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

Turzine 4/10 mg Film-coated Tablets for Small Cats and Kittens
Turzine 16/40 mg Film-coated Tablets for Cats

Date Created: 18th April 2018

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Turzine 4/10 mg Film-coated Tablets for Small Cats and Kittens Turzine 16/40 mg film-coated tablets for cats
Applicant	Elanco Europe Ltd Lilly House Priestley Road Basingstoke Hampshire RG24 9NL
Active substance	Name of active substances: Milbemycine oxime Praziquantel
ATC Vetcode	QP54AB51
Target species	Cats
Indication for use	In cats: treatment of mixed infections by immature and adult cestodes and 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.

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	17th January 2018

I. SCIENTIFIC OVERVIEW

These were generic applications in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The respective reference products are Milbemax Film-coated Tablets for Small Cats and Kittens and Milbemax Film-coated Tablets for Cats which have been authorised in the UK since April 2003.

The products are indicated in cats for the treatment of mixed infections by specific immature and adult cestodes and nematodes

The products are produced and controlled using validated methods and tests which ensure the consistency of the products released on the market. It has been shown that the products can be safely used in the target species, any reactions observed are indicated in the SPC.[1] The products are safe for the user, and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy[2] of the products was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting marketing authorisations.

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

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

Turzine 4/10 mg Film-coated Tablets for Small Cats and Kittens contains 4 mg milbemycin oxime and 10 mg praziquantel. Turzine 16/40 mg film-coated tablets for cats contains 16 mg milbemycin oxime and 40 mg praziquantel. The excipients in the tablet core are cellulose (microcrystalline), croscarmellose sodium, povidone, lactose monohydrate, silica (colloidal anhydrous) and magnesium stearate. The excipients in the tablet coating are hypromellose, macrogol, talc, iron oxide red (E172) and magnesium stearate. The pharmaceutical form of both products is an oblong artificial beef flavoured film-coated tablet with a score on both sides.

The container/closure system consists of PVC/PE/PVdC/aluminium blisters and is authorised in boxes containing 2, 4 10, 20, 50 or 100 tablets in a blister. 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 products are 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 products are manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method is simple process consisting of mixing of the active substances and excipients and compression into tablet form, followed by coating. Process validation data on the products have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance milbemycin oxime is an established active substance and the data provided complies with the monograph in the European pharmacopoeia. The active substance praziquantel is an established active substance described in the European pharmacopoeia and manufactured in accordance with a certificate of suitability. Both 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.

All excipients are describes in the European pharmacopoeia and batch analysis data have been provided for each excipient.

Praziquantel is supplied in low density polyethylene bags in a cardboard drum as stated in the certificate of suitability. Milbemycin oxime is supplied in a double-layer polythene bag sealed with a polyethylene tie and stored in a steel drum.

II.C.4. Substances of Biological Origin

The only ingredients derived from or potentially containing materials of animal origin are milbemycin oxime, and excipients lactose and magnesium stearate. Lactose, an excipient, and substances casein peptone and lactic yeast used during production of milbemycin oxime, are derived from bovine milk. Magnesium Stearate is declared to be derived from non-animal materials. 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 specifications control the relevant parameters for the pharmaceutical form. The tests in the specifications, and their limits, have been justified and are considered appropriate to adequately control the quality of the products. 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 products include those for: appearance, mean mass, dissolution of praziquantel and milbemycin oxime, identification of praziquantel and milbemycin oxime, loss on drying, total aerobic microbial count, total combine yeasts and moulds, specific species of microorganisms, uniformity of dosage units of praziquantel and milbemycin oxime, and related substances.

II.F. Stability

The stability of praziquantel is defined by the certificate of suitability and has a re-test period of three years. Stability data on milbemycin oxime 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 products throughout their shelf life when stored under the approved conditions.

G. Other Information

Shelf life of the veterinary medicinal products as packaged for sale: 3 years

In use shelf-life for half tablets is 6 months

Do not store above 25°C.
Keep blister in the outer carton to protect from light.
Half tablets should be returned to the open blister space and inserted back into the cardboard box until the next administration.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

These applications are for generic products in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The formulations are qualitatively and quantitatively identical to the reference products and therefore pharmacological and toxicological data are not required.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the formulations are identical to the reference products, and therefore the risks to users of the products or a child are also identical.

Warnings and precautions as listed on the product literature are identical to the reference products and are adequate to ensure safety to users of the products. Therefore the following applicant's user recommendations are appropriate:

Special precautions to be taken by the person administering the veterinary medicinal products to animals

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.

Other precautions
Echinococcosis represents a hazard for humans. As Echinococcosis is a notifiable disease to the World Organisation for Animal Health (OIE), specific guidelines on the treatment and follow-up, and on the safeguard of persons, need to be obtained from the relevant competent authority.

Environmental Safety

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

Phase I:
A Phase I environmental risk assessment was conducted. The products will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

The proposed wording regarding disposal advice is in line with that of the reference products and is acceptable. The products are not expected to pose a risk to the environment when used as recommended.

IV. CLINICAL DOCUMENTATION

These applications are for generic products in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The formulations are qualitatively and quantitatively identical to the reference products and therefore clinical and pre-clinical data were not required.

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 products. The current SPCs are 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 products.

The PAA for these products is available on the Product Information Database of the Veterinary Medicines Directorate website.

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