganisms, or sediment dwellers, were provided.

Concerning the risk characterisation, at Tier A, risks to dung organisms, fish (following direct excretion into surface water), aquatic invertebrates (following exposure via drainage/run-off and direct excretion), and the groundwater ecosystems have been identified. A proprietary bioaccumulation study in fish (in accordance with OECD GL 305) was provided. The BCF is below the trigger value (1000) and, therefore, a secondary poisoning assessment was not required.

With regard to mitigation of the risk to dung organisms, aquatic invertebrates, sediment organisms (for which the applicant provided a GLP-compliant Chironomid study conducted in accordance with OECD guideline 218), and fish, the applicant cited a number of references form the published literature in support of the argument that the adverse effects of doramectin on these populations were acute and localised (temporally and spatially), and the respective populations are able to recover due to the brief, temporal nature of exposure and the presence of unexposed populations of organism in the immediate vicinity which could facilitate the recovery of the affected populations in dung or surface water (downstream of exposure). The rationale of the

applicant is appreciated and presents some valid points. Nonetheless, the risk mitigation measures proposed for dung organisms and aquatic organisms following the CVMP Article 35 referral in 2013 (EMEA/V/A-35/81) for doramectin-containing injectable and pour-on veterinary medicines used in mammalian food producing species, have been proposed.

A PBT assessment was conducted, the conclusions of which are that doramectin is neither sufficiently persistent (DT_{50} at 12°C <120 days) nor bioaccumulative (BCF_{SSL} <2000 l/kg) to be classified as a PBT substance, this conclusion was supported.

The environmental precautions and warnings contained in the SPC reflect the outcome of the Article 35 referral on doramectin-containing injectables and pour-ons for cattle (EMEA/V/A-35/81). These mitigation measures relate to the risk identified for dung organisms and aquatic organisms and are supported. The disposal advice contained in the SPC is in line with current guidance and was considered acceptable.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because of the legal basis of the application.

MRLs

Doramectin is listed in Table 1 of Regulation 37/2010 (470/2009) and MRLs have been established for edible tissues. The marker substance is doramectin.

MRLs are listed below:

	Bovine
Muscle	10 µg/kg
Liver	100 µg/kg
Kidney	30 µg/kg
Fat	150 µg/kg

Withdrawal Periods

Based on the data provided, a withdrawal period of 35 days for meat in cattle is justified. Not permitted for use in lactating animals producing milk for human consumption.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Not required due to the legal basis of the application.

IV.II. Clinical Documentation

Not required due to the legal basis of the application.

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 product 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.

(www.gov.uk/check-animal-medicine-licensed)

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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