150 mg/mL ANTIMICROBIAL

For subcutaneous injection in beef and non-lactating dairy cattle only. Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

READ ENTIRE BROCHURE CAREFULLY BEFORE USING THIS PRODUCT.

DESCRIPTION

ZACTRAN® Injection for Cattle is a ready to use sterile parenteral solution containing gamithromycin, a macroclide subclass, 7a-azalide antimicrobial. Each mL of ZACTRAN contains 150 mg of gamithromycin as the free base, 1 mg of monomethylglycol and 40 mg of sucrose acid in a glycerol-formal vehicle.

The chemical name of gamithromycin is 1-Oxa-7-azacyclododecane-15-one, 13/[2,6-dideoxy-3-c-methyl-3-O-methyl-alpha-L-ribo-hexopyranosyloxy]-2-ethyl-3,4,10-trihydroxy-7-propyl-trihexamethyl-7-propyl-11-[3,4,6-trideoxy-3- (dimethylamino)-beta-D-xylene-hexopyranosyloxy]-[2R, 35, 4R, 55, 8R, 10R, 11R, 135, 135, 14R*]-, and the structure is shown below.

INDICATIONS

ZACTRAN is indicated for the treatment of bovine respiratory disease (BRD) associated with Mannheimia haemolytica, Pasteurella multocida, Histophilus somni and Mycoplasma bovis in beef and non-lactating dairy cattle. ZACTRAN is also indicated for the control of respiratory disease in cattle and non-lactating dairy cattle at high risk of developing BRD associated with Mannheimia haemolytica and Pasteurella multocida.

DOSEAGE AND ADMINISTRATION

Administer ZACTRAN one time as a subcutaneous injection in the neck at 6 mg/kg BW (2 mL/110 lb body weight (BW)). If the total dose exceeds 10 mL, divide the dose so that no more than 10 mL is administered at each injection site.

CONTRAINDICATIONS

As with all drugs, use of ZACTRAN is contraindicated in animals previously found to be hypersensitive to this drug.

WARNING:

FOR USE IN CATTLE ONLY.

NOT FOR USE IN HUMANS.

KEEP THIS AND ALL DRUGS OUT OF REACH OF CHILDREN.

NOT FOR USE IN CHICKENS OR TURKEYS.

FOR SAFETY REASONS, DO NOT USE IN CALVES TO BE PROCESSED FOR VEAL.

PRECAUTIONS

The effects of ZACTRAN on bovine reproductive performance, pregnancy, and lactation have not been determined. Subcutaneous injection of ZACTRAN may cause a transient local tissue reaction in some cattle that may result in trim loss of edible tissues at slaughter.

ADVERSE REACTIONS

Transient animal discomfort and mild to moderate injection site swelling may be seen in cattle treated with ZACTRAN.

CLINICAL PHARMACOLOGY

The macroclide antimicrobials as a class are weak bases and as such concentrate in some cells (such as pulmonary leukocytes). Prolonged exposure of extracellular pulmonary pathogens to macrolides appears to reflect the slow release of drug from its intracellular reservoir to the site of action, the pulmonary epithelial lining fluid (ELF). It is the ELF that is relevant to the subsequent treatment and control of BRD. Gamithromycin is primarily bacteriostatic at therapeutic concentrations. However, in vitro bacteriostatic activity has been observed at concentrations of 10 μg/mL (Mueller-Hinton broth) and after exposure to the 6-hour and 24-hour plasma samples derived from cattle dosed at 6 mg gamithromycin/kg BW. Macrolides typically exhibit substantially higher concentrations in the alveolar macrophages and ELF as compared to concentrations observed in plasma. Gamithromycin concentrations in the ELF and ELF cells exceed the concentrations observed in the plasma. Postmortem gamithromycin concentrations in ELF exceed the MICs, of M. haemolytica, H. somni and P. multocida through at least 72 hours after drug administration. Because M. haemolytica, P. multocida and H. somni are extracellular pathogens, drug concentrations in the ELF are considered to be clinically relevant.

The postmortem area under the concentration-time curve (AUC) observed in ELF cells (e.g., alveolar macrophages) are at least 300-times greater than that in the plasma. Although published studies suggest that inflammation can increase the release of drug from macrophages and neutrophils, these high concentrations in the alveolar macrophages should not be considered indicative of the magnitude or duration of response to the pathogens for which this product is indicated. ZACTRAN administered subcutaneously in the neck of cattle at a single dosage of 6 mg/kg BW is rapidly and completely absorbed, with peak concentrations generally occurring within 1 hour after administration. Based upon plasma and lung homogenate data, the terminal half-life (T1/2) of gamithromycin is approximately 3 days.

In vitro plasma protein binding studies show that 26% of the gamithromycin binds to plasma protein, resulting in free drug available for rapid and extensive distribution into body tissues. The free drug is rapidly cleared from the systemic circulation with a clearance rate of 712 mL/h/kg and a volume of distribution of 25 L/kg.

Dose proportionality was established based on AUC over a range of 3 mg/kg BW to 9 mg/kg BW. Biliary excretion of the unchanged drug is the major route of elimination.

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ZACTRAN is available in three ready-to-use bottle sizes. The 100, 250 and 1000 mL containers contain sufficient solution that will treat 10, 25 and 50 head of 550 lb (250 kg) cattle respectively.

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Made in Austria
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HOW SUPPLIED

ZACTRAN is available in three ready-to-use bottle sizes. The 100, 250 and 500 mL containers contain sufficient solution that will treat 10, 25 and 50 head of 550 lb (250 kg) cattle respectively.

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Table 1. Gamithromycin minimum inhibitory concentration (MIC) values* of indicated pathogens isolated from BRD treatment field studies in the U.S.

<table>
<thead>
<tr>
<th>Indicated Pathogen</th>
<th>Yeast of isolates</th>
<th>No. of isolates</th>
<th>MIC** (μg/mL)</th>
<th>MIC*** (μg/mL)</th>
<th>MIC range (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. haemolytica</td>
<td>2004</td>
<td>89</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5 to 3</td>
</tr>
<tr>
<td>P. multocida</td>
<td>2004</td>
<td>79</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5 to 3</td>
</tr>
<tr>
<td>H. somni</td>
<td>2004</td>
<td>32</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5 to 3</td>
</tr>
</tbody>
</table>

* The correlation between in vitro susceptibility data and clinical effectiveness is unknown.

** The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.