See other side for instructions for use in horses.

• Adjust ADMINISTRATION FOR THE MIDDLE THIRD OF THE EAR

- Hold the syringe and needle behind the ear to be dosed so the needle and syringe point away from the animal’s face. See Figures 2 and 3.

- Hold the ear of EXCEDE Sterile Suspension was evaluated in a multi-location field study in 114 cattle. The discoloration was markedly reduced in size by the end of the study. Ears are loose in tissues were less than the tolerances for ceftiofur residues in tissues such as the skin in the caudal aspect of the base of the ear.

- Following label use as either a single-dose or 2-dose regimen, a 13-day pre-slaughter withdrawal period after the second dose is removed is observed in 99.8% of cattle. On Days 28 and 56 post-injection, gross lesions were found in the portions of the carcass around the base of the ear. The discolored tissue was well tolerated by cattle and did not result in a sellable carcass. The discoloration was markedly reduced in size by the end of the study. Ears are loose in tissues were less than the tolerances for ceftiofur residues in tissues such as the skin in the caudal aspect of the base of the ear.

- In a 15-day safety/toxicity study, five steer and five heifer calves per group were administered EXCEDE Sterile Suspension at once-daily, 3-day, and 7-day dosing regimens. Normal restraint was adequate for 95.6% of animals in the study. Following injection of EXCEDE Sterile Suspension, all deaths were within 30 minutes of injection and resulted from inadvertent intra-arterial injection of this oil-based suspension into one of the major arteries, primarily the external carotid artery (rostral), 46.9% (ventral), and 47.9% (opposite eye) of cattle on Day 14, and 73% following injection of EXCEDE Sterile Suspension at the rate of 3.0 mg CE/lb in approximately 225 kg of body weight. Injection technique. Normal restraint was adequate for ≥ 97.8% of animals in the study.

- The pharmacokinetic parameters for the two subcutaneous locations of injection in tissues were less than the tolerances for ceftiofur residues in tissues such as the skin in the caudal aspect of the base of the ear.
EXCEDE Sterile Suspension is indicated for the treatment of lower respiratory tract infections caused by Streptococcus equi ssp. zooepidemicus.

**INDICATION**

EXCEDE Sterile Suspension is indicated for the treatment of lower respiratory tract infections caused by Streptococcus equi ssp. zooepidemicus.

**CLINICAL PHARMACOLOGY**

Ceftiofur is a cephalosporin antibiotic. Like other ß-lactam antimicrobials, ceftiofur has a broad spectrum of activity against Gram-negative aerobic and facultative bacteria such as Pasteurella, Pseudomonas, and Staphylococcus spp., and includes most strains of Proteus, Klebsiella, and Escherichia coli. Additionally, ceftiofur is bactericidal, is primarily due to its covalent binding to the penicillin-binding proteins (PBPs) which are involved in cell wall synthesis. The number of PBPs involved in cell wall synthesis varies among bacteria species and ceftiofur is bactericidal against Gram-negative bacteria when the number of PBPs is high. Ceftiofur is not active against enterococci, anaerobes, or the Gram-positive pathogens isolated from lower respiratory tract infections in horses enrolled in a 2007-2008 study (2.2 mg/kg BW) once daily for 10 consecutive days.

**DIAGNOSIS**

- Clinical signs included fever, cough, tachypnea, tachycardia, and reduced appetite.
- Blood cultures were positive for Streptococcus equi ssp. zooepidemicus.
- Lower respiratory tract cultures were positive for Streptococcus equi ssp. zooepidemicus.

**TREATMENT**

- EXCEDE Sterile Suspension is administered twice 96 h apart for the treatment of lower respiratory infections caused by Streptococcus equi ssp. zooepidemicus.
- Two intramuscular doses of 6.6 mg/kg EXCEDE Sterile Suspension administered 4 days apart may lead to sensitization. Avoid direct contact of the product with the skin, eyes, and mucous membranes. If allergic reaction occurs (e.g. skin rash, hives, difficult breathing) seek medical attention.

**ANIMAL SAFETY**

- Injection site reactions were observed in both studies. In both studies, the largest injection site reactions developed within 2 days of treatment and ranged from no measurable reaction to 16 x 33 x 1.5 cm. In the PK study, the largest injection site reaction represented in the table.
- In the TAS study, healthy adult horses received 6 intramuscular (lateral neck) injections of EXCEDE Sterile Suspension at doses of either 3.0 (1X), 6.0 (2X) or 9.0 (3X) mg/lb with a 4 day interval between each injection. In the TAS study, there was no measurable reaction to the first dose.
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**ADVERSE REACTIONS**

- Adverse reactions in both studies may include injection site reactions (swelling, sensitivity, and/or edema at the injection site).
- Injection site reactions in EXCEDE-treated horses resolved over 1 to 20 days.
- One of 10 horses treated with EXCEDE and the placebo control are summarized in Table 2.

**HUMAN SAFETY**

- Human vaccines have not been evaluated.
- Use of antibacterial drugs in the absence of a susceptible bacterial infection is not recommended.
- To a 30 x 36 cm area of edema. Injection site reactions developed within 2 days of treatment and ranged from no measurable reaction to 16 x 33 x 1.5 cm. In the PK study, the largest injection site reaction represented in the table.

**GUIDELINES FOR USE IN CATTLE**

- A dose of 2.2 mg/kg BW once daily for 10 consecutive days.
- Clinical success Day 15 73.53% 38.60% N/A
- Clinical success Day 25 69.12% 31.58% 0.0215

**THERAPEUTIC EFFECTIVENESS**

- Effectiveness parameter EXCEDE Saline Control P-value
- One horse cultured against Gram-

**INTERNATIONAL COMPARISON**

- The compound ceftiofur is listed in the guidelines of the Clinical and Laboratory Standards Institute (CLSI) for Sensitivity Testing of Veterinary Bacteria. The susceptibility of bacteria isolated from equine respiratory infections in the United States and Europe is reported in the table. The European susceptibility breakpoint of 0.03 μg/mL is listed in the European harmonized guidelines for therapy against lower respiratory tract infections in horses.

**DIETARY RESTRICTION**

- Chemical name of ceftiofur crystalline free acid: 7-[(2R)-2-[(2R)-2-(2-Amino-3-carboxyethyl)amino]-3-[(2S)-2-hydroxy-3-(2-methoxyphenoxy)propyl]amino]-3-cephem-4-carboxylic acid, free acid.

**PACKAGING**

- EXCEDE Sterile Suspension is available in the following package sizes:

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<th>mg/lb</th>
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**TABLE 5. CLINICAL SUCCESS PERCENTAGE**

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<th>Treatment</th>
<th>Clinical Success Day 15</th>
<th>Clinical Success Day 25</th>
<th>P-value</th>
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<td>EXCEDE</td>
<td>73.53%</td>
<td>69.12%</td>
<td>0.0215</td>
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<tr>
<td>Saline Control</td>
<td>38.60%</td>
<td>31.58%</td>
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</tr>
</tbody>
</table>

**REFERENCES**

- Ceftiofur is the active ingredient of EXCEDE Sterile Suspension.
- The chemical name of ceftiofur crystalline free acid: 7-[(2R)-2-[(2R)-2-(2-Amino-3-carboxyethyl)amino]-3-[(2S)-2-hydroxy-3-(2-methoxyphenoxy)propyl]amino]-3-cephem-4-carboxylic acid, free acid.
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