Date of Approval: December 21, 2023

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-760

Florfeniject™

(florfenicol)

Injectable Solution

Beef and Non-Lactating Dairy Cattle

Florfeniject™ Injectable Solution is indicated for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni*, and for the treatment of bovine interdigital phlegmon (foot rot, acute interdigital necrobacillosis, infectious pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*. Also, it is indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni*.

Sponsored by:

Cronus Pharma Specialities India Private Ltd.

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I. GENERAL INFORMATION

A. File Number

ANADA 200-760

B. Sponsor

Cronus Pharma Specialities India Private Ltd.,
Sy No–99/1, M/s GMR Hyderabad Aviation SEZ Ltd.,
Mamidipalli Village, Shamshabad Mandal,
Ranga Reddy, Hyderabad, Telangana, 501218, India

Drug Labeler Code: 069043

C. Proprietary Name

Florfeniject™

D. Drug Product Established Name

florfenicol

E. Pharmacological Category

Antimicrobial

F. Dosage Form

Injectable solution

G. Amount of Active Ingredient

300 mg/mL

H. How Supplied

100 mL, 250 mL, and 500 mL glass sterile multiple-dose vials

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

For treatment of bovine respiratory disease (BRD) and bovine interdigital phlegmon (foot rot): Florfeniject™ Injectable Solution should be administered by intramuscular injection to cattle at a dose rate of 20 mg/kg body weight (3 mL/100 lbs). A second dose should be administered 48 hours later. Alternatively, Florfeniject™ Injectable Solution can be administered by a single subcutaneous (SC) injection to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 lbs). Do not administer more than 10 mL at each site. The injection should be given only in the neck.

For control of respiratory disease in cattle at high-risk of developing BRD: Florfeniject™ Injectable Solution should be administered by a single subcutaneous injection to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 lbs). Do not administer more than 10 mL at each site. The injection should be given only in the neck.

K. Route of Administration

For treatment of BRD and bovine interdigital phlegmon (foot rot): intramuscular or subcutaneous

For control of respiratory disease in cattle at high-risk of developing BRD: subcutaneous

L. Species/Classes

Beef and non-lactating dairy cattle

M. Indication

Florfeniject™ Injectable Solution is indicated for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni*, and for the treatment of bovine interdigital phlegmon (foot rot, acute interdigital necrobacillosis, infectious pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*. Also, it is indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni*.

N. Reference Listed New Animal Drug (RLNAD)

Nuflor®; florfenicol; NADA 141-063; Intervet, Inc.

II. BIOEQUIVALENCE

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, allows for an abbreviated new animal drug application (ANADA) to be submitted for a generic version of an approved new animal drug (RLNAD). The ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. Effectiveness, target animal safety and human food safety data (other than tissue residue data) are not required for approval of an ANADA. If bioequivalence is demonstrated through a clinical endpoint study in a food-producing animal, then a tissue residue study to establish the withdrawal period for the generic product is also required. For certain dosage forms, the agency will grant a waiver from the requirement to perform *in vivo* bioequivalence studies (biowaiver) (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Cronus Pharma Specialities India Private Ltd., was granted a biowaiver for the generic product Florfeniject™ (florfenicol) injectable solution. The generic drug product is an injectable solution, contains the same active ingredient in the same concentration and dosage form as the RLNAD, and contains no inactive ingredients that may significantly affect the

bioavailability of the active ingredient. The RLNAD is Nuflor® (florfenicol) injectable solution, sponsored by Intervet, Inc., under NADA 141-063, and was approved for use in beef and non-lactating dairy cattle on May 31, 1996.

III. HUMAN FOOD SAFETY

The tolerances and R_m (the concentration of the marker residue in the target tissue when the residue of carcinogenic concern is equal to S_m [the concentration of a residue of carcinogenic concern in a specific edible tissue corresponding to no significant increase in the risk of cancer to the human consumer] (21 CFR 500.82)) for residues and withdrawal periods established for the RLNAD apply to the generic product. The following are assigned to this product for beef and non-lactating dairy cattle:

A. Acceptable Daily Intake, S_o, Tolerances, and R_m for Residues

The acceptable daily intake (ADI) for total residues of florfenicol is 10 µg/kg of body weight per day (21 CFR 556.283). The S_o (concentration of residue of carcinogenic concern in the total human diet that represents no significant increase in the risk of cancer to the human consumer (21 CFR 500.82)) for N-methyl-2-pyrrolidone (NMP) is 66.8 parts *per* million (ppm). The tolerances established for the RLNAD apply to the generic product. The tolerance for florfenicol amine (the marker residue) is 3.7 ppm in liver (the target tissue) and 0.3 ppm in muscle, under 21 CFR 556.283. The R_m for carcinogenic residues, established for parent NMP, is 180 ppm in cattle liver.

B. Withdrawal Periods

Because a biowaiver was granted, the withdrawal periods are those previously assigned to the RLNAD product. A withdrawal period of 28 days has been established for florfenicol in beef and non-lactating dairy cattle treated with two intramuscular injections of 20 mg florfenicol/kg body weight administered 48 hours apart. A withdrawal period of 38 days has been established for florfenicol in beef and non-lactating dairy cattle treated with a single subcutaneous injection of 40 mg florfenicol/kg body weight. Withdrawal periods of 28 and 38 days are consistent with the depletion of florfenicol and NMP residues in all edible tissues following treatment with Florfeniject™ for cattle, when administered as an intramuscular or subcutaneous injection, respectively.

C. Analytical Methods for Residues

Florfenicol
The validated regulatory method for analysis of residues of florfenicol is described in the RLNAD FOI Summary (NADA 141-063, dated May 31, 1996) and is on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855. To obtain a copy of the analytical method, please submit a Freedom of Information request to: https://www.accessdata.fda.gov/scripts/foi/FOIRequest/requestinfo.cfm.

NMP
The validated regulatory method for NMP as described in 21 CFR 500.1410 can be found at: https://www.fda.gov/about-fda/center-veterinary-medicine/cvm-foia-electronic-reading-room.

IV. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Florfeniject™:

USER SAFETY WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains materials that can be irritating to skin and eyes. Avoid direct contact with skin, eyes, and clothing. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately.

Reproductive and developmental toxicities have been reported in laboratory animals following high, repeated exposures to *N*-methyl-2-pyrrolidone (NMP). Pregnant women should wear gloves and exercise caution or avoid handling this product.

The Safety Data Sheet (SDS) contains more detailed occupational safety information.

V. AGENCY CONCLUSIONS

The data submitted in support of this ANADA satisfy the requirements of section 512(c)(2) of the FD&C Act. The data demonstrate that Florfeniject™, when used according to the label, is safe and effective for the conditions of use in the General Information Section above.

Additionally, data demonstrate that residues in food products derived from beef and non-lactating dairy cattle treated with Florfeniject™ will not represent a public health concern when the product is used according to the label.