FLORFENIJECT- florfenicol injection, solution
Cronus Pharma LLC

Florfenijject™
(florfenicol)
Injectable Solution
300 mg/mL

For intramuscular and subcutaneous use in beef and non-lactating dairy cattle only.

Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

CAUTION

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION

FLORFENIJECT Injectable Solution is a solution of the synthetic antibiotic florfenicol. Each milliliter of sterile FLORFENIJECT Injectable Solution contains 300 mg of florfenicol, 250 mg *N-methyl-2-pyrrolidone* (NMP), 150 mg propylene glycol, and polyethylene glycol qs. The chemical name for florfenicol is *2,2-Dichloro-N-[1-(fluoromethyl)-2-hydroxy-2-[4-(methylsulfonyl)phenyl]ethyl] acetamide.*

INDICATIONS

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.*

DOSAGE AND ADMINISTRATION

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.

NOTE: Intramuscular injection may result in local tissue reaction which persists beyond

28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe.

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.

FLORFENIJECT Injectable Solution DOSAGE GUIDE

ANIMAL WEIGHT (lbs)	IM FLORFENIJECT DOSAGE 3.0 mL/100 lb Body Weight (mL)	SC FLORFENIJECT DOSAGE 6.0 mL/100 lb Body Weight (mL)
100	3.0	6.0
200	6.0	12.0
300	9.0	18.0
400	12.0	24.0
500	15.0	30.0
600	18.0	36.0
700	21.0	42.0
800	24.0	48.0
900	27.0	54.0
1000	30.0	60.0

Recommended Injection Location

Do not inject more than 10 mL per injection site.

Clinical improvement should be evident in most treated subjects within 24 hours of initiation of treatment. If a positive response is not noted within 72 hours of initiation of treatment, the diagnosis should be re-evaluated.

CONTRAINDICATIONS

Do not use in animals that have shown hypersensitivity to florfenicol.

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.

CONTACT INFORMATION:

To report suspected adverse drug events, for technical assistance or to obtain a copy of the SDS, contact Cronus Pharma LLC at 1-844-227-6687. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

PRECAUTIONS:

Not for use in animals intended for breeding purposes. The effects of florfenicol on bovine reproductive performance, pregnancy, and lactation have not been determined. Toxicity studies in dogs, rats, and mice have associated the use of florfenicol with testicular degeneration and atrophy. Intramuscular injection may result in local tissue reaction which persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe.

RESIDUE WARNINGS:

Animals intended for human consumption must not be slaughtered within 28 days of the last intramuscular treatment. Animals intended for human consumption must not be slaughtered within 38 days of subcutaneous treatment. This product is not approved for use in female dairy cattle 20 months of age or older, including dry dairy cows. Use in these cattle may cause drug residues in milk and/or in calves born to these cows. A withdrawal period has not been established in pre-ruminating calves. Do not use in

calves to be processed for veal.

ADVERSE REACTIONS

Inappetence, decreased water consumption, or diarrhea may occur transiently following treatment.

CLINICAL PHARMACOLOGY

The pharmacokinetic disposition of Florfenicol Injectable Solution was evaluated in feeder calves following single intramuscular (IM) administration at the recommended dose of 20 mg/kg body weight. Florfenicol Injectable Solution was also administered intravenously (IV) to the same cattle in order to calculate the volume of distribution, clearance, and percent bioavailability1 (Table 1).

TABLE 1. Pharmacokinetic Parameter Values for Florfenicol Following IM Administration of 20 mg/kg Body Weight to Feeder Calves (n=10).

Parameter	Median	Range
C_{max} (μg/mL)	3.07*	1.43 - 5.60
t_{max} (hr)	3.33	0.75 - 8.00
T ½ (hr)	18.3†	8.30 - 44.0
AUC (μg.min/mL)	4242	3200 - 6250
Bioavailability (%)	78.5	59.3 - 106
Vd_{ss} (L/kg)‡	0.77	0.68 - 0.85
Cl_t (mL/min/kg)‡	3.75	3.17 - 4.31

C_{max} Maximum serum concentration

T_{max} Time at which C_{max} is observed

T ½ Biological half-life

AUC Area under the curve

Vd_{ss} Volume of distribution at steady state

Cl_t Total body clearance

*harmonic mean

†mean value

‡following IV administration

Florfenicol was detectable in the serum of most animals through 60 hours after intramuscular administration with a mean concentration of 0.19 µg/mL. The protein binding of florfenicol was 12.7%, 13.2%, and 18.3% at serum concentrations of 0.5, 3.0, and 16.0 µg/mL, respectively.

MICROBIOLOGY

Florfenicol is a synthetic, broad-spectrum antibiotic active against many Gram negative and Gram-positive bacteria isolated from domestic animals. It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis. Florfenicol is generally considered a bacteriostatic drug, but exhibits bactericidal activity against certain bacterial species. *In vitro* studies demonstrate that florfenicol is active against the bovine respiratory disease (BRD) pathogens *Mannheimia haemolytica*, *Pasteurella multocida,* and *Histophilus somni,* and that florfenicol exhibits bactericidal activity against strains of *M. haemolytica* and *H. somni*. Clinical studies confirm the efficacy of florfenicol against BRD as well as against commonly isolated bacterial pathogens in bovine interdigital phlegmon including *Fusobacterium necrophorum* and *Bacteroides melaninogenicus.*

The minimum inhibitory concentrations (MICs) of florfenicol for BRD organisms were determined using isolates obtained from natural infections from 1990 to 1993. The MICs for interdigital phlegmon organisms were determined using isolates obtained from natural infections from 1973 to 1997 (Table 2).

TABLE 2. Florfenicol Minimum Inhibitory Concentration (MIC) Values* of Indicated Pathogens Isolated From Natural Infections of Cattle.

Indicated pathogens	Year of isolation	Isolate Numbers	MIC $_{50}$† (µg/mL)	MIC $_{90}$† (µg/mL)
Mannheimia haemolytica	1990 to 1993	398	0.5	1
Pasteurella multocida	1990 to 1993	350	0.5	0.5
Histophilis somni	1990 to 1993	66	0.25	0.5
Fusobacterium necrophorum	1973 to 1997	33	0.25	0.25
Bacteroides melaninogenicus	1973 to 1997	20	0.25	0.25

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

†The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

ANIMAL SAFETY

A 10x safety study was conducted in feeder calves. Two intramuscular injections of 200 mg/kg were administered at a 48-hour interval. The calves were monitored for 14 days after the second dose. Marked anorexia, decreased water consumption, decreased

body weight, and increased serum enzymes were observed following dose administration. These effects resolved by the end of the study.

A 1x, 3x, and 5x (20, 60, and 100 mg/kg) safety study was conducted in feeder calves for 3x the duration of treatment (6 injections at 48-hour intervals). Slight decrease in feed and water consumption was observed in the 1x dose group. Decreased feed and water consumption, body weight, urine pH, and increased serum enzymes, were observed in the 3x and 5x dose groups. Depression, soft stool consistency, and dehydration were also observed in some animals (most frequently at the 3x and 5x dose levels), primarily near the end of dosing.

A 43-day controlled study was conducted in healthy cattle to evaluate effects of florfenicol injectable solution administered at the recommended dose on feed consumption. Although a transient decrease in feed consumption was observed, Florfenicol Injectable Solution administration had no long-term effect on body weight, rate of gain, or feed consumption.

STORAGE INFORMATION

Store at 20°C to 25°C (68°F to 77°F), with an excursion permitted between 15°C and 30°C (between 59°F and 86°F).
Protect from light when not in use.

Use within 30 days of first puncture. For the 100mL vials, puncture the stopper a maximum of 3 times. For the 250mL and 500mL vials, puncture the stopper a maximum of 17 times. If more than the specified punctures are anticipated, the use of multi-dosing equipment 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

FLORFENIJECT Injectable Solution is packaged in 100 mL (NDC 69043-044-10), 250 mL (NDC 69043-044-25), and 500 mL (NDC 69043-044-50) glass sterile multiple-dose vials.

REFERENCE

1. Lobell RD, Varma KJ, et al. Pharmacokinetics of florfenicol following intravenous and intramuscular doses to cattle. J Vet Pharmacol Therap. 1994;17:253-258.

Approved by FDA under ANADA # 200-760

Manufactured for:
Cronus Pharma LLC,
East Brunswick, NJ 08816.
Contact No: 1-844-227-6687
(1-844-2-CRONUS)
Made in India

PC044-00

Code No.: 4206162/TS/DRUGS/2023

January 2024

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 69043-044-10

Sterile

Florfeniject™

(florfenicol)

Injectable Solution

300mg/mL

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Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

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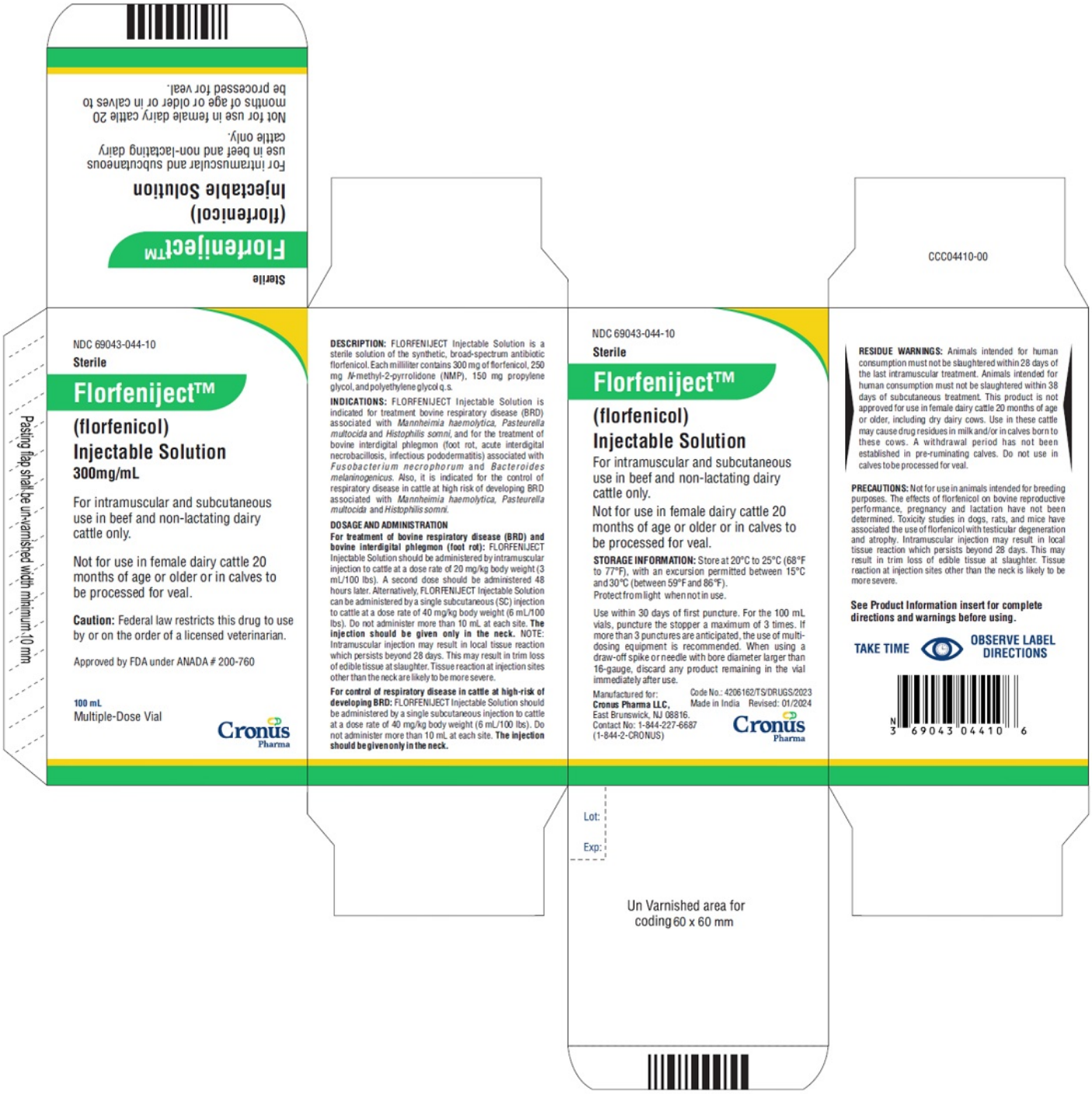
Approved by FDA under ANADA # 200-760

100 mL

Multiple-Dose Vial



PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 69043-044-25

Sterile

Florfeniject™

(florfenicol)

Injectable Solution

300mg/mL

For intramuscular and subcutaneous use in beef and non-lactating dairy cattle only.

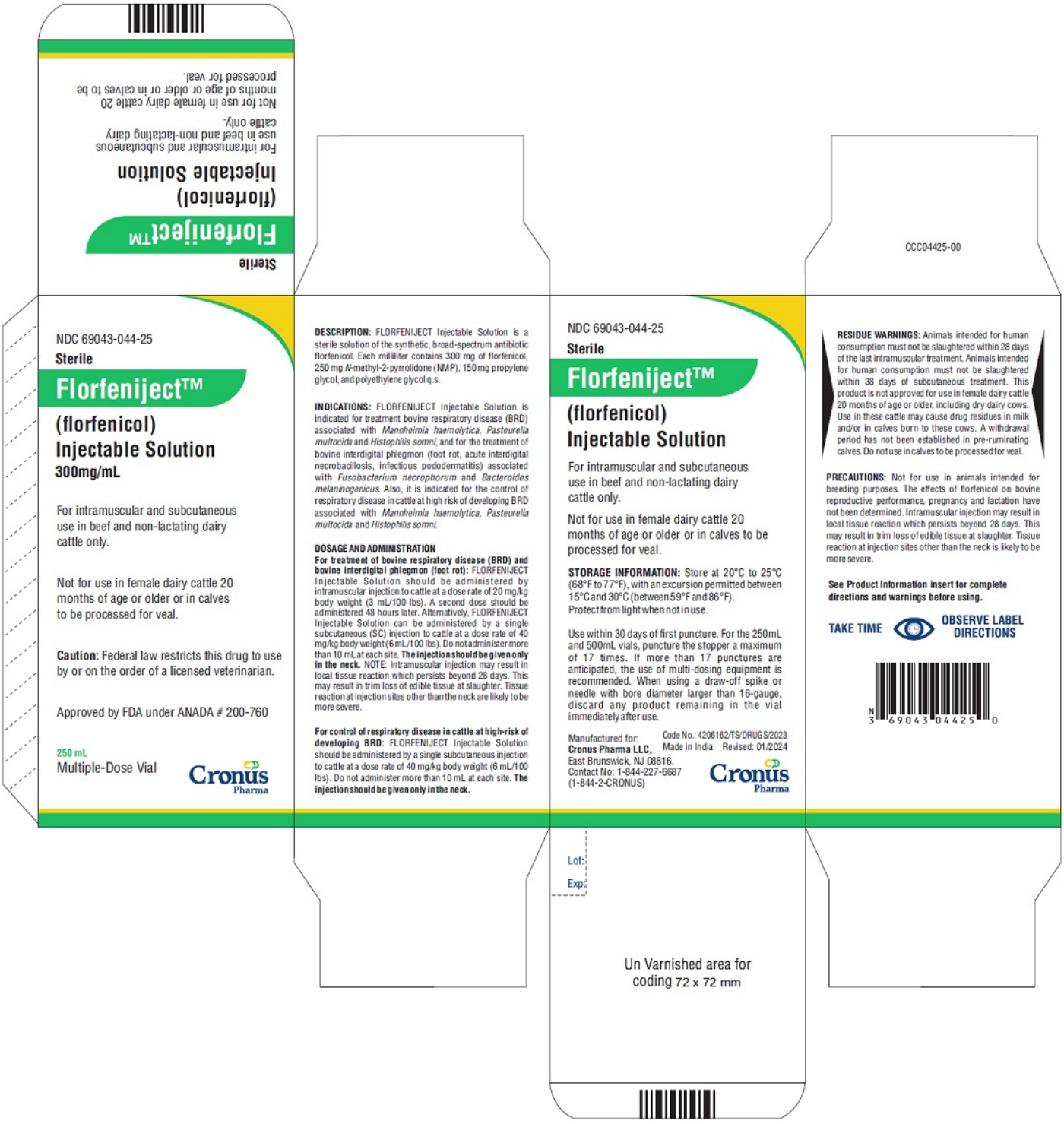
Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Approved by FDA under ANADA # 200-760

250 mL

Multiple-Dose Vial



NDC 69043-044-50

Sterile

Florfeniject™

(florfenicol)

Injectable Solution

300mg/mL

For intramuscular and subcutaneous use in beef and non-lactating dairy cattle only.

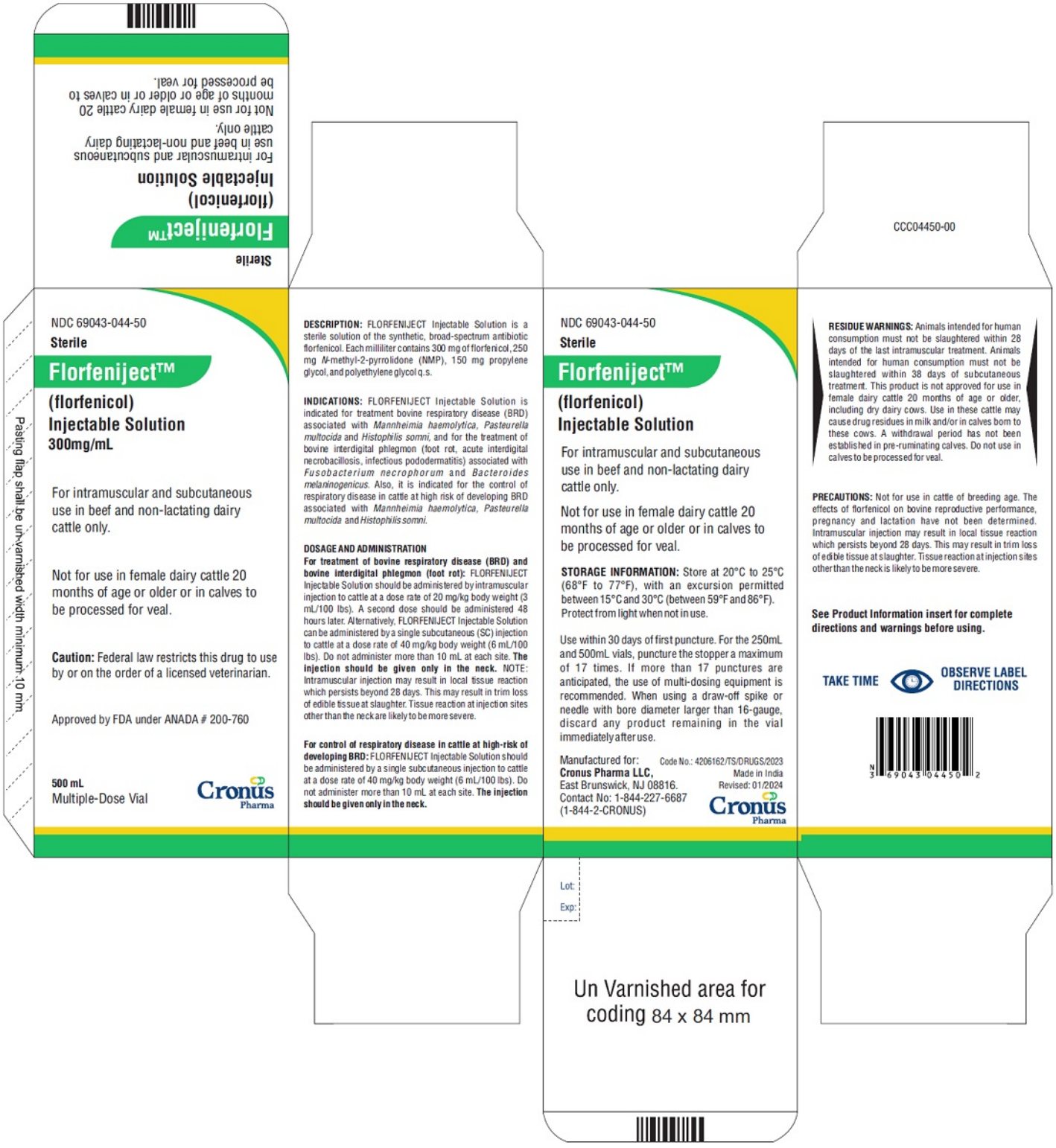
Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Approved by FDA under ANADA # 200-760

500 mL

Multiple-Dose Vial



FLORFENIJECT

florfenicol injection, solution

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:69043-044
Route of Administration	INTRAMUSCULAR, SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
FLORFENICOL (UNII: 9J97307Y1H) (FLORFENICOL - UNII:9J97307Y1H)	FLORFENICOL	300 mg in 1 mL

Product Characteristics			
Color	yellow	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:69043-044-10	1 in 1 CARTON		
1		100 mL in 1 VIAL, GLASS		
2	NDC:69043-044-25	1 in 1 CARTON		
2		250 mL in 1 VIAL, GLASS		
3	NDC:69043-044-50	1 in 1 CARTON		
3		500 mL in 1 VIAL, GLASS		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200760	04/15/2024	

Labeler - Cronus Pharma LLC (079421067)

Registrant - Cronus Pharma Specialities India Private Limited (876818318)

Establishment

Name	Address	ID/FEI	Business Operations
Cronus Pharma Specialities India Private Limited		876818318	analysis, manufacture, label, pack

Revised: 3/2024 Cronus Pharma LLC