MEDICINES EVALUATION BOARD AGENCY

Reference Member State: The Netherlands

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Sulfequine 333 mg/g + 67 mg/g oral paste for horses

Trimethoprim, Sulfadiazine

NL/V/0428/001/DC

Created: September 2025

PRODUCT SUMMARY

EU procedure number	NL/V/0428/001/DC
Name, strength and pharmaceutical form	Sulfequine 333 mg/g + 67 mg/g oral paste for horses
Applicant	CP-Pharma Handelsgesellschaft mbH
Active substance(s)	Trimethoprim, Sulfadiazine
ATC vetcode	QJ01EW10
Target species	Horses
Indication for use	Treatment of infections caused by microorganisms susceptible to the combination of trimethoprim and sulfadiazine.

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Hybrid application in accordance with Article 19 (change in strength) of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Norodine Vet.
Marketing authorisation holder	ScanVet Animal Health A/S
MS where the RP is or has been authorised	Denmark
Marketing authorisation number EU procedure number	18146
Date of authorisation	27/05/1998
Date of completion of the original decentralised procedure	6 June 2025
Concerned Member States for original procedure	AT, BE, CZ, DE, DK, EE, ES, FR, EL, HU, IE, IT, LT, LV, NO, PL, PT, SK, SE, UK(NI)
Concerned Member States for subsequent recognition procedure	N/A
Withdrawn CMS during original decentralised procedure	FI: The company decided to withdraw the application. At the time of withdrawal, the MS considered that the data provided could allow to conclude on a positive benefit-risk balance if the points for clarification were solved.

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMP 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 VMP was demonstrated according to the claims made in the SPC.

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

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP contains Trimethoprim 66.7 mg/g and Sulfadiazine 333.3 mg/g and the excipients methyl parahydroxybenzoate, propyl parahydroxybenzoate, propylene glycol, apple flavour, sucralose, sodium hydroxide, xanthan gum and water for injections.

The container/closure system pre–filled multi-dose LDPE syringe with adjustable screw ring closed with LDPE cap. Each syringe contains 45 g or 52.5 g paste.

The choice of the formulation is justified.

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

B. Description of the manufacturing method

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

Process validation data on the VMP have been presented in accordance with the relevant European guidelines.

C. Production and control of starting materials

The active substances are Trimethoprim and Sulfadiazine. Both are established active substance described in the European Veterinary Pharmacopoeia. For both substances the CEP procedure is used. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

D. Control tests carried out on isolated intermediates during the manufacturing process

No intermediates are manufactured.

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 VMP.

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 tests

Stability data on the active substances 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 VMP throughout its shelf life when stored under the approved conditions.

The claim of in-use stability is based on the demonstration of in-use stability study of 3 months at 25°C.

G. Other information

The VMP complies with the residual solvents requirements as stated in the current guidelines.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a hybrid application (change in strength) according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of safety tests are not required.

The safety aspects of this VMP are identical to the reference VMP.

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

A. Safety tests

Pharmacological studies

Results of pharmacological tests are not required. As no data on pharmacology are present in the SPC of the reference product, the applicant updated the SPC with relevant product specific data and literature data.

Toxicological studies

Results of toxicological tests are not required.

Observations in humans

The combined actives trimethoprim/sulfamethoxazole are also used in human medicine.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that hypersensitivity reactions may occur following contact, and accidental ingestion may lead to gastro-intestinal disturbances.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines. The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will be used to treat a small number of animals in a flock or herd. The VMP is not expected to pose an unacceptable risk for the environment when used according to the product literature.

B. Residues documentation

Residue tests

No residue depletion studies were conducted. As this is a hybrid application (change in strength) according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of safety tests are not required.

Maximum Residue Limits

The MRL status of the active ingredients and excipients propyl-4-hydroxybenzoate and propylene glycol at time of authorisation can be summarized as follows:

Pharmacologically active substance	**Marker residue**	**Animal Species**	**MRL**	**Target tissues**	**Other provision**	**Therapeutic Classification**
Trimethoprim	Trimethoprim	Equidae	100 µg/kg	Muscle Fat Liver Kidney	NO ENTRY	Anti-infectious agents/ Chemotheurapeutics
Sulfadiazine	Parent drug	All food producing species	100 µg/kg	Muscle Fat Liver Kidney	The combined total residues of all substances within the sulfonamide group should not exceed 100 µg/kg	Anti-infectious agents/ Chemotheurapeutics
Propyl 4-hydroxy-benzoate and its sodium salt	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	For use as preservative only	NO ENTRY
Propylene glycol	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	For use as preservative only	NO ENTRY

For the well-defined Ph. Eur. excipients Sucralose and Water (for injections) it can be concluded that they are outside the scope of (EEG) nr. 470/2009. The apple flavour is an established human food additive which complies to Regulation (EC) No 1334/2008 on flavouring. Methyl p-hydroxybenzoate (E218), Xanthan gum (E415) and Sodium hydroxide (E524) are approved food additives as listed in Regulation (EC) No 1333/2008.

Withdrawal Periods

Based on the demonstration of bioequivalence with the reference product, and the assessment of the proprietary residue depletion studies of the reference product, a withdrawal period of 15 days for meat in horses after a treatment period of up to 5 days is justified.

No residue depletion data is available for a treatment period of more than 5 days. A withdrawal period of 6 months is set to mitigate consumer safety risks in case a treatment duration longer than 5 days is required.

The agreement to set a withdrawal period of 6 months following treatment of more than 5 days, while only residue depletion data following 5 days treatment is present, is highly exceptional. The applicant has proposed and justified this withdrawal period, and agreement with the proposal was reached based on the following arguments:

- setting a maximum treatment duration of 5 days for a time-dependent antibiotic might lead to lack of expected efficacy and risk of development of resistance for certain infections requiring a longer treatment duration;
- requesting a new residue depletion study for a hybrid application which has satisfactorily demonstrated bioequivalence to the reference product would be inappropriate from a regulatory point-of-view;
- based on the available residue depletion data, it is scientifically justified that the extrapolated withdrawal period of 6 months will be sufficient to ensure consumer safety following a treatment duration of more than 5 days.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a hybrid application according to Article 19 of Regulation (EC) 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.

A. Pre-Clinical Studies

Pharmacology

Product specific pharmacokinetic data (as extracted from the bioequivalence study) on the active substances Trimethoprim and Sulfadiazine in horses are provided and reflected in the product literature. The pharmacodynamics section of the product literature is based on the information available in the reference product SPC as well as that of a different generic VMP.

Development of resistance and related risk in animals

The applicant presented an exhaustive summary of the literature regarding development of resistance in clinically relevant bacteria species in horses.

Warnings and precautions as listed on the product literature are adequate to ensure efficacious use of the VMP and to mitigate risks of development of resistance to the active substances. Mechanisms of resistance are also described in the product literature.

Dose determination and confirmation

No dose determination and confirmation studies were conducted.

Tolerance in the target species of animals

No target animal safety studies were conducted.

B. Clinical trials

The applicant has conducted one *in vivo* bioequivalence study. The study was conducted in accordance to GLP. A single-dose, two-period, two-sequence, cross-over design was used with a wash-out period of 7 days. Forty (40) clinically healthy warmblood horses of both sexes, similar breed and category were allocated to two groups of 20 animals. Following at least a 7-day acclimatisation period, each group was treated orally with the VMP or the reference product at a dose of 5.0 mg of trimethoprim and 25.0 mg of sulfadiazine per kg bodyweight.

The active substances were determined in blood plasma collected at set time points by a validated method after oral administrations of the VMP and/or the reference product. Clinical observations, physical examination, body weight, general tolerance, adverse effects, and other observed changes were recorded as well.

No animals died or were excluded during the study. The VMP and reference product were both well tolerated by all animals. The average sulfadiazine and trimethoprim plasma-concentration time curves are comparable between treatments. The sulfadiazine and trimethoprim plasma concentrations at each sampling point were considered for calculation of pivotal parameters (AUC_t and C_{max}), in order to demonstrate bioequivalence. Bioequivalence between the VMP and the refence product regarding the two active substances was shown for C_{max} and AUC_t .

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

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

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. 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 VMP.

None.