LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Triquest Vet
(trimethoprim, sulfadiazine)

SE/V/125/01/DC

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PRODUCT SUMMARY

EU Procedure number	SE/V/125/01/DC
Name, strength and pharmaceutical form	Triquest Vet, 333 mg/ml + 67 mg/ml, Oral suspension
Applicant	Alfasan Nederland BV, Kuipersweg 9 Woerden 3449 JA Netherlands
Active substance(s)	trimethoprim, sulfadiazine
ATC Vetcode	QJ01EW10
Target species	Horse
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.

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 of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Trimediazin Vet.
Marketing authorisation holder	Vetoquinol Scandinavia AB
MS where the RP is or has been authorised	RMS
Marketing authorisation number EU procedure number	MA.no: 12169 (national registration in Sweden)
Date of authorisation	1994-06-03 (deregistered 2021-06-02)
Date of completion of the original decentralised procedure	2024-05-08
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, EE, EL, ES, FR, HR, HU, IE, IS, IT, LT, LU, LV, NL, NO, PL, PT, RO, SI, SK, UK.
Withdrawn CMS during original decentralised procedure	DK and FI were withdrawn during the procedure.

*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 is formulated using excipients listed in section 2 in the Summary of Product Characteristics.

The container/closure system and details of any administration/dosing device are described in section 5.4 in the Summary of Product Characteristics.

The choice of any adjuvant, formulation and/or presence/absence of preservative are 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. The manufacturing process, as well as in-process controls have been acceptably described.

C. Production and control of starting materials

The active substance is an established active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

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

For substances within the scope of the TSE Guideline, scientific data and/or certificates of suitability issued by the EDQM have been provided and 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 tests carried out on isolated intermediates during the manufacturing process

The tests performed during manufacturing are described and results conforming to the specifications, are provided.

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<s> have been provided demonstrating compliance with the specification.

F. Stability tests

It has been ensured that the active substance complies with its specification immediately prior to its use in manufacture of the VMP.

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.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of toxicity and residue tests are not required. A user risk assessment (URA) and environmental risk assessment (ERA) were provided.

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

A. Safety tests

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that a risk for hypersensitivity, allergic reactions and irritation following dermal exposure to the product was identified. A risk for a child accidently ingesting the product was identified.

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.

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because this VMP 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.

B. Residues documentation

Residue tests

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

Maximum Residue Limits

Sulfadiazine (a sulfonamide) and trimethoprim are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010. For sulfonamides the MRL is 100 µg/kg for liver, kidney, fat and muscle in all food producing species as well as 100 µg/kg for milk in bovine, ovine and caprine. For trimethoprim the MRL is 50 µg/kg for liver, kidney, fat, muscle and milk in all food producing species except Equidae. The MRL for trimethoprim is 100 µg/kg in fat, muscle, liver and kidney derived from Equidae.

The excipients xanthan gum, sucralose, sodium hydroxide and hydrochloric acid are included in the Annex to Commission Regulation (EU) No 1333/2008.

The excipient anise aroma is in accordance to Commission Regulation (EC) No 1333/2008 and thus safe for human consumption.

Withdrawal Periods

As this is a hybrid 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, were proposed. However, during the procedure it was agreed to only use one withdrawal period, i.e. 20 days for both once and twice daily administration.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

This is a hybrid application according to Article 19 of Regulation (EC) 2019/6 since this product has a different pharmaceutical form and strength compared to the reference VMP.

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

The applicant has submitted one pilot (non-GLP) study and one pivotal (GLP) study comparing the product applied for to the reference product Trimediazine Oral Powder in the target species. The pilot study was performed in order to conclude on sample size and conditions in the pivotal study and is not further described in this report.

The pivotal study compared the product applied for, Triquest vet 333 mg/ml (SDZ) + 67 mg/ml (TMP) oral suspension for horses, to the reference product Trimediazin vet 250 mg/g (SDZ) + 50 mg/g (TMP) plain oral powder. This was a two-period, two-sequence, single dose cross-over trial performed in horses (36 animals) in the fasted state (except for small amount of feed given at dosing) 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. It would have been appropriate to perform the study according to the recommendations in the SmPC, ie by allowing additional feed once the feed containing the drug had been eaten. However, a fasted study is generally considered more sensitive in order to detect differences between formulations, and therefore no concern was raised regarding the fact that the study was performed in the fasted state. 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, Triquest vet is considered bioequivalent with Trimediazin vet in horses.

Development of resistance and related risk in animals

Adequate warnings and precautions appear on the product literature.

Tolerance in the target species of animals

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6, 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.

The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6, 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.

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.