



Baytril® 100 (enrofloxacin) Injectable Solution Technical Report



Clinical effectiveness of Baytril® 100 administered as a single injection of 7.5 mg/kg body weight for the treatment and control of naturally occurring bacterial respiratory disease in pigs.

Materials and Methods

Two studies were done to evaluate the effectiveness of Baytril 100.¹ Pigs from herds with known infections of swine respiratory disease (SRD) pathogens were purchased and transported to research facilities. Upon arrival at the research facility, the pigs were randomly assigned to pens of one of two treatment groups, Baytril 100 or saline. Five sentinel pigs were necropsied on arrival to confirm the presence of SRD pathogens.

Pigs were examined twice daily for signs of respiratory disease, and when disease outbreak appeared imminent, all pigs in the pen were evaluated to assign respiratory and attitude scores and record rectal temperatures. Pigs with temperatures $\geq 104.0^{\circ}\text{F}$, increased respiration rates, labored breathing and depressed attitudes were considered sick and febrile. When 3 or more pigs in a pen were sick and febrile, the pen was enrolled in the treatment and control study; that day became study day 0. The pigs in that pen were then given Baytril 100 at a dose of 7.5 mg/kg of body weight subcutaneously behind the ear or an equivalent volume of saline according to their random pen assignments.

Attitude was scored using a scale of 1 to 3, where 1 was normal. Respiratory character was scored using a scale of 1 to 4, where 1 was normal.

Attitude scores, respiratory scores and mortality were recorded daily for pigs remaining in the study through day 14. Rectal temperatures were recorded on day 0, day 4 and day 14. Weights were recorded on day 0 and day 14. Any pen with 3 or more sick and febrile pigs on day 4 was considered a treatment failure and no further evaluation was done on that pen.

Variables for evaluating control of respiratory disease were morbidity, mortality and rectal temperature on day 4. All pigs in the pen were used in the evaluation of disease control.

For use by or on the order of a licensed veterinarian. Extra-label use of this drug in food-producing animals is prohibited.





Treatment success was evaluated by comparing the respiratory and attitude scores and temperature of a sick and febrile pig on day 0 to that pig's scores and temperature on day 4. Thus, only those pigs classified as sick and febrile on day 0 were used in the treatment evaluation. A pig was considered a treatment success if it had a temperature of < 104.0°F and normal respiratory and attitude scores on day 4.

Results

Study 1 control of respiratory disease evaluation with a total of 275 pigs included.

Table 1 – Day 4 morbidity, mortality and rectal temperature results.

	Enrofloxacin	Saline	p-value
Morbidity	7.4% (10/137)	51% (71/138)	< 0.0001
Mortality	0% (0/137)	6.5% (9/138)	0.0325
Rectal Temperature	104.1°F	105.2°F	< 0.0001

Study 1 treatment of respiratory disease evaluation with a total of 98 pigs classified as sick and febrile on day 0.

Table 2 – Day 4 treatment success and individual parameter results using only those pigs classified as sick and febrile on day 0.

	Enrofloxacin	Saline	p-value
Treatment Success	33.0% (16/49)	0% (0/49)	< 0.0001
Median Attitude Score	1	2	< 0.01
Median Respiratory Score	1	2	< 0.01
Rectal Temperature	104.1°F	105.2°F	< 0.01

Actinobacillus pleuropneumoniae, *Pasteurella multocida*, *Haemophilus parasuis* and *Streptococcus suis* were cultured from the lungs of sentinel and saline-treated pigs that died or were euthanized during Study 1.





Study 2 control of respiratory disease evaluation with a total of 315 pigs included.

Table 3 – Day 4 morbidity, mortality and rectal temperature results.

	Enrofloxacin	Saline	p-value
Morbidity	5% (8/157)	61.4% (97/158)	< 0.0001
Mortality	0% (0/157)	1.9% (3/158)	0.2105
Rectal Temperature	103.1°F	104.0°F	< 0.0001

Study 2 treatment of respiratory disease evaluation with a total of 75 pigs classified as sick and febrile on day 0.

Table 4 – Day 4 treatment success and individual parameter results using only those pigs classified as sick and febrile on day 0.

	Enrofloxacin	Saline	p-value
Treatment Success	89.7% (35/39)	10.3% (3/39)	< 0.0001
Median Attitude Score	1	2	< 0.01
Median Respiratory Score	1	2.5	< 0.01
Rectal Temperature	103.2°F	104.1°F	< 0.01

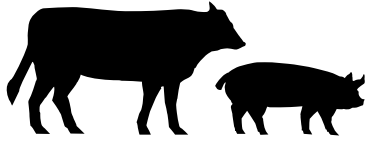
Actinobacillus pleuropneumoniae, *Pasteurella multocida*, *Haemophilus parasuis* and *Streptococcus suis* were cultured from the lungs of sentinel and saline-treated pigs that died or were euthanized during Study 2.

Conclusions

The combined results of these two studies indicate that Baytril 100 Injectable Solution is effective for the treatment and control of naturally occurring swine respiratory disease associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis* and *Streptococcus suis* when administered to pigs as a single subcutaneous dose of 7.5 mg/kg body weight.

Baytril® 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.

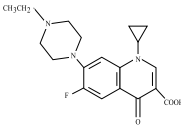
PRODUCT DESCRIPTION:

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: 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.

Swine: Baytril® 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:

Baytril® 100 provides flexible dosages and durations of therapy.

Baytril® 100 may be administered as a single dose for one day (cattle and swine) or for multiple days (cattle) 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.

Cattle:

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.

Table 1 – 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.

Swine:

Administer once, behind the ear, a subcutaneous 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 – Baytril® 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. 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.

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

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 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.

Baytril® 100 contains different excipients than other Baytril® 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.

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.

Swine: A total of 590 pigs were treated with Baytril® 100 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 $\geq 104.0^{\circ}\text{F}$) 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, 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*, 2nd ed, 59 - 75, 1993.
U.S. Patent No. 5,756,506

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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Injectable
Baytril® 100
(enrofloxacin)

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