[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrox Max 100 mg/ml solution for injection for cattle and pigs (AT, BE, BG, CZ, FR, HU, LV, LT, PT, RO, SI, SK, UK(NI))
Enroxal Max 100 mg/ml solution for injection for cattle and pigs (IT, DE)
Enrox 100, 100 mg/ml solution for injection for cattle and pigs (ES)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Enrofloxacin 100 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	20 mg
Butyl alcohol	30 mg
L-Arginine	
Water for injection	

Clear, yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and pigs.

3.2 Indications for use for each target species

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

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

3.3 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 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.
Do not use in known cases of resistance against other (fluoro)quinolones due to the potential for cross-resistance.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Official and local antimicrobial policies should be taken into account when the veterinary medicinal 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 veterinary medicinal 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.
If there is no clinical improvement observed within 2-3 days of therapy, re-evaluation of treatment and susceptibility testing may be necessary.
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 veterinary medicinal 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 veterinary medicinal 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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle:

Rare (1 to 10 animals / 10,000 animals treated):	Injection site inflammation (swelling, redness)[1] Circulatory shock[2]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Digestive tract disorder[3]

[1]Resolves within a few days, no treatment required
[2]Following intravenous administration
[3]Reported in calves

Pigs:

Rare (1 to 10 animals / 10,000 animals treated):	Injection site inflammation (swelling, redness)[1]

[1]Resolves within a few days, no treatment required

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

Can be used during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

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.

3.9 Administration routes and dosage

To ensure a correct dosage, body weight should be determined as accurately as possible.

Cattle:
For respiratory infections: administer by subcutaneous injection (s.c.):
A single dose of 7.5 mg enrofloxacin/kg body weight/day (7.5 ml of the veterinary medicinal product /100 kg body weight/day)
Not more than 15 ml of the veterinary medicinal product (7.5 ml in calves) should be administered at one subcutaneous injection site.
In cases of severe or chronic respiratory tract infections, a second injection may be required after 48 hours. Repeated injections should be administered at different sites.
For *E. coli* mastitis in cattle: administer by slow intravenous injection (i.v.).
5 mg enrofloxacin/kg body weight/day (5.0 ml of the veterinary medicinal product/100 kg body weight/day) daily for 2-3 days.

Pigs:
For respiratory infections: administer by intramuscular injection (i.m.) in neck musculature behind the ear:
A single dose of 7.5 mg enrofloxacin/kg bodyweight/day (0.75 ml of the veterinary medicinal product/10 kg body weight/day)
Not more than 7.5 ml of the veterinary medicinal product should be administered at one intramuscular injection site.
In cases of severe or chronic respiratory tract infections, a second injection may be required after 48 hours. Repeated injections should be administered at different sites.

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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. Clinical signs seen in gross overdosage include lethargy, lameness, ataxia, slight salivation and muscle tremors.
In pigs, doses of around 25 mg active ingredient per kg body weight and above may cause lethargy, loss of appetite and ataxia.

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

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Cattle:		
Meat and offal:	after subcutaneous administration (s.c.):	14 days
	after intravenous administration (i.v.):	7 days
Milk:	after subcutaneous administration (s.c.):	120 hours
	after intravenous administration (i.v.):	72 hours
Pigs:		
Meat and offal:	after intramuscular administration (i.m.):	12 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01MA90

4.2 Pharmacodynamics

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. Thus, the viability of bacetria is quickly reduced. The inhibitory and bactericidal concentrations of enrofloxacin are very close, being either identical or differing by no more than 1-2 dilution steps. Enrofloxacin has antimicrobial activity against many Gram-positive organisms, most Gram-negative organisms (including *Actinobacillus pleuropneumoniae*, *E. coli, Haemophilus parasuis*, *Histophilus somni*, *Mannheimia haemolytica, Pasteurella multocida*) and *Mycoplasma* spp.
Enrofloxacin reference breakpoints are available for *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* isolated from cattle (≥ 2 µg/ml, CLSI document VET01-S2) and for *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* isolated from pigs (≥ 1 µg/ml, CLSI document VET01-S2).
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.

4.3 Pharmacokinetics

Following subcutaneous administration in cattle and intramuscular administration in pigs, the active ingredient enrofloxacin is absorbed very rapidly and almost completely (high bioavailability). Peak serum concentrations of the active ingredient are reached after 1- 2 hours.
Therapeutic concentrations are maintained for a period of at least 48 hours.

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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 5 years.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Store in the original package. Do not freeze.

5.4 Nature and composition of immediate packaging

Cardboard box with one amber glass multi-dose vial (Type II) containing 100 ml with bromobutyl rubber stopper and aluminium seal.

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

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

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrox Max 100 mg/ml solution for injection (AT, BE, BG, CZ, FR, HU, LV, LT, PT, RO, SI, SK, UK(NI))
Enroxal Max 100 mg/ml solution for injection (IT, DE)
Enrox 100, 100 mg/ml solution for injection (ES)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 100 mg of enrofloxacin.

3. PACKAGE SIZE

100 ml

4. TARGET SPECIES

Cattle and pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Cattle: **s.c., i.v.**
Pigs: **i.m.**

7. WITHDRAWAL PERIODS

Withdrawal period:
Cattle:
Meat and offal: s.c.: 14 days
i.v.: 7 days
Milk: s.c.: 120 hours
i.v.: 72 hours

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

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days.

9. SPECIAL STORAGE PRECAUTIONS

Store in the original package. Do not freeze.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

GLASS VIAL 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrox Max 100 mg/ml solution for injection (AT, BE, BG, CZ, FR, HU, LV, LT, PT, RO, SI, SK, UK(NI))
Enroxal Max 100 mg/ml solution for injection (IT, DE)
Enrox 100, 100 mg/ml solution for injection (ES)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 100 mg of enrofloxacin.

3. TARGET SPECIES

Cattle and pigs

4. ROUTES OF ADMINISTRATION

Cattle: **s.c., i.v.**
Pigs: **i.m.**
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:
Cattle:
Meat and offal: s.c.: 14 days
i.v.: 7 days
Milk: s.c.: 120 hours
i.v.: 72 hours

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

6. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days.

7. SPECIAL STORAGE PRECAUTIONS

Store in the original package. Do not freeze.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Enrox Max 100 mg/ml solution for injection for cattle and pigs (AT, BE, BG, CZ, FR, HU, LV, LT, PT, RO, SI, SK, UK(NI))
Enroxal Max 100 mg/ml solution for injection for cattle and pigs (IT, DE)
Enrox 100, 100 mg/ml solution for injection for cattle and pigs (ES)

2. Composition

Each ml contains:

Active substance:
Enrofloxacin 100 mg

Excipients:
Benzyl alcohol (E1519) 20 mg
Butyl alcohol 30 mg

Clear, yellow solution.

3. Target species

Cattle and pigs.

4. Indications for use

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

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

5. 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 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.
Do not use in known cases of resistance against other (fluoro)quinolones due to the potential for cross-resistance.

6. Special warnings

Special precautions for safe use in the target species:
Official and local antimicrobial policies should be taken into account when the veterinary medicinal 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 veterinary medicinal 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.
If there is no clinical improvement observed within 2-3 days of therapy, re-evaluation of treatment and susceptibility testing may be necessary.
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 veterinary medicinal 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 veterinary medicinal 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.

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

Interaction with other medicinal products and other forms of interaction:
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.

Overdose:
In cattle, a dose of 25 mg/kg bodyweight administered by the subcutaneous route for 15 consecutive days is tolerated without any clinical symptoms. Clinical signs seen in gross overdosage include lethargy, lameness, ataxia, slight salivation and muscle tremors.
In pigs, doses of around 25 mg active ingredient per kg body weight and above may cause lethargy, loss of appetite and ataxia.
Do not exceed the recommended dose. In accidental overdose there is no antidote and treatment should be symptomatic.

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

7. Adverse events

Cattle:

Rare (1 to 10 animals / 10,000 animals treated): Injection site inflammation (swelling, redness)[1]

Circulatory shock[2]
Very rare (<1 animal / 10,000 animals treated, including isolated reports): Digestive tract disorder[3]

[1]Resolves within a few days, no treatment required
[2]Following intravenous administration
[3]Reported in calves

Pigs:

Rare (1 to 10 animals / 10,000 animals treated): Injection site inflammation (swelling, redness)[1]

[1]Resolves within a few days, no treatment required“

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

To ensure a correct dosage, body weight should be determined as accurately as possible.

Cattle:
For respiratory infections: administer by subcutaneous injection (s.c.):
A single dose of 7.5 mg enrofloxacin/kg body weight/day (7.5 ml of the veterinary medicinal product /100 kg body weight/day)
In cases of severe or chronic respiratory tract infections, a second injection may be required after 48 hours.
For *E. coli* mastitis in cattle: administer by slow intravenous injection (i.v.).
5 mg enrofloxacin/kg body weight/day (5.0 ml of the veterinary medicinal product/100 kg body weight/day) daily for 2-3 days.

Pigs:
For respiratory infections: administer by intramuscular injection (i.m.) in neck musculature behind the ear:
A single dose of 7.5 mg enrofloxacin/kg bodyweight/day (0.75 ml of the veterinary medicinal product/10 kg body weight/day)
In cases of severe or chronic respiratory tract infections, a second injection may be required after 48 hours.

9. Advice on correct administration

Repeated injections should be administered at different sites.
Cattle: not more than 15 ml of the veterinary medicinal product (7.5 ml in calves) should be administered at one subcutaneous injection site.
Pigs: not more than 7.5 ml of the veterinary medicinal product should be administered at one intramuscular injection site.

10. Withdrawal periods

Cattle:

Meat and offal:	after subcutaneous administration (s.c.):	14 days
	after intravenous administration (i.v.):	7 days
Milk:	after subcutaneous administration (s.c.):	120 hours
	after intravenous administration (i.v.):	72 hours

Pigs:

Meat and offal:	after intramuscular administration (i.m.):	12 days

11. Special storage precautions

Keep out of the sight and reach of children.

Store in the original package. Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

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

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Cardboard box with one 100 ml vial.

15. Date on which the package leaflet was last revised

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

To be completed nationally

Manufacturer responsible for batch release:
KRKA d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

Local representatives and contact details to report suspected adverse reactions:

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

17. Other information