**Draxxin® 25 (tulathromycin injection) Injectable Solution**

**Antibiotic**
25 mg of tulathromycin/mL. For use in suckling calves, dairy calves, veal calves, and swine. Not for use in ruminant cattle.

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

**DESCRIPTION**

Draxxin® 25 Injectable Solution is a ready-to-use sterile parenteral preparation containing tulathromycin, a semi-synthetic macrolide antibiotic of the subclass triazide. Each mL of DRAXXIN 25 contains 25 mg of tulathromycin as the free base in a 50% propylene glycol vehicle, monothioglycerol (5 mg/mL), citric acid (4.8 mg/mL) with hydrochloric acid and sodium hydroxide added to adjust pH. DRAXXIN 25 consists of an equilibrated mixture of two isomeric forms of tulathromycin in a 9:1 ratio.

The chemical names of the isomers are (2R,3S,4R,5R,8R,10R,11S,12S,14R)-13-[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[[propylamino][methyl]-(2S)-2-deoxy-3,4,10-trihydroxy-3,5,8,10,12,14-hexa-ethyl-11-[[3,4,6,8-dideoxy-3-(dimethylamino)-D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclododecan-15-one and (2R,3R,6R,8R,9S,11S,12S,14R)-13-[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[[propylamino][methyl]-(2R)-2-deoxy-3,4,10-trihydroxy-3,5,8,10,12,14-hexa-ethyl-11-[[3,4,6,8-dideoxy-3-(dimethylamino)-D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclododecan-15-one, respectively.

**INDICATIONS**

Swine

Draxxin® 25 Injectable Solution is indicated for the treatment of swine respiratory disease (SRD) associated with Actinobacillus pleuropneumoniae, Pasteurella multocida, Bordetella bronchiseptica, Haemophilus parasuis, and Mycoplasma hyopneumoniae and for the control of SRD associated with Actinobacillus pleuropneumoniae, Pasteurella multocida, and Mycoplasma hyopneumoniae in groups of pigs where SRD has been diagnosed.

Calves, Dairy Calves, and Veal Calves

BVD - DRAXXIN Injectable Solution is indicated for the treatment of bovine respiratory disease (BRD) associated with Mannheimia haemolytica, Pasteurella multocida, Histophilus somni, and Mycoplasma bovis.

**DOSAGE AND ADMINISTRATION**

Swine

Inject intramuscularly as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) Body Weight (BW). Do not inject more than 4 mL per injection site.

<table>
<thead>
<tr>
<th>Animal Weight (Pounds)</th>
<th>Dose Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>10</td>
<td>0.5</td>
</tr>
<tr>
<td>15</td>
<td>0.7</td>
</tr>
<tr>
<td>20</td>
<td>0.9</td>
</tr>
<tr>
<td>25</td>
<td>1.1</td>
</tr>
<tr>
<td>30</td>
<td>1.4</td>
</tr>
<tr>
<td>40</td>
<td>2.3</td>
</tr>
<tr>
<td>50</td>
<td>2.7</td>
</tr>
<tr>
<td>70</td>
<td>4.5</td>
</tr>
<tr>
<td>90</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Calves

Inject subcutaneously as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) Body Weight (BW). Do not inject more than 11.5 mL per injection site.

<table>
<thead>
<tr>
<th>Animal Weight (Pounds)</th>
<th>Dose Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>2.3</td>
</tr>
<tr>
<td>70</td>
<td>2.4</td>
</tr>
<tr>
<td>100</td>
<td>4.5</td>
</tr>
<tr>
<td>150</td>
<td>7.0</td>
</tr>
<tr>
<td>200</td>
<td>9.0</td>
</tr>
<tr>
<td>225</td>
<td>11.5</td>
</tr>
</tbody>
</table>

**CONTRAINdications**

The use of DRAXXIN Injectable Solution is contraindicated in animals previously found to be hypersensitive to the drug.

**WARNINGS**

**FOR USE IN ANIMALS ONLY. NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. NOT FOR USE IN CHICKENS OR TURKEYS.**

**RESIDUE WARNINGS**

Swine

Swine intended for human consumption must not be slaughtered within 5 days from the last treatment.

Calves

Calves intended for human consumption must not be slaughtered within 22 days from the last treatment with DRAXXIN Injectable Solution. This drug is not for use in ruminating cattle.

**PRECAUTIONS**

Swine

The effects of Draxxin Injectable Solution on porcine reproductive performance, pregnancy, and lactation have not been determined. Intramuscular injection can cause a transient local tissue reaction that may result in trim loss of edible tissue at slaughter.

Calves

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

**ADVERSE REACTIONS**

Swine

In one field study, one out of 40 pigs treated with DRAXXIN Injectable Solution (100 mg/mL) at 2.5 mg/kg BW exhibited mild salivation that resolved in less than four hours.

Calves

In one BRD field study, two calves treated with DRAXXIN Injectable Solution (100 mg/mL) at 2.5 mg/kg BW exhibited transient hypersalivation. One of these calves also exhibited transient dyspnea, which may have been related to pneumonia.

**Post Approval Experience**

The following adverse events are based on post approval adverse drug experience reporting for DRAXXIN Injectable Solution (100 mg/mL). Not all adverse events are reported to the FDA CVM. It is not possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of reporting frequency in cattle: injection site reactions and anaphylactic/anaphylactoid reactions. For a complete listing of adverse reactions for DRAXXIN Injectable Solution or DRAXXIN Injectable Solution reported to the CVM see: http://www.fda.gov/AnimalVeterinary.

**CLINICAL PHARMACOLOGY**

At physiological pH, tulathromycin (a weak base) is approximately 50 times more soluble in hydrophilic than lipophilic media. This solubility profile is consistent with the extracellular pathogen activity typically associated with the macrolides. Markedly higher tulathromycin concentrations are observed in the lung parenchyma as compared to serum. These elevated concentrations can remain in lung tissue for several days beyond which can be measured in the plasma. However the clinical relevance of these elevated lung concentrations is undetermined. As a class, macrolides tend to be primarily bacteriostatic, but may be bactericidal against some pathogens. When acting as a cidal compound, they tend to exhibit concentration independent killing; the rate of bacterial eradication does not change once serum drug concentrations reach 2 to 3 times the minimum inhibitory concentration (MIC) of the targeted pathogen. Under these conditions, the time that serum concentrations remain above the MIC becomes the major determinant of antimicrobial activity. Macrolides also exhibit a post-antibiotic effect (PAE), the duration of which varies from less than 1 hour to days and pathogens dependent. In general, by increasing the macrolide concentration and the exposure time, the PAE will increase to some maximal duration.

Tulathromycin is eliminated from the body by renal excretion via biliary excretion.

The MICs of tulathromycin against the pathogens cited in table 3 are based on post approval adverse drug experience reporting for DRAXXIN Injectable Solution or DRAXXIN Injectable Solution reported to the CVM. The correlation between in vitro susceptibility and clinical effectiveness is unknown. The lowest MIC is to encompass 90% of the most susceptible isolates, respectively.

**Comparative Bioavailability Summary**

Despite slightly lower peak concentrations with DRAXXIN Injectable Solution, a single IM dose of 2.5 mg/kg BW of either DRAXXIN Injectable Solution (100 mg/mL) or DRAXXIN Injectable Solution (25 mg/mL) resulted in comparable total systemic tulathromycin exposure. Therefore, DRAXXIN Injectable Solution is considered to be therapeutically equivalent to DRAXXIN Injectable Solution when administered to swine by IM injection at a dose of 2.5 mg/kg/mL/tulathromycin/kG BW.

Calves

Following intramuscular (IM) administration to feeder pigs at a dosage of 2.5 mg/kg BW, tulathromycin is nearly completely absorbed, with peak plasma concentrations achieved within ~0.25 hr. The volume of distribution exceeds 15 L/kg, which is consistent with extensive tissue binding. This large distribution volume results in a long terminal elimination half-life (60 to 90 hours) despite a rapid systemic free drug clearance (187 mL/hr/kg). No pharmacokinetic differences are observed in castrated male versus female calves.

**Microbiology**

**Swine**

Tulathromycin has demonstrated in vitro activity against A. pleuropneumoniae, P. multocida, B. bronchiseptica, H. parasuis, and M. hyopneumoniae. The MICs of tulathromycin against indicated pathogens collected from field studies were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLSI, 2001-A and 2003-A3). MICs for H. parasuis were determined using Veterinary Fastidious Medium and were incubated up to 48 hours at 35 °C to 37 °C in a CO2-enriched atmosphere. These values are represented in Table 3, below.

**Table 2. DRAXXIN Injectable Solution Comparative Bioavailability Summary**

<table>
<thead>
<tr>
<th>Indicated pathogen</th>
<th>Date isolated</th>
<th>No. of isolates</th>
<th>MIC&lt;sup&gt;c&lt;/sup&gt; (µg/mL)</th>
<th>MIC&lt;sup&gt;c&lt;/sup&gt; (µg/mL)</th>
<th>MIC range (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinobacillus pleuropneumoniae</td>
<td>2001-2002</td>
<td>134</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>2002-2003</td>
<td>89</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Haemophilus parasuis</td>
<td>2000-2001</td>
<td>31</td>
<td>2</td>
<td>0.25 to &gt; 64</td>
<td></td>
</tr>
<tr>
<td>Pasteurella multocida</td>
<td>2000-2001</td>
<td>39</td>
<td>1</td>
<td>2</td>
<td>0.5 to &gt; 64</td>
</tr>
<tr>
<td></td>
<td>2002-2003</td>
<td>40</td>
<td>1</td>
<td>2</td>
<td>0.03 to 2</td>
</tr>
<tr>
<td>Zootechnella bronchiseptica</td>
<td>2002-2003</td>
<td>42</td>
<td>8</td>
<td>2.68 g</td>
<td></td>
</tr>
</tbody>
</table>

<sup>c</sup> 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.

**Microbiology**

**Swine**

Tulathromycin has demonstrated in vitro activity against M. haemolytica, P. multocida, H. somni, and M. bovis, four pathogens associated with BRD. The MICs of tulathromycin against indicated pathogens collected from field studies using DRAXXIN Injectable Solution (100 mg/mL) were determined using methods recommended by the CLSI (M21-A3). These values are represented in Table 4, below.
was isolated from 106 saline-treated and non-treated sentinel calves with inflammatory changes induced by injections and were considered to be mild or moderate with progression to marked or pronounced lesions. In all groups, transient indications of pain after injection were seen, including head shaking and pawing at the ground. Injection site swelling, discoloration of the subcutaneous tissues at the injection site and corresponding histopathologic changes were seen in animals in all dosage groups. These lesions showed signs of resolving over time. No other drug-related lesions were observed macroscopically or microscopically.

An exploratory study was conducted in feeder calves receiving DRAXXIN Injectable Solution (100 mg/mL) as a single subcutaneous dose of 10, 12.5, or 15 mg/kg BW. Macroscopically, no lesions were observed. Microscopically, minimal to mild mucocutaneous degeneration was seen in one of six calves administered 12.5 mg/kg BW and two of six calves administered 15 mg/kg BW.

A safety study was conducted in prernitant calves 13 to 27 days of age receiving DRAXXIN Injectable Solution (100 mg/mL) at 2.5 mg/kg BW or 7.5 mg/kg BW once subcutaneously. With the exception of minimal to mild injection site reactions, no drug-related clinical signs or other lesions were observed macroscopically or microscopically.

Sixteen growing cattle were injected with either saline (eight animals) as a single injection of 11.5 mL or DRAXXIN 25 Injectable Solution (eight animals) as a single injection of either 2.5 mg/kg BW or a dose volume of 11.5 mL (whichever volume was higher). One calf in the DRAXXIN 25-treated group was observed to have firmness at the injection site for a single day. Two DRAXXIN 25-treated calves exhibited injection site swelling. In one calf, the swelling resolved within 48 hours. In the other calf, the swelling was observed over a three-day period, after which the calf underwent a scheduled necropsy, preventing further injection site observations. No injection site swelling was observed in saline-treated animals. At necropsy, three of the saline-treated calves and five of the DRAXXIN 25-treated calves had altered tissue present at the injection site.

**STORAGE CONDITIONS:** Store at or below 25°C (77°F). Use within 90 days of first vial puncture.

**HOW SUPPLIED** DRAXXIN 25 Injectable Solution is available in the following package sizes: 50 mL vial 100 mL vial 250 mL vial

NADA 141-349, Approved by FDA

Distributed by: Zoetis Inc., Kalamazo, MI 49007

To report a suspected adverse reaction or to request a safety data sheet call 1-888-963-8471. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/ AnimalVeterinary/SafetyHealth. For additional DRAXXIN 25 product information call: 1-888-DRAXXIN or go to www.DRAXXIN.com

**ANIMAL SAFETY**

**Swine**

Plasma concentrations of tulathromycin administered as DRAXXIN Injectable Solution (100 mg/mL) or as DRAXXIN 25 Injectable Solution were demonstrated to be therapeutically equivalent (see CLINICAL PHARMACOLOGY, Comparative Bioavailability Summary). Therefore effectiveness studies conducted with DRAXXIN Injectable Solution support the effectiveness for DRAXXIN 25 Injectable Solution.

A safety study was conducted in feeder calves receiving DRAXXIN Injectable Solution (100 mg/mL) as a single subcutaneous dose of 25 mg/kg BW, or 3 weekly subcutaneous doses of 2.5, 7.5, and 12.5 mg/kg BW. In all groups, transient indications of pain after injection were seen, including head shaking and pawing at the ground. Injection site swelling, discoloration of the subcutaneous tissues at the injection site and corresponding histopathologic changes were seen in animals in all dosage groups. These lesions showed signs of resolving over time. No other drug-related lesions were observed macroscopically or microscopically.

An exploratory study was conducted in feeder calves receiving DRAXXIN Injectable Solution (100 mg/mL) as a single subcutaneous dose of 10, 12.5, or 15 mg/kg BW. Macroscopically, no lesions were observed. Microscopically, minimal to mild mucocutaneous degeneration was seen in one of six calves administered 12.5 mg/kg BW and two of six calves administered 15 mg/kg BW.

A safety study was conducted in prernitant calves 13 to 27 days of age receiving DRAXXIN Injectable Solution (100 mg/mL) at 2.5 mg/kg BW or 7.5 mg/kg BW once subcutaneously. With the exception of minimal to mild injection site reactions, no drug-related clinical signs or other lesions were observed macroscopically or microscopically.

**STORAGE CONDITIONS:** Store at or below 25°C (77°F). Use within 90 days of first vial puncture.

**HOW SUPPLIED** DRAXXIN 25 Injectable Solution is available in the following package sizes: 50 mL vial 100 mL vial 250 mL vial

NADA 141-349, Approved by FDA

Distributed by: Zoetis Inc., Kalamazo, MI 49007

To report a suspected adverse reaction or to request a safety data sheet call 1-888-963-8471. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth. For additional DRAXXIN 25 product information call: 1-888-DRAXXIN or go to www.DRAXXIN.com

**ANIMAL SAFETY**

**Swine**

Plasma concentrations of tulathromycin administered as DRAXXIN Injectable Solution (100 mg/mL) or as DRAXXIN 25 Injectable Solution were demonstrated to be therapeutically equivalent (see CLINICAL PHARMACOLOGY, Comparative Bioavailability Summary). Therefore effectiveness studies conducted with DRAXXIN Injectable Solution support the effectiveness for DRAXXIN 25 Injectable Solution.

A safety study was conducted in feeder calves receiving DRAXXIN Injectable Solution (100 mg/mL) as a single subcutaneous dose of 25 mg/kg BW, or 3 weekly subcutaneous doses of 2.5, 7.5, and 12.5 mg/kg BW. In all groups, transient indications of pain after injection were seen, including head shaking and pawing at the ground. Injection site swelling, discoloration of the subcutaneous tissues at the injection site and corresponding histopathologic changes were seen in animals in all dosage groups. These lesions showed signs of resolving over time. No other drug-related lesions were observed macroscopically or microscopically.

An exploratory study was conducted in feeder calves receiving DRAXXIN Injectable Solution (100 mg/mL) as a single subcutaneous dose of 10, 12.5, or 15 mg/kg BW. Macroscopically, no lesions were observed. Microscopically, minimal to mild mucocutaneous degeneration was seen in one of six calves administered 12.5 mg/kg BW and two of six calves administered 15 mg/kg BW.

A safety study was conducted in prernitant calves 13 to 27 days of age receiving DRAXXIN Injectable Solution (100 mg/mL) at 2.5 mg/kg BW or 7.5 mg/kg BW once subcutaneously. With the exception of minimal to mild injection site reactions, no drug-related clinical signs or other lesions were observed macroscopically or microscopically.

Sixteen growing cattle were injected with either saline (eight animals) as a single injection of 11.5 mL or DRAXXIN 25 Injectable Solution (eight animals) as a single injection of either 2.5 mg/kg BW or a dose volume of 11.5 mL (whichever volume was higher). One calf in the DRAXXIN 25-treated group was observed to have firmness at the injection site for a single day. Two DRAXXIN 25-treated calves exhibited injection site swelling. In one calf, the swelling resolved within 48 hours. In the other calf, the swelling was observed over a three-day period, after which the calf underwent a scheduled necropsy, preventing further injection site observations. No injection site swelling was observed in saline-treated animals. At necropsy, three of the saline-treated calves and five of the DRAXXIN 25-treated calves had altered tissue present at the injection site. The gross and microscopic findings in the DRAXXIN 25-treated group were consistent with inflammatory changes induced by injections, were considered to be mild to marked, and progressed to macroscopic resolution and microscopic resolution by Day 42 post-injection.