S-TRIM 480

ORAL SUSPENSION

(FOR VETERINARY USE ONLY)

COMPOSITION

Each ml contents:

Sulfamethoxazole ..... 400 mg

Trimethoprim ..... 80 mg

PRODUCT DESCRIPTION

This product is a light yellowish color liquid with white suspension.

PHARMACODYNAMICS

Trimethoprim and sulfamethoxazole have a broad spectrum of activity against grampositive and gram-negative bacteria including *Streptococcus* spp. *Pasteurellamultocida, Actinobacilluspleuropneumoniae, Haemophilus parasuis, Avibacteriumparagallinarum* 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.

Environmental properties

Trimethoprim is persistent in soils.

TARGET SPECIES

Pigs (fattening pigs) and chickens (broilers)

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 *Pasteurellamultocida, Actinobacilluspleuropneumoniae, Streptococcus* spp. and *Haemophilus parasuis* susceptible to trimethoprim-sulfamethoxazole.

Broilers:

Treatment and metaphylaxis of:

- Colibacillosis caused by *Escherichia coli* susceptible to trimethoprimsulfamethoxazole.
- Coryza caused by *Avibacteriumparagallinarum* susceptible to trimethoprim-sulfamethoxazole.

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

ADMINISTRATION & DOSAGE

Route of administration: in drinking water use.

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 50 ml of the veterinary medicinal product per liter 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 16.0 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:

$$\frac{\text{Mean body weight (kg) of pigs to be treated}}{\text{Mean daily water consumption (liter) per pig} \times 16} = \text{xx ml veterinary medicinal product per liter drinking water}$$

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 10.67 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:

$$\frac{\text{Mean body weight (kg) of birds to be treated}}{\text{Mean daily water consumption (liter) per bird} \times 10.67} = \text{xx ml veterinary medicinal product per liter drinking water}$$

The body weight 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. Body weight and water consumption should be determined as accurately as possible to ensure administration of the correct dose. The uptake 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.

INTERACTION WITH OTHER MEDICAMENTS

Do not combine with other veterinary medicinal products.

WITHDRAWAL PERIODS

Pig (Meat and offal): 8 days.

Chicken (Meat and offal): 5 days.

Not authorised for use in birds producing eggs for human consumption.

WARNING AND PRECAUTIONS

1. 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 uptake of water, pigs should be treated parenterally.

2. Special precautions for use:

i. 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 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.

ii. 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.

Impermeable gloves, e.g. rubber or latex and protective glasses, should be worn when handling the product. Due to the risk of serious ocular damage, protective eyewear should be worn when mixing this product with drinking water. 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.

- Keep medicine out of reach of children.
- Jauhkan ubat dari kanak-kanak.

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

PREGNANCY AND LACTATION

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

SIDE EFFECT

A diminished water intake in chickens may occur occasionally.

Hypersensitivity reactions can occur rarely (more than1 but less than 10 animals in 10,000animals).

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 liters of the veterinary medicinal product per 1000 liters drinking water). Chronic overdose in chickens will result in a strongly diminished water- and feed intake and retarded growth.

SHELF LIFE: 36 months

SHELF LIFE after first opening: 24 hours

SHELF LIFE after dilution: 24 hours

STORAGE

Store at temperature not exceeding 30°C. Strictly avoid light & heat exposure.

PACKAGING

The product filled 1000 ml in HDPE plastic bottle.

DATE OF REVISION: 24th April 2020

MARKETING BY:

F. E VENTURE Sdn. Bhd.

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