1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Trisulfin vet. 25 mg/ 125 mg chewable tablets for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:

Trimethoprim	25 mg
Sulfadiazine	125 mg

Excipients:

Qualitative composition of excipients and other constituents
Povidone K30
Maize starch
Sodium laurilsulfate
Sodium starch glycolate (Type A)
Magnesium stearate
Chicken flavour
Yeast (dried)

Off-white to light brown with brown spots, round and convex tablet with a cross-shaped break line on one side. The tablet can be divided into 2 or 4 equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats.

3.2 Indications for use for each target species

For the treatment of:
- respiratory infections: including pneumonia, bronchitis, pharyngitis and tonsillitis.
- gastrointestinal tract infections: including gastritis, gastro-enteritis and enteritis.
- urogenital tract infections: including cystitis, urethritis, nephritis, vaginitis and metritis.
- skin infections: including interdigital abscess, dermatitis and infected wounds.
- eye and ear infections.
- mastitis.

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 case of severe liver or kidney insufficiency or blood dyscrasia.

3.4 Special warnings

Not to be used in animals less than 2.5 kg.

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.

P. aeruginosa and *Enterococcus spp*. are intrinsically resistant to the trimethoprim/sulfadiazine combination.

3.5 Special precautions for use

Special precautions for safe use in the target species:
In case of long-term treatment, periodic haematological examination is necessary.

In order to prevent renal disorders due to crystallisation in the urine an adequate hydration should be ensured during the 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 local/regional level.

Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

The routine use of systemic antibiotics for intestinal infections is not recommended.

Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach. This antimicrobial combination should only be used where diagnostic testing has indicated the need for simultaneous administration of each of the active substances.

The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Trimethoprim, sulfonamides and sodium lauryl sulfate may cause hypersensitivity reactions after skin contact or accidental ingestion. People with known hypersensitivity to these substances should avoid any direct contact with the veterinary medicinal product including hand-to-mouth contact.
If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the package leaflet or the label to the physician.
Wash hands after use.

This veterinary medicinal product may cause adverse gastrointestinal effects such as nausea and diarrhoea, particularly for children.
Care should be taken to avoid accidental ingestion.
In order to prevent children from accessing the product, tablets should be stored out of sight of children.
Divided tablets should be returned to the open blister and inserted into the outer box.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs and cats:

Undetermined frequency (cannot be estimated from the available data)	Keratoconjunctivitis sicca[1] Bone marrow suppression[2] Renal disorder[3] Hypersensitivity reactions

[1]: In dogs, in case of long-term use
[2]: In case of long-term use of high dosages, reversible suppression of haematopoiesis may occur.
[3]: In case of long-term use of high doses crystallisation in kidney can occur

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 its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Laboratory studies in mice have produced evidence of foetotoxic effects during long-term use, i.e. malformation in the foetus. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Para-aminobenzoic acid derivatives may reduce the effectiveness of the veterinary medicinal product.
Gelatine, albumin and serum can negatively affect the veterinary medicinal product due to possible binding with sulfadiazine.
Phenylbutazone and salicylates increase the effect of sulfonamides.
Sulfonamides reduce the effect of anticoagulants.

3.9 Administration routes and dosage

Oral use.

The single dose is 2.5 mg trimethoprim and 12.5 mg sulfadiazine per kg body weight, 2 times a day, for a minimum of 5 days. For certain indications longer treatment may be required.

For skin infections caused by staphylococci, treatment for 5-6 weeks is recommended.

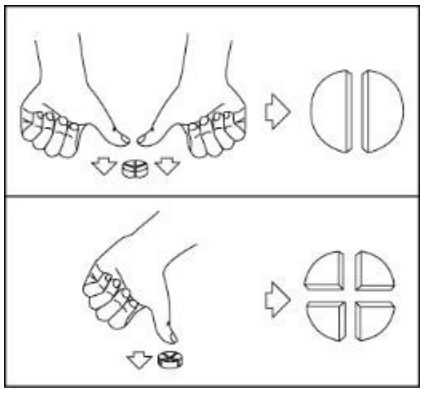
The appropriate treatment duration should be chosen based on the clinical needs and individual recovery of the treated animal. Consideration should be given to the accessibility of the target tissue and characteristics of the target pathogen.

To ensure administration of a correct dose, body weight should be determined as accurately as possible. For a single dose of 2.5 mg trimethoprim and 12.5 mg sulfadiazine per kg body weight, use the number of tablets given in the table below.

Dosage example:

Body weight range (kg)	Number of tablets In the morning	In the evening
>2.5 - 5	½	½
5.1 - 7.5	¾	¾
7.6 - 10	1	1
10.1 - 12.5	1 ¼	1 ¼
12.6 - 15	1 ½	1 ½
15.1 - 17.5	1 ¾	1 ¾
17.5 - 20	2	2

Tablets can be divided into 2 or 4 equal parts to ensure accurate dosage.



Halves: press down with your thumbs on both sides of the tablet.
Quarters: press down with your thumb in the middle of the tablet.

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

In case of overdose no other adverse events are known than those described 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

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01EW10

4.2 Pharmacodynamics

The spectrum of activity of the drug combination corresponds to that of sulfonamides. Its activity is therefore directed against numerous gram-positive and gram-negative bacteria.
Sulfadiazine belongs to the group of sulfonamides, trimethoprim belongs to the diaminopyrimidines. Both active substances have an inhibitory activity 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 dihydroproteosynthetase, this selective bacteriostatic activity 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

Sulfadiazine and trimethoprim are reasonably well absorbed after oral administration.
Trimethoprim and Sulfadiazine are well distributed to urine, bile, liver, lungs, gastrointestinal tract and synovia.

Sulfadiazine is intensively metabolized by oxidation and acetylation to 5 inactive metabolites.
Trimethoprim is metabolized by N-oxidation, O-demethylation and alpha-hydroxylation.
The half-life of trimethoprim in dogs is about 3 hours.

Trimethoprim is excreted unchanged in milk, urine and faeces.
The majority of sulfadiazine is excreted via the kidneys, partly unchanged, partly as a metabolite; in the dog in hydroxylated form.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 4 years.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Remaining tablet parts should be stored in the blister pack and be given at the next administration.

5.4 Nature and composition of immediate packaging

PVC/PE/PVDC – Aluminium blisters, containing 10 tablets each.

Package sizes:
Cardboard box with 1, 3, 5 or 10 blisters of 10 tablets.

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 NUMBERS

VPA10810/038/001

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).