# ANNEX I

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Baytril One 100 mg/ml solution for injection for cattle and pig (AT, CY, CZ, EL, PT, PL, SK)
Baytril uno 100 mg/ml solution for injection for cattle and pig (ES)
Baytril Max 100 mg/ml solution for injection for cattle and pig (BG, HR, SI)

## 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., as well as treatment of colimastitis.

Pigs:
For the treatment of bacterial bronchopneumonia caused by enrofloxacin-sensitive *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis* and *Pasteurella multocida*.

### 4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

Do not use in animals with central nervous system-associated seizure disorders, existing impairment of cartilage growth or damage to the locomotor apparatus involving joints subjected to heavy functional stresses or load-bearing joints.

Do not use in case of existing resistance against quinolones as this resistance is often almost complete, and there is cross-resistance with other fluoroquinolones.

For interactions with other medicinal products see section 4.8.

## 4.4 Special warnings for each target species

None.

## 4.5 Special precautions for use

**Special precautions for use in animals**

See also section 4.3 for contraindications

If no clinical improvement occurs within two or three days a renewed sensitivity test should be undertaken and the treatment changed, if necessary.

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.

Enrofloxacin is eliminated renally. As with all fluoroquinolones, delayed excretion can therefore be expected in the presence of existing renal damage.

**Prudent use**
Whenever possible fluoroquinolones should only be used based on susceptibility testing.

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.

Use of the product deviating from the instructions given by in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other fluoroquinolones due to the potential for cross resistance.

**Special precautions to be taken by the person administering the veterinary medicinal product to animals**
In case of accidental self-injection seek medical advice immediately and show the package leaflet or label to the physician.
If pain persists for more than 12 hours after medical examination, seek medical advice again.

People with known hypersensitivity to enrofloxacin should avoid contact to the veterinary medicinal product.

Wash any splashes from skin or eyes immediately with water.

Do not eat, drink or smoke while handling the product.

## 4.6 Adverse reactions (frequency and seriousness)

Possible adverse reactions attributed to the product when used as recommended and their frequency are:

- Very rare (less than 1 animal in 10,000 animals treated, including isolated reports):
  Transitory inflammatory reactions (swelling, redness) at the injection site.
  Calves: gastrointestinal disturbances during treatment.
  Cattle after i.v. application: shock reactions, presumably as a result of circulatory

impairment.

## 4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy and lactation.

## 4.8 Interaction with other medicinal products and other forms of interaction

Combination of enrofloxacin with macrolides antibiotics or tetracyclines may produce antagonistic effects. The elimination of theophylline may be delayed.

## 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 (s.c.) administration.

This is equivalent to

| **7.5 ml Baytril One solution for injection per 100 kg BW per 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 (BW) by intravenous administration (i.v.).

This is equivalent to

| **5 ml Baytril One solution for injection per 100 kg BW per day** |
|---|

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

Pigs:
The dosage for respiratory disease is 7.5 mg enrofloxacin per kg (BW) for a single treatment by intramuscular (i.m.) administration.

This is equivalent to

| **0.75 ml Baytril One solution for injection per 10 kg BW per 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:
Cattle:
For subcutaneous injection (respiratory disease) or for intravenous (colimastitis) injection.

Pigs:
For intramuscular injection into the neck muscles behind the ear.

To ensure a 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 pig may cause lethargy, lameness, ataxia, slight salivation and muscle tremors.

### 4.11 Withdrawal period(s)

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

Milk:
s.c.: 5 days
i.v.: 3 days

Pigs:
Meat and offal: i.m.: 12 days

## 5. PHARMACOLOGICAL 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.

### 5.2 Pharmacokinetic particulars

Following subcutaneous administration of the product in cattle or intramuscular administration in pigs, the active substance, 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*hr/L. Enrofloxacin is eliminated from the body at a half-life of 6.4 hr. Approximately 50% of enrofloxacin is metabolised to the active substance ciprofloxacin. Ciprofloxacin is eliminated from the body at a half-life of 6.8 hr.

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*hr/L. Enrofloxacin is eliminated from the body at a half-life of 0.9 hr. Approximately 50% of parent compound are metabolised to ciprofloxacin with peak plasma concentrations of 1.2 mg/L reached at 0.2 hr. Mean elimination half-life of ciprofloxacin is 2.1 hr.

In milk the metabolite ciprofloxacin mainly accounts for antibacterial activity (approx. 90%). Ciprofloxacin reaches peak milk concentrations of 4 mg/L within 2 hr after intravenous dosing. Total exposure in milk over 24 hours is approx. 21 mg*hr/L. Ciprofloxacin is eliminated from milk at a half-life of 2.4 hr. 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*hr/L. Enrofloxacin is eliminated from milk at 0.9 hr.

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*hr/L. The drug was eliminated from the central compartment at a terminal half-life of 13.1 hr. 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

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

### 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

Do not refrigerate or freeze.

### 6.5 Nature and composition of immediate packaging

Cardboard box with 1 brown glass bottle (glass type I, Ph. Eur.) of 100 ml with butyl rubber stopper and 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 product should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORIZATION HOLDER

(Name and Address)
(Tel.:)
(Fax:)
(Email)

## 8. MARKETING AUTHORIZATION NUMBER

## 9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

DD/MM/YYYY

## 10. DATE OF REVISION OF THE TEXT

MM /YYYY

**PROHIBITION OF SALE, SUPPLY AND/OR USE**

To be supplied only on veterinary prescription

**Annex III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE**

**Card box and package leaflet for brown glass bottles (Type 1)**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Baytril One 100 mg/ml solution for injection for cattle and pig (AT, CY, CZ, EL, PT, PL, SK)
Baytriluno 100 mg/ml solution for injection for cattle and pig (ES)
Baytril Max 100 mg/ml solution for injection for cattle and pig (BG, HR, SI)

Enrofloxacin

## 2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains:

**Active substance:**
Enrofloxacin 100 mg

**Excipients:**
n-Butanol 30 mg
Benzyl alcohol (E 1519) 20 mg

## 3. PHARMACEUTICAL FORM

Solution for injection

## 4. PACKAGE SIZE

100 ml

## 5. TARGET SPECIES

Cattle and Pig

## 6. INDICATION(S)

Read the package leaflet before use.

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD(S)

Withdrawal periods:

Cattle:
Meat and offal:
subcutaneous: 14 days
intravenous: 7 days

Milk:
subcutaneous: 5 days
intravenous: 3 days

Pig:
Meat and offal: intramuscular: 12 days

## 9. SPECIAL WARNING(S), IF NECESSARY

Accidental injection is dangerous- read the package leaflet before use.

## 10. EXPIRY DATE

EXP{month/year}
Shelf life after first opening of the container: 28 days
Once broached use within…

## 11. SPECIAL STORAGE CONDITIONS

Do not refrigerate or freeze.

## 12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

## 13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription.

## 14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

## 15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

**{Name Address}**
**<{Tel}>**
**<{Fax}>**
**<{E-mail}>**

## 16. MARKETING AUTHORISATION NUMBER(S)

## 17. MANUFACTURER'S BATCH NUMBER

**Lot {number}**

# B. PACKAGE LEAFLET

**PACKAGE LEAFLET:**
Baytril One 100 mg/ml solution for injection for cattle and pig

## 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
National Bayer Animal Health subsidary

Manufacturer responsible for the batch release:
KVP Pharma + Veterinär Produkte GmbH
Projensdorfer Str. 324
D-24106 Kiel

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Baytril One 100 mg/ml solution for injection for cattle and pig (AT, CY, CZ, EL, PL, PT, SK)
Baytriluno 100 mg/ml solution for injection for cattle and pig (ES)
Baytril Max 100 mg/ml solution for injection for cattle and pig (BG, HR, SI)

Enrofloxacin

## 3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

1 ml contains:

**Active substance:**
Enrofloxacin 100 mg

**Excipients:**
n-Butanol 30 mg
Benzyl alcohol (E 1519) 20 mg

Yellow, clear solution.

## 4. INDICATION(S)

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

Pigs:
For the treatment of bacterial bronchopneumonia caused by enrofloxacin-sensitive *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis* and *Pasteurella multocida.*

## 5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with central nervous system-associated seizure disorders, existing impairment of cartilage growth or damage to the locomotor apparatus involving joints subjected to heavy functional stresses or load-bearing joints.

Do not use in case of existing resistance against quinolones as this resistance is often almost complete, and there is cross-resistance with other fluoroquinolones.

## 6. ADVERSE REACTIONS

Possible adverse reactions attributed to the product when used as recommended and their frequency are:

- Very rare (less than 1 animal in 10,000 animals treated, including isolated reports):
  Transitory inflammatory reactions (swelling, redness) at the injection site.
  Calves: gastrointestinal disturbances during treatment.
  Cattle after i.v. application: shock reactions, presumably as a result of circulatory impairment.

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

## 7. TARGET SPECIES

Cattle, Pig

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Cattle:

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

This is equivalent to

**7.5 ml Baytril One solution for injection per 100 kg BW per 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 (BW) by intravenous administration (i.v.).

This is equivalent to

**5 ml Baytril One solution for injection per 100 kg BW per day**

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

Pigs:

The dosage for respiratory disease is 7.5 mg enrofloxacin per kg (BW) for a single treatment by intramuscular (i.m.) administration.

This is equivalent to

**0.75 ml Baytril One solution for injection per 10 kg BW per 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:
Cattle:
For subcutaneous injection (respiratory disease) or for intravenous (colimastitis) injection.

Pigs:
For intramuscular injection into the neck muscles behind the ear.

The stopper may be safely punctured up to 20 times.

## 9. ADVICE ON CORRECT ADMINISTRATION

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

If no clinical improvement occurs within two or three days a renewed sensitivity test should be undertaken and the treatment changed, if necessary.

## 10. WITHDRAWAL PERIOD

Cattle:
Meat and offal:

s.c.: 14 days
i.v.: 7 days

Milk:

s.c.: 5 days
i.v.: 3 days

Pig:
Meat and offal: i.m.: 12 days

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not refrigerate or freeze.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton and label after {EXP}. The expiry date refers to the last day of that month.

Shelf-life after first opening the container: 28 days.

## 12. SPECIAL WARNING(S)

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 by in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other fluoroquinolones 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:
In case of accidental self-injection seek medical advice immediately and show the package leaflet or label to the physician.
If pain persists for more than 12 hours after medical examination, seek medical advice again.
People with known hypersensitivity to enrofloxacin should avoid contact with the veterinarian medicinal product.
Wash any splashes from the skin or eyes immediately with water.
Do not eat, drink or smoke while handling the product.

Pregnancy and lactation:
Can be used during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:
Combination of enrofloxacin with macrolides antibiotics or tetracyclines may produce antagonistic effects. The elimination of theophylline may be delayed.

Overdose (symptoms, emergency procedures, antidotes):
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 pig may cause lethargy, lameness, ataxia, slight salivation and muscle tremors.

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

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

## 15. OTHER INFORMATION

Package sizes: 100 ml

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.