For Veterinary Use Only.

Actimisin®

Injectable Solution

Veterinary Systemic Antibacterial

COMPOSITION

Actimisin Injectable Solution is a light yellow, viscous liquid containing 300mg tilmicosin and 25% propylene glycol.

PHARMACOLOGICAL PROPERTIES

Actimisin Injectable Solution contains tilmicosin, a semi-synthetic macrolide antibiotic. Due to its high affinity for the lung tissue, tilmicosin is used for the treatment of pneumoniae infections in cattle. Tilmicosin, as all macrolide antibacterial group, prevents the protein synthesis with inhibiting the peptide translocation by conjugating the 50S subunit of bacterial ribosome. Gram positive microorganisms and some gram negative microorganisms like Mannheimia (Pasteurella) haemolytica, Haemophillus sumnus, Pasteurella multocida, Mycoplasma dispar, M.bovoculi, M.bovinitis are susceptible to tilmicosin. E.coli, Enterobacter aerogenes,Klepsiella pneumoniae, Pseudomonas aeroginosa, Sallmonella and Serratia spp and Actinomyces spp are resistant microorganisms. In spite of low serum concentration ratio, Tilmicosin, as all macrolide antibacterial group, has high tissue diffusion ratio. This is the reason of tilmicosin concentration is 4.29 microgram/ml in lung tissue when it is 0.31 microgram/ml in serum after 8 hours of 10mg/kg single dose subcutaneous injection. Minimum inhibitor concentration of Mannheimia (Pasteurella) haemolytica is above 3.2 microgram/ml in lung tissue. In 21 days, 24% is by urine and 64% is by feces is excreted as the main composition.

FIELD OF APPLICATION/INDICATIONS

It is used for the treatment of respiratory system infections caused by susceptible bacteria in cattle and sheep.

ADMINISTRATION AND DOSE

Unless recommended otherwise by the Veterinary Surgeon, it is administrated as a single dose subcutaneous injection at 10 mg/kg (1ml/30kg BW) in cattle and sheep. Do not inject more than 15ml / injection site in cattle and 5 ml/injection site in sheep

UNDESIRABLE/ADVERSE EFFECTS

A temporal and slight edema may occur at the site of injection. The high fever decreases, feed consumption and general condition improved in the 24 hours period after injection. In laboratory and dominant animal researches, Tilmicosin is found toxic in heart muscle. The major effects on heart muscle are tachycardia and decreasing contraction power (negative inotropic effect). In cattle, subcutaneous doses of 10, 30 and 50 mg/kg of body weight, each injected 3 times at 72 hour intervals did not cause any deaths. As expected, edema at the site of injection was noted. The only lesion observed at necropsy was minimal myocardial necrosis in some animals in the 50 mg/kg group. Subcutaneous doses of 150 mg/kg injected at 72-hour intervals resulted in deaths. Edema was marked at the site of injection. Minimal myocardial necrosis was the only lesion observed at necropsy. Deaths of cattle have been observed with a single intravenous dose of 5 mg/kg of body weight.

DRUG INTERACTIONS

Competitive antagonism occurs by the administration with chloramphenicol, florinephenicol, lincosamids and other macrolide antibiotics. Beta adrenergic antagonists (e.g. propranolol) may increase the tilmicosin based tachycardia. Intravenous epinephrine administration with tilmicosin may cause death in pigs.

OVERDOSE SIGNS, PRECAUTIONS AND ANTIDOTE

In case of overdose, cardiac toxicity risk increases. It is stated that administration of 50 mg/kg dose causes myocardial necroses in healthy cattle. Horse and goats are more susceptible than cattle in high dose administrations. No specific antidote is known. The beta adrenergic antagonists as Propranolol are not recommended because of decreasing the contraction power of heart in spite of decreasing the tachycardia.

WARNINGS FOR THE DRUG RESIDUES IN FOOD

Withholding Period (WHP): The cattle and sheep that are being grown for human consumption should not be slaughtered during the treatment or before 60 and 42 days, respectively, following the drug administration. The milk of sheep should not be used for human consumption before 15 days (30 milking) of drug administration. The drug is not appropriate for administration in dairy cows from which milk for human consumption is produced. It is not recommended of administration in sheep which are used for human milk consumption, because of the long lasting withdrawal time in milk

CONTRAINDICATIONS

Macrolide antibiotics are metabolized in liver, therefore it should not be used in animals with hepatic disorders. It should not be administrated in intravenous injection way. Should not be administrated in sheep at below 15 kg of weight; may cause death.

Use during pregnancy: There is not enough data about reliability in pregnant animals

GENERAL WARNINGS

Veterinary surgeon should be consulted before the administration and in the case of adverse effects. Keep away from children. Use only in target species.

SPECIAL PROTECTION MEASURES FOR THE ADMINISTRATOR AND WARNINGS FOR THE SURGEONS

Be careful during injection. 30 mg/kg intramuscular injection caused death in monkeys. A doctor should be consulted in the case of accidental injection in human. In this type of cases cardiovascular system is mostly affected. This antibiotic exists in the tissues for a few days. Cardiovascular system should be monitored and supportive treatment should be administrated. The negative inotropic effect in dogs is partially cured by dobutamine. Beta-adrenergic receptors as propranol increases the negative inotropic effect in tachycardia. Some researches indicates the usage of epinephrine may be contraindicate. Single high dosage administration of epinephrine increased the lethal effects in a research about pigs. The beta-adrenergic antagonist, as propranol, administration is contraindicated in any tachycardia case, because of increasing effect on negative inotrop effect.

STORAGE CONDITIONS AND SHELF LIFE

Store it in its original package at room temperature of not more than 25 ℃ (15-25 ℃). Keep away from d irect sunlight. A shelf life of 2 years (24 months) has been reported from the date of manufacture.

WARNINGS FOR THE NON-TARGET SPECIES

Tilmicosin may cause death in dog, horse, pig, monkey and goats. Tachycardia and decrease in heart contraction may occur in dogs.

COMMERCIAL PRESENTATION FORM

Actimicin Injectable Solution is presented in 20ml, 50ml and 100ml amber vials.

SELLING AREA AND CONDITIONS

To be sold in pharmacies and veterinary clinics upon prescription of veterinary surgeon (Veterinary Surgeon Prescription.

DATE OF APPROVAL OF THE PACKAGE INSERT: 03.05.2005

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