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- ***M. hyo* predisposes pigs to additional respiratory infections and increases their severity.**
- **In a 60-day study, pigs treated with one dose of Draxxin[®] (tulathromycin) for SRD due to *M. hyo* had reduced mortality and better average daily gain and feed consumption compared to controls.**
- **Because Draxxin only requires one dose and is indicated for *M. hyo* as well as other important causes of respiratory disease, it provides pork producers with a convenient option for treating complex SRD.**

M. hyo treatment with Draxxin[®] plays important role in SRD management

Pigs treated for *Mycoplasma hyopneumoniae* (*M. hyo*) with a single dose of the injectable antimicrobial Draxxin[®] (tulathromycin) had significantly better average daily gain and feed consumption in a 60-day controlled study.¹

They also had lower mortality and a markedly better overall feed-to-gain ratio compared to controls (Table 1), reports Lucina Galina, DVM, PhD, director, US Pork technical services, Zoetis.

For the study, 200 pigs negative for *M. hyo* were infected with an *M. hyo* field isolate via the trachea and nose 3 days in a row. After challenge, 96 pigs met criteria for swine respiratory disease (SRD), and of these, half received one intramuscular (IM) dose of Draxxin at 2.5 mg/kg bodyweight, as indicated. The remaining pigs served as controls and received an IM injection of saline, she explains.

continued

Table 1. Results in pigs with SRD treated with Draxxin as compared to controls

Treatment group	Average daily gain, 0-60 days (lb/head/day)	Average daily feed intake, 0-60 days (lb/day)	Feed-to-gain ratio, 0-60 days	Mortality
Draxxin (48 pigs)	1.99*	5.17**	2.78	4.2%
Control (48 pigs)	1.77*	4.85**	3.58	8.7%

* Significantly different (p = 0.0015)

** Significantly different (p ≤ 0.0861)

M. hyo treatment with Draxxin® plays important role in SRD management



“The results [of the study] are significant because *M. hyo* not only causes enzootic pneumonia, it plays an important role in the establishment and severity of complex SRD.”

LUCINA GALINA, DVM, PHD

The researchers also scored pigs for attitude/depression and respiratory character. After challenge, all pigs had moderate depression, and almost all had moderately severe respiratory signs. By 10 days after treatment, the proportion of treated pigs scoring normal was 11% higher for attitude/depression and 24% higher for respiratory character compared to controls. In addition, only three treated pigs needed additional antibiotic therapy compared to five controls, Galina says.

Study significance

“The results are significant because *M. hyo* not only causes enzootic pneumonia, it plays an important role in the establishment and severity of complex SRD,” the veterinarian says.

M. hyo predisposes pigs to other SRD bacterial pathogens such as *Actinobacillus pleuropneumoniae* (APP) and *Pasteurella multocida* (PM).^{2,3} Many pigs with severe SRD are positive for both *M. hyo* and porcine reproductive and respiratory syndrome virus (PRRSV), and *M. hyo* increases the severity of PRRSV.⁴

“This knowledge underscores the importance of treating *M. hyo*, especially considering the cost of respiratory disease rises from less than \$1 per pig when *M. hyo* alone is present to an estimated \$10 per pig when there are co-infections with pathogens such as PRRSV,”⁵ Galina says.

Only one dose required

Draxxin, she continues, is approved for treating not only *M. hyo* but the other four major bacterial causes of SRD: APP, PM, *Bordetella bronchiseptica* and *Haemophilus parasuis*. It reaches peak lung concentrations within 12 hours and provides prolonged exposure of pathogens to the antibiotic,⁶ she says.

“Pork producers can appreciate the convenience of one-dose treatment. There are fewer labor costs and less stress on pigs since they don’t have to be handled as often as needed

with multi-dose injectables,” she says. “It’s a plus that Draxxin is also indicated for other important bacterial causes of respiratory disease.”

Considering *M. hyo* predisposes pigs to other respiratory diseases and worsens their severity, effective treatment of this pathogen can yield multiple disease-control benefits and minimize the economic consequences of SRD, Galina says.

For more information, contact Dr. Galina (lucina.galina@zoetis.com) or your local Zoetis representative.

Important Safety Information for Swine: Withdraw Draxxin/Draxxin 25 five (5) days prior to slaughter in swine. Do not use in animals known to be hypersensitive to the product. See the full Prescribing Information attached.

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LUCINA GALINA, DVM, PHD

¹ Data on file, Study Report No. 1121R-60-07-292, Zoetis LLC.

² Ciprian A, Pijoan C, Cruz T, et al. *Mycoplasma hyopneumoniae* increases the susceptibility of pigs to experimental *Pasteurella multocida* pneumonia. *Can J Vet Res.* 1988;52:434-438.

³ Marois C, et al. Experimental infection of SPF pigs with *Actinobacillus pleuropneumoniae* serotype 9 alone or in association with *Mycoplasma hyopneumoniae*. *Vet Microbiol.* 2009 March;135(3-4):283-291.

⁴ Thacker E, Halbur P, Ross RF, et al. *Mycoplasma hyopneumoniae* potentiation of porcine reproductive and respiratory syndrome virus-induced pneumonia. *J Clin Microbiol.* 1999;37(3):620-627.

⁵ Haden DC, Painter T, Fangman T, et al. Assessing production parameters and economic impact of swine influenza, PRRS and *Mycoplasma hyopneumoniae* on finishing pigs in a large production system. In: Proceedings 43rd Annual Meeting Am Assoc Swine Veterinarians. Denver, Colorado. 2012:75-76.

⁶ Benchaoui HA, Nowakowski M, Sherington J, et al. Pharmacokinetics and lung tissue concentrations of tulathromycin in swine. *J Vet Pharmacol Therap.* 2004;27:203-210.

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Antibiotic
100 mg of tulathromycin/mL

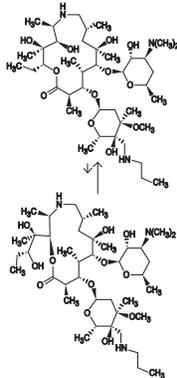
For use in swine.

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

DESCRIPTION

DRAXXIN Injectable Solution is a ready-to-use sterile parenteral preparation containing tulathromycin, a semi-synthetic macrolide antibiotic of the subclass triamylide. Each mL of DRAXXIN contains 100 mg of tulathromycin, 500 mg propylene glycol, 19.2 mg citric acid and 5 mg monothiolglycerol. Sodium hydroxide or hydrochloric acid may be added to adjust pH.

DRAXXIN consists of an equilibrated mixture of two isomeric forms of tulathromycin in a 9:1 ratio. Structures of the isomers are shown below. Figure 1.



The chemical names of the isomers are (2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino)methyl]-α-L-ribo-hexopyrano-syl]oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]-oxy]-1-oxa-6-azacyclotridecan-15-one and (2R,3R,6R,8R,9R,10S,11S,12R)-11-[[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino)methyl]-α-L-ribo-hexopyrano-syl]oxy]-2-[[1R,2R)-1,2-dihydroxy-1-methylbutyl]-8-hydroxy-3,6,8,10,12-pentamethyl-9-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]oxy]-1-oxa-4-azacyclotridecan-13-one, respectively.

INDICATIONS

Swine
DRAXXIN 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.

DOSAGE AND ADMINISTRATION

Swine
Inject intramuscularly as a single dose in the neck at a dosage of 2.5 mg/kg (0.25 mL/22 lb) BW. Do not inject more than 2.5 mL per injection site.

Table 21. DRAXXIN Swine Dosing Guide

Animal Weight (Pounds)	Dose Volume (mL)
15	0.2
30	0.3
50	0.6
70	0.8
90	1.0
110	1.3
130	1.5
150	1.7
170	1.9
190	2.2
210	2.4
230	2.6
250	2.8
270	3.1
290	3.3

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.

PRECAUTIONS

Swine
The effects of DRAXXIN 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.

ADVERSE REACTIONS

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

POST APPROVAL EXPERIENCE

The following adverse events are based on post approval adverse drug experience reporting. Not all adverse events are reported to the FDA CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. For a complete listing of adverse reactions for DRAXXIN (tulathromycin injection) 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 hydrophobic media. This solubility profile is consistent with the extracellular pathogen activity typically associated with the macrolides.¹ Markedly higher tulathromycin concentrations are observed in the lungs as compared to the plasma. The extent to which lung concentrations represent free (active) drug was not examined. Therefore, the clinical relevance of these elevated lung concentrations is undetermined.

Although the relationship between tulathromycin and the characteristics of its antimicrobial effects has not been characterized, as a class, macrolides tend to be primarily bacteriostatic, but may be bactericidal against some pathogens.² They also 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 tends to be both drug and pathogen dependent. In general, by increasing the macrolide concentration and the exposure time, the PAE will increase to some maximal duration. Of the two variables, concentration and exposure time, drug concentration tends to be the most powerful determinant of the duration of PAE.

Tulathromycin is eliminated from the body primarily unchanged via biliary excretion.

¹ Carbon, C. 1998. *Pharmacodynamics of Macrolides, Azalides, and Streptogramins: Effect on Extracellular Pathogens. Clin. Infect. Dis., 27:28-32.*

² Nightingale, C.J. 1997. *Pharmacokinetics and Pharmacodynamics of Newer Macrolides. Pediatr. Infect. Dis. J., 16:438-443.*

Swine

Following intramuscular administration to feeder pigs at a dosage of 2.5 mg/kg BW, tulathromycin is completely and rapidly absorbed (T_{max} ~0.25 hour). Subsequently, the drug rapidly distributes into body tissues, achieving a volume of distribution exceeding 15 L/kg. The free drug is rapidly cleared from the systemic circulation ($Cl_{systemic}$ = 187 mL/hr/kg). However, it has a long terminal elimination half-life (60 to 90 hours) owing to its extensive volume of distribution. Although pulmonary tulathromycin concentrations are substantially higher than concentrations observed in the plasma, the clinical significance of these findings is undetermined. There are no gender differences in swine tulathromycin pharmacokinetics.

MICROBIOLOGY

Swine

In vitro activity of tulathromycin has been demonstrated against *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Bordetella bronchiseptica*, *Haemophilus parasuis*, and *Mycoplasma hyopneumoniae*.

The MICs of tulathromycin against indicated SRD pathogens were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLSI, M31-A and M31-A3). MICs for *Haemophilus parasuis* were determined using Veterinary Fastidious Medium and were incubated up to 48 hours at 35 to 37°C in a CO₂-enriched atmosphere. All MIC values were determined using the 9:1 isomer ratio of this compound. Isolates obtained in 2000 and 2002 were from lung samples from saline-treated pigs and non-treated sentinel pigs enrolled in Treatment of SRD field studies in the U.S. and Canada. Isolates obtained in 2007 and 2008 were from lung samples from saline-treated and DRAXXIN-treated pigs enrolled in the Control of SRD field study in the U.S. and Canada. The results are shown in Table 4.

Table 4. Tulathromycin minimum inhibitory concentration (MIC) values* for indicated pathogens isolated from field studies evaluating SRD in the U.S. and Canada.

Indicated pathogen	Date isolated	No. of isolates	MIC ₅₀ ** (µg/mL)	MIC ₉₀ ** (µg/mL)	MIC range (µg/mL)
<i>Actinobacillus pleuropneumoniae</i>	2000-2002	135	16	32	16 to 32
	2007-2008	88	16	16	4 to 32
<i>Haemophilus parasuis</i>	2000-2002	31	1	2	0.25 to > 64
<i>Pasteurella multocida</i>	2000-2002	55	1	2	0.5 to > 64
	2007-2008	40	1	2	≤0.03 to 2
<i>Bordetella bronchiseptica</i>	2000-2002	42	4	8	2 to 8

* 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.

EFFECTIVENESS

Swine

In a multi-location field study to evaluate the treatment of naturally occurring SRD, 266 pigs were treated with DRAXXIN. Responses to treatment were compared to saline-treated controls. Success was defined as a pig with normal attitude, normal respiration, and rectal temperature of < 104°F on Day 7. The treatment success rate was significantly greater (P ≤ 0.05) in DRAXXIN-treated pigs (70.5%) compared to saline-treated pigs (46.1%). *M. hyopneumoniae* was isolated from 106 saline-treated and non-treated sentinel pigs in this study.

Two induced infection model studies were conducted to confirm the effectiveness of DRAXXIN against *M. hyopneumoniae*. Ten days after inoculation intranasally and intratracheally with a field strain of *M. hyopneumoniae*, 144 pigs were treated with either DRAXXIN (2.5 mg/kg BW) intramuscularly or an equivalent volume of saline. Pigs were euthanized and necropsied 10 days post-treatment. The mean percentage of gross pneumonic lung lesions was statistically significantly lower (P < 0.0001) for DRAXXIN-treated pigs than for saline-treated pigs in both studies (8.52% vs. 23.62% and 11.31% vs. 26.42%).

The effectiveness of DRAXXIN for the control of SRD was evaluated in a multi-location natural infection field study. When at least 15% of the study candidates showed clinical signs of SRD, all pigs were enrolled and treated with DRAXXIN (226 pigs) or saline (227 pigs). Responses to treatment were evaluated on Day 7. Success was defined as a pig with normal attitude, normal respiration, and rectal temperature of < 104°F. The treatment success rate was significantly greater (P < 0.05) in DRAXXIN-treated pigs compared to saline-treated pigs (59.2% vs. 41.2%).

ANIMAL SAFETY

Swine

Safety studies were conducted in pigs receiving a single intramuscular dose of 25 mg/kg BW, or 3 weekly intramuscular doses of 2.5, 7.5, or 12.5 mg/kg BW. In all groups, transient indications of pain after injection were seen, including restlessness and excessive vocalization. Tremors occurred briefly in one animal receiving 7.5 mg/kg BW. Discoloration and edema of injection site tissues and corresponding histopathologic changes were seen in animals at all dosages and resolved over time. No other drug-related lesions were observed macroscopically or microscopically.

STORAGE CONDITIONS

Store below 25°C (77°F), with excursions up to 40°C (104°F). Use this product within 45 days of the first puncture and puncture a maximum of 20 times. If more than 20 punctures are anticipated, the use of automatic injection equipment of a repeater syringe is recommended. When using a draw-off spike or needle with bore diameter larger than 16 gauge, discard any product remaining in the vial immediately after use.

HOW SUPPLIED

DRAXXIN Injectable Solution is available in the following package sizes:
50 mL vial
100 mL vial
250 mL vial
500 mL vial

NADA 141-244, Approved by FDA



Distributed by:
Zoetis Inc.
Kalamazoo, 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 product information call: 1-888-DRAXXIN or go to www.DRAXXIN.com



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