PRESCRIPTION ANIMAL REMEDY
KEEP OUT OF REACH OF CHILDREN
FOR ANIMAL TREATMENT ONLY

Tulieve® Injection

100 mg/mL Tulathromycin

For the treatment of respiratory infections in cattle and pigs. For subcutaneous injection in cattle, including dairy heifers up to the point of first mating, and intramuscular injection in pigs.

INDICATIONS

Cattle

Tulieve® Injection is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma bovis* sensitive to tulathromycin.

Pigs

Tulieve® Injection is indicated for the treatment of swine respiratory disease (SRD) associated with *Pasteurella multocida*, *Mycoplasma hyopneumoniae,* and *Haemophilus parasuis* sensitive to tulathromycin.

DIRECTIONS FOR USE:

Restraints

USE ONLY in respiratory infections of cattle and swine.
DO NOT USE in cows, except replacement dairy heifers, which are producing or may in the future produce milk that may be used or processed for human consumption.
DO NOT USE in bobby calves.
DO NOT USE in dairy heifers following the first mating.
RE-TREATMENT INTERVALS
Cattle: DO NOT RE-TREAT cattle for 12 weeks after last treatment.
Dairy heifers: DO NOT RE-TREAT dairy heifers.
Pigs: DO NOT RE-TREAT pigs for 8 weeks after last treatment.

Precautions

Avoid using the product simultaneously with other macrolides or lincosamides. Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. However, the effects of Tulieve® Injection on bovine and porcine reproductive performance, pregnancy and lactation have not been determined.

Side Effects

Subcutaneous administration to cattle frequently causes transient pain reactions and local swellings at the injection site that can persist for up to 30 days.
Pain reactions have not been observed in pigs after intramuscular administration, but local swellings at the injection site can persist for up to 30 days. These swellings may result in trim loss of edible tissue at slaughter. In one pig field study, one out of 40 pigs exhibited mild salivation that resolved in less than four hours.

Dosage and Administration

In use shelf life: 50mL and 100mL vials - Use within 60 days of the first puncture and puncture a maximum of 52 times. 250 ml vial - Use within 60 days of the first puncture and puncture a maximum of 80 times.
Cattle: 1 mL/40 kg body weight (2.5 mg tulathromycin/kg) by a subcutaneous injection high on the neck. For cattle over 400 kg body weight, divide the dose so that no more than 10 mL are injected at one site.
Pigs: 1 mL/40 kg body weight (2.5 mg tulathromycin/kg) by an intramuscular injection in the neck. For pigs over 100 kg body weight, divide the dose so that no more than 2.5 mL are injected at one site.

General Directions

DESCRIPTION

Tulieve® Injection is a ready-to-use sterile parenteral preparation containing tulathromycin, a semi-synthetic macrolide antimicrobial agent. Each mL of Tulieve® Injection contains 100 mg of tulathromycin as the free base in a 50% propylene glycol vehicle with citric and hydrochloric acids added to adjust pH.

PHARMACOLOGY

Tulathromycin is a semi-synthetic macrolide antimicrobial agent, which originates from a fermentation product. It differs from many other macrolides in that it has a long duration of action that is, in part, due to its three amine groups; therefore it has been given the chemical subclass designation of triamilide. Macrolides are bacteriostatic acting antibiotics and inhibit essential protein biosynthesis by virtue of their selective binding to bacterial ribosomal RNA. They act by stimulating the dissociation of peptidyl-tRNA from the ribosome during the translocation process.
Resistance to macrolides can develop by mutations in genes encoding ribosomal RNA (rRNA) or some ribosomal proteins; by enzymatic modification (methylation) of the 23S rRNA target site, generally giving rise to cross-resistance with lincosamides and group B streptogramins (MLSB resistance); by enzymatic inactivation; or by macrolide efflux. MLSB resistance may be constitutive or inducible. Resistance may be chromosomal or plasmid encoded and may be transferable if associated with transposons or plasmids.
In cattle, the pharmacokinetic profile of tulathromycin when administered as a single subcutaneous dose of 2.5 mg/kg body weight, was characterised by rapid and extensive absorption followed by high distribution and slow elimination.
The maximum concentration (C_{max}) in plasma was approximately 0.5 µg/mL; this was achieved approximately 30 minutes post-dosing (T_{max}). Tulathromycin concentrations in lung homogenate were considerably higher than those in plasma. There is strong evidence of substantial accumulation of tulathromycin in neutrophils and alveolar macrophages. Tulathromycin was present in pulmonary epithelial lining fluid (alveolar) cells at concentrations exceeding 10 µg/mL from days 2 to 15 post-treatment, achieving a C_{max} in these cells of 19.5 µg/mL. Peak concentrations were followed by a slow decline in systemic exposure with an apparent elimination half-life ($t_{1/2}$) of 90 hours in plasma. Plasma protein binding was low, approximately 40%. The volume of distribution at steady-state (Vss) determined after intravenous administration was 11L/kg.

The bioavailability of tulathromycin after subcutaneous administration in cattle was approximately 90%.
In pigs, the pharmacokinetic profile of tulathromycin when administered as a single intramuscular dose of 2.5 mg/kg body weight, was also characterised by rapid and extensive absorption followed by high distribution and slow elimination.

The maximum concentration (C_{max}) in plasma was approximately 0.6 µg/mL; this was achieved approximately 30 minutes post-dosing (T_{max}). Tulathromycin concentrations in lung homogenate were considerably higher than those in plasma. There is strong evidence of substantial accumulation of tulathromycin in neutrophils and alveolar macrophages. However, the *in vivo* concentration of tulathromycin at the infection site of the lung is not known. Peak concentrations were followed by a slow decline in systemic exposure with an apparent elimination half-life ($t_{1/2}$) of approximately 91 hours in plasma. Plasma protein binding was low, approximately 40%. The volume of distribution at steady-state (Vss) determined after intravenous administration was 13.2L/kg. The bioavailability of tulathromycin after intramuscular administration in pigs was approximately 88%.

Prudent Use
Indiscriminate use of tulathromycin can contribute to the development of antibiotic resistance. Culture and sensitivity tests should be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly.

WITHHOLDING PERIODS:
MEAT: Cattle: DO NOT USE less than 35 days before slaughter for human consumption.
Pigs: DO NOT USE less than 14 days before slaughter for human consumption.
MILK: DO NOT USE in cows, except replacement dairy heifers, which are producing or may in the future produce milk that may be used or processed for human consumption.
DO NOT USE in bobby calves.
DO NOT USE in dairy heifers following the first mating.

Any variation by the prescribing veterinarian to the approved dose, frequency, duration, route, disease or target species may result in the need to extend the approved withholding period.

EXPORT SLAUGHTER INTERVALS (ESI):
Cattle: DO NOT USE less than 35 days before slaughter for export.
Pigs: DO NOT USE less than 26 days before slaughter for export.
The ESIs on this label were correct at the time of label approval. Before using this product, confirm the ESI from the manufacturer on 1800 665 866 or the APVMA website (www.apvma.gov.au/residues/).

First Aid Instructions
If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126.

Additional User Safety
Tulathromycin is irritating to eyes. If accidental eye exposure occurs, flush the eyes immediately with clean water.
Users should wear a face shield or goggles when administering Tulieve® Injection, to prevent exposure from syringe or needle breakage. Tulathromycin may cause sensitisation by skin contact. If accidental skin exposure occurs, wash the skin immediately with soap and water. In case of accidental self injection, seek medical advice immediately and show the package insert or the label to the physician.

DISPOSAL
Dispose of container by wrapping with paper and putting in garbage.

STORAGE
Store below 30ºC (Room Temperature). Do not freeze. Protect from light.

PRESENTATION
Tulieve® Injection is available in 50 mL, 100 mL and 250 mL vials.

APVMA Approval No. 88653/121910
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