LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Equibactin vet. sulfadiazine & trimethoprim

SE/V/120/01/DC

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

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MODULE 1

PRODUCT SUMMARY

DCP Procedure number Asp no	SE/V/120/01/DC 2017-0382

Name, strength and pharmaceutical form	Equibactin vet., 250 mg/g + 50 mg/g, Oral powder
Applicant	Dechra Regulatory B.V. Handelsweg 25 5531 AE Bladel The Netherlands
Active substance(s)	sulfadiazine & trimethoprim
ATC Vetcode	QJ01EW10
Target species	Horses
Indication for use	For the treatment of infections in horses caused by micro-organisms susceptible to the combination of trimethoprim and sulfadiazine, such as infections of the upper respiratory tract, the urogenital system and wound infections.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

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 completion of the original decentralised procedure	2019-02-06
Date product first authorised in the Reference Member State Sweden	2019-03-08
Concerned Member States for original procedure	AT, BE, CY, DE, EE, EL, ES, FR, HR, HU, IE, IS, IT, LT, LU, LV, NL, NO, PL, PT, RO, SI, SK, UK

I. SCIENTIFIC OVERVIEW

The product is 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 product can be safely used in the target species; the slight reactions observed are indicated in the SPC.
The product is 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.

II. QUALITY ASPECTS

A. Drug Substances

The structures of the drug substances have been adequately proven and their physicochemical properties are sufficiently described.

The manufacture of the drug substances has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substances specifications include relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest periods.

B. Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmaco-toxicological tests are not required.

The safety aspects of this product, i.e. user safety, consumer safety and environmental risk, are identical to the reference product.

Warnings and precautions as listed on the product literature are the same, or as for the user somewhat extended (in line with the current guidelines, i.e. Guideline on user safety for pharmaceutical veterinary medicinal products [EMA/CVMP/543/03-Rev.1]) as those of the reference product and are adequate to ensure safety of the product to users / the environment / consumers.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the main risk with this product is related to the content of sulfadiazine, a sulphonamide which can cause hypersensitivity reactions following skin contact, inhalation or accidental ingestion. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

Phase I

The environmental risk assessment can stop in Phase I because this product will be used to treat a small number of animals in a flock or herd, i.e. it is not expected to pose a risk for the environment when used according to the product literature.

III.B Residues documentation

Residue Studies

No residue

depletion studies were conducted because this is a generic application for an oral formulation with no potential to leave local residues and for which bioequivalence with the reference product has been demonstrated.

MRLs

Sulfadiazine (a sulphonamide) and trimethoprim are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 with MRLs of 100 µg/kg for liver, kidney, fat, muscle and milk in all food producing species (sulphonamides) and in horses (trimethoprim), respectively. For trimethoprim the MRL for liver, kidney, fat, muscle and milk in all food producing species except horses is 50 µg/kg.

Withdrawal Periods

As this is a generic application for an oral formulation with no potential to leave local residues, and for which bioequivalence with the reference product has been demonstrated, the withdrawal periods for the reference product in meat, i.e. 10 days for once daily administration of 30 mg (/kg for 5 days and 20 days for twice daily administration of 30 mg/kg for 5 days, are justified. During the procedure it was agreed to only use one withdrawal period, i.e. 20 days for both once and twice daily administration.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application 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.

IV.A Pre-Clinical Studies

Pharmacology

The applicant has conducted one bioequivalence study comparing the applied product Equibactin vet oral powder for horses and the reference product Trimediazin vet plain oral powder in the target species. This was a two-period, two-sequence, single dose cross-over trial performed in horses (24 animals) in the fasted state with a 7 days washout period between doses. The dose given in each period was 5 mg of trimethoprim and 25 mg of sulfadiazine per kg administered orally. The study design is satisfactory. Blood samples were collected pre-dose and up to 48 hours after dose. Plasma concentrations of sulfadiazine and trimethoprim were determined with a sufficiently validated LC/MS/MS method. For AUC_{0-t} and C_{max}, the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80-125% for both active substances.

Based on the submitted bioequivalence study, Equibactin vet is considered bioequivalent with Trimediazin vet in horses.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, target animal safety studies are not required. The safety profile of this product is equivalent to that of the reference product.

Resistance

Adequate warnings and precautions appear on the product literature to reduce the risk for resistance development.

IV.B Clinical Studies

Laboratory Trials

As this is a generic application 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.

Field Trials

As this is a generic application 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.

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.

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 product. The current SPC is available on the Heads of Veterinary Medicines Agencies website (www.HMA.eu). The current SPC is available on the Medical Products Agency's website (http://www.lakemedelsverket.se/english/).

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:

None