Veterinary Package Insert

KHC TRIMETHOMIX 400/80MG/G PREMIX POWDER (40% Sulfadimidine & 8% Trimethoprim)

PRODUCT DESCRIPTION

White or almost white colour powder, which contains 400mg of sulfadimidine (as sulfamidine sodium 432mg) and 80mg of Trimethoprim in 1g of product.

PHARMACODYNAMICS & PHARMACOKINETICS

Pharmacodynamics:

Sulfadimidine: Bacteriostatic. Sulfonamides interfere with the biosynthesis of folic acid in bacterial cells; they compete with para-aminobenzoic acid (PABA) for incorporation in the folic acid molecule. By replacing the PABA molecule and preventing the folic acid formation required for DNA synthesis, the sulfonamides prevent multiplication of the bacterial cell. Only organisms that synthesize their own folic acid are susceptible; mammalian cells use preformed folic acid and, therefore, are not susceptible. Cells that produce excess PABA or environments with PABA, such as necrotic tissues, allow for resistance by competition with the sulfonamide.

Alone, sulfonamides are bacteriostatic agents and trimethoprim is bactericidal, but when used in combination, the potentiated sulfas are bactericidal. Potentiated sulfas sequentially inhibit enzymes in the folic acid pathway, inhibiting bacterial thymidine synthesis.

Pharmacokinetics:

Sulfadimidine

Absorption

Most sulfonamides are well absorbed orally with the exception of the enteric sulfonamides, such as sulfaquinoxaline, which are minimally absorbed. Delays in absorption may occur in adult ruminants or when sulfonamides are administered with food to monogastric animals.

Distribution

Sulfonamides are widely distributed throughout the body. They cross the placenta, and a few penetrate into the cerebrospinal fluid. Sulfonamides may be distributed into milk; however, they vary greatly in their ability to do so. The process depends on several factors, including protein binding and pKa values.

Protein Binding

Binding can vary depending on serum concentration and other factors.

Biotransformation

Sulfonamides are primarily metabolized in the liver but metabolism also occurs in other tissues. Biotransformation occurs mainly by acetylation, glucuronide conjugation, and aromatic hydroxylation in many species. The types of metabolites formed and the amount of each varies depending on the specific sulfonamide administered; the species, age, diet, and environment of the animal; the presence of disease; and, with the exception of pigs and ruminants, even the sex of the animal. Dogs are considered to be unable to acetylate sulfonamides to any significant degree.

Duration of Action

Duration of action may be estimated by the length of time target serum concentrations are maintained. Target concentrations are generally based on minimum inhibitory concentrations for each organism.

Elimination

Alkalization of the urine increases the fraction of the dose that is eliminated in the urine. In general, the metabolites of the parent drug are more quickly eliminated by the kidney than the original sulfonamide is, but the proportions of metabolites formed can vary, depending on many factors.

Sulfonamides are also distributed in relatively small amounts into milk, saliva, and into the gastrointestinal tract.

Trimethoprim

Absorption

Trimethoprim is rapidly and almost completely absorbed from the gastrointestinal tract and peak concentrations in the circulation occur about 1 to 4 hours after an oral dose.

Distribution

Trimethoprim is widely distributed to various tissues and fluids including kidneys, liver, lung and bronchial secretions, saliva, aqueous humour, prostatic tissue and fluid, and vaginal secretions; concentrations in many of these tissues are reported to be higher than serum concentrations but concentrations in the CSF are about one-quarter to one-half of those in serum. Trimethoprim readily crosses the placenta and it appears in breast milk.

Elimination

Trimethoprim is excreted primarily by the kidneys through glomerular filtration and tubular secretion. About 10 to 20% of trimethoprim is metabolised in the liver and small amounts are excreted in the faeces via the bile, but most, about 40 to 60% of a dose, is excreted in urine, predominantly as unchanged drug, within 24 hours. Trimethoprim is removed from the blood by haemodialysis to some extent.

INDICATION

For the treatment of infections in pigs and poultry due to organisms susceptible to the combination of sulfadimidine and trimethoprim.

TARGET SPECIES

Pigs and poultry.

RECOMMENDED DOSAGE AND ADMINISTRATION

To be administered orally.

Administer mixed thoroughly with food or dissolved into drinking water.

Pigs: 3.13gm of product per 50kg bodyweight daily.

Poultry: 3.13gm to 6.25 gm of product per 12L drinking water for 3 - 5 days.

CONTRAINDICATIONS

Except under special circumstances, this medication should not be used when the following medical problem exists:

» Hypersensitivity to sulfonamides (animals that have had a previous reaction to sulfonamides may be much more likely to react on subsequent administration)

Risk-benefit should be considered when the following medical problems exist:

» Hepatic function impairment (systemically absorbed sulfonamides are metabolized by the liver; delayed biotransformation may increase the risk of adverse effects)

» Renal function impairment (systemically absorbed sulfonamides are renally excreted; delayed elimination could cause accumulation of sulfonamide and metabolites, increasing the risk of adverse effects)

WARNINGS & PRECAUTIONS.

Patients allergic to one sulfonamide may be allergic to other sulfonamides also.

INTERACTIONS WITH OTHER MEDICATIONS

Drug interactions relating specifically to the use of sulfonamides in animals are rarely reported in veterinary literature.

Trimethoprim may increase serum concentrations and potentiate the effect of a number of drugs, including phenytoin, digoxin, and procainamide. The effect may be due to competitive inhibition of renal excretion, decreased metabolism, or both. It has been suggested that trimethoprim may potentiate the effects of warfarin. Trimethoprim has been reported to reduce the renal excretion and increase blood concentrations of zidovudine, zalcitabine, and lamivudine. Trimethoprim and dapsone increase each other's serum concentrations, whereas rifampicin may decrease trimethoprim concentrations.

PREGNANCY AND LACTATION

Sulfonamides cross the placenta in pregnant animals. Some teratogenic effects have been seen when very high doses were given to pregnant mice and rats.

Safety of trimethoprim/sulfa has not been clearly established in pregnant animals. Use of this product in nursing animals with caution. However, it is not recommended for use in pregnant or nursing animals.

ADVERSE EFFECTS

Crystallization of sulfonamides can occur in the kidneys or urine with high doses of sulfonamide or when an animal is dehydrated. Solubility in the urine is dependent on the concentration of drug in the urine, urinary pH (less soluble in an acidic pH), the patient's hydration, and the amount of drug in the acetylated form. It can be minimized in susceptible animals by maintaining a high urine flow and, if necessary, alkalinizing the urine.

Trimethoprim is teratogenic in animals.

OVERDOSE & TREATMENT

Toxicities secondary to acute overdose of sulfonamides are not typically reported. Side effects may be more likely to occur with high doses and long-term administration, but are seen at recommended doses as well.

WITHDRAWAL PERIOD

Meat (pigs and poultry):
Do not use less than 14 days before slaughter for human consumption.

Eggs:
Do not use in birds which are producing or may in the future produce eggs or egg products for human consumption

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

SHELF LIFE
2 years.
After 1st opening, reconstitution or dilution, use within 24 hours.

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
Sulfadimidine	Edible offal (chicken and mammalian), muscle (chicken and mammalian)	100

PACKING
1000g

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No.49 Lorong Alma Jaya 12,
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