2023 Fall Bonus

Elanco Producer Rebate Offer

August 1 – October 31, 2023

Earn up to a 20% rebate when you spend across multiple product categories with Elanco.*

Buy from two categories → get a **10% rebate.**

Buy from three categories → get a **15% rebate.**

Buy from four categories → get a **20% rebate.**

*Producers must spend a minimum amount per category to earn a rebate:

Category	Qualifying products	Purchase Minimum
Anti-infectives: Group A	Micotil® (tilmicosin injection)	**$5,000**
	Increxxa™ (tulathromycin injection)	
Anti-infectives: Group B	Baytril® 100 (enrofloxacin injection)	**$2,500**
	Loncor® (florfenicol injection)	
Vaccines	Titanium®	**$2,500**
	NUPLURA® PH	
Implants	Component® with Tylan® (All SKUs)	**$2,500**
	Compudose® (estradiol)	
	Encore® (estradiol)	

ElancoCattleRebates.com.

Right for cattle. Right by you.

Elanco™

Program Terms & Conditions:

Ways to claim your rebate:

1. Online claims: Scan the QR code to be directed to the rebate claim forms online, or visit ElancoCattleRebates.com.
2. Mail-in claims: Complete a mail-in claim form and submit with proof of purchase (invoice) via mail.
3. Supplier Reported Claims (EDI): Qualifying purchases billed through an EDI-reporting distributor be aggregated at the end of the program. EDI-reporting distributor must report EDI sales to Elanco. Qualifying customers will automatically receive a rebate check in the mail.

Program Terms:

- Only producers are eligible for this program. Producers enrolled in any special Elanco pricing programs are not eligible for this rebate offer.
- Purchases are cumulative August 1 – October 31, 2023. Eligible purchases must be invoiced by October 31, 2023.
- Minimum rebate check amount is $50.00. Allow at minimum 6 weeks for processing following program conclusion.
- Eligible products for the offer include: Baytril, Increxxa, Micotil, Loncor, Titanium, Nuplura PH, Component with Tylan, Compudose, Encore. All SKUs are eligible. Offers valid while supplies last.
- Products that are on backorder and qualify for the rebate offer must ship during the program term to receive the rebate. Products that are on backorder and do not ship during the program term will not qualify for any rebate in this program. All product returns will be applied toward the subsequent program payout period.
- Producers who submit coupons via mail or online will not be eligible for EDI reported claims.
- Limit 10 mail or online claim submissions per household. Multiple proofs of purchase can be used per submission. One rebate will be calculated per submission. Qualifying rebates will be calculated for all invoices included in a submission and will not be calculated across multiple submissions.
- Mail and online rebate claim form and invoice(s) must be postmarked or submitted by November 30, 2023.
- Elanco reserves the right to vary the terms and conditions of this program or to cancel this program at any time upon notice through the website Elanco.com.
- For more information regarding this rebate program and eligibility, contact your Elanco Animal Health representative or call 800-364-2014.

Buy from two categories, get a 10% rebate. Buy from three categories, get a 15% rebate. Buy from four categories, get a 20% rebate.

Categories	Product	Amount purchased	Rebate	TOTAL $
Anti-infectives: Group A	Micotil® (tilmicosin injection)			
	Increxxa™ (tulathromycin injection)			
Anti-infectives: Group B	Baytril® 100 (enrofloxacin injection)			
	Loncor® (florfenicol injection)			
Vaccines	Titanium®			
	NUPLURA® PH			
Implants	Component® with Tylan® (All SKUs)			
	Compudose® (estradiol)			
	Encore® (estradiol)			
			Number of categories	
			TOTAL Rebate request	$

Submit rebate claim form and invoice(s)
POSTMARKED NO LATER THAN November 30, 2023, to:

Cattle Health and Productivity Rebate Offer
PO Box 1080
Dept: R12747
Grand Rapids, MN 55745-1080

Invoice copy(ies) or invoice statement(s) must accompany this form to obtain rebate.
Invoices or statements must clearly show:

1. Product name(s), product size(s) and date(s) purchased.
2. Name of company where product(s) was/were purchased and price paid.
3. Limit of 10 mail or online claim submission per household.

Producer Name

Physical Address

Mailing Address

City State ZIP

Phone Number

Email Address

❑ I would like to receive future communications from Elanco about farm animal products.

IMPORTANT SAFETY INFORMATION FOR MICOTIL

Before using this product, it is important to read the entire product insert, including the boxed human warning. Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Not for human use. Injection of this drug in humans has been associated with fatalities. Keep out of reach of children. Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately and apply ice or cold pack to injection site while avoiding direct contact with the skin. Avoid contact with eyes. Always use proper drug handling procedures to avoid accidental self-injection. Consult your veterinarian on the safe handling and use of all injectable products prior to administration. For use in cattle or sheep only. Inject subcutaneously. Injection of this antibiotic has been shown to be fatal in swine and non-human primates, and may be fatal in horses and goats. Do not use in lambs less than 15 kg body weight. Do not use in female dairy cattle 20 months of age or older. Use in lactating dairy cattle or sheep may cause milk residues. The following adverse reactions have been reported: in cattle: injection site swelling and inflammation, lameness, collapse, anaphylaxis/anaphylactoid reactions, decreased food and water consumption, and death; in sheep: dyspnea and death. Micotil has a pre-slaughter withdrawal time of 42 days.

Elanco™

Micotil™ 300

250 mL™

(tilmicosin injection)

300 mg tilmicosin, USP as tilmicosin phosphate per mL

For Subcutaneous Use in Cattle and Sheep Only

Solo Para Uso Subcutáneo en Ganado Vacuno y Ovino

Approved by FDA under NADA # 140-929

Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices.
Contact Elanco at 1-800-428-4441, or your distributor, for a tube-fed safety syringe for use with this product. Administrar únicamente con una jeringa de seguridad con tubo. No administrar con jeringas accionadas automáticamente, jeringas de un solo uso u otros dispositivos de aplicación. Contactar a Elanco al 1-800-428-4441, o al distribuidor, para obtener una jeringa de seguridad con tubo para usar con este producto.

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

Description: Micotil (tilmicosin injection) is a solution of the antibiotic tilmicosin. Each mL contains 300 mg of tilmicosin, USP as tilmicosin phosphate in 25% propylene glycol, phosphoric acid as needed to adjust pH and water for injection, Q.S. Tilmicosin, USP is produced semi-synthetically and is in the macrolide class of antibiotics.

Indications: Micotil is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni* and for the treatment of ovine respiratory disease (ORD) associated with *Mannheimia haemolytica*. Micotil is indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*.

Micotil must be used with the quick-fit connector made specifically for its use. Contact Elanco or your distributor for this equipment. Read product labeling, including Safe Handling Practices, before use.

Micotil debe usarse con un conector de ajuste rápido hecho específicamente para su uso. Contacte a Elanco o al distribuidor para obtener este equipo. Lea la ficha técnica, incluidas las Prácticas De Manejo Seguro, antes de usar.

Dosage and Administration: Follow instructions for activation of the shroud before first usage.

Inject Subcutaneously in Cattle and Sheep Only. See Safe Handling Practices, Contraindications, and Warnings prior to use. In cattle, administer a single subcutaneous dose of 10 to 20 mg/kg of body weight (1 to 2 mL/30 kg or 1.5 to 3 mL per 100 lbs). **In sheep** greater than 15 kg, administer a single subcutaneous dose of 10 mg/kg of body weight (1 mL/30 kg or 1.5 mL per 100 lbs). Do not inject more than 10 mL per injection site.
If no improvement is noted within 48-hours, the diagnosis should be reevaluated.
For cattle and sheep, injection under the skin in the neck is suggested. If not accessible, inject under the skin behind the shoulders and over the ribs.

Note: Swelling at the subcutaneous site of injection may be observed.

CONTRAINDICATIONS: Do not use in automatically powered syringes, single-use syringes, or other delivery devices not specified in the labeling. Do not administer intravenously to cattle or sheep.
Intravenous injection in cattle or sheep will be fatal. Do not use in lambs less than 15 kg body weight. Do not administer to animals other than cattle or sheep. Injection of tilmicosin has been shown to be fatal in swine and non-human primates. Death following exposure to tilmicosin injection has been reported to FDA/CVM in goats, rabbits, pheasants, pigs, dogs, deer, cats, alpacas, and horses.

Warnings:

HUMAN WARNINGS: Not for human use. Injection of this drug in humans has been associated with fatalities. Keep out of reach of children. Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately and apply ice or cold pack to injection site while avoiding direct contact with the skin. Emergency medical telephone numbers are 1-800-722-0987 or 1-800-428-4441. Avoid contact with skin, eyes, or mucous membranes.

NOTE TO THE PHYSICIAN: The cardiovascular system is the target of toxicity and should be monitored closely. Cardiovascular toxicity may be due to calcium channel blockade. In dogs, administration of intravenous calcium offset Micotil-induced tachycardia and negative inotropy (decreased contractility). Dobutamine partially offset the negative inotropic effects induced by Micotil in dogs. ß-adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil in dogs. Epinephrine potentiated lethality of Micotil in pigs. This antibiotic persists in tissues for several days.

ADVERTENCIAS PARA EL SER HUMANO: Este producto no es para uso humano. La inyección de este medicamento al ser humano se ha asociado con muertes. Mantenga fuera del alcance de los niños. Utilice únicamente con una jeringa de seguridad con tubo. No use en jeringas operadas automáticamente, jeringas de un solo uso u otros dispositivos de aplicación. Proceda con extrema cautela para evitar la autoinyección accidental. En caso de inyección en seres humanos, consulte inmediatamente a un médico y aplique hielo o una compresa fría en el lugar de la inyección, evitando el contacto directo con la piel. Los números de teléfono para emergencias médicas son 1-800-722-0987 o 1-800-428-4441. Evite el contacto con la piel, los ojos o las membranas mucosas.

NOTA PARA EL MÉDICO: El sistema cardiovascular es el blanco de la toxicidad y debe vigilarse estrechamente. La toxicidad cardiovascular puede deberse al bloqueo de los canales de calcio.
En los perros, la administración intravenosa de calcio compensó la taquicardia y los efectos inotrópicos negativos (reducción de la contractilidad) inducidos por Micotil (tilmicosina inyectable). La dobutamina compensó parcialmente los efectos inotrópicos negativos inducidos por Micotil en perros. Los antagonistas ß-adrenérgicos, como propranolol, exacerbaron el inotropismo negativo de Micotil en los perros. La epinefrina potenció la letalidad de Micotil en cerdos. Este antibiótico persiste en los tejidos por varios días.

Residue Warnings: Animals intended for human consumption must not be slaughtered within 42 days of the last treatment. Not for use in lactating dairy cattle 20 months of age or older. Use of tilmicosin in this class of cattle may cause milk residues. Not for use in lactating ewes producing milk for human consumption.

Precautions: The effects of tilmicosin on bovine and ovine reproductive performance, pregnancy and lactation have not been determined. Intramuscular injection will cause a local reaction which may result in trim loss of edible tissue at slaughter.

Adverse Reactions: The following adverse reactions have been reported post-approval: In cattle: injection site swelling and inflammation, lameness, collapse, anaphylaxis/anaphylactoid reactions, decreased food and water consumption, and death.

In sheep: dyspnea and death.

For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae

Clinical Pharmacology: A single subcutaneous injection of Micotil (tilmicosin injection) at 10 mg/kg of body weight dose in cattle resulted in peak tilmicosin levels within one hour and detectable levels (0.07 µg/mL) in serum beyond 3 days. However, lung concentrations of tilmicosin remained above the tilmicosin MIC 95% of 3.12 µg/mL for *Mannheimia haemolytica* for at least 3 days following the single injection. Serum tilmicosin levels are a poor indicator of total body tilmicosin. The lung/serum tilmicosin ratio in favor of lung tissue appeared to equilibrate by 3 days post-injection at approximately 60. In a study with radioactive tilmicosin, 24% and 68% of the dose was recovered from urine and feces respectively over 21 days. After a single subcutaneous injection of Micotil at 10 mg/kg of body weight, tilmicosin concentrations in excess of 4 µg/mL were maintained in the alveolar macrophages and neutrophils of most cattle for at least 10 days. The clinical relevance of these findings has not been determined.

Microbiology: Tilmicosin has an *in vitro* antibacterial spectrum that is predominantly Gram-positive with activity against certain Gram-negative microorganisms. *In vitro* activity against several *Mycoplasma* species has also been observed.

Effectiveness: In a multi-location field study, 1508 calves with naturally occurring BRD were treated with Micotil. Responses to treatment were compared to saline-treated controls. A cure was defined as a calf with normal attitude and activity, normal respiration, and a rectal temperature of <104°F on Day 13. The cure rate was significantly higher (P=0.004) in Micotil-treated calves (63.1%) compared to saline-treated calves (29.2%). During the treatment phase of the study, there were 10 BRD-related deaths in the Micotil-treated calves compared to 47 in the saline-treated calves.

Animal Safety: A safety study was conducted in feeder calves receiving subcutaneous doses of 20, 30, 40, or 60 mg/kg of body weight, injected 3 times at 72-hour intervals. Death was not seen in any of the treatment groups. Injection site swelling and mild hemorrhage at the injection site were seen in animals in all dosage groups. Lesions were described as being generally more severe and occurred at higher frequency rates in the animals treated with higher doses of tilmicosin. Lameness associated with the injection site was noted in two of twenty-four animals (one animal in the 30 mg/kg body weight treatment group and one animal in the 60 mg/kg treatment group). No other drug related lesions were observed macroscopically or microscopically. Decreases in food and water consumption were noted in all treatment groups compared to the control group.

A separate safety study conducted in feeder calves, subcutaneous doses of 10, 30, or 50 mg/kg of body weight, injected 3 times at 72-hour intervals did not cause any deaths. Edema at the site of injection was noted. The only lesion observed at necropsy was minimal myocardial necrosis in some animals dosed at 50 mg/kg.

In an additional safety study, subcutaneous doses of 150 mg/kg body weight injected at 72-hour intervals resulted in death of two of the four treated animals. Edema was marked at the site of injection. Minimal myocardial necrosis was the only lesion observed at necropsy. Deaths of cattle have been observed with a single intravenous dose of 5 mg/kg of body weight.

In sheep, single subcutaneous injections of 10 mg/kg body weight dose did not cause any deaths and no adverse effects of tilmicosin were observed on blood pressure, heart rate, or respiratory rate.

Toxicology: The heart is the target of toxicity in laboratory and domestic animals given Micotil (tilmicosin injection) by oral or parenteral routes. The primary cardiac effects are increased heart rate (tachycardia) and decreased contractility (negative inotropy). Cardiovascular toxicity may be due to calcium channel blockade.

Upon subcutaneous injection, the acute median lethal dose of tilmicosin in mice is 97 mg/kg, and in rats is 185 mg/kg of body weight. Given orally, the median lethal dose is 800 mg/kg and 2250 mg/kg body weight in fasted and nonfasted rats, respectively.

No compound-related lesions were found at necropsy.

In dogs, intravenous calcium offset Micotil-induced tachycardia and negative inotropy, restoring arterial pulse pressure. Dobutamine partially offset the negative inotropic effects induced by Micotil in dogs. ß- adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil in dogs.

In monkeys, a single intramuscular dose of 10 mg/kg body weight caused no signs of toxicity. A single dose of 20 mg/kg body weight caused vomiting and 30 mg/kg body weight caused the death of the only monkey tested.

In swine, intramuscular injection of 10 mg/kg body weight caused increased respiration, emesis, and a convulsion, 20 mg/kg body weight resulted in mortality in 3 of 4 pigs, and 30 mg/kg body weight caused the death of all 4 pigs tested. Injection of 4.5 and 5.6 mg/kg body weight intravenously followed by epinephrine, 1mL (1:1000) intravenously 2 to 6 times, resulted in death of all pigs injected. Pigs given 4.5 mg/kg and 5.6 mg/kg body weight intravenously with no epinephrine all survived.

These results suggest intravenous epinephrine may be contraindicated.

Results of genetic toxicology studies were all negative. Results of teratology and reproduction studies in rats were negative.
The no effect level in dogs after daily oral doses for up to one year is 4 mg/kg of body weight.

Storage Conditions: Store at or below 86°F (30°C). Protect from direct sunlight. Use within 84 days of first puncture. Store upright between product dispensing. Disconnect and clean dosing equipment for storing as per manufacturer's instructions.
Conservar a 86 °F (30 °C). Proteger de la luz solar directa. Usar dentro de los 84 días de la primera punción. Guardar en posición vertical entre cada suministro del producto. Desconectar y limpiar el dispositivo de dosificación para el almacenamiento según las instrucciones del fabricante.

To report adverse effects, access medical information, or obtain additional product information, call 1-800-428-4441.

How Supplied: Micotil (tilmicosin injection) is supplied in 250 mL multi-dose amber glass bottles in a non-removable polymer protector.

Manufactured for: **Elanco US, Inc. Greenfield, IN 46140, USA**

Revised: 09/2021

Baytril® 100

(enrofloxacin)

100 mg/mL Antimicrobial Injectable Solution

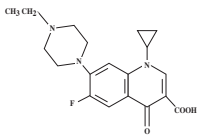
For Subcutaneous Use In Beef Cattle And Non-Lactating Dairy Cattle
Not For Use In Female Dairy Cattle 20 Months Of Age Or Older
Or In Calves To Be Processed For Veal

CAUTION:
Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.
Federal (U.S.A.) law prohibits the extra-label use of this drug in food-producing animals.

PRODUCT DESCRIPTION:
Baytril® 100 is a sterile, ready-to-use injectable antimicrobial solution that contains enrofloxacin, a broad-spectrum fluoroquinolone antimicrobial agent.
Each mL of Baytril® 100 contains 100 mg of enrofloxacin. Excipients are L-arginine base 200 mg, n-butyl alcohol 30 mg, benzyl alcohol (as a preservative) 20 mg and water for injection q.s.

CHEMICAL NOMENCLATURE AND STRUCTURE:
1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid.

INDICATIONS:
Cattle - Single-Dose Therapy: Baytril® 100 is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma bovis* in beef and non-lactating dairy cattle; and for the control of BRD in beef and non-lactating dairy cattle at high risk of developing BRD associated with *M. haemolytica, P. multocida, H. somni* and *M. bovis*.
Cattle - Multiple-Day Therapy: Baytril® 100 is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni* in beef and non-lactating dairy cattle.



DOSAGE AND ADMINISTRATION:
Baytril® 100 provides flexible dosages and durations of therapy.
Baytril® 100 may be administered as a single dose for one day for treatment and control of BRD, or for multiple days for BRD treatment. Selection of the appropriate dose and duration of therapy for BRD treatment in cattle should be based on an assessment of the severity of the disease, pathogen susceptibility and clinical response.
Cattle:
Single-Dose Therapy (BRD Treatment): Administer, by subcutaneous injection, a single dose of 7.5-12.5 mg/kg of body weight (3.4-5.7 mL/100 lb).
Multiple-Day Therapy (BRD Treatment): Administer daily, a subcutaneous dose of 2.5-5 mg/kg of body weight (1.1-2.3 mL/100 lb). Treatment should be repeated at 24-hour intervals for three days. Additional treatments may be given on Days 4 and 5 to animals that have shown clinical improvement but not total recovery.
Single-Dose Therapy (BRD Control): Administer, by subcutaneous injection, a single dose of 7.5 mg/kg of body weight (3.4 mL/100 lb).
Examples of conditions that may contribute to calves being at high risk of developing BRD include, but are not limited to, the following:

- Transportation with animals from two or more farm origins.
- An extended transport time with few to no rest stops.
- An environmental temperature change of ≥30°F during transportation.
- A ≥30°F range in temperature fluctuation within a 24-hour period.
- Exposure to wet or cold weather conditions.
- Excessive shrink (more than would be expected with a normal load of cattle).
- Stressful arrival processing procedures (e.g., castration or dehorning).
- Exposure within the prior 72 hours to animals showing clinical signs of BRD.

Administered dose volume should not exceed 20 mL per injection site.

Table 1 – Baytril® 100 Dose and Treatment Schedule for Cattle*

Weight (lb)	Treatment		Control
	Single-Dose Therapy 7.5 - 12.5 mg/kg Dose Volume (mL)	Multiple-Day Therapy 2.5 - 5.0 mg/kg Dose Volume (mL)	Single-Dose Therapy 7.5 mg/kg Dose Volume (mL)
100	3.5 - 5.5	1.5 - 2.0	3.5
200	7.0 - 11.0	2.5 - 4.5	7.0
300	10.5 - 17.0	3.5 - 6.5	10.5
400	14.0 - 22.5	4.5 - 9.0	14.0
500	17.0 - 28.5	5.5 - 11.5	17.0
600	20.5 - 34.0	7.0 - 13.5	20.5
700	24.0 - 39.5	8.0 - 16.0	24.0
800	27.5 - 45.5	9.0 - 18.0	27.5
900	31.0 - 51.0	10.0 - 20.5	31.0
1000	34.0 - 57.0	11.0 - 23.0	34.0
1100	37.5 - 62.5	12.5 - 25.0	37.5

*Dose volumes have been rounded to the nearest 0.5 mL within the dose range.

RESIDUE WARNINGS:
Cattle: Animals intended for human consumption must not be slaughtered within 28 days from the last treatment. This product is not approved for 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 for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

HUMAN WARNINGS:
Not for use in humans. Keep out of reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with copious amounts of water for 15 minutes. In case of dermal contact, wash skin with soap and water. Consult a physician if irritation persists following ocular or dermal exposures. Individuals with a history of hypersensitivity to quinolones should avoid this product. In humans, there is a risk of user photosensitization within a few hours after excessive exposure to quinolones. If excessive accidental exposure occurs, avoid direct sunlight. For customer service or to obtain product information, including a Safety Data Sheet, call 1-800-633-3796. For medical emergencies or to report adverse reactions, call 1-800-422-9874.

PRECAUTIONS:
The effects of enrofloxacin on cattle reproductive performance, pregnancy and lactation have not been adequately determined. Subcutaneous injection in cattle can cause a transient local tissue reaction that may result in trim loss of edible tissue at slaughter. Baytril® 100 contains different excipients than other Baytril® products. The safety and efficacy of this formulation in species other than cattle have not been determined. Quinolone-class drugs should be used with caution in animals with known or suspected Central Nervous System (CNS) disorders. In such animals, quinolones have, in rare instances, been associated with CNS stimulation which may lead to convulsive seizures. Quinolone-class drugs have been shown to produce erosions of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species. See Animal Safety section for additional information.

ADVERSE REACTIONS:
No adverse reactions were observed during clinical trials.
For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/reportanimalae.

MICROBIOLOGY:
Enrofloxacin is bactericidal and exerts its antibacterial effect by inhibiting bacterial DNA gyrase (a type II topoisomerase) thereby preventing DNA supercoiling and replication which leads to cell death.[1] Enrofloxacin is active against Gram-negative and Gram-positive bacteria.

EFFECTIVENESS:
Cattle: A total of 845 calves with naturally-occurring BRD were treated with Baytril® 100 in eight field trials located in five cattle-feeding states. Response to treatment was compared to non-treated controls. Single-dose and multiple-day therapy regimens were evaluated. BRD and mortality were significantly reduced in enrofloxacin-treated calves. No adverse reactions were reported in treated animals.
The effectiveness of Baytril® 100 for the control of respiratory disease in cattle at high risk of developing BRD was evaluated in a six-location study in the U.S. and Canada. A total of 1,150 crossbred beef calves at high risk of developing BRD were enrolled in the study. Baytril® 100 (7.5 mg/kg BW) or an equivalent volume of sterile saline was administered as a single subcutaneous injection within two days after arrival. Cattle were observed daily for clinical signs of BRD and were evaluated for success on Day 14 post-treatment. Treatment success in the Baytril® 100 group (497/573, 87.83%) was significantly higher ($P = 0.0013$) than success in the saline control group (455/571, 80.92%). In addition, there were more treatment successes ($n = 13$) than failures ($n = 3$) in the group of animals positive for *M. bovis* on Day 0 that were treated with Baytril® 100. No product-related adverse reactions were reported.

TOXICOLOGY:
The oral LD50 for laboratory rats was greater than 5000 mg/kg of body weight. Ninety-day feeding studies in dogs and rats revealed no observable adverse effects at treatment rates of 3 and 40 mg/kg respectively. Chronic studies in rats and mice revealed no observable adverse effects at 5.3 and 323 mg/kg respectively. There was no evidence of carcinogenic effect in laboratory animal models. A two-generation rat reproduction study revealed no effect with 10 mg/kg treatments. No teratogenic effects were observed in rabbits at doses of 25 mg/kg or in rats at 50 mg/kg.

ANIMAL SAFETY:
Cattle: Safety studies were conducted in feeder calves using single doses of 5, 15 and 25 mg/kg for 15 consecutive days and 50 mg/kg for 5 consecutive days. No clinical signs of toxicity were observed when a dose of 5 mg/kg was administered for 15 days. Clinical signs of depression, incoordination and muscle fasciculation were observed in calves when doses of 15 or 25 mg/kg were administered for 10 to 15 days. Clinical signs of depression, inappetance and incoordination were observed when a dose of 50 mg/kg was administered for 3 days. No drug-related abnormalities in clinical pathology parameters were identified. No articular cartilage lesions were observed after examination of stifle joints from animals administered 25 mg/kg for 15 days.
A safety study was conducted in 23-day-old calves using doses of 5, 15 and 25 mg/kg for 15 consecutive days. No clinical signs of toxicity or changes in clinical pathology parameters were observed. No articular cartilage lesions were observed in the stifle joints at any dose level at 2 days and 9 days following 15 days of drug administration.
An injection site study conducted in feeder calves demonstrated that the formulation may induce a transient reaction in the subcutaneous tissue and underlying muscle. No painful responses to administration were observed.

STORAGE CONDITIONS: Protect from direct sunlight. Do not refrigerate or freeze. Store at 20-30ºC (68-86ºF), excursions permitted up to 40ºC (104ºF). Precipitation may occur due to cold temperature. To redissolve, warm and then shake the vial.

HOW SUPPLIED:
Baytril® 100:

100 mg/mL	100 mL Bottle
100 mg/mL	250 mL Bottle
100 mg/mL	500 mL Bottle

REFERENCES:
1. Hooper, D. C., Wolfson, J. S., Quinolone Antimicrobial Agents, 2nd ed, 59 - 75, 1993.
For customer service or to obtain product information, including a Safety Data Sheet, call 1-800-633-3796.
For medical emergencies or to report adverse reactions, call 1-800-422-9874.

LV2010
October, 2020

Baytril® 100
Approved by FDA under NADA # 141-068
Elanco US Inc
Shawnee, KS 66216 USA
Made in Germany

Elanco™

FULL PRESCRIBING INFORMATION FOR USE IN CATTLE ONLY

Elanco™ Increxxa™ (tulathromycin injection)

Injectable Solution

Antibiotic

100 mg of tulathromycin/mL

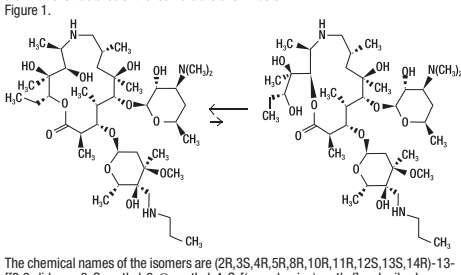
For use in beef cattle (including suckling calves), non-lactating dairy cattle (including dairy calves), veal calves, and swine. Not for use in female dairy cattle 20 months of age or older.

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

DESCRIPTION

Increxxa Injectable Solution is a ready-to-use sterile parenteral preparation containing tulathromycin, a semi-synthetic macrolide antibiotic of the subclass triamilide. Each mL of Increxxa contains 100 mg of tulathromycin, 500 mg propylene glycol, 19.2 mg citric acid and 5 mg monothioglycerol. Sodium hydroxide or hydrochloric acid may be added to adjust pH. Increxxa consists of an equilibrated mixture of two isomeric forms of tulathromycin in a 9:1 ratio. Structures of the isomers are shown below.

Figure 1.



The chemical names of the isomers are (2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino) methyl]-α-L-ribo-hexopyrano-syl]oxy]-2-ethyl-3,4,10- trihydroxy-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]-oxy]-1-oxa-6-azacyclopentadecan-15-one and (2R,3R,6R,8R,9R,10S,11S,12R)-11-[[2,6-dideoxy-3-C-methyl- 3-O-methyl-4-C-[(propylamino)methyl]-α-L-ribo-hexopyrano-syl]oxy]-2-[(1R,2R)-1,2-dihydroxy-1-methylbutyl]-8-hydroxy-3,6,8,10,12-pentamethyl-9-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]oxy]-1-oxa-4-azacyclotridecan-13-one, respectively.

INDICATIONS

Beef and Non-Lactating Dairy Cattle

BRD – Increxxa Injectable Solution is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, 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*.

IBK – Increxxa Injectable Solution is indicated for the treatment of infectious bovine keratoconjunctivitis (IBK) associated with *Moraxella bovis*.

Foot Rot – Increxxa Injectable Solution is indicated for the treatment of bovine foot rot (interdigital necrobacillosis) associated with *Fusobacterium necrophorum* and *Porphyromonas levii*.

Suckling Calves, Dairy Calves, and Veal Calves

BRD – Increxxa Injectable Solution is indicated for the treatment of BRD associated with *M. haemolytica*, *P. multocida*, *H. somni*, and *M. bovis*.

DOSAGE AND ADMINISTRATION

Cattle

Inject subcutaneously as a single dose in the neck at a dosage of 2.5 mg/kg (1.1 mL/100 lb) body weight (BW). Do not inject more than 10 mL per injection site.

Table 1. Increxxa Cattle Dosing Guide

Animal Weight (Pounds)	Dose Volume (mL)
100	1.1
200	2.3
300	3.4
400	4.5
500	5.7
600	6.8
700	8.0
800	9.1
900	10.2
1000	11.4

CONTRAINDICATIONS

The use of Increxxa Injectable Solution is contraindicated in animals previously found to be hypersensitive to the drug.

WARNINGS

FOR USE IN ANIMALS ONLY.

NOT FOR HUMAN USE.

KEEP OUT OF REACH OF CHILDREN.

NOT FOR USE IN CHICKENS OR TURKEYS.

RESIDUE WARNINGS

Cattle

Cattle intended for human consumption must not be slaughtered within 18 days from the last treatment. This drug 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.

PRECAUTIONS

Cattle

The effects of Increxxa on bovine reproductive performance, pregnancy, and lactation have not been determined. Subcutaneous injection can cause a transient local tissue reaction that may result in trim loss of edible tissue at slaughter.

ADVERSE REACTIONS

Cattle

In one BRD field study, two calves treated with tulathromycin injection at 2.5 mg/kg BW exhibited transient hypersalivation. One of these calves also exhibited transient dyspnea, which may have been related to pneumonia.

POST APPROVAL EXPERIENCE

The following adverse events are based on post approval adverse drug experience reporting. Not all adverse events are reported to the FDA CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of reporting frequency in cattle: Injection site reactions and anaphylaxis/anaphylactoid reactions. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY

At physiological pH, tulathromycin (a weak base) is approximately 50 times more soluble in hydrophilic than hydrophobic media. This solubility profile is consistent with the extracellular pathogen activity typically associated with the macrolides.[1] Markedly higher tulathromycin concentrations are observed in the lungs as compared to the plasma. The extent to which lung concentrations represent free (active) drug was not examined. Therefore, the clinical relevance of these elevated lung concentrations is undetermined. Although the relationship between tulathromycin and the characteristics of its antimicrobial effects has not been characterized, as a class, macrolides tend to be primarily bacteriostatic, but may be bactericidal against some pathogens.[2] They also tend to exhibit concentration independent killing; the rate of bacterial eradication does not change once serum drug concentrations reach 2 to 3 times the minimum inhibitory concentration (MIC) of the targeted pathogen. Under these conditions, the time that serum concentrations remain above the MIC becomes the major determinant of antimicrobial activity. Macrolides also exhibit a post-antibiotic effect (PAE), the duration of which tends to be both drug and pathogen dependent. In general, by increasing the macrolide concentration and the exposure time, the PAE will increase to some maximal duration. Of the two variables, concentration and exposure time, drug concentration tends to be the most powerful determinant of the duration of PAE. Tulathromycin is eliminated from the body primarily unchanged via biliary excretion.

1 *Carbon, C. 1998. Pharmacodynamics of Macrolides, Azalides, and Streptogramins: Effect on Extracellular Pathogens. Clin. Infect. Dis.,* ***27****:28-32.*

2 *Nightingale, C.J. 1997. Pharmacokinetics and Pharmacodynamics of Newer Macrolides. Pediatr. Infect. Dis. J.,* ***16****:438-443.*

Cattle

Following subcutaneous administration into the neck of feeder calves at a dosage of 2.5 mg/kg BW, tulathromycin is rapidly and nearly completely absorbed. Peak plasma concentrations generally occur within 15 minutes after dosing and product relative bioavailability exceeds 90%. Total systemic clearance is approximately 170 mL/hr/kg. Tulathromycin distributes extensively into body tissues, as evidenced by volume of distribution values of approximately 11 L/kg in healthy ruminating calves.[3] This extensive volume of distribution is largely responsible for the long elimination half-life of this compound [approximately 2.75 days in the plasma (based on quantifiable terminal plasma drug concentrations) versus 8.75 days for total lung concentrations (based on data from healthy animals)]. Linear pharmacokinetics are observed with subcutaneous doses ranging from 1.27 mg/kg BW to 5.0 mg/kg BW. No pharmacokinetic differences are observed in castrated male versus female calves.

3 *Clearance and volume estimates are based on intersubject comparisons of 2.5 mg/kg BW administered by either subcutaneous or intravenous injection.*

MICROBIOLOGY

Cattle

Tulathromycin has demonstrated *in vitro* activity against *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*, four pathogens associated with BRD; against *Moraxella bovis* associated with IBK; and against *Fusobacterium necrophorum* and *Porphyromonas levii* associated with bovine foot rot. The MICs of tulathromycin against indicated BRD and IBK pathogens were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLSI, M31-A2). The MICs against foot rot pathogens were also determined using methods recommended by the CLSI (M11-A6). All MIC values were determined using the 9:1 isomer ratio of this compound.

BRD - The MICs of tulathromycin were determined for BRD isolates obtained from calves enrolled in therapeutic and at-risk field studies in the U.S. in 1999. In the therapeutic 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 at-risk 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. The results are shown in Table 3.

IBK - The MICs of tulathromycin were determined for *Moraxella bovis* isolates obtained from calves enrolled in IBK field studies in the U.S. in 2004. Isolates were obtained from pre-treatment conjunctival swabs of calves with clinical signs of IBK enrolled in the tulathromycin injection and saline-treated groups. The results are shown in Table 3.

Foot Rot - The MICs of tulathromycin were determined for *Fusobacterium necrophorum* and *Porphyromonas levii* obtained from cattle enrolled in foot rot field studies in the U.S. and Canada in 2007. Isolates were obtained from pre-treatment interdigital biopsies and swabs of cattle with clinical signs of foot rot enrolled in the tulathromycin injection and saline-treated groups. The results are shown in Table 3.

Table 3. Tulathromycin minimum inhibitory concentration (MIC) values* for indicated pathogens isolated from field studies evaluating BRD and IBK in the U.S. and from foot rot field studies in the U.S. and Canada.

Indicated pathogen	Date isolated	No. of isolates	MIC_{50} ** (µg/mL)	MIC_{90} ** (µg/mL)	MIC range (µg/mL)
Mannheimia haemolytica	1999	642	2	2	0.5 to 64
Pasteurella multocida	1999	221	0.5	1	0.25 to 64
Histophilus somni	1999	36	4	4	1 to 4
Mycoplasma bovis	1999	43	0.125	1	≤ 0.063 to > 64
Moraxella bovis	2004	55	0.5	0.5	0.25 to 1
Fusobacterium necrophorum	2007	116	2	64	≤ 0.25 to > 128
Porphyromonas levii	2007	103	8	128	≤ 0.25 to > 128

* The correlation between *in vitro* susceptibility data and clinical effectiveness is unknown.
** The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

EFFECTIVENESS

Cattle

BRD – In a multi-location field study, 314 calves with naturally occurring BRD were treated with tulathromycin injection. Responses to treatment were compared to saline-treated controls. A cure was defined as a calf with normal attitude/activity, normal respiration, and a rectal temperature of ≤ 104°F on Day 14. The cure rate was significantly higher ($P \leq 0.05$) in tulathromycin injection-treated calves (78%) compared to saline-treated calves (24%). There were two BRD-related deaths in the tulathromycin injection-treated calves compared to nine BRD-related deaths in the saline-treated calves. Fifty-two tulathromycin injection-treated calves and 27 saline-treated calves from the multi-location field BRD treatment study had *Mycoplasma bovis* identified in cultures from pre-treatment nasopharyngeal swabs. Of the 52 tulathromycin injection-treated calves, 37 (71.2%) calves were categorized as cures and 15 (28.8%) calves were categorized as treatment failures. Of the 27 saline-treated calves, 4 (14.8%) calves were categorized as cures and 23 (85.2%) calves were treatment failures.

A Bayesian meta-analysis was conducted to compare the BRD treatment success rate in young calves (calves weighing 250 lbs or less and fed primarily a milk-based diet) treated with tulathromycin injection to the success rate in older calves (calves weighing more than 250 lbs and fed primarily a roughage and grain-based diet) treated with tulathromycin injection. The analysis included data from four BRD treatment effectiveness studies conducted for the approval of tulathromycin injection in the U.S. and nine contemporaneous studies conducted in Europe. The analysis showed that the BRD treatment success rate in young calves was at least as good as the BRD treatment success rate in older calves.

As a result, tulathromycin injection is considered effective for the treatment of BRD associated with *M. haemolytica*, *P. multocida*, *H. somni*, and *M. bovis* in suckling calves, dairy calves, and veal calves.

In another multi-location field study with 399 calves at high risk of developing BRD, administration of tulathromycin injection resulted in a significantly reduced incidence of BRD (11%) compared to saline-treated calves (59%). Effectiveness evaluation was based on scored clinical signs of normal attitude/activity, normal respiration, and a rectal temperature of ≤ 104°F on Day 14. There were no BRD-related deaths in the tulathromycin injection-treated calves compared to two BRD-related deaths in the saline-treated calves.

Fifty saline-treated calves classified as non-responders in this study had *Mycoplasma bovis* identified in cultures of post-treatment nasopharyngeal swabs or lung tissue.

Two induced infection model studies were conducted to confirm the effectiveness of tulathromycin injection against *Mycoplasma bovis*. A total of 166 calves were inoculated intratracheally with field strains of *Mycoplasma bovis*. When calves became pyrexic and had abnormal respiration scores, they were treated with either tulathromycin injection (2.5 mg/kg BW) subcutaneously or an equivalent volume of saline. Calves were observed for signs of BRD for 14 days post-treatment, then were euthanized and necropsied. In both studies, mean lung lesion percentages were statistically significantly lower in the tulathromycin injection-treated calves compared with saline-treated calves (11.3% vs. 28.9%, $P = 0.0001$ and 15.0% vs. 30.7%, $P < 0.0001$).

IBK – Two field studies were conducted evaluating tulathromycin injection for the treatment of IBK associated with *Moraxella bovis* in 200 naturally-infected calves. The primary clinical endpoint of these studies was cure rate, defined as a calf with no clinical signs of IBK and no corneal ulcer, assessed on Days 5, 9, 13, 17, and 21. Time to improvement, defined as the first day on which a calf had no clinical signs of IBK in both eyes, provided that those scores were maintained at the next day of observation, was assessed as a secondary variable. At all time points, in both studies, the cure rate was significantly higher ($P < 0.05$) for tulathromycin injection-treated calves compared to saline-treated calves. Additionally, time to improvement was significantly less ($P < 0.0001$) in both studies for tulathromycin injection-treated calves compared to saline-treated calves.

Foot Rot - The effectiveness of tulathromycin injection for the treatment of bovine foot rot was evaluated in 170 cattle in two field studies. Cattle diagnosed with bovine foot rot were enrolled and treated with a single subcutaneous dose of tulathromycin injection (2.5 mg/kg BW) or an equivalent volume of saline. Cattle were clinically evaluated 7 days after treatment for treatment success, which was based on defined decreases in lesion, swelling, and lameness scores. In both studies, the treatment success percentage was statistically significantly higher in tulathromycin injection-treated calves compared with saline-treated calves (60% vs. 8%, $P < 0.0001$ and 83.3% vs. 50%, $P = 0.0088$).

ANIMAL SAFETY

Cattle

Safety studies were conducted in feeder calves receiving a single subcutaneous dose of 25 mg/kg BW, or 3 weekly subcutaneous doses of 2.5, 7.5, or 12.5 mg/kg BW. In all groups, transient indications of pain after injection were seen, including head shaking and pawing at the ground. Injection site swelling, discoloration of the subcutaneous tissues at the injection site and corresponding histopathologic changes were seen in animals in all dosage groups. These lesions showed signs of resolving over time. No other drug-related lesions were observed macroscopically or microscopically. An exploratory study was conducted in feeder calves receiving a single subcutaneous dose of 10, 12.5, or 15 mg/kg BW. Macroscopically, no lesions were observed. Microscopically, minimal to mild myocardial degeneration was seen in one of six calves administered 12.5 mg/kg BW and two of six calves administered 15 mg/kg BW.

A safety study was conducted in preruminant calves 13 to 27 days of age receiving 2.5 mg/kg BW or 7.5 mg/kg BW once subcutaneously. With the exception of minimal to mild injection site reactions, no drug-related clinical signs or other lesions were observed macroscopically or microscopically.

STORAGE CONDITIONS

Store below 25°C (77°F), with excursions up to 40°C (104°F).

100 mL: Use within 2 months of first puncture and puncture a maximum of 67 times. If more than 67 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.

250 mL: Use within 2 months of first puncture and puncture a maximum of 100 times. If more than 100 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

Increxxa (tulathromycin injection) Injectable Solution is available in the following package sizes:
100 mL vial
250 mL vial
500 mL vial

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet, contact Elanco at 1-800-422-9874. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

Approved by FDA under ANADA # 200-666

Product of China.

Manufactured by: Elanco US Inc, Shawnee, KS 66216

October, 2020

TAKE TIME

OBSERVE LABEL DIRECTIONS

Elanco™

90198370 LV2011

Loncor™ 300

(florfenicol)

300 mg/mL 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.

DESCRIPTION
LONCOR 300 Injectable Solution is a solution of the synthetic antibiotic florfenicol. Each milliliter of sterile LONCOR 300 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
LONCOR 300 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): LONCOR 300 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, LONCOR 300 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: LONCOR 300 should be administered by a single subcutaneous injection to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 lbs).

LONCOR 300 DOSAGE GUIDE

ANIMAL WEIGHT (lbs)	IM LONCOR 300 DOSAGE 3.0 mL/100 lb Body Weight (mL)	SC LONCOR 300 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

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.

RECOMMENDED INJECTION LOCATION

Do not inject more than 10 mL per injection site.

Do not administer more than 10 mL at each site. The injection should be given only in the neck.

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 Elanco at 1-800-428-4441. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or 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 was evaluated in feeder calves following single intramuscular (IM) administration at the recommended dose of 20 mg/kg body weight. Florfenicol was also administered intravenously (IV) to the same cattle in order to calculate the volume of distribution, clearance, and percent bioavailability[1] (Table 1).

Parameter	Median	Range
C_{max} (µg/mL)	3.07*	1.43 - 5.60
T_{max} (hr)	3.33	0.75 - 8.00
T 1/2 (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

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

* harmonic mean
** mean value
*** following IV administration
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
Cl_t Total body clearance

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).

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
Histophilus 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.
** 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 administered at the recommended dose on feed consumption. Although a transient decrease in feed consumption was observed, florfenicol administration had no long-term effect on body weight, rate of gain, or feed consumption.

STORAGE INFORMATION
Store below 30°C (86°F). Protect from light when not in use.
Once opened, use contents within 6 months.
The solution is light yellow to straw colored. Color does not affect potency.

HOW SUPPLIED
Loncor 300 is packaged in 250 mL and 500 mL 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.

Made in China

Approved by FDA under ANADA # 200-582
Revised: April 2023

LONCOR 300

Manufactured for:
Elanco US Inc.
Greenfield, IN 46140 U.S.A.

Elanco™