

METOTRIM ORAL SOLUTION

METOTRIM ORAL SOLUTION appears to be a light-yellow colour clear solution.

Composition:

Each ml contains	
Sulfamethoxazole	100 mg
Trimethoprim	20 mg

Pharmacodynamics:

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. Sulphonamides block the conversion of para-aminobenzoic acid to dihydrofolic acid. Its effect is bacteriostatic.

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

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.

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. Sulphonamides are metabolised in various ways. The degree of acetylation, hydroxylation and glucuronidation depends, among other things, on the species and age of the animal. Trimethoprim is metabolised to a large extent in the liver. Important metabolic pathways are O-methylation, N-oxidation in the ring structure and alpha hydroxylation. Sulfamethoxazole and trimethoprim are primarily excreted through the kidneys.

Indications:

Fattening pigs:

Treatment and metaphylaxis of:

- Post-weaning diarrhoea caused by beta-haemolytic K88-positive, K99-positive or 987P *Escherichia coli* strains susceptible to trimethoprim-sulfamethoxazole.
- Secondary bacterial infections caused by *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, *Streptococcus* spp. and *Haemophilus parasuis* susceptible to trimethoprim-sulfamethoxazole.

Broilers:

Treatment and metaphylaxis of:

- Colibacillosis caused by *Escherichia coli* susceptible to trimethoprim-sulfamethoxazole.
- Coryza caused by *Avibacterium paragallinarum* susceptible to trimethoprim-sulfamethoxazole.

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

Recommended Dosage:

Route of administration: for use in drinking water.

Warning and Precautions:

Special warnings for each target species

Severely diseased animals can have a decreased appetite and water consumption. If necessary the concentration of the product in the drinking water should be adjusted to make sure that the recommended dosage is being consumed. However if the concentration of the 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 intake of water, pigs should be treated parenterally.

Special precautions for use in animals

Due to the likely variability (time, geographical) 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 product should be based on culture and sensitivity of micro-organisms from diseased cases on farm or from recent previous experience on the farm. Use of the product deviating from the instructions given in the package insert 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. Official and local antimicrobial policies should be taken into account when the product is used.

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.

Do not handle this product if you know you are sensitive to sulphonamides. If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the physician this warning. The excipient N-methylpyrrolidone (NMP) may damage unborn children; therefore, women of child bearing age must be very careful to avoid exposure via spillage onto the skin when administering the product. If you are pregnant, think you may be pregnant or are attempting to conceive, you should not administer the product. This product may cause skin- and respiratory irritation as well as eye damage. Impermeable gloves, e.g. rubber or latex and protective glasses, should be worn when handling the product including when mixing the product with drinking water. Avoid inhalation. In the event of eye contact, rinse the eye with large amounts of clean water and, if irritation occurs, seek medical attention. In the event of accidental ingestion, seek medical advice. Wash hands and contaminated skin immediately after handling the product.

Interactions with Other Medicaments:

Do not combine with other veterinary medicinal products.

Use during pregnancy, lactation or lay:

The safety of the veterinary medicinal product has not been established during pregnancy, lactation or lay.

Side effects:

A diminished water intake in chickens may occur rarely.

Hypersensitivity reactions can occur rarely.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)

The 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 a day, for 4-7 days. This corresponds to 1 ml of the veterinary medicinal product per 4.0 kg body weight per day. Based on the recommended dose, daily water consumption, and the number and weight of the pigs to be treated, the exact daily amount of the veterinary medicinal product required can be calculated according to the following formula:

$$\frac{\text{Mean body weight (kg) of pigs to be treated}}{\text{Mean daily water consumption (litre) Per pig x 4.0}} = \frac{\text{xx ml veterinary medicinal product per litre drinking water}}$$

Broilers:

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

Based on the recommended dose, daily water consumption, and the number and weight of the birds to be treated, the exact daily amount of the veterinary medicinal product required can be calculated according to the following formula:

$$\frac{\text{Mean body weight (kg) of birds to be treated}}{\text{Mean daily water consumption (litre) Per bird x 2.67}} = \frac{\text{xx ml veterinary medicinal product per litre drinking water}}$$

The body weight and water consumption should be determined as accurately as possible, to ensure a correct dosage. 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. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of the veterinary medicinal products has to be adjusted accordingly.

Contraindication:

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 case of known hypersensitivity to sulphonamides or trimethoprim or any of the excipients.

- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

Overdose and Treatment:

In chickens an acute overdose will likely not 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.

Withdrawal Period (s):

Pig: Meat and offal: 8 days.

Chicken: Meat and offal: 5 days.

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

Storage Condition:

Store below 30°C. Protect from heat and sunlight exposure.

Keep out of reach of children/ Jauhkan dari kanak-kanak.

Any unused product or packaging should be disposed of in accordance with local and national legislation.

Shelf Life as packaged for Sale: 3 years.

Shelf Life after first opening: 28 days.

Shelf life after reconstitution: 24 hours.

Packaging Available: 1L

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Product Holder/ Manufacturer:

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