Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Milbetab 16 mg/40 mg Film-coated Tablets for Cats
Wormax Film-coated Tablets for Cats 16/40 mg
Wormit Film-coated Tablets for Cats 16/40 mg

Date Created: April 2025

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Milbetab 16 mg/40 mg Film-coated Tablets for Cats Wormax Film-coated Tablets for Cats 16/40 mg, Film-coated tablet Wormit Film-coated Tablets for Cats 16/40 mg, Film-coated tablet
Applicant	C&H Generics Ltd, c/o Michael McEvoy and Co, Seville House, New Dock Street, Galway, Ireland
Active substance	Milbemycin Oxime (A3 and A4) Praziquantel
ATC Vet code	QP54AB51
Target species	Cats
Indication for use	Treatment of mixed infections by immature and adult cestodes as well as nematodes of the following species: Cestodes: • *Dipylidium caninum* • *Taenia* spp. • *Echinococcus multilocularis* Nematodes: • *Ancylostoma tubaeforme* • *Toxocara cati* Prevention of heartworm disease (*Dirofilaria immitis*) if concomitant treatment against cestodes is indicated. The veterinary medicinal product is only indicated when use against cestodes and nematodes is indicated at the same time.

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 8 of VMRs 2013 (Schedule 1, Para 10) as amended.
Date of conclusion of the procedure	09/04/2025

I. SCIENTIFIC OVERVIEW

These are generic applications in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10) as amended, for authorisations in Great Britain (GB) and Northern Ireland (NI). The reference product for GB is Milbemax Film-coated Tablets for Cats, which has been authorised in the UK since April 2003. The reference product for NI is Milbemax Film-coated Tablets for Cats, which has been authorised in IE since August 2003. The applicant provided evidence of bioequivalence with the reference products.

Milbetab, Wormax and Wormit tablets contain 16mg milbemycin oxime and 40mg praziquantel. The products are indicated for the treatment of mixed infections by immature and adult cestodes and nematodes of certain species and the prevention of heartworm disease, if concomitant treatment against cestodes is indicated. The certain parasite species that the product is effective against are listed in the SPC[1]. The minimum recommended dose rate is 2 mg milbemycin oxime and 5 mg praziquantel per kg, given once orally.

The distribution category for each product is POM-V, a veterinary medicinal product subject to prescription.

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[2]. 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[3] 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.

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

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains milbemycin oxime and praziquantel and the excipients lactose monohydrate, croscarmellose sodium, microcrystalline cellulose, povidone, colloidal anhydrous silica and magnesium stearate in the core and titanium dioxide (E171), iron oxide yellow, iron oxide red, polyvinyl alcohol, polyethylene glycol, macrogol/PEG, talc and grilled meat flavour in the coat.

The container/closure system consists of cardboard boxes containing blister packs, made up of a cold form laminate of OPA/ALU/PVC of thickness 25µm/47µm/60µm, with a 20µm hard tempered aluminium foil. 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 regulatory 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:

- Standard granulation
- Blending
- Compression
- Coating of tablets prior to packaging

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

II.C. Control of Starting Materials

The active substances are milbemycin oxime and praziquantel, both established active substances described in the European Pharmacopoeia and supplied in accordance with appropriate Certificates of Suitability (CEPs). The active substances are 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.

The excipients are tested for compliance with the requirements of their respective current European Pharmacopoeia monographs.

The tablet packaging is compliant with EU Regulations 10/2011 and 1935/2004/EC for materials in contact with food, and satisfactory certificates of analysis for packaging materials, showing compliance with specifications, were provided.

II.C.4. Substances of Biological Origin

Scientific data and/or certificates of suitability issued by the EDQM have been provided and 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.

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 appropriate for this pharmacological form.

II.F. Stability

Stability data on the active substances have been provided in accordance with applicable regulatory 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 regulatory guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information

The shelf life of the veterinary medicinal product as packaged for sale is 4 years. The product should be used immediately after first opening the immediate packaging. The blister should be kept in the outer carton in order to protect from light and there are no special temperature storage conditions.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

Due to the legal basis of the applications, no new pharmacological or toxicological studies were submitted. Appropriate bioequivalence data to the reference product was provided.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users/the environment.

III.A Safety Documentation

Pharmacological Studies

The applicant submitted an *in vivo* bioequivalence study in cats in comparison to the reference product. This was concluded as appropriate to prove evidence of bioequivalence with the reference product.

Milbemycin oxime belongs to the group of macrocyclic lactones and is active against mites, larval and adult stages of nematodes and larvae of *Dirofilaria immitis*.

The mode of action of milbemycin is related to its action on invertebrate neurotransmission. It increases nematode and insect membrane permeability to chloride ions via glutamate-gated chloride ion. This leads to hyperpolarisation of the neuromuscular membrane and flaccid paralysis and death of the parasite.

Praziquantel is an acylated pyrazino-isoquinoline derivative and is active against cestodes and trematodes. It modifies the permeability for calcium in the membranes of the parasite, inducing an imbalance in the membrane structures, leading to membrane depolarisation and almost instantaneous contraction of the musculature, rapid vacuolization of the syncytial tegument and subsequent tegumental disintegration, resulting in easier expulsion from the gastrointestinal tract or death of the parasite.

In the cat, praziquantel reaches peak plasma concentrations within an hour after oral administration. The half-life of elimination is around 3 hours. In the dog, there is rapid hepatic biotransformation, principally to monohydroxylated derivatives. The principal route of elimination in the dog is renal. After oral administration in the cat, milbemycin oxime reaches peak plasma concentrations within 2 hours. The half-life of elimination is around 13 hours (± 9 hours). In the rat, metabolism appears to be complete although slow, since unchanged milbemycin oxime has not been found in urine or faeces. Main metabolites in the rat are monohydroxylated derivatives, attributable to hepatic biotransformation. In addition to relatively high liver concentrations, there is some concentration in fat, reflecting its lipophilicity.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the products do not present an unacceptable risk to the user if used as directed.

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:

- Accidental ingestion of the product may be harmful.
- Dispose of unused tablet halves.
- In the event of accidental ingestion of the tablets, particularly by a child, seek medical advice immediately 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 producing animals and as a result environmental exposure will be low. A Phase II ERA was not required. No unacceptable risk to the environment is expected if the products are used as directed.

IV. CLINICAL DOCUMENTATION

As these are generic applications, and bioequivalence with the reference product has been established, efficacy studies are not required. The efficacy claims, dosing regimens, and pharmacology for this product are equivalent to those of the reference product.

Resistance

The bibliography/information provided suggests that there are currently no known significant resistance issues in the target parasites in the UK. Adequate warnings and precautions appear on the product literature.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the products are 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.

(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.

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