Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Turzine 12.5/125 mg tablets for dogs
Turzine 2.5/25 mg tablets for small dogs and puppies

Date Created: 18th April 2018

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Turzine 12.5/125 mg Tablets for Dogs Turzine 2.5/25 mg Tablets for Small Dogs and Puppies
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	Dogs
Indication for use	In dogs: treatment of mixed infections by adult cestodes and nematodes of the following species: - 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) *Thelazia callipaeda* 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	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 Tablets for Small Dogs and Puppies, and Milbemax Tablets for Dogs which have been authorised in the UK since April 2003.

The products are indicated in dogs for the treatment of mixed infections by adult cestodes and nematodes of several species. The products can also be used in the prevention of heartworm disease (*Dirofilaria immitis)* if concomitant treatment against cestodes is indicated. The recommended dose rate is a minimum of 0.5 mg of milbemycin oxime and 5 mg of praziquantel per kg bodyweight, given once daily.

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 were demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a 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 2.5/25 mg tablets for small dogs and puppies contains 2.5 mg milbemycin oxime and 25.0 mg praziquantel. Turzine 12.5/125 mg tablets for dogs contains 12.5 mg milbemycin oxime and 125.0 mg praziquantel. The excipients are, cellulose (microcrystalline), croscarmellose sodium, povidone, lactose monohydrate, silica (colloidal anhydrous) and magnesium stearate. Turzine 2.5/25 mg tablets for small dogs and puppies is one divisible oblong tablet of 125 mg with a score line of both sides and Turzine 12.5/125 mg tablets for dogs is a round tablet of 625 mg.

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 established pharmaceutical forms and their 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. Process validation data on the product 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 described 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 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 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 product throughout its shelf life when stored under the approved conditions.

For Turzine 2.5/25 mg tablets for small dogs and puppies half tablets an in use shelf-life for half tablets in 1 month when stored in the open blister space and placed back in the cardboard box.

G. Other Information

Turzine 2.5/25 mg tablets for small dogs and puppies:

Shelf life of the veterinary medicinal product as packaged for sale: 2 years
In use shelf-life for half tablets is 1 month

Do not store above 30°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.
Half tablets should be stored below 25°C.

Turzine 12.5/125 mg tablets for dogs:

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

Do not store above 30°C.
Keep blister in the outer carton to protect from light.

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 as the formulations are identical to the reference products, and therefore the risks to users of the product 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 product. Therefore the following applicant's user recommendations are appropriate.,

Special precautions to be taken by the person administering the veterinary medicinal product 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 formulation is qualitatively and quantitatively identical to the reference product 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.

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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 these products are available on the Product Information Database of the Veterinary Medicines Directorate website.

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