Key Points

• DRAXXIN™ (tulathromycin) Injectable Solution administered as a single subcutaneous (SC) injection was safe and effective for the control of respiratory disease in cattle at high risk of developing bovine respiratory disease (BRD) caused by *Mannheimia haemolytica*, *Histophilus somni* (*Haemophilus somnus*) and *Pasteurella multocida*.

• When DRAXXIN was administered during arrival processing in a multi-location (4 sites) short-term study and a 229-day feedlot study, fewer animals developed BRD, as demonstrated by defined clinical signs, than did cattle that received Micotil® (tilmicosin) Injection during arrival processing.

• Fewer animals that received DRAXXIN required multiple hospital treatments than did animals that received Micotil.

• In the 229-day feedlot study, fewer animals (*P*=0.014) that received DRAXXIN than received Micotil became BRD-associated removals (mortalities plus chronics) from days 3 through 28.

Introduction

DRAXXIN contains the active ingredient tulathromycin, the first of a new subclass of macrolide, the triamilides, discovered and developed by Pfizer Animal Health. DRAXXIN is a highly effective, single-dose antimicrobial medication indicated for treatment of BRD, and control of respiratory disease in cattle at high risk of developing BRD, caused by *M haemolytica*, *P multocida* and *H somni* (*Haemophilus somnus*).

DRAXXIN is formulated with excellent syringeability, even at low temperatures, and has a convenient low-volume dose (1mL/40 kg; 1.1 mL/100 lb). When administered at the label dose of 2.5 mg tulathromycin/kg body weight (BW), tulathromycin is rapidly absorbed, distributes widely (large apparent volume of distribution) and provides concentrations in bovine lung for an extended period.¹ Clinical efficacy of DRAXXIN for control of respiratory disease in cattle at high risk of developing BRD has been well documented by results of multiple studies in feedlot and stocker settings.²,³,⁴ Reported here are results of a multi-location (4 sites), short-term study submitted for regulatory approval of DRAXXIN and
longer-term feedlot study that compared the efficacy of DRAXXIN with that of Micotil for the control of respiratory disease in cattle at high risk of developing BRD, and the subsequent feedlot performance and carcass characteristics of animals that completed the study.

**Multi-location Short-term Study**

**Materials and Methods**

During the fall and winter of 1999, feeder steers were acquired from multiple auction markets in Mississippi, Washington, Idaho, South Carolina, Kentucky, Missouri and California, were transported to 4 research feedlots (1 each in Texas, Nebraska, California and Idaho) and were at high risk of developing BRD. A common protocol was used so that the data could be pooled for analysis. Cattle were processed, typical for commercial feedlot practices, and enrolled in the study within 1 to 2 days of their arrival. Animals were randomly assigned to receive saline, DRAXXIN (2.5 mg tulathromycin/kg BW), or Micotil (10 mg tilmicosin/kg BW) once by SC injection at the time of processing. Calves from all study groups were commingled during the study.

On days 1 through 14, animals that were assigned abnormal respiratory and clinical attitude scores (CAS) were removed from study pens so that rectal temperatures could be measured and recorded. Calves with rectal temperatures <104°F were returned to their pens. Calves received their 1st hospital treatment if they exhibited, on days 1 through 14, abnormal CAS, abnormal respiratory score, and rectal temperatures ≥104°F. Clinical attitude scores were assigned as follows: 0 = normal, bright, alert, responsive; 1 = mild depression; 2 = moderate to marked depression (may be reluctant to stand); 3 = severe depression (unable to stand without assistance); 4 = moribund, unable to rise. Respiratory scores were assigned as follows: 0 = normal, 1 = abnormal. The primary clinical end point for this study was the determination of animals that required treatment, as per treatment criteria above, or that were BRD-associated mortalities. For purposes of this study an animal was determined to be a clinical success if it did not meet those treatment criteria or was not classified as a BRD-related mortality. Animals that met treatment criteria received standard feedlot treatment and were returned to their pens.

Nasopharyngeal samples were obtained from animals in the saline-control group before they received their 1st hospital treatment, and were submitted to veterinary microbiological laboratories for isolation and identification of organisms associated with the outbreak of BRD.

This study was conducted and analyzed according to the experimental design contained in the study protocol, which included random allocation of animals to groups, response data to be analyzed, and statistical methods to be used.

**Results**

Twelve animals were removed for non-BRD reasons (4 that received saline, 3 that received DRAXXIN, and 5 that received Micotil). Clinical signs exhibited by animals that required treatment were typical of those for naturally occurring BRD. Morbidity was significantly (P=0.0001) lower for calves that received DRAXXIN (13.2%) than for those that received saline (58%) or Micotil (28.7%; Table 1). Microbiological results of samples from lungs of calves that died, or from nasopharyngeal swabs obtained from calves that received saline and required treatment, supported bacterial and mycoplasmal etiologies of the respiratory disease (Table 2).

No adverse drug-related experiences were reported.

**229-Day Feedlot Study**

**Materials and Methods**

During the fall of 2001, in a feedlot study, the efficacy of DRAXXIN or Micotil for the control of respiratory disease in cattle at high risk of developing BRD, and the subsequent performance and carcass characteristics of those cattle were compared (Figure 1). Five-hundred crossbred steers (430 to 714 lb, 195 to 325 kg) were acquired from auction markets in Colorado and Wyoming, were transported to a feedlot in Colorado and were at high risk for developing undifferentiated BRD. At arrival, 250 animals per group were

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**Table 1. Successes Following Administration of DRAXXIN, Micotil or Saline at Arrival Processing: Short-term Study, n (%)**

<table>
<thead>
<tr>
<th>DRAXXIN</th>
<th>P Value</th>
<th>Micotil</th>
<th>P Value</th>
<th>Saline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animals Enrolled*</td>
<td>n=410</td>
<td>n=408</td>
<td>n=409</td>
<td></td>
</tr>
<tr>
<td>No Observed BRD Through Day 14</td>
<td>356 (86.8%)</td>
<td>NA</td>
<td>291 (71.3%)</td>
<td>NA</td>
</tr>
<tr>
<td>Animals Treated</td>
<td>54 (13.2%)</td>
<td>0.0001</td>
<td>117 (28.7%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mortalities</td>
<td>0 (0.0%)</td>
<td>NA</td>
<td>0 (0.0%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Number of animals enrolled minus non-BRD removals. NA = not analyzed.

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**Table 2. Pathogens Isolated at the Time of First Treatment from 226 of 236 Animals that Received Saline at Arrival Processing Plus 2 BRD Mortalities: Short-term Study, n (%)**

<table>
<thead>
<tr>
<th>M haemolytica</th>
<th>P multocida</th>
<th>H somnus</th>
<th>Mycoplasma species</th>
</tr>
</thead>
<tbody>
<tr>
<td>143 (63.3%)</td>
<td>60 (26.5%)</td>
<td>18 (8.0%)</td>
<td>123 (54.4%)</td>
</tr>
</tbody>
</table>
randomly assigned to receive DRAXXIN (2.5 mg tulathromycin/kg BW) or Micotil (10 mg tilmicosin/kg BW). There were 5 replicates per group, 50 animals per pen, 1 group per pen. Arrival processing also included administration of BOVI-SHIELD™ 4, DECTOMAX®, DURASECT® II, and Synovex® S Implants.

This study was divided into 2 phases, days 0 to 28 and day 29 to close. For days 3 through 28, hospital-treatment criteria included a CAS of 1 or 2 (see description above) and rectal temperature ≥104° F, or a CAS ≥3. Throughout the study, animals requiring 1st hospital treatment received LA-200® (20 mg oxytetracycline/kg BW) and animals requiring 2nd hospital treatment received Baytril® (11 mg enrofloxacin/kg BW). Animals were allowed approximately 2 to 3 days following each treatment before subsequent treatment was administered. Animals that met the hospital-treatment criteria 3 times were classified as chronics and removed from the study. For days 29 to close, animals were treated if they demonstrated clinical signs of BRD, regardless of rectal temperature. The original treatment regimen for hospital treatment was used for those animals remaining in the study from day 29 to close.

Body weights for individual animals were recorded on day 0, if the animal required additional treatment, when an animal was removed from the study, and at re-implant. Re-implant occurred on day 80 or 82. All animals that completed the study were weighed individually and harvested on a single day, either day 227 or day 229, depending on day of enrollment. Hot carcass weight was recorded. After an overnight chill, yield and quality grades, kidney/pelvic/heart fat, marbling and ribeye area were recorded.

**Figure 1.** Experimental Design for the 229-Day Feedlot Study: DRAXXIN or Micotil

- **DRAXXIN**
  - n=250
  - Arrival processing, Day 0
  - Eligible for 1st treatment 3 days
  - LA-200
  - Eligible for 2nd treatment 2 - 3 days
  - Baytril
  - Eligible for 3rd treatment 2 - 3 days
  - Removals (mortalities plus chronics) Days 3 to 28: Days 29 to close

- **Micotil**
  - n=250
  - Arrival processing, Day 0
  - Eligible for 1st treatment 3 days
  - LA-200®
  - Eligible for 2nd treatment 2 - 3 days
  - Baytril®
  - Eligible for 3rd treatment 2 - 3 days
  - Removals (3rd Pull)

This study was conducted and analyzed according to the experimental design contained in the study protocol, which included random allocation of animals to groups, response data to be analyzed, and statistical methods to be used.

**Results**

Success for days 3 through 28 and days 3 through close was significantly higher (P=0.001) for animals that received DRAXXIN (94.8% and 80.3%, respectively) than for animals that received Micotil (80.3% and 62.8%, respectively; Table 3). Frequency distribution of 1st hospital treatments during days 3 to 28 (Figure 2a) revealed daily numerical differences for animals in each group. Cumulative distribution of 1st hospital treatments during days 3 to 28 (Figure 2b) revealed marked differences between groups when the day-to-day variability of the frequency distribution accumulated. Fewer animals that received DRAXXIN at arrival required hospital treatment than did those animals that received Micotil. Because eligibility for hospital treatment was re-initiated on day 29, some animals received 4 hospital treatments before being classified as chronics and removed from the study. Removals (mortalities plus chronics) from days 3 through 28 (P=0.014) and days 3 through 222 (P=0.094) were lower for animals that received DRAXXIN (0% and 2.1%, respectively) than those for animals that received Micotil (2.4% and 5%, respectively; Table 3).

The average daily gain (ADG) at close was not significantly higher (P=0.4528) for animals that received DRAXXIN (3.57 lb) than for animals that received Micotil (3.55 lb; Table 4). Animals that received DRAXXIN yielded a least-squares mean carcass weight of 841.0 lb compared to a carcass weight of 845.5 lb for animals that received Micotil (P=0.5322; Table 5). Differences in individual carcass variables (yield grade, quality grade, kidney/pelvic/heart fat, marbling, ribeye area) were not statistically significant (P>0.05).

No adverse drug-related experiences were
Table 3. Successes for Arrival Processing and Hospital Treatment; 229-Day Feedlot Study: DRAXXIN or Micotil,* n (%)  

<table>
<thead>
<tr>
<th>Animals Enrolled</th>
<th>Days 3-28</th>
<th>Days 3-Close**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DRAXXIN</td>
<td>Micotil</td>
</tr>
<tr>
<td>Successes§</td>
<td>237 (94.8%)</td>
<td>200 (80.3%)</td>
</tr>
<tr>
<td>1st Hospital treatment</td>
<td>11 NA</td>
<td>30 NA</td>
</tr>
<tr>
<td>2nd Hospital treatment</td>
<td>2 NA</td>
<td>13 NA</td>
</tr>
<tr>
<td>3rd Hospital treatment</td>
<td>0 NA</td>
<td>0 NA</td>
</tr>
<tr>
<td>4th Hospital treatment</td>
<td>NA NA</td>
<td>NA NA</td>
</tr>
<tr>
<td>BRD Removals§</td>
<td>0 (0.0%)</td>
<td>6 (2.4%)</td>
</tr>
<tr>
<td>Chronics</td>
<td>0 NA</td>
<td>4 NA</td>
</tr>
<tr>
<td>BRD Mortalities</td>
<td>0 NA</td>
<td>2 NA</td>
</tr>
<tr>
<td>Non-BRD Removals§§</td>
<td>0 NA</td>
<td>1 NA</td>
</tr>
</tbody>
</table>

NA = not analyzed.
* Arrival Processing = DRAXXIN or Micotil
1st hospital treatment = animal met treatment criteria 1 time (LA-200)
2nd hospital treatment = animal met treatment criteria 2 times (Baytril)
3rd hospital treatment = animal met treatment criteria 3 times (classified as chronic and removed from study)
4th hospital treatment = animal met treatment criteria 4 times (classified as chronic and removed from study)
Chronic = received ≥ 3 hospital treatments and removed from study
Treatment Criteria
Days 3-28 - CAS of 1 or 2 and a rectal temperature of ≥ 104°F, or CAS of 3 or 4
Days >28 - CAS of ≥ 1
** Close was either day 227 or day 229.
§ All percents calculated with number enrolled minus non-BRD removals as denominator.
§§ Non-BRD removals included non-BRD-associated mortalities.

Figure 2a. Frequency Distribution of Animals that Received 1st Hospital Treatment by Day, from Days 3 through 28; 229-Day Feedlot Study (Colorado): DRAXXIN or Micotil

Figure 2b. Cumulative Distribution of Animals that Received 1st Hospital Treatment by Day, from Days 3 through 28; 229-Day Feedlot Study (Colorado): DRAXXIN or Micotil
Table 4. Body Weights (lb),* Average Daily Gain (lb/day),* and Feed Efficiencies; 229-Day Feedlot Study: DRAXXIN or Micotil

<table>
<thead>
<tr>
<th></th>
<th>Days 0 to 80/82</th>
<th>Days 0 to 227/229</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DRAXXIN</td>
<td>P Value</td>
</tr>
<tr>
<td>Initial Body Weight</td>
<td>543.0</td>
<td>0.3257</td>
</tr>
<tr>
<td>Final Body Weight**</td>
<td>842.1</td>
<td>0.2515</td>
</tr>
<tr>
<td>Average Daily Gain**</td>
<td>3.69</td>
<td>0.0914</td>
</tr>
<tr>
<td>Feed Consumption§</td>
<td>14.96</td>
<td>0.2940</td>
</tr>
<tr>
<td>Feed Conversion§§</td>
<td>4.04</td>
<td>0.0536</td>
</tr>
</tbody>
</table>

* Repeated measures mixed model least-squares mean estimates, based on pen-average body weight. Removals (mortalities plus chronics) are not included.

** Mortalities and chronics removed. Day 227/229 final body weight is an average based on pen weight.

§ Feed consumption: Pounds of feed calculated on a dry matter basis.

§§ Feed conversion: Pound of feed/pound of weight gain. Number of animal-days accounted for removals per time period.

Table 5. Carcass Adjusted Least-Squares Mean Final Body Weight, Weight Gain, Average Daily Gain, and Hot Carcass Weight at Close; 229-Day Feedlot Study: DRAXXIN or Micotil,* n (SEM)

<table>
<thead>
<tr>
<th></th>
<th>DRAAXIN</th>
<th>P Value</th>
<th>Micotil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Animals</td>
<td>233</td>
<td></td>
<td>230</td>
</tr>
<tr>
<td>Final Body Weight, lb</td>
<td>1293.88 (7.42)</td>
<td>0.5322</td>
<td>1300.76 (7.47)</td>
</tr>
<tr>
<td>Weight Gain, lb</td>
<td>751.9 (6.24)</td>
<td>0.7311</td>
<td>749.1 (6.28)</td>
</tr>
<tr>
<td>Average Daily Gain, lb/day</td>
<td>3.37 (0.03)</td>
<td>0.7311</td>
<td>3.36 (0.03)</td>
</tr>
<tr>
<td>Hot Carcass Weight, lb</td>
<td>841.0 (4.82)</td>
<td>0.5322</td>
<td>845.5 (4.86)</td>
</tr>
</tbody>
</table>

* Mortalities and chronics removed.
Discussion

Animals used in these studies were at high risk of developing BRD and were randomly assigned to receive the respective medication so that the expected incidence of disease would be the same for both groups of animals. Bacteria isolated during the short-term study (M. haemolytica, P. multocida and H. somni) were consistent with those associated with BRD. In addition, Mycoplasma species were isolated in 54% of sampled individuals (Table 1).

Based on number of animals that received hospital treatment and number of BRD removals (mortalities plus chronics), the results of the short-term, multi-location study are evidence of the efficacy of DRAXXIN for control of respiratory disease in cattle at high risk of developing BRD. Frequency distribution and cumulative distribution for 1st treatments should be considered when evaluating clinical response to medication used for the control of BRD, because they provide excellent, though different, views of the same information.

Treatment criteria were consistent within each phase of the 229-day feedlot study, but were different in the first phase (days 3 through 28) from those in the second phase (days 29 through close). As a result, a few animals received 4 hospital treatments before being classified as chronics and removed from the study. Removals (mortalities plus chronics) from days 3 through 28 (P=0.014) and days 3 through 222 (P=0.094) were lower for animals that received DRAXXIN (0% and 2.1%, respectively) than those for animals that received Micotil (2.4% and 5%, respectively; Table 3). A P value of 0.094 indicates that there was a 90.6% probability that the difference in BRD removals was actually attributable to DRAXXIN. There was no difference in ADG for animals that completed the study in either of the 2 groups.

In order to minimize confounding influences on results, animals were randomly assigned to receive one of the respective medications being evaluated. Management practices and processing at each site of investigation were consistent for all animals within a given study. Recording of the disposition of animals removed from the studies (BRD-associated or non-BRD-associated removals) was not included in the protocol; therefore, that information is not available for analysis or discussion. Before each study began, regimens for administration of those medications as well as subsequent medication (if needed) were stated in the respective protocols. Criteria for administration of subsequent medication and for classifying the responses were also defined to be consistent within the study. Because those steps were implemented, results within a given study could be attributed to the respective medication being evaluated.
Conclusions

DRAXXIN administered as a single SC injection was safe and significantly more effective than was Micotil for the control of respiratory disease in cattle at high risk of developing BRD caused by *M haemolytica, H somni* and *P multocida.*

Do not use DRAXXIN in female dairy cattle 20 months of age or older. Effects on reproductive performance, pregnancy and lactation have not been determined. Do not use in calves to be processed for veal. Do not use in chickens or turkeys. Do not use in animals known to be hypersensitive to the product.

References


Prepared from studies 1133C-60-99-309, 1133C-60-99-310, 1133C-60-99-311, 1133C-60-99-312, and 2132T-60-01-069.