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

Alpramil 5 mg/50 mg Tablets for Dogs
Alpramil 12.5 mg/125 mg Tablets for Dogs
Alpramil 20 mg/200 mg Tablets for Dogs

Date Created: July 2022

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Alpramil Tablets for Dogs; 5 mg/50 mg, 12.5 mg/125 mg, and 20 mg/200 mg
Applicant	Alfasan Nederland BV Kuipersweg 9 3449 JA Woerden The Netherlands
Active substance	Milbemycin Oxime (A3 and A4) Praziquantel
ATC Vetcode	QP54AB51
Target species	Dogs
Indication for use	Treatment of mixed infections by adult cestodes and nematodes of the following species susceptible to praziquantel and milbemycin oxime: - Cestodes: • Dipylidium caninum • Taenia spp. • Echinococcus spp. • Mesocestoides spp. - Nematodes: • *Ancylostoma caninum* • *Toxocara canis* • *Toxascaris leonina* • *Trichuris vulpis* • *Crenosoma vulpis* (Reduction of the level of infection) • *Angiostrongylus vasorum* (Reduction of the level of infection by immature adult (L5) and adult parasite stages; see specific treatment and disease prevention schedules under SPC point "4.9 Amounts to be administered and administration route") • *Thelazia callipaeda* (See specific

	treatment schedule under section 4.9 “Amounts to be administered and administration route”) The product can also be used in the prevention of heartworm disease (*Dirofilaria immitis*) if concomitant treatment against cestodes is indicated.

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	Alpramil 12.5/125mg: Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended. Alpramil 5/50mg and 20/200mg: Generic hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	

I. SCIENTIFIC OVERVIEW

Alpramil 12.5/125mg:

The quality / safety / efficacy aspects of this product are identical to Milbemax film coated tablets for cats. The initial application for Milbemax was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

Alpramil 5/50mg and 20/200mg:

This was determined a generic 'hybrid' application because of a quantitative change to the active substances with regard to the reference medicinal product have been made.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains milbemycin oxime and praziquantel and the excipients povidone, microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, colloidal hydrated silica, magnesium stearate, chicken flavour, and dried yeast. The proposed tablets contain chicken and yeast as additional excipients.

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.

The packaging consists of aluminium blister packs.

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: wet granulation and compression.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

II.C. Control of Starting Materials

The active substances are milbemycin oxime and praziquantel and are both 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 specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been 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

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

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 sites have been provided demonstrating compliance with the specification.

II.F. Stability

The active substance is fully tested to ensure compliance with its specification immediately prior to its use in manufacture of the product.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years

Shelf life of divided tablets after first opening the immediate packaging: 7 days

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

The applicant submitted a pilot and a pivotal bioequivalence study between the 12.5/125 mg test product and the reference product. Due to the legal basis of the application, further studies for the additional tablet strengths were exempted.

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:,

- Wash hands after use.
- 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 doctor.

Environmental Safety

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

Phase I:

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

Pharmacokinetics

The applicant has submitted a pilot and pivotal bioequivalence study between the 12.5/125 mg test product and the reference product. An *in vivo* bioequivalence study to demonstrate bioequivalence between the test and reference products is considered appropriate for both actives. Bioequivalence was established. The applicant also conducted an *in vivo* study to claim an

exemption from conducting further studies with the additional tablet strengths which suggested the dissolution profiles are similar.

Tolerance in the Target Species

Tolerance studies were not required but the applicant provided literature supporting the general safety.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that the benefit/risk profile of the products are 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)