
Florfeniject™ (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.

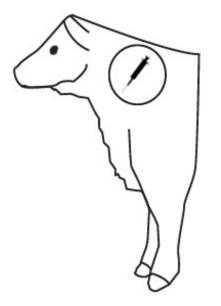
For control of respiratory disease in cattle at high-risk of developing BRD:

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 GOIDE				
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		

FLORFENIJECT Injectable Solution DOSAGE GUIDE

Recommended Injection Location



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

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 IMAdministration 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 ¹/₂ Biological half-life

AUC Area under the curve

Vd_{ss} Volume of distribution at steady state

Clt Total body clearance

*harmonic mean

[‡]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 μ g/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 μ g/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).

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

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

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

 $^{\dagger}\text{The}$ 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.

Florfeniject[™] is the trademark of Cronus Pharma LLC

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

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

100 mL

Multiple-Dose Vial

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

For intramuscular and subcutaneous use in beet and non-lactating dairy

NDC 69043-044-10

(florfenicol)

300mg/mL

cattle only.

100 mL Multiple-Dose Vial

be processed for yeal.

Florfeniject™

Injectable Solution

For intramuscular and subcutaneous

use in beef and non-lactating dairy

Not for use in female dairy cattle 20

months of age or older or in calves to

Caution: Federal law restricts this drug to use

Cronus

by or on the order of a licensed veterinarian.

Approved by FDA under ANADA # 200-760

Sterile

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Injectable Solution (florfenicol)

FlortenijectTM

Sterile

DESCRIPTION: FLORFENIJECT Injectable Solution is a sterile solution of the symhetic, broad-spectrum antibiotic florfenicol. Each milliller contains 300 mg of florfenicol. 250 mg //methyf-2pyrrolidome (MMP), 150 mg propylene glycol.andpolyethylene glycol.g.s.

glycol, and polyethylene glycol q.s. INDICATIONS: FLORFENIJECT Injectable Solution is indicated for treatment bovine respiratory disease (BRD) associated with Mannheimia haemolytica, Pasteurella multocida and Histophilis sommi, and for the treatment of bovine interdigital philegmon (toot rot, acute interdigital necrobacillosi; infectious pododermatitis) associated with Fus obacterium 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 Histophilis sonni.

DO SAGE AND ADMINISTRATION

DOSAGE AND ADMINISTRATION For treatment of bovine respiratory disease (BRD) and bovine interdigital pheymon (teot rot): FLORFENLECT injectable Solution should be administered by intramuscular injection to catife at a dose rate of 20 mg/kg body weight (3 mU100 lbs). A second does bloud be administered 48 hours later. Atternatively, FLORFENLECT 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 m, at each site. The to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 bs). Do not administer more than 10 m, 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 dolbe tissue at slaughter. Tissue reaction at injection sites other than the neck are likely to be more severe.

Other than the next at a wey to be more severe. For control of respiratory discess in cattle at high-risk of developing BRD: FLOFFENUECT Injectable Solution should be administered by a single subcularnous 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.

NDC 69043-044-10 Sterile

Florfeniject[™]

(florfenicol) Injectable Solution

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 yeal.

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 100 mL vials, puncture the stopper a maximum of 3 times. If more than 3 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.

Code No.: 4206162/TS/DRUGS/2023 Made in India Revised: 01/2024 Manufactured for: Coo Cronus Pharma LLC, Ma East Brunswick, NJ 08816. Contact No: 1-844-227-6687 (1-844-2-CRONUS)

Cronus

RESIDUE WARNINGS: Animals intended for human consumption must not be shuphtered within 28 days of the last intramuscular treatment. Animals intended for human consumption must not be slauphtered within 38 days of subcutaneous treatment. This product is not approved for use in female dairy catlle 20 months of age or older, including dry dairy cows. Use in these catle may cause drog residues in milk and/or in calves born to these cows. A withdrawal period has not been established in one-turning not calves. Do not use in the setablished in one-turning not calves. Do not use in the setablished in one-turning not calves. Do not use in the setablished in one-turning not calves. Do not use in the setablished in the seta established in pre-ruminating calves. Do not use in calves to be processed for yeal. PRECAUTIONS: Not for use in animals intended for breed

CCC04410-00

RESIDUE WARNINGS: Animals intended for human

PRECAUTIONS: Not for use in animals intended to breeding purposes. The effects of florfiencial 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 ingetion may result in local tissue reaction which persists beyond 28 days. This may result in trim loss of edible tissue at slauphter. Tissue reaction at injection sites other than the neck is likely to be more seven. moreseve

See Product Information insert for complete directions and warnings before using.



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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.

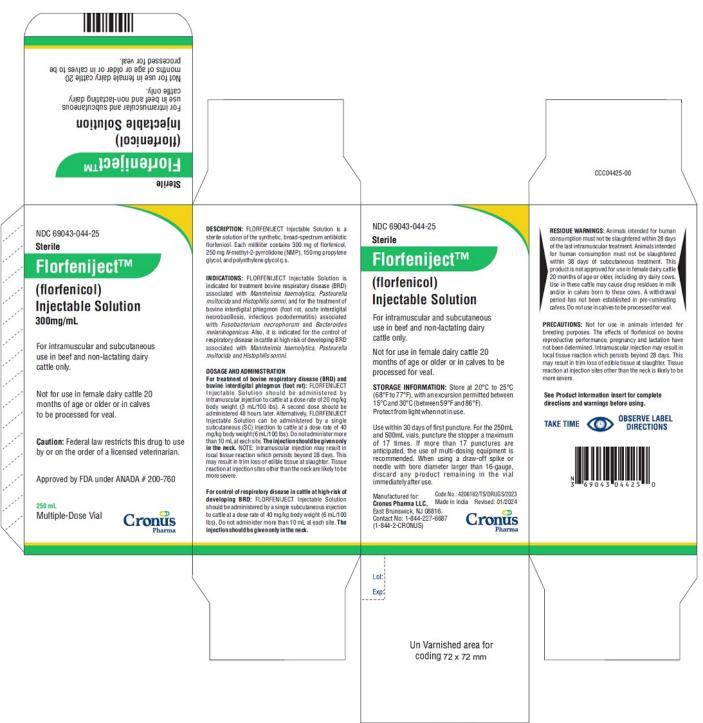
Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

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

months of age or older or in calves to be processed for veal. Not for use in female dairy cattle 20 cattle only. use in beef and non-lactating dairy For intramuscular and subcutaneous Injectable Solution (locinstroll) CCC04450-00 ^{m1}Jo9[in9Trol] Sterile NDC 69043-044-50 NDC 69043-044-50 **DESCRIPTION:** FLORFENIJECT Injectable Solution is a RESIDUE WARNINGS: Animals intended for human sterile solution of the synthetic, broad-spectrum antibiotic florfenicol. Each milliliter contains 300 mg of florfenicol, 250 consumption must not be slaughtered within 28 Sterile Sterile days of the last intramuscular treatment. Animals intended for human consumption must not be slaughtered within 38 days of subcutaneous mg N-methyl-2-pyrrolidone (NMP), 150 mg propylene **Florfeniject**[™] Florfeniiect[™] glycol, and polyethylene glycol q.s. 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 (florfenicol) (florfenicol) INDICATIONS: FLORFENIJECT Injectable Solution is indicated for treatment bovine respiratory disease (BRD) associated with Mannheimia haemolytica, Pasteurella multocida and Histophilis somni, and for the treatment of Pasting flap shall be **Injectable Solution Injectable Solution** these cows. A withdrawal period has not been 300mg/mL established in pre-ruminating calves. Do not use in calves to be processed for yeal. bovine interdigital phlegmon (foot rot, acute interdigital For intramuscular and subcutaneous nerobacilosis, infectious pododernatiis) associated with Fusobacterium necrophorum and Bacteroides melaninogenicus. Also, it is indicated for the control of use in beef and non-lactating dairy cattle only. For intramuscular and subcutaneous respiratory disease in cattle at high risk of developing BRD PRECAUTIONS: Not for use in cattle of breeding age. The associated with Mannheimia haemolytica, Pasteurella effects of florfenicol on bovine reproductive performance, pregnancy and lactation have not been determined. use in beef and non-lactating dairy Not for use in female dairy cattle 20 multocida and Histophilis somni cattle only. months of age or older or in calves to un-varnished width minimum Intramuscular injection may result in local tissue reaction which persists beyond 26 days. This may result in first losar sectors of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe. be processed for yeal. DOSAGE AND ADMINISTRATION For treatment of bovine respiratory disease (BRD) and bovine interdigital phlegmon (toot rot): FLORFENIJECT Injectable Solution should be administered by intramuscular STORAGE INFORMATION: Store at 20°C to 25°C Not for use in female dairy cattle 20 (68°F to 77°F), with an excursion permitted between 15°C and 30°C (between 59°F and 86°F). months of age or older or in calves to 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. Aternatively, FLORFENIJECT Injectable Solution be processed for veal. Protect from light when not in use. See Product Information insert for complete directions and warnings before using. can be administered by a single subcutaneous (SC) injection Use within 30 days of first puncture. For the 250mL to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 10s). Do not administer more than 10 mL at each site. The injection should be given only in the neck. NOTE: Caution: Federal law restricts this drug to use and 500mL vials, puncture the stopper a maximum of 17 times. If more than 17 punctures are by or on the order of a licensed veterinarian. **OBSERVE LABEL** 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 are likely to be more severe. ~10 mm TAKE TIME anticipated, the use of multi-dosing equipment is DIRECTIONS recommended. When using a draw-off spike or needle with bore diameter larger than 16-gauge, Approved by FDA under ANADA # 200-760 discard any product remaining in the vial immediately after use. For control of respiratory disease in cattle at high-risk of developing BRD: FLORFENIJECT Injectable Solution should Wanufactured for: Code No.: 4206162/TS/DRUGS/2023 Cronus Pharma LLC, East Brunewidth Clifford 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. East Brunswick, NJ 08816. Contact No: 1-844-227-6687 500 mL Revised: 01/2024 Cronus Multiple-Dose Vial Cronus (1-844-2-CRONUS)

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

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	ctive Ingredien		-		Pacia of Ch	rongth	Strongth
		-	ent Name		Basis of Strength		Strength
FLORFENICOL (UNII: 9J97307Y1H) (FLORFENICOL - UNII:		9J97307Y1H)	FLORFENICOL		300 mg in 1 mL		
Ρ	roduct Charact	eristics					
С	olor		yellow	Score			
Shape			Size				
FI	avor			Imprint Cod	le		
С	ontains						
P	ackaging						
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1	NDC:69043-044-10	1 in 1 CAR	TON				
1		100 mL in	1 VIAL, GLASS				
2	NDC:69043-044-25	1 in 1 CAR					
2		250 mL in	1 VIAL, GLASS				
3	NDC:69043-044-50	1 in 1 CAR	TON				
3		500 mL in	1 VIAL, GLASS				
	larketing In	formati	on				
Μ	Marketing	Applicat	lication Number or Monograph Citation		Marketing Start M Date		Aarketing End Date
M	Category		Citation		Dutt		Date

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