Veterinary Package Insert

TP-KSM 125/625 MG/G WATER SOLUBLE POWDER

PRODUCT DESCRIPTION
Beige to light brown colour powder, which contains 625mg of sulfachloropyridazine sodium (580.2mg of sulfachloropyridazine) and 125mg of trimethoprim per gram in sachet.

PHARMACODYNAMICS & PHARMACOKINETICS
The antibacterial activity of veterinary drug is based on a double sequential inhibition of microbial synthesis of tetrahydrofolic acid. Trimethoprim is an antibacterial derivative of diaminopyrimidine with bactericidal and synergistic activity with sulfonamides. Sulfachloropyridazine is an antibacterial sulfonamide that acts by preventing bacterial growth. The combination of the two active substances has a synergistic effect, which influences the dosage (reduction of the doses of the active substances) and the bactericidal effect in a positive manner and broadens the spectrum of activity. Moreover, the appearance of bacterial resistance is slowed down.

In chickens the veterinary medicinal product, administered at a dose of 200 mg / kg body weight, is active against respiratory and septic infections by wild-type *E. coli* and against septic infections by *P. multocida* and *S. aureus*.

Resistance develops slowly through transferable elements and results from a chromosomal mutation as a result of one or more of the mechanisms described below:

- permeability barrier and / or active efflux;

- insensitive natural target enzymes;

- adjustable modifications of the target enzyme;

- mutational or recombination modifications of the target enzyme;

- resistance acquired by target enzymes resistant to the veterinary drug.

The pharmacokinetic parameters in chickens following a single administration of the veterinary medicinal product at the recommended daily dose are summarized in the table below, as well as steady state plasma concentrations (Css) by continuous medication in drinking water.

Significantly higher plasma levels are achieved with sulfachloropyridazine.

	Trimethoprim	Sulfachloropyridazine
Cmax (µg/ml)	0,52	18,65
AUC24h (µg.h/ml)	2,14	103,4
T_{max} (h)	1,55	1,32
T1/2el (h)	1,41	2,60
C_{ss} (µg/ml)	0,089	4,31

Protein binding in plasma reached 24.1% for trimethoprim and 35.1% for sulfachloropyridazine.

These results translate into an effective steady state Css of 0.068 µg / ml for trimethoprim and 2.797 µg / ml for sulfachloropyridazine. Both active components are almost absorbed as quickly and excreted relatively quickly.

INDICATION
Treatment of infections caused by trimethoprim / sulfachloropyridazine-sensitive organisms, taking into account the ability of the antibiotic to reach the site of infection in effective concentrations.

TARGETED SPECIES
Chicken (non-egg laying).

RECOMMENDED DOSAGE AND ADMINISTRATION
For oral administration via the drinking water.

Dosage: 32mg of product per kg of body weight per day (= 24mg of active substance in total). Particularly in case of primary and secondary infections with *E. coli*, it is recommended to administer a higher dose.

Administration mode:

Chickens: mix product in drinking water for 3 to 6 days.

... mg product / kg bodyweight / day *
x average live weight (kg) of poultry to be treated
---------- = ...mg of product per liter of drinking
Daily water consumption (liter) per animal

* 24mg TMP + Sulfa / kg body weight is equivalent to 32mg veterinary drug / kg body weight.

CONTRAINDICATIONS
Do not use in hypersensitive animals or animals with liver or kidney disease.

Do not administer to animals with hematopoietic function.

Do not use in case of known hypersensitivity to sulfonamides, trimethoprim or any of the excipients.

WARNINGS & PRECAUTIONS.

Special warnings for each target species

Avoid underdosing. Sick animals can drink less water than normal. If the animals can be isolated, the concentration of the veterinary drug can be increased proportionally in the water.

The watering should be checked regularly, especially in broilers.

Special precautions for use in animals

Due to the variable sensitivity (in time and space) of bacteria to potentiated sulphonamides, bacterial resistance is likely to fluctuate from one region to another, or even from one farm to another. Therefore, it is recommended to take bacteriological samples and perform sensitivity tests. The administration of the veterinary medicinal product in question must be based on the culture and sensitivity of the micro-organisms in the sick farm animals or on the basis of recent experience on the site concerned. If the veterinary medicinal product is used in ways other than those indicated in the summary of product characteristics, there is no risk of an increase in the prevalence of sulfachloropyridazine and trimethoprim-resistant bacteria and the reduction of effectiveness of combinations of trimethoprim with other sulfonamides due to cross-resistance. During any use of the veterinary medicinal product, the official and local antimicrobial.

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

Sulfonamides may cause hypersensitivity reactions (allergy) after injection, inhalation, ingestion or skin contact. Hypersensitivity to sulfonamides may result in cross-reactions with other antibiotics. The allergic reactions caused by these substances can be serious in some cases.

Avoid contact with this veterinary medicinal product if you are sensitive to sulphonamides.

If after exposure to the veterinary medicinal product, symptoms such as rash appear, seek immediate medical attention and show the package leaflet.

Put on a pair of waterproof latex or rubber gloves and put on a pair of safety glasses before using this veterinary medication.
In case of eye contact, rinse thoroughly with clean water and, if irritation occurs, call a doctor.

In case of accidental ingestion, consult a doctor.

Wash hands and contaminated skin immediately after handling the veterinary medicinal product.

INTERACTIONS WITH OTHER MEDICATIONS

Do not combine with other veterinary drugs.

PREGNANCY AND LACTATION

The safety of the veterinary medicinal product has not been established in case of lay.

ADVERSE EFFECTS

Sulfonamides may affect renal function (crystalluria, hematuria, urinary obstruction) and hematopoiesis (thrombocytopenia, anemia).

The frequency of adverse events is defined as follows:

- very common (adverse effects in more than 1 animal in 10 treated animals)

- frequent (between 1 and 10 animals out of 100 treated animals)

- uncommon (between 1 and 10 animals per 1000 treated animals)

- rare (between 1 and 10 animals out of 10,000 treated animals)

- very rare (less than one in 10,000 animals treated, including isolated cases)

OVERDOSE & TREATMENT

Target species support doses at least 5 times higher than the recommended dose that is administered during a treatment period at least three times the maximum recommended period, without any adverse effects being demonstrated.

WITHDRAWAL PERIOD

Chicken :

Meat and offal: 7 days.

Eggs: Do not use in laying hens for eggs intended for human consumption.

MAXIMUM RESIDUAL LIMIT (MRL)

Substance/ Drug Definition of residues in which MRL was set	Food	Maximum Residue Limits (MRLs) in food µg/kg
Trimethoprim	Edible offal, muscle (mammalian and chicken), egg (chicken)	50
Sulphonamide	Muscle, liver, kidney, fat (all food producing species)	100

STORAGE CONDITION
Store below 30°C. Protect from direct sunlight.

SHELF LIFE
2 years.

After 1st opening, reconstitution or dilution, use within 24 hours.

PACKING
150g
500g
1kg

THYE PHARMA SDN. BHD.
(manufacturer & product registration holder)
No.2 Lorong Industri Ringan Permatang Tinggi 8,
Kawasan Industri Ringan Permatang Tinggi,
14000 Bukit Mertajam,
Pulau Pinang.

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