Date of Approval: September 26, 2007

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-244

DRAXXIN Injectable Solution

Tulathromycin
Cattle (Beef and Non-lactating Dairy)

To add *Mycoplasma bovis* to the list of target pathogens for the bovine respiratory disease control "at high risk" indication.

Sponsored by:

Pfizer, Inc.

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I. GENERAL INFORMATION:

A. File Number:	NADA 141-244
B. Sponsor:	Pfizer, Inc. 235 East 42d St. New York, NY 10017 Drug Labeler Code: 000069
C. Proprietary Name(s):	DRAXXIN Injectable Solution
D. Established Name(s):	Tulathromycin
E. Pharmacological Category:	Antimicrobial
F. Dosage Form(s):	Sterile injectable solution
G. Amount of Active Ingredient(s):	100 mg/mL
H. How Supplied:	50 mL, 100 mL, 250 mL, and 500 mL glass vials
I. How Dispensed:	Rx
J. Dosage(s):	2.5 mg/kg body weight (BW), administered once
K. Route(s) of Administration:	Subcutaneous (cattle) or intramuscular (swine) injection in the neck
L. Species/Class(es):	Beef and non-lactating dairy cattle, and swine
M. Indication(s):	Cattle: DRAXXIN Injectable Solution is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* (*Haemophilus somnus*), and *Mycoplasma bovis;* and for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni,* ***and Mycoplasma bovis*****.** Swine: DRAXXIN Injectable Solution is indicated for the treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae, Pasteurella multocida*,

Bordetella bronchiseptica, and *Haemophilus parasuis*.

N. Effect(s) of Supplement: This supplement provides for the addition of *Mycoplasma bovis* to the list of target pathogens for the BRD control "at high risk" indication.

II. EFFECTIVENESS:

A. Dosage Characterization:

This supplemental approval does not change the previously approved dosage. The FOI Summary for the original approval of NADA 141-244 dated May 24, 2005, contains dosage characterization information for cattle.

B. Substantial Evidence:

Effectiveness of tulathromycin for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* (*Haemophilus somnus*); and for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* was previously demonstrated in the original approval, and is summarized in the FOI Summary for DRAXXIN Injectable Solution (NADA 141-244) dated May 24, 2005.

Effectiveness of tulathromycin for the treatment of BRD associated with *Mycoplasma bovis* was demonstrated using two experimentally-induced infection model studies and examining *M. bovis* data from cattle used in the BRD treatment studies conducted for the original approval of DRAXXIN Injectable Solution. These data are summarized in the FOI Summary for DRAXXIN Injectable Solution (NADA 141-244) dated August 18, 2006.

Effectiveness of tulathromycin for the control of respiratory disease in cattle at high risk of developing BRD associated with *M. bovis* was further demonstrated by examining *M. bovis* data from cattle used in the BRD control studies conducted for the original approval of DRAXXIN Injectable Solution.

1. Identification of *Mycoplasma bovis* in Cattle Enrolled in BRD Control Studies

The presence of *M. bovis* in calves enrolled in the BRD control studies (1133C-60-99-310, 1133C-60-99-311, and 1133C-60-99-312) summarized in the FOI Summary for DRAXXIN Injectable Solution (NADA 141-244) dated May 24, 2005, was examined. None of the isolates obtained from the Texas site (1131C-60-99-309) survived transport to the laboratory.

M. bovis was identified by fluorescent antibody (FA) test from samples which were cultured from nasopharyngeal swabs of saline-treated non-responders and from lung swabs or lung tissue of saline-treated calves that died during the studies. A total of 50 FA-positive isolates were identified, as shown in Table 1.

Table 1. Number of isolates from cattle with naturally-occurring BRD which were positive for *M. bovis* by FA test.

Study Number and Location	No. of Isolates Positive for *M. bovis* by FA
1133C-60-99-310 Idaho	11
1133C-60-99-311 Nebraska	4
1133C-60-99-312 California	35
Total	**50**

2. Determination of Minimum Inhibitory Concentrations (MICs)

The MICs of tulathromycin were determined for *M. bovis* isolates obtained from calves enrolled in BRD treatment and control field studies in the U.S. in 1999. In the treatment studies, isolates were obtained from pre-treatment nasopharyngeal swabs from all study calves and from lung swabs or lung tissue of saline-treated calves that died. In the control studies, isolates were obtained from nasopharyngeal swabs of saline-treated non-responders and from lung swabs or lung tissue of saline-treated calves that died. MICs were determined using methods recommended by the Clinical and Laboratory Standards Institute (M31-A2). The results are shown in Table 2.

Table 2. Tulathromycin minimum inhibitory concentration (MIC) values* for *M. bovis* isolated from field studies evaluating BRD in the U.S.

Indicated pathogen	Date isolated	No. of isolates	MIC_{50}** (µg/mL)	MIC_{90}** (µg/mL)	MIC range (µg/mL)
Mycoplasma bovis	1999	43	0.125	1	≤ 0.063 to > 64

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

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

III. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-244 dated May 24, 2005, contains a summary of target animal safety studies for cattle.

IV. HUMAN FOOD SAFETY:

A. Toxicology:

CVM did not require toxicology studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-244 dated May 24, 2005, contains a summary of all toxicology studies.

B. Residue Chemistry:

CVM did not require residue chemistry studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-244 dated May 24, 2005, contains a summary of residue chemistry studies for cattle.

C. Microbial Food Safety:

The impact of the proposed change in the control indication for tulathromycin in cattle from "For the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni (Haemophilus somnus)*" to "For the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*" on microbial food safety was carefully considered by the Agency. The Agency determined that this change should not significantly impact public health, and therefore an evaluation of microbial food safety regarding this change was not necessary at this time.

D. Analytical Method for Residues:

The FOI Summary for the original approval of NADA 141-244 dated May 24, 2005, contains the analytical method summaries for tulathromycin in cattle.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to DRAXXIN Injectable Solution:

For use in animals only. Not for human use. Keep out of reach of children.

To request a material safety data sheet, call 1-800-733-5500.

VI. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514. The data demonstrate that DRAXXIN Injectable Solution, when used according to the label, is safe and effective for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mycoplasma bovis*. Additionally, data demonstrate that residues in food products derived from cattle treated with DRAXXIN Injectable Solution will not represent a public health concern when the product is used according to the label.

A. Marketing Status:

Labeling restricts this drug to use by or on order of a licensed veterinarian. This decision was based on the following factors: (a) adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this product to treat BRD, and (b) restricting this drug to use by or on order of a licensed veterinarian should help prevent indiscriminate use which could result in violative tissue residues.

B. Exclusivity:

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval. The three years of marketing exclusivity applies only to the control of respiratory disease in cattle at high risk of developing BRD associated with *Mycoplasma bovis* for which this supplement is approved.

C. Supplemental Applications:

This supplemental NADA did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR §514.106(b)(2)).

D. Patent Information:

Tulathromycin is under the following U.S. patent numbers:

U.S. Patent Number	Date of Expiration
6,329,345	November 18, 2019
6,420,536	May 29, 2018
6,514,945	January 24, 2021
6,583,274	May 2, 2020
6,777,393	May 29, 2018

VII. ATTACHMENTS:

Facsimile Labeling:

a. DRAXXIN Injectable Solution – 50 mL vial label and insert
b. DRAXXIN Injectable Solution – 50 mL carton
c. DRAXXIN Injectable Solution – 50 mL shipper label
d. DRAXXIN Injectable Solution – 100 mL vial label and insert
e. DRAXXIN Injectable Solution – 100 mL carton
f. DRAXXIN Injectable Solution – 100 mL shipper label
g. DRAXXIN Injectable Solution – 250 mL vial label and insert
h. DRAXXIN Injectable Solution – 250 mL carton
i. DRAXXIN Injectable Solution – 250 mL shipper label
j. DRAXXIN Injectable Solution – 500 mL vial label and insert
k. DRAXXIN Injectable Solution – 500 mL carton
l. DRAXXIN Injectable Solution – 500 mL shipper label