

NORFENICOL- florfenicol injection, solution
Norbrook Laboratories Limited

Norfenicol®
(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.

DESCRIPTION:

Norfenicol® Injectable Solution is a solution of the synthetic antibiotic florfenicol. Each milliliter of sterile Norfenicol Injectable Solution contains 300 mg of florfenicol, 250 mg 2-pyrrolidone, and glycerol formal qs.

INDICATIONS:

Norfenicol 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): Norfenicol 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, Norfenicol 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:

Norfenicol Injectable Solution should be administered by a single subcutaneous injection to cattle at a dose rate of 40 mg/kg body weight (6 mL/100lbs). Do not administer more than 10 mL at each site. The injection should be given only in the neck.

NORFENICOL INJECTABLE SOLUTION DOSAGE GUIDE

ANIMAL WEIGHT (lbs)	IM DOSAGE 3.0 mL/100 lb Body Weight (mL)	SC 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.

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

For customer service, adverse effects reporting, and/or a copy of the MSDS, call 1-866-591-5777.

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 33 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

* harmonic mean

** mean value

*** following IV administration

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

Florfenicol was detectible 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	Number of isolates	MIC ₅₀ ** (µg/mL)	MIC ₉₀ ** (µg/mL)
<i>Mannheimia haemolytica</i>	1990 to 1993	398	0.5	1
<i>Pasteurella multocida</i>	1990 to 1993	350	0.5	0.5
<i>Histophilus somni</i>	1990 to 1993	66	0.25	0.5
<i>Fusobacterium necrophorum</i>	1973 to 1997	33	0.25	0.25
<i>Bacteroides melaninogenicus</i>	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% to 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 or below 77°F (25°C). Refrigeration is not required. Excursions permitted up to 86°F (30°C). Brief exposure to temperature up to 104°F (40°C) may be tolerated provided the mean kinetic temperature does not exceed 77°F (25°C); however, such exposure should be minimized. The solution is light yellow to straw colored.

Color does not affect potency.

Use within 28 days of first vial puncture.

HOW SUPPLIED:

Norfenicol Injectable Solution is packaged in 100 mL, 250 mL, and 500 mL 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.

Restricted Drug - California. Use Only as Directed.

Made in the UK.

Manufactured by: Norbrook Laboratories Limited,
Newry, BT35 6PU, Co. Down,
Northern Ireland.

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Norbrook®

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March 2015

Principal Display Panel - 100 mL Carton Label

NDC 55529-155-02

Sterile

Norfenicol®

(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 veal.

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

ANADA 200-591,

Approved by FDA

100 mL (3.4 fl oz)

Multiple-Dose Vial

300 mg/mL

Norbrook®



Principal Display Panel - 100 mL Bottle Label

NDC 55529-155-02

Sterile

Norfenicol®

(florfenicol)

Injectable Solution

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cattle only.

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ANADA 200-591,

Approved by FDA

100 mL (3.4 fl oz)

Multiple-Dose Vial

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Norbrook®

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STORAGE INFORMATION: Store at or below 77°F (25°C). Refrigeration is not required. Excursions permitted up to 88°F (30°C). Brief exposure to temperature up to 104°F (40°C) may be tolerated provided that mean kinetic temperature does not exceed 77°F (25°C); however, such exposure should be minimized. The solution is light yellow to straw colored. Color does not affect potency. Use within 28 days of first vial puncture. Made in the UK. Manufactured by: Norbrook Laboratories Limited, Newry, BT35 6PU, Co. Down, Northern Ireland.

March 2015 000000L01

NDC 55529-155-02 Sterile

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

100 mL (3.4 fl oz)
Multiple-Dose Vial
300 mg/mL

ANADA 200-591,
Approved by FDA

Norbrook

See Product Information insert for complete directions and warnings before using.
DESCRIPTION: Each milliliter contains 300 mg of florfenicol, 250 mg 2-pyrrolidone, and glycerol formal qs.
DOSAGE AND ADMINISTRATION: For treatment of bovine respiratory disease (BRD) and bovine interdigital phlegmon (foot rot): Norfenicol® 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, Norfenicol 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: Norfenicol 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.

Lot No.:
Exp. Date:

OVERPRINT AREA
18 x 18mm

Principal Display Panel - 250 mL Bottle Label

NDC 55529-155-04

Sterile

Norfenicol®

(florfenicol)

Injectable Solution

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

ANADA 200-591,

Approved by FDA

250 mL (8.5 fl oz)

Multiple-Dose Vial

300 mg/mL

Norbrook®

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

DESCRIPTION: Each milliliter contains 300 mg of florfenicol, 250 mg 2-pyrrolidone, and glycerol formal qs.

DOSAGE AND ADMINISTRATION: For treatment of bovine respiratory disease (BRD) and bovine interdigital phlegmon (foot rot); Norfenicol® 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, Norfenicol 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: Norfenicol 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.**



NDC 55529-155-04 Sterile

Norfenicol®
(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 veal.

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

250 mL (8.5 fl oz)
Multiple-Dose Vial
300 mg/mL

ANADA 200-591,
Approved by FDA



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 33 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.

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STORAGE INFORMATION: Store at or below 77°F (25°C). Refrigeration is not required. Excursions permitted up to 86°F (30°C). Brief exposure to temperature up to 104°F (40°C) may be tolerated provided that mean kinetic temperature does not exceed 77°F (25°C); however, such exposure should be minimized. The solution is light yellow to straw colored. Color does not affect potency. Use within 28 days of first vial puncture.

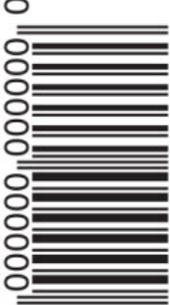
Made in the UK

Manufactured by: Norbrook Laboratories Limited, Newry, BT35 6PU, Co. Down, Northern Ireland.

Exp. Date:

Lot No.:

March 2015



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NORFENICOL

florfenicol injection, solution

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:55529-155
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

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:55529-155-02	1 in 1 CARTON		
1		100 mL in 1 BOTTLE, PLASTIC		
2	NDC:55529-155-04	250 mL in 1 BOTTLE, PLASTIC		
3	NDC:55529-155-05	500 mL in 1 BOTTLE, PLASTIC		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200591	09/30/2015	

Labeler - Norbrook Laboratories Limited (214580029)

Establishment

Name	Address	ID/FEI	Business Operations
Norbrook Laboratories Limited		211218325	ANALYSIS, LABEL, MANUFACTURE, PACK

Revised: 2/2022

Norbrook Laboratories Limited