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Publicly Available Assessment Report for a
Veterinary Medicinal Product

Cubarmix Equi 400 mg/g and 80 mg/g oral powder for horses

PRODUCT SUMMARY

EU Procedure number	IE/V/0673/001/DC
Name, strength and pharmaceutical form	Cubarmix Equi 400 mg/g + 80 mg/g oral powder for horses
Active substance(s)	Sulfadiazine, trimethoprim
Applicant	Dopharma Research B.V. Zalmweg 24, Raamsdonksveer, Noord-Brabant, 4941 VX, Netherlands
Target species	Horses
Indication(s) for use	Treatment of infections caused by micro-organisms susceptible to the combination of sulfadiazine and trimethoprim, such as infections of the upper respiratory tract and wound infections.
ATCvet code	QJ01EW10

SUMMARY OF ASSESSMENT

Legal basis of original application	Hybrid application in accordance with Article 19(1) of Regulation (EU) 2019/6 as amended.
Reference product (RP) Marketing authorisation holder MS where the RP is or has been authorised Marketing authorisation number Date of authorisation	Trimediazine Plain Oral Powder Vetoquinol Ireland Limited Ireland VPA10983/059/001 01/10/1988
Date of completion of the original decentralised procedure	17/12/2025
Concerned Member States for original procedure	AT, BE, DE, DK, ES, FR, HU, IT, NL, PL, RO, SE, UK(NI)
Withdrawn CMS during original decentralised procedure	FI

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in relevant articles of Regulation (EU) 2019/6. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland. The Summary of Product Characteristics (SPC), the labelling and package leaflet for this product are available in the Union Product Database (UPD).

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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

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A. Qualitative and Quantitative Particulars

The product contains the active substances sulfadiazine and trimethoprim at 400 mg/ g and 80 mg/g respectively and the excipients vanilla flavour and lactose monohydrate. The container/closure system consists of a cylindrical polypropylene container, covered with a low density polyethylene lid or heat-sealed, white coloured, 4-layer sachets. The product is an established pharmaceutical form, and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site. Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substances sulfadiazine and trimethoprim are established active substances described in the European Pharmacopoeia. The active substances 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 has been provided.

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

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. 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 has been provided. Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substance has 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 has been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Tests
Pharmacological Studies
As this is a hybrid application according to Article 19 of Regulation (EU) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of pharmacodynamic tests are not required.
An in vivo bioequivalence study conducted in accordance with the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4) and VICH GL52 guideline Bioequivalence: blood level bioequivalence study (EMA/CVMP/VICH/751935/2013-Corr) has been provided. The applicant specified a-priori in the study

protocol that bioequivalence may be concluded if the 90% confidence intervals for the ratio of the means of the parameters Cmax and AUCt are included within the interval 80-125%. The results of the study indicated that the 90% confidence intervals for C_{max} and AUC_t lie within the narrower limits of 80-125%. Based on these data it was accepted that the product is bioequivalent to the reference product.

Toxicological Studies
As this is a hybrid application according to Article 19 of Regulation (EU) 2019/6 and essential similarity to a reference VMP has been demonstrated, results of toxicological tests are not required.

User Safety
The applicant has provided a user safety assessment in compliance with the relevant guideline. A qualitative risk characterisation has been conducted identifying a potential risk of skin and eye irritation and irritation following inhalation. Exposure to trimethoprim or sulfonamides may cause hypersensitivity reactions. In addition, a quantitative risk characterisation has identified a potential risk to the user following accidental ingestion including hand-to-mouth contact.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment
A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.
Phase I:
The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP will be used to treat a small number of animals in a flock or herd.

III.B Residues Documentation
Residue tests
No residue depletion studies were conducted because bioequivalence with the reference product is claimed, and it is assumed that residue depletion from edible tissues (muscle, fat, liver and kidney) will be comparable for both products.

Maximum Residue Limits
Sulfadiazine and trimethoprim are listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	Marker residue	Animal Species	MRL (µg/kg)	Target tissues	Other provision
Sulfonamides (all substances belonging to the sulfonamide group)	Parent drug	All food-producing species	100 100 100 100	Muscle Fat Liver Kidney	The combined total residues of all substances within the sulfonamide group should not exceed 100 µg/kg.
Trimethoprim	Trimethoprim	Equidae	100 100 100 100	Fat Muscle Liver Kidney	

The MRL status of the excipients of the product is indicated in the following table:

Excipients	MRL status
Lactose monohydrate ('Carbohydrates naturally occurring')	Out of scope
Vanilla Flavour	Constituents are either considered as out of scope, listed in Table 1 as 'no MRL required', or allowed feed additives

These excipients are either substances considered as not falling within the scope of Regulation (EC) No. 470/2009, allowed substances for which Table I of the Annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required, or authorised for use in feed according to Regulation (EC) No. 1831/2003, therefore no concern is anticipated.
Withdrawal Periods
Based on the data provided above, the following withdrawal period is justified:
Meat and offal: 6 months.
Not authorised for use in animals producing milk for human consumption.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies

As this is a hybrid application according to Article 19 of Regulation (EU) 2019/6 and bioequivalence with a reference VMP has been demonstrated, pre-clinical studies are not required.

***Development of resistance* and related risks in animals**

A number of references from the published literature considering the antimicrobial spectrum of trimethoprim/sulfonamide combinations and mechanisms of resistance were provided. It was concluded that antimicrobial resistance levels in horse populations based on the EU national reports remain stable for most pathogen-trimethoprim/sulfonamide combinations.
The VMP includes the same active substances, to be administered at the same concentration as the reference product. Given the legal basis of this application, and the fact that the VMP is intended to be used for the same indications, in the same target species, via the same route of administration and at the same posology as the reference product, the potential for resistance development is not expected to differ between the VMP and reference product.
Adequate warnings and precautions appear on the product literature.

Tolerance in the Target Species of Animals

No target animal tolerance studies in the target species were conducted.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical trials

As this is a hybrid application according to Article 19 of Regulation (EU) 2019/6 and bioequivalence with a reference VMP has been demonstrated, efficacy studies are not required.
The efficacy claims for this VMP are equivalent to those of the reference VMP.

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 benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI. 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 in the Union Product Database (UPD).
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.

Changes:

None.