AGENCE NATIONALE DU

MEDICAMENT VETERINAIRE

FRENCH AGENCY FOR FOOD, ENVIRONNEMENTAL AND OCCUPATIONAL HEALTH SAFETY

FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

14 RUE CLAUDE BOURGELAT – PARC D'ACTIVITES DE LA GRANDE MARCHE JAVENE – CS 70611 – 35306 FOUGERES

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

MILBETAB 2.5 mg/25 mg tablets for small dogs and puppies
MILIPRAZ 2.5 mg/25 mg tablets for small dogs and puppies

PRODUCT SUMMARY

EU procedure number	FR/V/0494/001/DC FR/V0495/001/DC
Name, strength and pharmaceutical form	MILBETAB 2.5 mg/25 mg tablets for small dogs and puppies MILIPRAZ 2.5 mg/25 mg tablets for small dogs and puppies
Applicant	Chanelle Pharmaceuticals Manufacturing ltd., Loughrea, Co. Galway, Ireland
Active substance(s)	Milbemycin oxime and Praziquantel
ATC vetcode	QP54A B51
Target species	Dogs (1-5kg)
Indication for use	For dogs with, or at risk from mixed infections by cestodes, gastro-intestinal nematodes, eyeworm, lungworms and/or heartworm. This veterinary medicinal product is only indicated when use against cestodes and nematodes or prevention of heartworm disease/angiostrongylosis is indicated at the same time. <u>Cestodes:</u> Treatment of tapeworms: *Dipylidium caninum, Taenia* spp*., Echinococcus* spp*., Mesocestoides* spp*.* <u>Gastrointestinal Nematodes:</u> Treatment of: Hookworm: *Ancylostoma caninum,* Roundworms: *Toxocara canis, Toxascaris leonina* Whipworm: *Trichuris vulpis* <u>Eyeworm</u> Treatment of *Thelazia callipaeda* (see specific treatment schedule under section 3.9 “Administration routes and dosage”). <u>Lungworms</u> Treatment of: *Angiostrongylus vasorum* (Reduction of the level of infection by immature adult (L5) and adult parasite stages; see specific treatment and prevention disease schedules under section 3.9 “Administration routes and dosage”), *Crenosoma vulpis* (Reduction of the level of infection).

	<u>Heartworm</u> Prevention of heartworm disease (*Dirofilaria immitis*) if concomitant treatment against cestodes is indicated.
Date of completion of the original procedure	26/02/2025
Concerned Member States	FR/V/0494/001/DC CMS: AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, HR, HU, IE, IT, LT, LV, NL, NO, PL, PT, RO, SE, SK FR/V/0495/001/DC CMS: IE

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Chanelle Pharmaceuticals Manufacturing ltd	DCP
Publicly available assessment report	

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Application in accordance with Article 18 of Regulation (EC) 2019/6, as amended.
Reference product (RP)	MILBEMAX COMPRIMES POUR PETITS CHIENS ET CHIOTS
Marketing authorisation holder	Elanco
Marketing authorisation number EU procedure number	FR/V/673855 1/2002 - FR/V/0135/001
Date of authorisation	17-07-2002

1. SCIENTIFIC OVERVIEW

The veterinary medicinal products (VMPs) are produced and controlled using validated methods and tests, which ensure the consistency of the VMPs released on the market.

It has been shown that the VMPs can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMPs are 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 VMPs was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP contains 2.5 mg of milbemycin oxime and 25 mg of praziquantel and the excipients lactose monohydrate, croscarmellose sodium, grilled meat flavour, yeast extract, povidone K30, cellulose microcrystalline, silica colloidal anhydrous, talc and magnesium stearate.

The tablets are packaged in blister made of OPA/ALU/PVC with a tempered aluminium foil placed in cardboard box.

The choice of the excipients are justified.

The VMP is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

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

C. Production and control of starting materials

The active substances are milbemycin oxime and praziquantel, two established substances described in the European Pharmacopeia. 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 this specification have been provided.

The product contains several excipients: lactose monohydrate, croscarmellose sodium, grilled meat flavour, yeast extract, povidone, cellulose microcrystalline, silica colloidal anhydrous, talc and magnesium stearate. Except grilled meat flavour, there are all described in Ph. Eur. monographs and they are controlled accordingly. Grilled Meat Flavour is not described in a pharmacopoeia but controlled according a satisfactory in-house monograph. The specifications are considered adequate to control the quality of the materials.

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.

Quality control of the container-closure system is described and considered adequate.

D. Control tests carried out on isolated intermediates during the manufacturing process

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 VMP.

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.

F. Stability tests

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. Milbemycin oxime (Line I) has a retest period of 48 months and Milbemycin oxime (Line II) has a retest period of 36 months. Retest period of Praziquantel of 48 months is also acceptable.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the VMP throughout its shelf life of 30 months when stored under the approved conditions.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of safety tests are not required.

The toxicological aspects of these VMP are identical to the reference VMP.

A. Safety tests

Pharmacological studies

Please refer to part 4.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:
The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP will only be used in non-food animals.

No warning is necessary.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, efficacy studies are not required. The efficacy claims for this VMP are equivalent to those of the reference VMP.

A. Pre-Clinical Studies

Pharmacology

A bioequivalence study was conducted between the candidate and the reference product. Comparative dissolution studies were also performed too.

Satisfactory bioequivalence was demonstrated between the reference and the candidate products

Development of resistance and related risk in animals

The bibliography reported resistance of *Dipylidium caninum* to praziquantel as well as cases of multi-drug resistance of *Ancylostoma caninum* to milbemycin oxime and resistance of *Dirofilaria immitis* to macrocyclic lactones

Adequate warnings and precautions appear on the product literature.

Dose determination and confirmation

The applicant has not conducted dose determination and confirmation studies. As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, dose determination and dose confirmation studies are not required.

Tolerance in the target species of animals

No tolerance studies have been conducted with the VMP.
The tolerance profile is similar to the reference VMP.
The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

No clinical trials were performed.
The absence of clinical trials was justified based on the generic application according to Article 18 of Regulation (EC) 2019/6).

Claimed indications are the same as those of the reference VMP.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the VMP for humans and the environment is acceptable.