

SULFOLAN POWDER

Ingredient(s):
Tylosin (as Tylosin tartrate) 88mg/g
Sulfamethazine 88mg/g

Pharmacology (Summary of Pharmacodynamics and Pharmacokinetics):
Pharmacodynamics
Tylosin –
Tylosin is thought to have the same mechanism of action as erythromycin (binds to 50S ribosome and inhibits protein synthesis). It is a bacteriostatic antibiotic.
Sulfamethazine –
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.

Pharmacokinetics
Tylosin –
Tylosin tartrate is well absorbed from the GI tract, primarily from the intestine. Tylosin is well distributed in the body after systemic absorption, with the exception of penetration into the CSF. The volume of distribution of tylosin is reportedly 1.7L/kg in small animals and 1~2.3L/kg in cattle. In lactating dairy cattle, the milk to plasma ratio is reported to be between 1 and 5.4. Tylosin is eliminated in the urine and bile apparently as unchanged drug. The elimination half-life of tylosin is reportedly 54 minutes in small animals, 139 minutes in newborn calves, and 64 minutes in calves 2 months of age or older.
Sulfamethazine –
Most sulfonamides are well absorbed orally. Delays in absorption may occur in adult ruminants or when sulfonamides are administered with food to monogastric animals. The oral bioavailability is 86% in pigs and 84% in ponies. Sulfonamides are widely distributed throughout the body. They cross the placenta into the cerebrospinal fluid. Sulfonamides may be distributed into milk.
Protein binding in cows is 51~79% (depends on plasma concentrations), 86% in goats, 70% in horses, and 77% in sheep. Sulfonamides are primarily metabolized in the liver.
Biotransformation occurs mainly by acetylation, glucuronide conjugation, and aromatic hydroxylation in many species. In pigs, sulfamethazine is metabolized into N4-acetylsulfamethazine, desaminosulfamethazine and the N4-glucose conjugate of sulfamethazine. In general, metabolites of sulfonamides are cleared more quickly than the parent drug. The desaminosulfamethazine half-life of elimination can vary from 1~9 days, while sulfamethazine and other metabolites have a shorter half-life of 10~20 hours. It has been theorized that diets containing nitrate, which is then reduced by bacteria to nitrite, will greatly increase the amount of sulfamethazine biotransformed to the desaminosulfamethazine metabolite and prolong tissue residues of metabolite.
The elimination half-lives of sulfamethazine are 9.8~16.9 hours in pigs, 4.5~10.8 hours in sheep, 5.4~11.4 hours in horses, 2.4~9.6 hours in goats, and 5~11.3 hours in cattle. Renal excretion is the primary route of elimination 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. 11~37% (cattle), 7.8% (horses), 24.5% (pigs), and 18% (sheep) of a dose of sulfamethazine is excreted in the urine as parent drug. 52.1% (pigs) and 53% (sheep) are excreted in urine as measured metabolites.

Indications:
Swine:
- For reduction in the severity of effects of atrophic rhinitis; lowering the incidence and severity of *Bordetella bronchiseptica* rhinitis.
- For control of swine dysentery associated with *Brachyspira hyodysenteriae*.
- For control of swine pneumonias caused by bacterial pathogens (*Pasteurella multocida* and/or *Arcanobacterium pyogenes*).

Dosage and Administrations:
Thoroughly mix 1.14kg Sulfolan Powder in one ton of feed to provide 100g of Tylosin and 100g of Sulfamethazine per ton.

Target Species
Swine.

Mode of Administration
Orally via feed mixing.

Contraindications:
1) Tylosin is contraindicated in patients hypersensitive to it or other macrolide antibiotics.
2) Tylosin is contraindicated in horses, as severe and sometimes fatal diarrheas may result from its use in that species.
3) Animals that have had a previous reaction to sulfonamides may be much more likely to react on subsequent administration. Except under special circumstances, this medication should not be used.
4) Risk-benefit should be considered when hepatic function impairment exists. Since systemically absorbed sulfonamides are metabolized by the liver, delayed biotransformation may increase the risk of adverse effects.
5) Risk-benefit should be considered when renal function impairment exists. Since systemically absorbed sulfonamides are renally excreted; delayed elimination could cause accumulation of sulfonamide and metabolites, increasing the risk of adverse effects.

Precaution(s) / Warning(s):
1) An idiosyncratic sulfonamide toxicosis can occur in any breed of dog, but has been reported more frequently in the Doberman Pinscher than in other breeds. This specific type of drug reaction includes blood dyscrasias, nonseptic polyarthritis, and skin rash. Dogs given sulfonamides may also develop cutaneous eruptions, hepatitis, or keratitis sicca.
2) Patients allergic to one sulfonamide may be allergic to other sulfonamides also (cross-sensitivity).
3) High doses of sulfamethazine have been shown to induce follicular cell hyperplasia of the thyroid gland and splenic changes in specific-pathogen-free mice.

Special precautions for use
Official, national and regional antimicrobial policies should be taken into account when the product is used.

Special precautions for use in animals
1) For use in pig feeds only.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
1) Tylosin may induce irritation. Macrolides, such as tylosin, may also cause hypersensitivity (allergy) following injection, inhalation, ingestion or contact with skin or eye. Hypersensitivity to tylosin may lead to cross reactions to other macrolides and vice versa. Allergic reactions to these substances may occasionally be serious and therefore direct contact should be avoided.
2) To avoid exposure during preparation of the medicated feed, wear overalls, safety glasses, impervious gloves and wear either a disposable half mask respirator or a non-disposable respirator. Wash hands after use.
3) In the event of accidental skin contact, wash thoroughly with soap and water. In case of accidental eye contact, flush the eyes with plenty of clean, running water.
4) Do not handle the product if you are allergic to ingredients in the product.
5) If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the physician this warning. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

Interaction with Other Medicaments
None observed

Pregnancy and Lactation:
1) No information was located with regards to the reproductive safety of tylosin, but it is unlikely to have serious teratogenic potential.
2) Sulfonamides cross the placenta in pregnant animals. Some teratogenic effects have been seen when very high doses were given to pregnant mice and rats.
3) Sulfonamides are distributed into milk; however, the sulfonamides that are clinically relevant to food-producing animals are distributed into milk in concentrations too low to be therapeutic but high enough to produce residues. For lactating dairy cattle, concentration of the active parent compound of sulfamethazine, measured at a specific time in milk, is about 20% of the concentration in the blood.

Side Effect / Adverse Reactions:
1) Most likely adverse effects with tylosin are pain and local reactions at intramuscular injection sites, and mild GI upset (anorexia, and diarrhea).
2) Tylosin may induce severe diarrheas if administered orally to ruminants or by any route to horses.
3) In swine, adverse effects reported include edema of rectal mucosa and mild anal protrusion with pruritus, erythema, and diarrhea.
4) Shock and death have been reported in baby pigs overdosed with tylosin.
5) 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.
6) In dogs, adverse effects of sulfonamides may include cutaneous drug eruption, hepatitis, hypothyroidism, idiosyncratic toxicosis (blood dyscrasias, including anemia, leukopenia or thrombocytopenia, fever, focal retinitis, lymphadenopathy, nonseptic polyarthritis, polymyositis, and skin rash), and keratoconjunctivitis sicca

Environmental Property
Tylosin -
1) Practically nontoxic to fish, birds, earthworms, and aquatic invertebrates.
2) Highly toxic to algae.
3) No volatility expected.
4) Not expected to bioconcentrate in aquatic organisms.
5) Low mobility in soil.
6) Not persistent in the environment due to degradation and possible photolysis.
Sulfamethazine -
1) Practically nontoxic to aquatic organisms.
2) If released into air, material is expected to exist primarily in the particulate-phase and may be removed by wet or dry deposition processes.
3) Vapor-phase material is expected to rapidly degrade in the atmosphere.
4) Material may covalently bond with humic materials in soil and water.
5) Material not covalently bonded may leach into groundwater.
6) Volatilization is not expected to occur.
7) Material is not expected to bioconcentrate in aquatic organisms.

Symptoms and Treatment For Overdosage, and Antidotes:
Tylosin
Produced no adverse effects when fed to pigs at 600 ppm in the feed (six times the recommended maximum level) for 28 days.
Sulfonamides
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.

Storage Conditions:
Store at temperature below 30°C.

Shelf-life:
3 years.

Product description and Packing:
A white to slightly yellow powder, and without other foreign matter.
Aluminum Pouch of 100g, 1kg. Paper Bag of 20kg.

For food producing animals product
Withdrawal Periods
15 days before slaughtering.

Maximum Residual Limit (MRL)
Tylosin –
All food producing species: Muscle, fat, liver, kidney 100µg/kg, milk 50µg/kg, eggs 200µg/kg.
Sulfamethazine –
Cattle, sheep, pigs, poultry: Muscle, fat, liver, kidney 0.1mg/kg, milk 0.025mg/L.



Made by YSP
Manufacturer:
Y.S.P. INDUSTRIES VIETNAM CO., LTD
Road No.6, Nhon Trach Industrial Zone 3, Nhon Trach Dist.,
Dong Nai Province, Vietnam Tel: +84251 3569 993

Product Registration Holder :
Y.S.P. INDUSTRIES (M) SDN. BHD.(192593 U)
Lot 3, 5 & 7, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor Darul Ehsan Malaysia.
Ordering Line: 1 800 88 3027 Product Info: 1 800 88 3679