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

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CENFLOX 100 mg/ml solution for injection for cattle and pigs

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**
n-Butanol	30 mg
Benzyl alcohol (E 1519)	20 mg
Arginine	
Water for injection	

Clear, yellow solution for injection.

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-sensitive *Histophilus somni*, *Mannheimia haemolytica*, *Pasteurella multocida* and *Mycoplasma* spp.
For the treatment of Mastitis caused by enrofloxacin-sensitive *E. coli*.

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

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipient.
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 case of resistance against other fluoroquinolone 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 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.
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.

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

People with known hypersensitivity to (fluoro)quinolones and/or benzyl alcohol should avoid contact with the veterinary medicinal product.
Direct contact with the skin should be avoided due to sensitisation, contact dermatitis and possible hypersensitivity reactions.
Wash hands after use.
In case of accidental contact with the eye, rinse with large amounts of clean water. If irritation occurs, seek medical advice.
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.
Do not eat, drink or smoke while handling the product.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site inflammation[1] (Swelling, Redness)

[1] These are transitory and regress within a few days without further therapeutic measures.

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site inflammation[1] (Swelling, Redness) Circulatory shock[2] Digestive tract disorders[3]

[1] These are transitory and regress within a few days without further therapeutic measures.
[2] After intravenous treatment, probably as a result of circulatory disturbances.
[3] During treatment of calves.

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

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

Intramuscular, intravenous, or subcutaneous use.

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 veterinary medicinal product per 100 kg bw and day.
Do not administer more than 15 ml (cattle) or 7.5 ml (calf) per injection site (subcutaneous).
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 veterinary medicinal product per 100 kg bw and day.
The treatment of colimastitis should be exclusively by intravenous application on 2 to 3 consecutive days.

Pigs
The dosage for respiratory tract infections is 7.5 mg enrofloxacin per kg body weight for a single administration. This is equivalent to 0.75 ml of the veterinary medicinal product per 10 kg bw and day.
Do not administer more than 7.5 ml per injection site (intramuscular).
In case 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 injection (colimastitis).

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

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

The stopper may be safely punctured up to 30 times.

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. 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.

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

Administration by a veterinarian surgeon (in case of intravenous route) or under their direct responsibility.

3.12 Withdrawal periods

Cattle:

Following intravenous injection:
Meat and offal: 7 days.
Milk: 72hours (3 days).

Following subcutaneous injection:
Meat and offal: 14 days.
Milk: 120 hours (5 days).

Pig:
Meat and offal: 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 targeting DNA gyrase and topoisomerase IV with the resulting selective inhibition of these enzymes.
DNA gyrase and topoisomerase IV are the two type II topoisomerases present in bacteria. 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.
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 a spectrum of activity which includes enrofloxacin-sensitive *Histophilus somni*, *Mannheimia haemolytica, Pasteurella multocida, Mycoplasma* spp., *E. coli* in cattle as well as *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Haemophilus parasuis* in pigs.
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.

Enrofloxacin clinical breakpoints (Susceptible, Intermediate, Resistant) are available for:
Mannheimia haemolytica, *Pasteurella multocida* and *Histophilus somni* isolated from cattle ($S \leq 0.25$ μg/ml; I = 0.5-1 μg/ml; $R \geq 2$ μg/ml, CLSIVET08ED4-2018 document), *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* isolated from pigs ($S \leq 0.25$ μg/ml; I = 0.5 μg/ml; $R \geq 1$ μg/ml, CLSIVET08ED4-2018 document).

No clinical breakpoints are available for *E.coli* isolates from cattle/mastitis *(ECOFF = 0.125* μg/ml, EUCAST 2019).
MIC_{90} for isolates *E.coli* from clinical mastitis 0.06 - 0.125 μg/ml (SE: 0.125 μg/ml 2013-2017, No isolates 503; CZ: 0.125 μg/ml 2015-2017, No isolates 192); DE: 0.06 μg/ml 2004 – 2014, No isolates 1756).

4.3 Pharmacokinetics

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*h/L. Enrofloxacin is excreted from the body at a half-life of 6.4 h. Approximately 50% of enrofloxacin is metabolized to the active substance ciprofloxacin. Ciprofloxacin is excreted from the body at a half-life of 6.8 h.
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*h/L. Enrofloxacin is excreted from the body at a half-life of 0.9 h. Approximately 50% of parent compound are metabolized to ciprofloxacin with peak plasma concentrations of 1.2 mg/L reached at 0.2 h. Elimination half-life is at a mean of 2.1 h.
In milk mainly the metabolite ciprofloxacin 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*h/L. Ciprofloxacin is excreted from milk at a half-life of 2.4 h. Peak concentrations of 1.2 mg enrofloxacin per liter are reached in milk within 0.5 hours with an total enrofloxacin exposure in milk of approx. 2.2 mg*h/L. Enrofloxacin is excreted from milk at 0.9 h.

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*h/L. The drug was excreted from the central compartment at a terminal half-life of 13.1 h. 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 excreted renally.

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 in glass vials: 3 years
Shelf life of the veterinary medicinal product as packaged for sale in polypropylene vials: 2 years
Shelf life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

Do not freeze.
Keep the container in the outer carton.

5.4 Nature and composition of immediate packaging

Amber glass type II vials, with bromobutyl stopper and aluminium cap with FLIP-OFF seal.
Amber polypropylene vials, with bromobutyl stopper and aluminium cap with FLIP-OFF seal.

Pack sizes:

- Box with 1 vial of 100 ml
- Box with 1 vial of 250 ml
- Box with 10 vials of 100 ml
- Box with 10 vials of 250 ml

Not all pack sizes may be marketed.

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

CENAVISA, S.L.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/YYYY}

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

Boxes for a vial of 100 ml and 250 ml
Boxes containing 10 vials of 100 ml or 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CENFLOX 100 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Enrofloxacin ..... 100 mg

3. PACKAGE SIZE

1 x 100 ml
1 x 250 ml
10 vials x 100 ml
10 vials x 250 ml

4. TARGET SPECIES

Cattle and pigs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Cattle: intravenous and subcutaneous route.
Pigs: intramuscular route.

7. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:

Meat and offal:	s.c.: 14 days.
	i.v.: 7 days.
Milk:	s.c.: 120 hours (5 days).
	i.v.: 72 hours (3 days).

Pig:

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

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days.
Once opened, use by …

9. SPECIAL STORAGE PRECAUTIONS

Do not freeze.
Keep the container in the outer carton.

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

CENAVISA, S.L.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot{number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vials of 100 ml and 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CENFLOX 100 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Enrofloxacin ..... 100 mg

3. TARGET SPECIES

Cattle and pigs.

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:

Meat and offal:	s.c.:14 days.
	i.v.: 7 days.
Milk:	s.c.: 120 hours (5 days).
	i.v.: 72 hours (3 days).

Pig:

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

6. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 28 days.
Once opened, use by …

7. SPECIAL STORAGE PRECAUTIONS

Do not freeze.
Keep the container in the outer carton.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

CENAVISA, S.L.

9. BATCH NUMBER

Lot{number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

CENFLOX 100 mg/ml solution for injection for cattle and pigs

2. Composition

Each ml contains:

Active substance:
Enrofloxacin.....100 mg
Excipients:
n-Butanol .....30 mg
Benzyl alcohol (E 1519) .....20 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-sensitive *Histophilus somni*, *Mannheimia haemolytica*, *Pasteurella multocida* and *Mycoplasma* spp.
For the treatment of Mastitis caused by enrofloxacin-sensitive *E. coli*.

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

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipient.
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 case of resistance against other fluoroquinolone due to the potential for cross-resistance.

6. Special warnings

None.

Special precautions for safe use in the target species:

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.
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.

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

People with known hypersensitivity to (fluoro)quinolones and/or benzyl alcohol should avoid contact with the veterinary medicinal product.
Direct contact with the skin should be avoided due to sensitisation, contact dermatitis and possible hypersensitivity reactions.
Wash hands after use.
In case of accidental contact with the eye, rinse with large amounts of clean water. If irritation occurs, seek medical advice.
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.
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:

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

Special restrictions for use and special conditions for use:

Administration by a veterinarian surgeon (in case of intravenous route) or under their direct responsibility.

Major incompatibilities:

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

7. Adverse events

Pigs:

Very rare	Injection site inflammation[1] (Swelling, Redness)

(<1 animal / 10,000 animals treated, including isolated reports):	

[1] These are transitory and regress within a few days without further therapeutic measures.

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site inflammation[1] (Swelling, Redness) Circulatory shock[2] Digestive tract disorders[3]

[1] These are transitory and regress within a few days without further therapeutic measures.
[2] After intravenous treatment, probably as a result of circulatory disturbances.
[3] During treatment of calves.

Reporting adverse events is important. It allows continuous safety monitoring of a 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

Intramuscular, intravenous, or subcutaneous use.

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 veterinary medicinal product per 100 kg bw and day.
Do not administer more than 15 ml (cattle) or 7.5 ml (calf) per injection site (subcutaneous).
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 veterinary medicinal product per 100 kg bw and day.
The treatment of colimastitis should be exclusively by intravenous application on 2 to 3 consecutive days.

Pigs
The dosage for respiratory tract infections is 7.5 mg enrofloxacin per kg body weight for a single administration. This is equivalent to 0.75 ml of the veterinary medicinal product per 10 kg bw and day.
Do not administer more than 7.5 ml per injection site (intramuscular).
In case of serious or chronic respiratory disease a second injection may be required after 48 hours.

9. Advice on correct administration

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

Pig
For intramuscular injection into the neck muscles behind the ear.

To ensure a correct dosage, body weight should be determined as accurately as possible.
The stopper may be safely punctured up to 30 times.

10. Withdrawal periods

Cattle:

Following intravenous injection:
Meat and offal: 7 days.
Milk: 72 hours (3 days).

Following subcutaneous injection:
Meat and offal: 14 days.
Milk: 120 hours (5 days).

Pig:
Meat and offal: 12 days.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not freeze. Keep the container in the outer carton.

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

Pack sizes:
Box containing 1 vial of 100 ml
Box containing 1 vial of 250 ml
Box containing 10 vials of 100 ml
Box containing 10 vials of 250 ml

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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, manufacturer responsible for batch release and contact details to report suspected adverse reactions:

CENAVISA, S.L.
C/ dels Boters 4
43205 Reus (SPAIN)
Tel: +34 977 75 72 73
farmacovigilancia@cenavisa.com

17. Other information