

A New

# BRD THERAPY

For Dairy Replacement Heifers

Question & Answer  
Guide



Injectable  
**Baytril® 100**  
(enrofloxacin)

Right the first time®



## Q Why is Baytril® 100 (enrofloxacin) now entering the dairy replacement heifer market?

A There is no time to wait when a calf has BRD, especially valuable dairy replacement heifers. Baytril 100 will help save the lives of dairy replacement heifers with BRD, and protect producers' investment.

Bovine veterinarians and producers trust and rely on Baytril 100 as the first line of defense to save the lives of cattle with bovine respiratory disease.

With FDA approval, dairy replacement heifers less than 20 months of age can now be treated and benefit from the fast-acting, broad-spectrum therapy Baytril 100 provides.

## Q What is Baytril® 100 (enrofloxacin)?

A Baytril® 100 (enrofloxacin) from Bayer Animal Health was the first Food and Drug Administration (FDA)-approved fluoroquinolone antimicrobial for use against bovine respiratory disease (BRD) in beef cattle and remains the fast-acting, broad-spectrum, first-line therapy on which bovine veterinarians and producers depend.

Baytril 100 helps save animals' lives by quickly killing the three major BRD-causing bacteria in a single dose and is concentration-dependent, not time-dependent, delivering therapeutic concentrations to the lungs in just 60 minutes<sup>1</sup> to clear the infection quickly.

## Q Is Baytril® 100 a new antibiotic?

A Baytril 100 has a 10-year history of performance in the beef cattle market and is field-tested and proven with more than 30 million animals treated in the United States alone. Baytril 100 is now available for use in dairy replacement heifers less than 20 months of age.

Not for use in dairy heifers greater than 20 months of age.

## Q How is Baytril® 100 different from other antimicrobials?

A Baytril 100 is bactericidal, while many other antibiotics are bacteriostatic. Bacteriostatic antibiotics do not kill bacteria immediately, but inhibit bacterial growth. The unique mode of action of Baytril 100 kills all three major BRD-causing bacteria in both the resting and growth phases of bacteria development – essentially killing the “heart” of the bacteria.

In addition, Baytril 100 is concentration-dependent, not time-dependent. Concentration-dependent therapies exert their effect by achieving high drug concentrations in relationship to the level required to kill the bacteria. Time-dependent drugs must sustain concentrations above the level required to inhibit bacteria growth over a longer period of time. Baytril 100 reaches therapeutic lung levels in just 60 minutes and peak killing concentration levels in only 4.5 hours.<sup>1</sup>

For use by or on the order of a licensed veterinarian.

**Q** What were the steps Bayer Animal Health took to get FDA approval for Baytril® 100 (enrofloxacin) in the dairy replacement heifer market?

**A** Iowa State University, Cornell University, and Bayer Animal Health collaborated to conduct an extensive quantitative Risk Assessment to determine any potential impact on food safety as a result of use in dairy replacement heifers. The FDA Center for Veterinary Medicine evaluated the Risk Assessment as the final step in the food safety evaluation process prior to approval.

Bayer Animal Health is proud of the safety and performance legacy of Baytril® 100 (enrofloxacin), which has been proven with more than 30 million animals treated in the U.S. over the past decade.

**Q** What is a Risk Assessment?

**A** A Risk Assessment is a qualitative and quantitative assessment of risk factors that could potentially impact human health. Typically, Risk Assessments take into consideration available data to evaluate, and quantify the potential risk associated with the use of a product. During a Risk Assessment, wide margins of safety are utilized when existing data are not available.

## What was the purpose and the result of the Risk Assessment?

The objective was to determine the probability of any potential impact on food safety in the United States.

According to the Risk Assessment, use of Baytril® 100 (enrofloxacin) in dairy heifers results in a near zero risk of additional human illness as indicated below.

### Risk Estimates:

One additional human case of campylobacter enteritis every 18 years

- Risk of 1 case of persistent symptoms in 3.8 billion

One additional human case of salmonella enteritis every 501 years

- Risk of 1 case of persistent symptoms in 105 billion

One additional human case of MDR salmonella enteritis every 292 years

- Risk of 1 case of persistent symptoms in 61 billion

During the Risk Assessment, many conservative assumptions and margins of safety were utilized when existing data were not available, giving the Risk Assessment a large margin of safety.

The safety of Baytril 100 is well documented. The product has been approved by the FDA for use in dairy replacement heifers as a BRD therapy because the Risk Assessment indicates risk estimates to public health at or near zero; and because Baytril 100 is an effective, lifesaving tool for producers and veterinarians.

**Q** Can Baytril® 100 (enrofloxacin) be used in lactating cows?

**A** No. Baytril 100 can not be used in lactating dairy cows. The additional FDA-approved label use of Baytril 100 is for the treatment of BRD in dairy heifers under 20 months of age.

**Q** What is Bayer Animal Health doing to support the proper use of Baytril® 100?

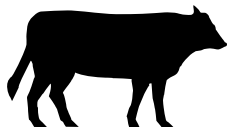
**A** Bayer Animal Health strongly encourages veterinarians and producers to familiarize themselves with and follow responsible antibiotic use guidelines. Antibiotics are lifesaving tools and are not a substitute for proper animal husbandry. Prudent use of antibiotics is beneficial for treated animals, public health, and the producer or veterinarian's business.

Do not use in calves to be processed for veal.



Extra-label use of this product in food-producing animals is prohibited.

# Baytril® 100 (enrofloxacin)



## 100 mg/mL Antimicrobial Injectable Solution

For 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:

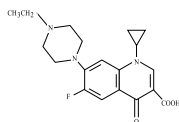
Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.  
Federal (U.S.A.) law prohibits the extra-label use of this drug in food-producing animals.

### PRODUCT DESCRIPTION:

Baytril® 100 is a sterile, ready-to-use injectable antimicrobial solution that contains enrofloxacin, a broad-spectrum fluoroquinolone antimicrobial agent. Therapeutic treatment with Baytril® 100 may be administered as a single-dose or as a multiple-day therapy. Each mL of Baytril® 100 contains 100 mg of enrofloxacin. Excipients are L-arginine base 200 mg, n-butyl alcohol 30 mg, benzyl alcohol (and 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-quinolincarboxylic acid.



### INDICATION:

Baytril® 100 is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* (previously *Haemophilus somnus*) 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 or for multiple days of therapy. 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.

**Single-Dose Therapy:** Administer once, a subcutaneous dose of 7.5 - 12.5 mg/kg of body weight (3.4 - 5.7 mL/100 lb).

**Multiple-Day Therapy:** Administer daily, a subcutaneous dose of 2.5 - 5.0 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.

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

### Baytril® 100 Dose and Treatment Schedule for Cattle\*

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

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

### RESIDUE WARNINGS:

Animals intended for human consumption must not be slaughtered within 28 days from the last treatment. Do not use in female dairy cattle 20 months of age or older. Use of enrofloxacin in this class of cattle may cause milk residues. 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:

**For use in animals only. Keep out of the 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 Material 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 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.

### 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. Enrofloxacin is active against Gram-negative and Gram-positive bacteria.

### EFFECTIVENESS:

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.

### 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:

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.

**STORAGE CONDITIONS:** Protect from direct sunlight. Do not refrigerate, freeze or store at or above 40°C (104°F). Precipitation may occur due to cold temperature. To redissolve, warm and then shake the vial.

### HOW SUPPLIED:

Baytril® 100:  
Code: 08711170-023699 100 mg/mL 100 mL Bottle  
Code: 08711278-032199 100 mg/mL 250 mL Bottle

### REFERENCES:

1. Hooper, D. C., Wolfson, J. S., *Quinolone Antimicrobial Agents*, 2<sup>nd</sup> ed, 59 - 75, 1993.  
U.S. Patent No. 4,670,444

For customer service or to obtain product information, including a Material Safety Data Sheet, call 1-800-633-3796.

For medical emergencies or to report adverse reactions, call 1-800-422-9874.

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NADA 141-068, Approved by FDA



**Bayer**

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Footnotes:

1. A Study to Compare the Plasma Pharmacokinetics of danofloxacin and enrofloxacin in Ruminating Cattle. Bayer Report 75646 (Bayer Study 151.603) ©2003 Bayer HealthCare LLC

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