Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Baytril Max 100 mg/ml Solution for Injection for Cattle and Pigs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:
Active substance:
Enrofloxacin 100 mg
Excipients:
n-Butanol 30 mg
Benzyl alcohol (E 1519) 20 mg
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
Clear, yellow solution

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle, Pig

4.2 Indications for use, specifying the target species

Cattle:
For the treatment of respiratory tract infections caused by enrofloxacin-sensitive *Histophilus somni, Mannheimia haemolytica, Pasteurella multocida* and *Mycoplasma* spp.
For the treatment of mastitis caused by enrofloxacin-sensitive E. coli.

Pig:
For the treatment of bacterial bronchopneumonia caused by enrofloxacin-sensitive *Actinobacillus pleuropneumoniae, Pasteurella multocida* and complicated by *Haemophilus parasuis* as a secondary pathogen in pigs.

4.3 Contraindications

Do not use for prophylaxis.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients. Do not use in known cases of resistance to other (fluoro)quinolones due to the potential for cross-resistance.

Do not use in animals with central nervous system-associated seizure disorders. Do not use in the presence of existing disorders of cartilage development or musculoskeletal damage around functionally significant or weight-bearing joints.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

For repeated injection or for injection volumes exceeding 15 ml (cattle) or 7.5 ml (pigs, calves) in divided doses, a new site must be chosen for each injection.
Official and local antimicrobial policies should be taken into account when the product is used.
Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials.
Whenever possible, fluoroquinolones should only be used based on susceptibility testing.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.
Enrofloxacin is eliminated renally. As with all fluoroquinolones, delayed excretion can therefore be expected in the presence of existing renal damage.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Direct contact with the skin should be avoided due to sensitisation, contact dermatitis and possible hypersensitivity reactions.
People with known hypersensitivity to (fluoro)quinolones should avoid contact with the product.
Wash hands after use.
In the event of accidental splash into the eye, rinse with large amounts of clean water. If irritation occurs, seek medical advice.
Do not eat, drink or smoke while handling the product.
Take care to avoid accidental self-injection.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or label to the physician.

4.6 Adverse reactions (frequency and seriousness)

In rare cases, transitory inflammatory reactions (swelling, redness) can occur at the injection site. These regress within a few days without further therapeutic measures.
In rare cases, intravenous treatment can cause shock reactions in cattle, probably as a result of circulatory disturbances.
Gastrointestinal disturbances may occur in isolated cases during treatment of calves.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports)

4.7 Use during pregnancy, lactation or lay

May be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interactions

Antagonist effects due to concurrent administration of macrolides and tetracyclines may occur. Enrofloxacin may interfere with the metabolism of theophylline, decreasing theophylline clearance resulting in increased plasma levels of theophylline.

4.9 Amounts to be administered and administration route

Cattle:
The dosage for respiratory disease is 7.5 mg enrofloxacin per kg body weight (BW) for a single treatment by subcutaneous administration (s.c.).

This is equivalent to

7.5 ml of the product per 100 kg BW and day

Do not administer more than 15 ml (cattle) or 7.5 ml (calf) per injection site (s.c.). In case of serious or chronic respiratory disease a second injection may be required after 48 hours.

The dosage for the treatment of colimastitis is 5 mg enrofloxacin per kg body weight (BW) by intravenous administration (i.v.).

This is equivalent to

5 ml of the product per 100 kg BW and day

The treatment of colimastitis should be exclusively by intravenous application on 2 to 3 consecutive days.

Pig:
The dosage for respiratory tract infections is 7.5 mg enrofloxacin per kg body weight for a single treatment by intramuscular administration (i.m.).
This is equivalent to

0.75 ml of the product per 10 kg BW and day

Do not administer more than 7.5 ml per injection site (i.m.). In cases of serious or chronic respiratory disease a second injection may be required after 48 hours.

Method of administration:
Repeated injections should be made at different injection sites.

Cattle:
For subcutaneous injection (respiratory disease) or for intravenous injection (colimastitis).

Pig:
For intramuscular injection into the neck muscles behind the ear.
To ensure administration of the correct dosage, body weight should be determined as accurately as possible to avoid underdosing. The stopper may be safely punctured up to 20 times.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In cattle a dose of 25 mg/kg bodyweight administered by the subcutaneous route for 15 consecutive days is tolerated without any clinical symptoms. Higher doses in cattle and doses of around 25 mg/kg and above in pigs may cause lethargy, lameness, ataxia, slight salivation and muscle tremors.

Do not exceed the recommended dose. In accidental overdose there is no antidote and treatment should be symptomatic.

4.11 Withdrawal period(s)

Cattle:
Meat and offal:
s.c.: 14 days
i.v.: 7 days

Milk:
s.c.: 120 hours
i.v.: 72 hours

Pig:
Meat and offal: 12 days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterials for systemic use, Fluoroquinolones,
ATCvet code: QJ01MA90

5.1 Pharmacodynamic properties

Enrofloxacin has a spectrum of activity which includes enrofloxacin-sensitive *Histophilus somni, Mannheimia haemolytica, Pasteurella multocida, Mycoplasma* spp., and *E. coli* in cattle as well as *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Haemophilus parasuis* in pigs.

Enrofloxacin belongs to the fluoroquinolone group of antibiotics. The substance has bactericidal activity which is mediated by binding to subunit A of DNA gyrase and the resulting selective inhibition of this enzyme.
DNA gyrase is a topoisomerase. These enzymes are involved in the replication, transcription and recombination of bacterial DNA. Fluoroquinolones also influence bacteria in the stationary phase by altering cell wall permeability.
Resistance to fluoroquinolones has been reported to arise from five sources, (i) point mutations in the genes encoding for DNA gyrase and/or topoisomerase IV leading to alterations of the respective enzyme, (ii) alterations of drug permeability in Gram-negative bacteria, (iii) efflux mechanisms, (iv) plasmid mediated resistance and (v) gyrase protecting proteins. All mechanisms lead to a reduced susceptibility of the bacteria to fluoroquinolones. Cross-resistance within the fluoroquinolone class of antimicrobials is common.
The inhibitory and bactericidal concentrations of enrofloxacin are very close, being either identical or differing by no more than 1-2 dilution steps.

MIC-Data

Cattle:

Species	**Country**	**Year of Isolation**	**Number of strains**	**MIC_{50}** (µg/mL)	**MIC_{90}** (µg/mL)	**Resistance (%)**
Mannheimia haemolytica	EU[(1)]	2009-12	149	0.03	0.25	0.7
Pasteurella multocida	EU[(1)]	2009-12	134	0.015	0.03	3.0
Histophilus somni	EU[(1)]	2009-12	66	0.03	0.06	0.0
Escherichia coli (mastitis)	EU[(2)]	2009-12	207	0.03	0.06	n.a.[(5)]
Mycoplasma bovis	EU[(3)]	2010-12	156	0.25	4	n.a.[(5)]

	F[4]	2010-12	143	0.5	0.5	n.a.[5]

EU: Europe; F: France; [1] VET MICROBIOL 194, 2016, 11-22; [2] INT J ANTIMICROB AGENTS 46, 2015, 13-20; [3] VET MICROBIOL 204, 2017, 188-193; [4] PLoS One, 2014; 9(2): e87672; [5] n.a.: not applicable.

Pig:

Species	**Country**	**Year of Isolation**	**Number of strains**	**MIC_{50}** (µg/mL)	**MIC_{90}** (µg/mL)	**Resistance (%)**
Actinobacillus pleuropneumoniae	EU[1]	2009-12	158	0.03	0.06	1.3
Pasteurella multocida	EU[1]	2009-12	152	0.015	0.03	0.0
Haemophilus parasuis	EU[1]	2009-12	68	0.008	0.06	n.a.[2]

EU: Europe; [1] VET MICROBIOL 194, 2016, 11-22; [2]n.a.: not applicable.

Enrofloxacin resistance breakpoints [R] are available for *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* isolated from cattle (R ≥ 2 µg/ml, CLSI document VET01S 3rd Edition) and for *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* isolated from pigs (R ≥ 1 µg/ml, CLSI document VET01S 3rd Edition).

5.2 Pharmacokinetic particulars

Following subcutaneous administration of the product in cattle or intramuscular administration in pigs, the active ingredient, enrofloxacin, is absorbed very rapidly and almost completely (high bioavailability).

Cattle:
After subcutaneous administration at a dose rate of 7.5 mg enrofloxacin per kg body weight to non-lactating cattle peak plasma concentrations of 0.82 mg/L are reached within 5 hours. The overall drug exposure in plasma is 9.1 mg*hour/L. Enrofloxacin is eliminated from the body at a half-life of 6.4 hours. Approximately 50% of enrofloxacin is metabolised to the active substance ciprofloxacin. Ciprofloxacin is eliminated from the body at a half-life of 6.8 hours.

After intravenous injection at a dose rate of 5.0 mg enrofloxacin per kg body weight to lactating cows, peak plasma concentrations of approx. 23 mg/L are reached immediately. The overall drug exposure in plasma is 4.4 mg*hour/L. Enrofloxacin is eliminated from the body at a half-life of 0.9 hours. Approximately 50% of parent compound are metabolised to ciprofloxacin with peak plasma concentrations of 1.2 mg/L reached at 0.2 hours. Elimination half-life is at a mean of 2.1 hours.

In milk mainly the metabolite ciprofloxacin accounts for antibacterial activity (approx. 90%). Ciprofloxacin reaches peak milk concentrations of 4 mg/L within 2 hours after intravenous dosing. Total exposure in milk over 24 hours is approx. 21 mg*hour/L. Ciprofloxacin is eliminated from milk at a half-life of 2.4 hours. Peak concentrations of 1.2 mg enrofloxacin per litre are reached in milk within 0.5 hours with an total enrofloxacin exposure in milk of approx. 2.2 mg*hour/L. Enrofloxacin is eliminated from milk at 0.9 hours.

Pig:
After intramuscular administration of 7.5 mg/kg body weight to pigs a mean peak serum concentration of 1.46 mg/L was achieved within 4 hours. The overall drug exposure over 24 hours was 20.9 mg*hour/L. The drug was eliminated from the central compartment at a terminal half-life of 13.1 hours. With peak concentrations less than 0.06 mg/L mean serum concentrations of ciprofloxacin were very low.

Enrofloxacin has a high volume of distribution. The concentrations in the tissues and organs mostly significantly exceed serum levels. Organs in which high concentrations can be expected include the lungs, liver, kidneys, gut and muscle tissue. Enrofloxacin is eliminated renally.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E 1519)
Arginine
n-Butanol
Water for injection

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening of the immediate packaging: 28 days

6.4 Special precautions for storage

Protect from frost.

6.5 Nature and composition of immediate packaging

Cardboard box with one brown glass bottle (Type I) containing 100 ml with chlorobutyl rubber stopper secured by an aluminium crimp cap.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann-Strasse 4
27472 Cuxhaven
Germany

8 MARKETING AUTHORISATION NUMBER(S)

VPA22020/053/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 November 2012
Date of latest renewal: 25 August 2017

10 DATE OF REVISION OF THE TEXT

October 2020