Enroflox® 100
(enrofloxacin)

APPROVED FOR SINGLE-DOSE BRD TREATMENT & CONTROL

Enroflox® 100
(enrofloxacin)

Federal law restricts this drug to use by or on the order of a licensed veterinarian. Federal law prohibits the extra-label use of this drug in food-producing animals. Cattle 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 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. Use with caution in animals with known or suspected CNS disorders. Observe label directions and withdrawal times. See product labeling for full product information.

www.norbrookinc.com

FOR VETERINARY USE ONLY

Norbrook®

BEEF PRODUCERS ASKED FOR IT, NORBROOK DELIVERS...

Enroflox® 100
Approved for Single Dose & Multi-Day Treatment and Control

- **Same active ingredient and dosing regimen as Baytril®100 Injection in beef and non-lactating dairy cattle**
- **FDA-Approved for the treatment and control of Bovine Respiratory Disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni* and now *Mycoplasma bovis* in beef and non-lactating dairy cattle**
- **Easy-to-inject, safe and effective**

Enroflox® 100 . . . Three Convenient Dosing and Treatment Options

Single-Dose Therapy (BRD Treatment):

Enroflox 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.

Multiple-Day Therapy (BRD Treatment):

Enroflox 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.

Single-Dose Therapy (BRD Control in High-Risk Cattle):

Enroflox 100 is approved 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*. Administer a single dose to cattle at high risk of BRD due to stresses including transportation, extreme environmental conditions and processing (e.g. castration, dehorning).

Enroflox® 100 Dosing Chart*

	Treatment		Control
	Single-Dose Therapy 7.5-12.5 mg/kg	Mutiple-Day Therapy 2.5-5.0 mg/kg	Single-Dose Therapy 7.5 mg/kg
Weight (lb)	Dose Volume (mL)	Dose Volume (mL)	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. Administerd dose volume should not exceed 20 mL per injection site.

Enroflox® 100
(enrofloxacin)

What is Enroflox® 100 Injection?

Enroflox 100 is an FDA-approved sterile, ready-to-use injectable antimicrobial solution that contains enrofloxacin, a broad-spectrum fluoroquinolone antimicrobial agent.

Enroflox 100 is approved for the treatment and control of Bovine Respiratory Disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and now *Mycoplasma bovis* in beef and non-lactating dairy cattle.

Enroflox 100 is also approved for use in dairy replacement heifers < 20 months of age.

What is enrofloxacin?

Enrofloxacin, the active ingredient in **Enroflox 100**, is a fluoroquinolone antibiotic. Fluoroquinolones interfere with bacterial DNA replication. Enrofloxacin exhibits a broad spectrum of antibacterial activity against both Gram-positive and Gram-negative bacteria.

How does Enroflox® 100 compare to Baytril® 100?

Enroflox 100 has the same active ingredient (enrofloxacin) and dosing regimen as Baytril® 100 in beef and non-lactating dairy cattle.

How is Enroflox® 100 supplied?

Enroflox 100 is supplied in convenient and cost competitive 100 mL, 250 mL and 500 mL bottles to fit any size operation.

How is Enroflox® 100 administered in cattle?

Enroflox 100 can be administered three ways in beef 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 (3.4mL/100 lb.).

Selection of the appropriate dose and duration of therapy should be based on an assessment of the severity of disease, pathogen susceptibility and clinical response. **Enroflox 100** dose volume should not exceed 20 mL per injection site.

How quickly does Enroflox® 100 start killing BRD-causing bacteria?

Enroflox 100 is concentration-dependent, delivering effective therapeutic drug concentrations with a single dose. In vitro*, enrofloxacin kills 97% of BRD-causing bacteria in 1-2 hours[1,2]

* The clinical significance of in vitro data has not been demonstrated.

1 Blondeau J.M., Borsos S., Blondeau L.D., Blondeau B.J., Hesje C. The killing of clinical isolates of *Mannheimia haemolytica* (MH) by enrofloxacin (ENR) using minimum inhibitory and mutant prevention drug concentrations and over a range of bacterial inocula. In: ASM Conference on Pasteurellaceae; 2005 October 23-26; Kohala Coast, Big Island, Hawaii: American Society of Microbiology; 2005. Abstract B12.

2 Blondeau J.M., Borsos S.D., Hesje C.H., Blondeau L.D., Blondeau B.J. Comparative Killing of Bovine Isolates of *Mannheimia haemolytica* by Enrofloxacin, Florfenicol Tilmicosin and Tulathromycin Using the Measured Minimum Inhibitory Concentration (MIC) and Mutant Prevention Concentration (MPC) Drug Values. In: International Meeting of Emerging Diseases and Surveillance (IMED), Vienna, Austria, February 23-25, 2007. Figures 8-10.

Observe label directions and withdrawal. See product labeling (following page) for full product information.

ANADA 200-495, Approved by FDA

Enroflox® 100
(enrofloxacin)

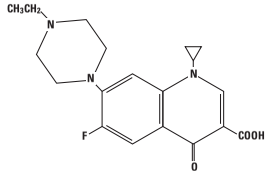
100 mg/mL Antimicrobial Injectable Solution

For Subcutaneous Use in Beef Cattle, Non-Lactating Dairy Cattle and Swine Only.
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:
Enroflox® 100 is a sterile, ready-to-use injectable antimicrobial solution that contains enrofloxacin, a broad-spectrum fluoroquinolone antimicrobial agent. Each mL of Enroflox 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: Enroflox 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: Enroflox 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.

Swine: Enroflox 100 is indicated for the treatment and control of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae, Pasteurella multocida, Haemophilus parasuis* and *Streptococcus suis*.

DOSAGE AND ADMINISTRATION:
Enroflox 100 provides flexible dosages and durations of therapy.
Enroflox 100 may be administered as a single dose for one day for treatment and control of BRD (cattle) and SRD (swine), or for multiple days for BRD treatment (cattle). 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.
For the 500 mL bottle, do not enter the vial with a needle more than 56 times or enter the vial with a dosage delivery device more than 4 times. Any product remaining after these maximum numbers of entries should be discarded.

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 for 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 – Enroflox 100 Dose and Treatment Schedule for Cattle*

	Treatment		Control
WEIGHT (lb)	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.

Swine:
Administer, by subcutaneous (behind the ear) injection, a single dose of 7.5 mg/kg of body weight (3.4 mL/100 lb).

Administered dose volume should not exceed 5 mL per injection site.

Table 2 – Enroflox 100 Dose and Treatment Schedule for Swine

WEIGHT (lb)	Dose Volume (mL)
50	1.7
100	3.4
150	5.1
200	6.8
250	8.5

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.
Swine: Animals intended for human consumption must not be slaughtered within 5 days of receiving a single-injection dose.

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, to obtain a copy of the Safety Data Sheet (SDS) or to report adverse reactions, call Norbrook at 1-866-591-5777.

PRECAUTIONS:
The effects of enrofloxacin on cattle or swine reproductive performance, pregnancy and lactation have not been adequately determined.
The long-term effects on articular joint cartilage have not been determined in pigs above market weight.
Subcutaneous injection can cause a transient local tissue reaction that may result in trim loss of edible tissue at slaughter.
Enroflox 100 contains different excipients than other enrofloxacin products. The safety and efficacy of this formulation in species other than cattle and swine 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 adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

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 enrofloxacin injection 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 enrofloxacin injection 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. Enrofloxacin injection (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 enrofloxacin injection 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 enrofloxacin injection. No product-related adverse reactions were reported.

Swine: A total of 590 pigs were treated with enrofloxacin injection or saline in two separate natural infection SRD field trials. For the treatment of SRD, the success rate of enrofloxacin-treated pigs that were defined as "sick and febrile" (increased respiratory rate, labored or dyspneic breathing, depressed attitude and a rectal temperature ≥104.0°F) was statistically significantly greater than the success rate of saline-treated "sick and febrile" pigs. For the control of SRD, mean rectal temperature, mortality (one trial) and morbidity were statistically significantly lower for enrofloxacin-treated pigs in pens containing a percentage of "sick and febrile" pigs compared to saline-treated pigs.

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, inappetence 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.

Swine: A safety study was conducted in 32 pigs weighing approximately 57 kg (125 lb) using single doses of 5, 15, or 25 mg/kg daily for 15 consecutive days. Incidental lameness of short duration was observed in all groups, including the saline-treated controls. Musculoskeletal stiffness was observed following the 15 and 25 mg/kg treatments with clinical signs appearing during the second week of treatment. Clinical signs of lameness improved after treatment ceased and most animals were clinically normal at necropsy.

A second study was conducted in two pigs weighing approximately 23 kg (50 lb), treated with 50 mg/kg for 5 consecutive days. There were no clinical signs of toxicity or pathological changes.

An injection site study conducted in pigs demonstrated that the formulation may induce a transient reaction in the subcutaneous tissue. No painful responses to administration were observed.

STORAGE CONDITIONS:
Protect from direct sunlight. Do not refrigerate or freeze. Store below 77°F (25°C). Precipitation may occur due to cold temperature. To redissolve, warm and then shake the vial.

HOW SUPPLIED:
Enroflox 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, to obtain a copy of the Safety Data Sheet (SDS) or to report adverse reactions, call Norbrook at 1-866-591-5777.

Restricted Drug - California. Use Only as Directed.

Made in the UK.

TAKE TIME
OBSERVE LABEL DIRECTIONS

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

September 2016
101670I02

Norbrook®