College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

METRONIDAVET 250 mg tablets for dogs and cats
METRONIDAVET 500 mg tablets for dogs and cats

Date: 4 March 2021

MODULE 1

PRODUCT SUMMARY

Dutch Application numbers	REG NL 126481, 126483
EU Procedure number	NL/V/0324/001-002/DC
NL Case number(s) registration	795594
Names, strengths and pharmaceutical form	Metronidavet 250 mg tablets for dogs and cats Metronidavet 500 mg tablets for dogs and cats
Applicant	Vet-Agro Multi-Trade Company Sp. z.o.o.
Active substance(s)	Metronidazole
ATC Vet code	QP51AA01
Target species	dogs and cats
Indication for use	Treatment of gastrointestinal tract infections caused by *Giardia* spp. and *Clostridia* spp. (i.e. *C. perfringens* or *C. difficile*). 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

Legal basis of original application	250 mg: Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended. 500 mg: Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	10 February 2021
Concerned Member States for original procedure	AT, BE, BG, CZ, EL, ES, FR, HU, IT, LT, PL, PT, RO

I. SCIENTIFIC OVERVIEW

Metronidavet 250 mg, 500 mg tablets for dogs and cats 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.
Metronidavet 250 mg, 500 mg tablets for dogs and cats 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 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 Metronidavet 250 mg, 500 mg tablets for dogs and cats are based on bioequivalence with the Reference product Metrazol REG NL 5757 and the EU Reference product Metronidazole VET-AGRO 250 mg tabletten voor honden en katten REG NL124309. 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 and 500 mg Metronidazole and the following core excipients: Colloidal silica hydrated, Sodium starch glycolate (type A), Hydroxypropyl cellulose, Magnesium stearate, Microcrystalline cellulose, Yeast extract and Iron oxide (E172).
The tablet is cross scored and meant to be broken into equal halves or quarters.
The products are packed in Al-Al 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 auto-generic Metronidazole 250 mg tablets. The 500 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 Yeast extract, 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 Yeast extract a BSE/TSE declaration is 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 18 months stability results provided the claimed shelf life of 30 months claim can be granted.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application (250 mg) respectively a hybrid application (500 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 (250 mg, 500 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) 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) 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**