AGENCE NATIONALE DU

MEDICAMENT VETERINAIRE

FRENCH AGENCY FOR FOOD, ENVIRONNEMENTAL AND OCCUPATIONAL HEALTH SAFETY

FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

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PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Milbetab 16 mg/40 mg film-coated tablets for cats
Milipraz 16 mg/40 mg film-coated tablets for cats

Product name Milbetab 16 mg/40 mg film-coated tablets for cats Milipraz 16 mg/40 mg film-coated tablets for cats	Application number FR/V/0475/001/DC FR/V/0476/001/DC
Applicant Chanelle Pharmaceuticals Manufacturing Ltd	DCP
Publicly available assessment report	

PRODUCT SUMMARY

EU procedure number	FR/V/0475/001/DC FR/V/0476/001/DC
Name, strength and pharmaceutical form	Milbetab 16 mg/40 mg film-coated tablets for cats Milipraz 16 mg/40 mg film-coated tablets for cats
Applicant	Chanelle Pharmaceuticals Manufacturing Limited Ida Industrial Estate Dublin Road Loughrea Co Galway H62 FH90 Ireland
Active substance(s)	Milbemycin oxime/Praziquantel
ATC vetcode	QP54A B51
Target species	Cats
Indication for use	For cats with, or at risk from mixed infections of cestodes, gastrointestinal nematodes, and/or heartworm. This veterinary medicinal product is only indicated when use against cestodes and nematodes or prevention of heartworm disease is indicated at the same time. Cestodes: Treatment of tapeworms: Dipylidium caninum Taenia spp. Echinococcus multilocularis Gastrointestinal nematodes: Treatment of Hookworm: Ancylostoma tubaeforme Roundworm: Toxocara cati Heartworm Prevention of heartworm disease (Dirofilaria immitis) if concomitant treatment against cestodes is indicated.

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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).

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1. SCIENTIFIC OVERVIEW

The veterinary medicinal products (VMP) 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 16 mg milbemycin oxime and 40 mg praziquantel and the excipients lactose monohydrate, croscarmellose sodium, microcrystalline cellulose, povidone K30, colloidal anhydrous silica, magnesium stearate in the tablet core. The coating agent is constituted of polyvinyl alcohol, macrogol 3350, talc, grilled meat flavour and a pink colouring agent containing titanium dioxide, iron oxide yellow and iron oxide red.

The film-coated tablets are packed in blisters made of a laminate of OPA/ALU/PVC with a hard tempered aluminium foil, placed in cardboard box.

The choice of the formulation is 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 active substances described in the European Pharmacopeia. Both active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substances specification are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

The quality control of the excipients is described and considered adequate.
The container-closure system is appropriately controlled.

Scientific data and 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.

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.

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 when stored under the approved conditions.

G. Other information

Not applicable

3. SAFETY DOCUMENTATION (safety and residues tests)

A. Safety tests

Pharmacological studies

Please refer to part 4

Toxicological 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, results of toxicological tests are not required.

Other 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, results of toxicological tests are not required.

Development of resistance and related risk in humans

The bibliographic information provided with this application indicates that there is recent clinical evidence of emerging resistance of *Dipylidium caninum* to praziquantel. Resistance of *Dirofilaria immitis* to milbemycin has been confirmed.

Adequate warnings and precautions concerning resistance appear on the product literature.

User safety

The applicant has identified the different exposure scenarios. Since both the reference product and the generic product have the same qualitative composition in active substance and that the route of administration and posology for the two products is also the same, the quantitative risk to the user or a child will be the same. The inclusion of additional excipients in the generic product is not expected to have an adverse impact on the qualitative risk.

Warnings and precautions, which have been updated, 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.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

It is a generic application for a marketing authorisation in accordance with Article 18 of the European regulation (UE) 2019/6.
The cited reference product is MILBEMAX COMPRIMES PELLICULES POUR CHATS. This reference product is marketed by Elanco GmbH and was first authorised in France on 12/08/2002.

A. Pre-Clinical Studies

Pharmacology

Pharmaceutical form
The test and the reference products have the same pharmaceutical form: tablet film coated.

Active substance qualitative and quantitative composition

The test and reference products have the same qualitative and quantitative composition in active substances: 16 mg of milbemycin oxime and 40 mg of praziquantel per tablet.

Bioequivalence studies

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

Dose determination and confirmation

These data are not required for a generic application where bioequivalence with a reference VMP has been demonstrated.

Tolerance in the target species of animals

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 tolerance tests in the target animal species are not required.

B. Clinical trials

As this is a generic application according to Article 18 of Regulation (EC) 2019/6, and bioequivalence with a reference product has been demonstrated, the results of clinical trials are not required. The efficacy profile of the candidate product is accepted as being the same as that of the reference product.

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.