SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Trimsulfasol 20/100 mg/ml solution for use in drinking water for pigs and chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:

Active substances:

Trimethoprim	20 mg
Sulfamethoxazole	100 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
N-methyl pyrrolidone	691 mg
Propylene glycol	
Sodium hydroxide	
Water, purified	

Clear yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Pigs (fattening pigs) and chickens (broilers).

3.2 Indications for use for each target species

Fattening pigs:
Treatment and metaphylaxis of:
- Post weaning diarrhoea caused by ß-haemolytic K-88positive, K99- positive or 987P *Escherichia coli* strains.
- Secondary bacterial infections caused by *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, *Streptococcus spp.* and *Haemophilus parasuis*.

Broilers:
Treatment and metaphylaxis of:
- Colibacillosis caused by *Escherichia coli*.

- Coryza caused by *Avibacterium paragallinarum*.

The presence of the disease in the group/flock must be established before the veterinary medicinal product is used.

3.3 Contraindications

Do not use in animals suffering from severe liver or kidney disease, oliguria or anuria.
Do not use in animals with impaired haematopoietic systems.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

3.4 Special warnings

Severely diseased animals can have a decreased appetite and water consumption. If necessary, the concentration of the veterinary medicinal product in the drinking water should be adjusted to make sure that the recommended dosage is being consumed. However, if the concentration of the veterinary medicinal product is increased too much, the intake of the medicated drinking water decreases for palatability reasons. Therefore, water intake should be monitored regularly, especially in broilers.
In case of insufficient uptake of water, pigs should be treated parenterally.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Due to the likely variability (time or geographically) in susceptibility of bacteria for potentiated sulphonamides, occurrence of resistance of bacteria may differ from country to country and even from farm to farm, and therefore bacteriological sampling and susceptibility testing are recommended. 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 deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to sulfamethoxazole and trimethoprim and may also decrease the effectiveness of combinations of trimethoprim with other sulphonamides due to the potential for cross resistance. 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:

Sulphonamides may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to sulphonamides may lead to cross reactions with other antibiotics. Allergic reactions to these substances may occasionally be serious.

People with known hypersensitivity (allergy) to sulphonamides or trimethoprim should avoid contact with the veterinary medicinal product. If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the package leaflet or the label to the physician.

This veterinary medicinal product may cause skin- and respiratory irritation as well as eye damage. During preparation and administration of the medicated drinking water, skin and eye contact with the drug should be avoided. Personal protective equipment consisting of

impermeable gloves e.g. rubber or latex and protective glasses should be worn when handling the veterinary medicinal product.

Avoid inhalation. Wash hands and contaminated skin immediately after handling the veterinary medicinal product.
In the event of eye contact, rinse the eye with large amounts of clean water and, if irritation occurs, seek medical attention.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. The veterinary medicinal product should not be administered by pregnant women and women suspected of being pregnant. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product by women of childbearing age.

Special precautions for the protection of the environment:

Manure from animals treated with this veterinary medicinal product may cause toxic effects to plants after spreading onto land. This risk can be reduced by avoiding too frequent and repeated use of the veterinary medicinal product.

3.6 Adverse events

Chickens:

Rare (1 to 10 animals / 10,000 animals treated):	Hypersensitivity reaction
Undetermined frequency (cannot be estimated from the available data):	Decreased drinking

Pigs:

Rare (1 to 10 animals / 10,000 animals treated):	Hypersensitivity reaction

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 also section ‘Contact details’ of the package leaflet or the combined label and package leaflet.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established in pigs and chickens during pregnancy, lactation, lay or in animals intended for breeding.
Laboratory studies in rats conducted with trimethoprim have shown evidence of teratogenicity at higher doses than recommended therapeutic ones.

Laboratory studies in rabbits and rats with the excipient N-methylpyrrolidone have shown evidence of foetotoxic effects.
Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Do not combine with other veterinary medicinal products.

3.9 Administration routes and dosage

In drinking water use.

The veterinary medicinal product can be added directly to the drinking water to prepare a therapeutic solution at the calculated concentration, but can also be used in a concentrated stock solution by adding 200 ml of the veterinary medicinal product per litre of water and diluting this further.

Fattening pigs:
5 mg trimethoprim and 25 mg sulfamethoxazole per kg body weight per day, for 4-7 consecutive days. This corresponds to 1 ml of the veterinary medicinal product per 4.0 kg body weight per day.

Broilers:
7.5 mg trimethoprim and 37.5 mg sulfamethoxazole per kg body weight per day, for 3 consecutive days. This corresponds to 1 ml of the veterinary medicinal product per 2.67 kg body weight per day.

To ensure a correct dosage, body weight should be determined as accurately as possible.

The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of trimethoprim/sulfamethoxazole may need to be adjusted accordingly.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{…ml veterinary medicinal product/ kg body weight/day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily water intake (l/animal)}} = \text{… ml veterinary medicinal product per litre of drinking water}$$

The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water and stock solutions should be freshly prepared every 24 hours. During the treatment period animals should not have access to water sources other than the medicated water. However, it should be ensured that animals always have sufficient water available. After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of active substance.

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

In chickens an acute overdose is unlikely to occur because the birds will be reluctant to drink the strongly concentrated drinking water (too bitter taste if above 2 litres of the veterinary medicinal product per 1000 litres drinking water). Chronic overdose in chickens will result in a strongly diminished water- and feed intake and retarded growth.

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

Pigs: meat and offal: 8 days.
Chickens: meat and offal: 5 days.

Not for use in birds producing or intended to produce eggs for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01EW11

4.2 Pharmacodynamics

Sulphonamides block the conversion of para-aminobenzoic acid to dihydrofolic acid. Their activity is bacteriostatic.
Trimethoprim inhibits dihydrofolic acid reductase, which converts dihydrofolic into tetrahydrofolic acid. The activity of trimethoprim is bacteriostatic and in combination with sulphonamides it is bactericidal.
Sulphonamides and trimethoprim thus cause a successive blockade of two enzymes that play an important role in the metabolism of bacteria. Their effect is synergistic.

Trimethoprim and sulfamethoxazole have a broad spectrum of activity against Gram-positive and Gram-negative bacteria including *Streptococcus spp*.

Pasteurella multocida, *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis*, *Avibacterium paragallinarum* and *E. coli* in vitro.

Bacterial resistance to trimethoprim and to sulphonamides can be mediated via 5 main mechanisms: (1) changes in the permeability barrier and/or efflux pumps, (2) naturally insensitive target enzymes, (3) changes in the target enzymes, (4) mutational or recombinational changes in the target enzymes, and (5) acquired resistance by drug-resistant target enzymes.

4.3 Pharmacokinetics

Following oral administration, trimethoprim and sulfamethoxazole are rapidly and almost completely absorbed from the gut. The bioavailability of sulfamethoxazole is slightly higher than that of trimethoprim. It is distributed to all tissues except the brain. The highest concentrations can be found in the lungs, the liver and the kidneys.
Sulfonamides are metabolised in various ways. The degree of acetylation, hydroxylation and glucuronidation depends on, among other things, the species and the age of the animal. Trimethoprim is metabolised to a large extent in the liver. Major metabolic pathways are O-methylation, N-oxidation in the ring structure and alpha hydroxylation. Sulfamethoxazole and trimethoprim are primarily excreted through the kidneys.

Environmental properties

The mixture of sulfamethoxazole and trimethoprim shows to have phytotoxic effects on terrestrial plants.
Trimethoprim is persistent in soils.

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: 3 years.
Shelf life after first opening the immediate packaging: 3 months.
Shelf life after dilution in drinking water: 24 hours.

5.3 Special precautions for storage

Do not refrigerate or freeze.
Protect from frost.

5.4 Nature and composition of immediate packaging

- High-density polyethylene bottles with low-density polyethylene screw cap containing 1 litre of veterinary medicinal product;
- High-density polyethylene jerrycan with high-density polyethylene screw cap containing 5 litres of veterinary medicinal product.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Dopharma Research B.V.

7. MARKETING AUTHORISATION NUMBER

Vm 28365/3004

8. DATE OF FIRST AUTHORISATION

22 August 2017

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

October 2023

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).

Approved: 12 April 2024