**College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board**

**Graadt van Roggenweg 500**
**3531 AH Utrecht**
**The Netherlands**

**DECENTRALISED PROCEDURE**

# PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

**Metrotab vet. Flavoured 250 mg Tablets for dogs and cats**
**Metrotab vet. Flavoured 500 mg Tablets for dogs and cats**
**Metrotab vet. Flavoured 1000 mg Tablets for dogs**

**Date: 5 February 2021**

# MODULE 1

## PRODUCT SUMMARY

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| Dutch Application numbers | REG NL 126405, 126407, 126408 |
| EU Procedure number | NL/V/0350/001-003/DC |
| NL Case numbers registration | 793646, 793652, 793653 |
| Names, strengths and pharmaceutical form | Metrotab vet. Flavoured 250 mg Tablets for dogs and cats<br>Metrotab vet. Flavoured 500 mg Tablets for dogs and cats<br>Metrotab vet. Flavoured 1000 mg Tablets for dogs |
| Applicant | CP-Pharma Handelsgesellschaft mbH |
| Active substance(s) | Metronidazole |
| ATC Vetcode | QP51AA01 |
| Target species | 250 mg, 500 mg: dogs and cats<br>1000 mg: dogs |
| Indication for use | Treatment of gastrointestinal tract infections caused by *Giardia* spp. and *Clostridia* spp. (i.e. *C. perfringens* or *C. difficile*).<br>Treatment of infections of the urogenital tract, oral cavity, throat and skin caused by obligate anaerobic bacteria (e.g. *Clostridia* spp.) susceptible to metronidazole. |

# MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website:

http://www.cbg-meb.nl/CBG/en/veterinary-medicines/database-veterinary-medicines/default.htm

# MODULE 3

## PUBLIC ASSESSMENT REPORT

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| Legal basis of original application | 250 mg: Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.<br>500 mg, 1000 mg: Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended. |
| Date of completion of the original decentralised procedure | 16 December 2020 |
| Concerned Member States for original procedure | AT, BE, DE, DK, ES, FI, FR, HU, IE, IT, PL, PT, SE, UK |

## I. SCIENTIFIC OVERVIEW

Metrotab vet. Flavoured 250 mg, 500 mg Tablets for dogs and cats and Metrotab vet. Flavoured 1000 mg Tablets for dogs are produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.
It has been shown that the products can be safely used in the target species; the slight reactions observed are indicated in the SPC.
Metrotab vet. Flavoured 250 mg, 500 mg Tablets for dogs and cats and Metrotab vet. Flavoured 1000 mg Tablets for dogs are safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

The quality, safety and efficacy aspects of Metrotab vet. Flavoured 250 mg, 500 mg Tablets for dogs and cats and Metrotab vet. Flavoured 1000 mg Tablets for dogs are based on bioequivalence with the Reference product Metrazol REG NL 5757 and the EU Reference product Metrotab flavour 250 mg tabletten voor honden en katten REG NL 123390. Warnings statements and precautions are adopted from the (EU) Reference product.
Additional statements have been added, based on increased knowledge and the current state of science. Adverse events, warnings and contraindications are indicated in the SPC.

## II. QUALITY ASPECTS

### *A. Composition*

The tablets contain 250 mg, 500 mg and 1000 mg Metronidazole and the following core excipients: Colloidal silica hydrated, Sodium starch glycolate (type A), Hydroxypropyl cellulose, Magnesium stearate, Microcrystalline cellulose and Chicken flavour.

The tablet is cross scored and meant to be broken into equal halves or quarters.

The products are packed in Al-PVC/PE-PVDC blisters, each containing 10 tablets.

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

A bioequivalence study is waived for the generic Metronidazole 250 mg Flavoured tablets. The 500 mg and 1000 mg tablets fulfil the requirements of the biowaiver for strengths.

## *B. Method of Preparation of the Product*

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

The product is manufactured using conventional manufacturing techniques. However, suitable pre-approval validation results on two small production batches have been provided.

The tests performed during production are described.

## *C. Control of Starting Materials*

The active substance, Metronidazole, is an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

A CEP procedure has been employed. The copy of the CEP provided represents the current version.

The active substance specification is considered adequate to control the quality of the material from the supplier. Batch analytical data demonstrating compliance with this specification have been provided.

All excipients are in conformity with the Ph.Eur. requirements with the exception of Chicken flavour which have been adequately specified.

The packaging is in conformity with the Ph. Eur. and EU Food Directive.

*Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies.*

The Magnesium stearate is of vegetable origin. In regard to Chicken flavour A TSE declaration and Viral Safety Evaluation are provided.

## *D. Control on intermediate products*

Not applicable.

## *E. Control Tests on the Finished Product*

The finished product specification controls the relevant parameters for the pharmaceutical form. Relevant 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.

## *F. Stability*

According to the statement on the CEP the claimed retest period of 60 months can be granted.

Stability data on the finished product has been provided in accordance with applicable European guidelines.

According to the stability results provided the claimed shelf life of 30 months can be granted for all tablet strength.

### *G. Other Information*

Not applicable.

## III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

### For generics, insert in the relevant sections as appropriate:

As this is a generic application (250 mg) respectively a hybrid application (500 mg, 1000 mg) according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological, pharmacological and clinical tests are not required.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users / the environment / consumers.

Additional statements have been added, based on increased knowledge and the current state of science. Adverse events, warnings and contraindications are indicated in the SPC.

### *User Safety*

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

Combined with increased knowledge and the current state of science, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

### *Ecotoxicity*

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

The environmental risk assessment can stop in Phase I because this product is intended for use in dogs and cats (100 mg, 250 mg) respectively dogs (750 mg) and a Phase II assessment is not deemed necessary.

The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

# IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application (250 mg) respectively a hybrid application (500 mg, 1000 mg) according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

### *Tolerance in the Target Species of Animals*

Additionally to the above, based on increased knowledge and the current state of science, warning statements and precautions have been added to the product literature ensuring safety to the target animals. Adverse events, warnings and contraindications are indicated in the SPC.

### *Resistance*

As this is a generic application (250 mg) respectively a hybrid application (500 mg, 1000 mg) according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological and pharmacological and clinical tests are not required. However, the SPC and Product Literature are updated according to the Revised Guideline on the SPC for Antimicrobial Products (EMEA/CVMP/SAGAM/383441/2005).

# V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product 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 product for humans and the environment is acceptable.

## 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 Heads of Veterinary Medicines Agencies website (www.HMA.eu ).

This section 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.

| **Summary of change (Application number)** | **Section updated in Module 3** | **Approval date** |
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