Veterinary Package Insert

COCCI 25% W/W PREMIX POWDER (25% Sulfaquinoxaline)

PRODUCT DESCRIPTION

Pale yellow to yellow colour powder, which contains 250mg of sulfaquinoxaline per gram.

PHARMACODYNAMICS & PHARMACOKINETICS

Sulfaquinoxaline belongs to a group of antibiotics called the sulphonamides. It is 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.

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.

N_4-acetyl metabolites have no antimicrobial activity and hydroxymetabolites have 2.5 to 39.5% of the activity of the parent compound. Metabolites may compete with the parent drug for involvement in folic acid synthesis but have little detrimental effect on the bacterial cell, and so could lower the activity of the remaining parent drug.

Duration of Action

The sulfonamides have been loosely categorized according to their plasma concentration versus time profiles:

Intermediate- to long-acting—Sulfadimethoxine, sulfamethazine. Enteric (minimally absorbed)—Sulfaquinoxaline.

Note: 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. Many sources use 50 mcg sulfonamide per mL (5 mg per decaliter) of blood as the minimum effective concentration for sulfonamides in animals.

Elimination

Renal excretion is the primary route of elimination for most nonenteric sulfonamides and it occurs by glomerular filtration of parent drug, tubular excretion of unchanged drug and metabolites, and passive reabsorption of nonionized drug. 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.

INDICATION

Chickens:

As an aid in preventing outbreaks of coccidiosis caused by Eimeria tenella, E. necatrix, E. acervulina, E. maxima, and E. brunetti where excessive exposure to coccidia is increased due to overcrowding or other management factors.

As an aid in controlling outbreaks of coccidiosis caused by Eimeria tenella, E. necatrix, E. acervulina, E. maxima, and E. brunetti.

As an aid in preventing outbreaks of coccidiosis caused by Eimeria tenella, E. necatrix, E. acervulina, E. maxima, and E. brunetti under average conditions of exposure.

Chickens and turkeys:
As an aid in the control of acute fowl cholera caused by Pasteurella multocida susceptible to sulfaquinoxaline and fowl typhoid caused by Salmonella gallinarum susceptible to sulfaquinoxaline.

Turkeys:
As an aid in controlling outbreaks of coccidiosis caused by Eimeria meleagrimitis and E. adenoeides.

As an aid in preventing outbreaks of coccidiosis caused by Eimeria meleagrimitis and E. adenoeides.

TARGET SPECIES
Chickens and turkeys.

RECOMMENDED DOSAGE AND ADMINISTRATION
To be administered orally.

Chickens:
As an aid in preventing outbreaks of coccidiosis caused by Eimeria tenella, E. necatrix, E.

acervulina, E. maxima, and E. brunetti where excessive exposure to coccidia is increased due to overcrowding or other management factors.

280.5 g/tonne (0.028%)

Feed continuously from the time birds are placed on litter and continue past the age when coccidiosis is ordinarily a hazard. If death losses caused by coccidiosis exceed 0.5% in a 2-day period, use the sulfaquinoxaline levels recommended for control of outbreaks, returning to the original prevention dosage schedule after the outbreak has subsided. Losses may result from intercurrent disease, other conditions affecting drug intake, or variant strains of coccidia species which can contribute to the virulence of coccidiosis under field conditions. Do not treat chickens within 10 days of slaughter for food. Do not medicate chickens producing eggs for human consumption.

As an aid in controlling outbreaks of coccidiosis caused by Eimeria tenella, E. necatrix, E. acervulina, E. maxima, and E. brunetti.

1603.5 g/tonne (0.16%) and 802.6 g/tonne (0.08%)

Feed at 1603.5g/tonne (0.16 percent) level for first 48 to 72 hours. Skip 3 days; 802.6 g/tonne (0.08 percent) for 2 days, skip 3 days; 802.6 g/tonne (0.08 for 2 days. If bloody droppings recur give 802.6 g/tonne (0.08%) for another 2 days. Do not treat chickens within 10 days of slaughter for food.

Do not medicate chickens producing eggs for human consumption.

As an aid in preventing outbreaks of coccidiosis caused by Eimeria tenella, E. necatrix, E. acervulina, E. maxima, and E. brunetti under average conditions of exposure.

239.9 g/tonne (0.024%)

Feed continuously from the time birds are placed on litter and continue past the age when coccidiosis is ordinarily a hazard. If death losses caused by coccidiosis exceed 0.5% in a 2-day period, use the sulfaquinoxaline levels recommended for control of outbreaks, returning to the original prevention dosage schedule after the outbreak has subsided. Losses may result from intercurrent disease, other conditions affecting drug intake, or variant strains of coccidia species which can contribute to the virulence of coccidiosis under field conditions. Do not treat chickens within 10 days of slaughter for food. Do not medicate chickens producing eggs for human consumption.

Chickens and turkeys:
As an aid in the control of acute fowl cholera caused by Pasteurella multocida susceptible to

sulfaquinoxaline and fowl typhoid caused by Salmonella gallinarum susceptible to sulfaquinoxaline.

1603.5 g/tonne (0.16%) and 802.6 g/tonne (0.08%).

Feed 1603.5 g/tonne (0.16%) for 48 to 72 hours. Mortality should be brought under control. After medication, move birds to clean ground or to a clean house. If disease recurs, use 802.6 g/tonne (0.08%) in feed again for 2 days. Do not treat chickens or turkeys within 10 days of slaughter for food. Do not medicate chickens or turkeys producing eggs for human consumption.

Turkeys:
As an aid in controlling outbreaks of coccidiosis caused by Eimeria meleagrimitis and E.adenoeides.

802.6 g/tonne (0.08%).

Feed 802.6 g/tonne (0.08%) for 2 days. Follow with 3 days on regular feed and 2 more days on 802.6 g/tonne (0.08%) sulfaquinoxaline feed. Again follow with 3 days on regular feed and 2 more days on 802.6 g/tonne (0.08%) sulfaquinoxaline feed. Continue this schedule if necessary till all signs of the outbreaks have subsided. Do not medicate turkeys producing eggs for human consumption. Do

not treat turkeys within 10 days of slaughter for food.

As an aid in preventing outbreaks of coccidiosis caused by Eimeria meleagrimitis and E. adenoeides.

280.5 g/tonne (0.028%).

Feed 0.028% continuously during time birds are closely confined. May be continued for a week to 10 days after flock is transferred to range to reduce danger of an outbreak following moving of the flock. Do not medicate turkeys producing eggs for human consumption. Do not treat turkeys within 10 days of slaughter for food.

CONTRAINDICATIONS

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

Hypersensitivity to sulphonamides (animals that have had a previous reaction to sulphonamides 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 sulphonamide 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.

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.

Do not medicate chickens or turkeys producing eggs for human consumption.

ADVERSE EFFECTS

Crystallization in the urinary tract

Note: 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. Because dogs do not produce acetylated metabolites, they may be less susceptible to this adverse effect. It can be minimized animals by maintaining a high urine flow and, if necessary, alkalinizing the urine.

Hemorrhagic syndrome (anorexia, epistaxis, hemoptysis, lethargy, pale mucous membranes, possibly death)

Note: Hemorrhagic syndrome has been reported in chickens but may occur in other species. It is most often reported with the addition of sulfaquinoxaline to feed for chickens. Sulfaquinoxaline is a vitamin K antagonist that inhibits vitamin K eposide and vitamin K quinone reductase and causes an effect similar to that of coumarin anticoagulants. Sulfaquinoxaline may have an additional adverse effect on specific cell types; this may explain why supplementation of chicken feeds with vitamin K has not always prevented the syndrome in chickens. Rapid discontinuation of medication and initiation of therapy with vitamin K1 may reverse the effects.

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.

Dosage and length of treatment recommendations should be followed; high doses or long-term use can increase the risk of side effects.

Animals should have a good water supply and should be monitored to ensure adequate water consumption during treatment.

WITHDRAWAL PERIOD

Meat and offal: 10 days.

Do not use in chickens and turkeys which eggs are produced for human consumption.

STORAGE CONDITION

Store below 30ºC. 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 residue in which MRL was set	Food	Maximum Residue Limits (MRLs) in food µg/kg
Sulfaquinoxaline	Edible offal, muscle (poultry)	100

PACKING
1000gm

LIM SENG PHARMACHEM SDN. BHD.
(product registration holder)
2692,Tingkat Perusahaan Enam,
Kawasan Perusahaan Prai Mk 1,
13600 Prai, Pulau Pinang.

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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