1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sulfequine (333 mg/g + 67 mg/g) oral paste for horse

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substances:
Sulfadiazine 333.0 mg
Trimethoprim 67.0 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Methyl parahydroxybenzoate (E218)	1.80 mg
Propyl parahydroxybenzoate	0.20 mg
Propylene glycol	
Apple flavour	
Sucralose	
Sodium hydroxide, for pH adjustment	
Xanthan gum	
Water for injection	

Homogenous white to almost white paste.

3. CLINICAL INFORMATION

3.1 Target species

Horses.

3.2 Indications for use for each target species

Treatment of infections caused by microorganisms susceptible to the combination of trimethoprim and sulfadiazine.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substances (or any other sulfonamide) or to any of the excipients.
Do not use in detomidine-treated horses.
Do not use in horses with impaired liver function or kidney disease.

3.4 Special warnings

Cross-resistance has been shown between sulfadiazine and other sulfonamides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to sulfonamides because its effectiveness may be reduced.

In case of infections involving purulent conditions, trimethoprim-sulfonamides combinations are not recommended due to a diminished efficacy under such conditions.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Caution should be exercised when treating horses with blood dyscrasia.
Throughout the treatment, animals should have free access to drinking water to avoid possible crystalluria.
Caution should be exercised when treating new-born animals. Renal impairment leads to risk of accumulation, increasing the risk of adverse events in long term treatment.
Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.
Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

This veterinary medicinal product may cause hypersensitivity reactions. People with known hypersensitivity to sulfonamides, trimethoprim or any of the excipients (parabens, polyethylene glycol) should avoid contact with the product. In case of accidental skin contact, wash skin thoroughly. In case of hypersensitivity reactions (such as skin rash), seek medical advice and show the package leaflet or label to the physician.

Swelling of the face, lips or eyes are more serious symptoms and require urgent medical attention.

This veterinary medicinal product may cause adverse effects, such as gastro-intestinal disturbances. Care should be taken to avoid accidental ingestion, particularly by a child. Do not leave the syringe unattended. Oral syringes and partially used syringes should be stored in the original outer carton in a safe place and should be used at the next administration. In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Horses:

Undetermined frequency (cannot be estimated from the available data)	Hypersensitivity reaction (e.g. urticaria) Inappetence Digestive tract disorder (e.g. loose faeces, diarrhoea and colitis) Hepatic disorder. Renal disorder, renal tubular disorder[1] Haematologic effects (e.g. anaemia, thrombocytopenia, or leukopenia) Haematuria, crystalluria

[1]Tubular obstruction

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for the respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Laboratory studies in rats and mice have shown evidence of teratogenic effects.
The safety of the veterinary medicinal product during pregnancy and lactation has not been assessed in the target species. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Trimethoprim/sulfonamide-containing preparations can trigger fatal cardiac arrhythmias in detomidine-sedated horses.

3.9 Administration routes and dosage

Oral use.

The single daily dose is 30 mg of active substance (5 mg trimethoprim and 25 mg sulfadiazine), per kg body weight, corresponding to 3.75 grams of the veterinary medicinal product per 50 kg bodyweight, usually for 5 days. For certain indications longer treatment may be required.

The appropriate treatment duration should be chosen based on the clinical needs and individual recovery of the treated animal. Consideration should be given to the accessibility of the target tissue and characteristics of the target pathogen.

Absorption is increased if food is withheld in the last few hours before dosing.

To ensure a correct dosage, body weight should be determined as accurately as possible.
The 45 g syringe is intended for horses up to 600 kg body weight and the 52.5 g syringe is for horses up to 700 kg body weight.
The plunger of each prefilled oral syringe is divided into 50 kg markings.
The calculated dose is provided by adjusting the ring on the plunger according to the body weight of the horse.

After removing the cap, the paste is administered orally by inserting the nozzle of the syringe through the interdental space and depositing the required amount of veterinary medicinal product on the back of the tongue. The animal's mouth should be free of any food. Immediately after administration, elevate the head of the horse for a few seconds to ensure the dose is swallowed.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

In case of overdose, no other adverse events are known than those mentioned in section 3.6.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Meat and offal:
For a treatment period of up to 5 days: 15 days.
For a treatment period of more than 5 days: 6 months.

Not authorised for use in animals producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01EW10

4.2 Pharmacodynamics

Sulfadiazine belongs to the group of sulfonamide chemotherapeutics, trimethoprim belongs to the diaminopyrimidines. Both active substances have an inhibitory effect on the folic acid metabolism of microorganisms at two different stages (sequential effect). Blocking individual steps disrupts the synthesis of nucleic acids and proteins in sensitive bacteria.
Sulfadiazine inhibits the incorporation of p-aminobenzoic (PABA) acid into dihydrofolic acid. Sulfadiazine specifically competes with PABA for the enzyme dihydroproteo synthetase, this selective bacteriostatic effect depends on the difference in the formation of folic acid in bacterial and mammalian cells. Susceptible microorganisms synthesize folic acid, whereas mammalian cells use preformed folic acid.
Trimethoprim selectively inhibits the enzyme dihydrofolate reductase, thus preventing the conversion of dihydrofolic acid to tetradihydrofolic acid.

Sulfonamide resistance genes are linked chromosomally (*folP* genes) or extrachromosomally, e.g. to integron 1 (*sul1* genes) and plasmids (*sul2* genes). The result of the expression of these genes is a change in the structure of the dihydropteroate synthetase enzyme so that sulfonamides lose their ability to bind and the mechanism of their action is disrupted. There is mutual cross-resistance in the sulfonamide group.
Trimethoprim resistance genes (*dfr* genes) are linked chromosomally or extrachromosomally, e.g. on integrons 1 and 2 or on transposons. Extrachromosomal *dfr* genes are divided into two subgroups. More than 30 *dfr* genes are currently described. Their action is manifested by a change in the structure of the dihydrofolate reductase enzyme and its sensitivity to trimethoprim. Chromosomally linked resistance is manifested either by overproduction of dihydrofolate reductase or loss of function of the thymidylate synthase enzyme.

4.3 Pharmacokinetics

The pharmacokinetic profile of sulfadiazine when administered at an oral dose of 25 mg/kg body weight to horses was characterised by a maximum concentration (C_{max}) in plasma of approximately 15.9 mcg/ml; this was achieved at 2.5 hours post-dosing (T_{max}). Peak concentrations were followed by a decline in systemic exposure with an apparent elimination half-life ($t_{½}$) of 5.6 hours.
The pharmacokinetic profile of trimethoprim when administered at an oral dose of 5 mg/kg body weight to horses was characterised by a maximum concentration (C_{max}) in plasma of approximately 2.1 mcg/ml; this was achieved at 1.8 hours post-dosing (T_{max}). Peak concentrations were followed by a decline in systemic exposure with an apparent elimination half-life ($t_{½}$) of 2.1 hours.

Excretion of both actives is mainly by the kidneys.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 33 months.
Shelf-life after first opening the immediate packaging: 3 months.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

White 50 mL pre-filled oral syringe, delivering 45.0 or 52.5g of paste, composed of:
Barrel: LDPE
Plunger: LDPE
Screw ring: LDPE
Cap: LDPE

The plunger is sub-divided into increments of 50 kg body weight.

Pack sizes:
Cardboard box containing 1 oral syringe containing 45 grams paste
Cardboard box containing 5 oral syringes containing 45 grams paste
Cardboard box containing 6 oral syringes containing 45 grams paste
Cardboard box containing 10 oral syringes containing 45 grams paste
Cardboard box containing 1 oral syringe containing 52.5 grams paste
Cardboard box containing 5 oral syringes containing 52.5 grams paste
Cardboard box containing 6 oral strings containing 52.5 grams paste
Cardboard box containing 10 oral syringes containing 52.5 grams paste

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

CP-Pharma Handelsgesellschaft mbH

7. MARKETING AUTHORISATION NUMBER(S)

VPA10810/034/001

8. DATE OF FIRST AUTHORISATION

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).