ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Xeden 150 mg tablet for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:
Enrofloxacin ..... 150.0 mg

Excipients:

Qualitative composition of excipients and other constituents
Pig liver powder
Yeast
Cellulose microcrystalline
Croscarmellose sodium
Copovidone
Silica colloidal anhydrous
Hydrogenated castor oil
Lactose monohydrate

Clover-shaped scored beige tablet.
The tablet can be divided into four equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

- Treatment of lower urinary tract infections (associated or not with prostatitis) and upper urinary tract infections caused by *Escherichia coli* or *Proteus mirabilis*.
- Treatment of superficial and deep pyoderma.

3.3 Contraindications

Do not use in young or growing dogs (dogs aged less than 12 months (small breed) or less than 18 months (large breed)) as the veterinary medicinal product may cause epiphyseal cartilage alterations in growing puppies.
Do not use in dogs having seizure disorders, since enrofloxacin may cause CNS stimulation.
Do not use in cases of hypersensitivity to the active substance, to fluoroquinolones or to any of the excipients.Do not use in the case of resistance to quinolones, as there exists almost complete cross resistance to other quinolones and complete cross resistance to other fluoroquinolones.
See also section 3.7 and 3.8.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
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.
Wherever possible, fluoroquinolones should be used based on susceptibility testing.
Use of the veterinary medicinal product deviating from instructions given in the SPC may increase the prevalence of bacteria resistant to fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.
Official and local antimicrobial policies should be taken into account when the veterinary medicinal product is used.
Use the veterinary medicinal product with caution in dogs with severe renal or hepatic impairment.
Pyoderma is mostly secondary to an underlying disease. It is advisable to determine the underlying cause and to treat the animal accordingly.
The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Persons with a known hypersensitivity to (fluoro)quinolones should avoid any contact with the veterinary medicinal product.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after handling the veterinary medicinal product.
In case of contact with eyes, rinse immediately with plenty of water.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Vomiting Anorexia Hypersensitivity reaction[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Neurological signs (Ataxia, Tremor, Seizure, Excitation) Joint cartilage disorder[2]

[1]In this case, the administration of the product should be stopped.
[2]Possible alterations in growing puppies (see 3.3 contra-indications).

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:
Laboratory studies in rats and chinchillas have not produced any evidence of teratogenic, foetotoxic, maternotoxic effects.
Use only according to the benefit/risk assessment by the responsible veterinarian.

Lactation:
As enrofloxacin passes into the maternal milk, the use is not recommended during lactation.

3.8 Interaction with other medicinal products and other forms of interaction

Concurrent use of flunixin should be under careful veterinary monitoring, as the interactions between these drugs may lead to adverse events related to delayed elimination.
Concomitant administration of theophylline requires careful monitoring as serum levels of theophylline may increase.
Concurrent use of magnesium or aluminum containing substances (such as antacids or sucralfate) may reduce absorption of enrofloxacin. These drugs should be administered two hours apart.
Do not use with tetracyclines, phenicols or macrolides because of potential antagonistic effects.

3.9 Administration routes and dosage

Oral use.
5 mg of enrofloxacin/kg/day as a single daily dosing, i.e. one tablet for 30 kg daily for:

- 10 days in lower urinary tract infections.
- 15 days in upper urinary tract infections and lower urinary tract infections associated with prostatitis.
- Up to 21 days in superficial pyoderma depending on clinical response.
- Up to 49 days in deep pyoderma depending on clinical response.

The treatment should be reconsidered in case of lack of clinical improvement at half of the treatment duration.

Xeden 50 mg Number of tablets per day	Xeden 150 mg Number of tablets per day	Dog weight (kg)		
¼		≥ 2	-	< 4
½		≥ 4	-	< 6.5
¾	¼	≥ 6.5	-	< 8.5
1	¼	≥ 8.5	-	< 11
1 ¼	½	≥ 11	-	< 13.5
1 ½	½	≥ 13.5	-	< 17
	¾	≥ 17	-	< 25
	1	≥ 25	-	< 35
	1 ¼	≥ 35	-	< 40
	1 ½	≥ 40	-	< 50
	1 ¾	≥ 50	-	< 55
	2	≥ 55	-	< 65

To ensure a correct dosage body weight should be determined as accurately as possible.
The tablets are flavoured and are well accepted by dogs. The tablets may be administered directly in the mouth of the dog or simultaneously with food if necessary.
Instruction on how to divide the tablet: Put the tablet on an even surface, with its scored side facing down (convex face up). With the tip of the forefinger, exert slight vertical pressure on the middle of the tablet to break it along its width into halves. Then, in order to obtain quarters, exert slight pressure on the middle of one half with the forefinger to break it into two parts.

3.10 Symptoms of overdose (and where applicable, emergency procedures, and antidotes)

Overdosing can cause vomiting and nervous signs (muscle tremor, incoordination and convulsions) which may require treatment discontinuation.
In the absence of any known antidote, apply drug elimination methods and symptomatic treatment.
If necessary, administration of aluminium- or magnesium-containing antacids or activated carbon can be used to reduce absorption of enrofloxacin.
According to literature, signs of overdosage with enrofloxacin in dogs such as inappetence and gastrointestinal disturbance were observed at approximately 10 times the recommended dose when administered for two weeks. No signs of intolerance were observed in dogs administered 5 times the recommended dose for a month.

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

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01MA90

4.2 Pharmacodynamics

Enrofloxacin is a synthetic fluoroquinolone antibiotic that exerts its activity by inhibiting topoisomerase II, an enzyme involved in the mechanism of bacterial replication.

Enrofloxacin exerts bactericidal activity concentration-dependant with similar values of minimal inhibit concentration and minimal bactericide concentrations. It also possesses activity against bacteria in the stationary phase by an alteration of the permeability of the outer membrane phospholipid cell wall.

In general, enrofloxacin exhibits good activity against most gram-negative bacteria, especially those of the Enterobacteriaceae. *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., and *Enterobacter* spp. are generally susceptible.
Pseudomonas aeruginosa is variably susceptible and, when it is susceptible, usually has a higher MIC than other susceptible organisms.
Staphylococcus aureus and *Staphylococcus intermedius* usually are susceptible.
Streptococci, *enterococci*, anaerobic bacteria can generally be considered resistant.

Induction of resistance against quinolones can develop by mutations in the gyrase gene of bacteria and by changes in cell permeability towards quinolones.

4.3 Pharmacokinetics

Enrofloxacin is rapidly metabolised to form an active compound, ciprofloxacin.
After oral administration of veterinary medicinal product 150 mg (5 mg/kg) in dogs:

- The maximal plasma concentration of enrofloxacin of 1.72 mcg/mL was observed one hour following administration.
- The maximal plasma concentration of ciprofloxacin (0.32 mcg/mL) was observed two hours following administration.

Enrofloxacin is primarily excreted via the kidneys. A major portion of the parent drug and its metabolites is recovered in urine.
Enrofloxacin is widely distributed in the body. The tissue concentrations are often higher than the serum concentrations. Enrofloxacin crosses the blood-brain barrier. The degree of protein binding in serum is 14% in dogs. The half-life in serum is 3-5 hours in dogs (5 mg/kg). Approximately 60 % of the dose is excreted as unchanged enrofloxacin and the remainder as metabolites, amongst others ciprofloxacin. The total clearance is approximately 9 ml/minute/kg bodyweight in dogs.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not known.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale:3 years.
Shelf-life of divided tablets:3 days.

5.3 Special precautions for storage

Store in the original container.
Protect from light.
This veterinary medicinal product does not require any special temperature storage conditions.
Any divided tablets should be returned to the original blister for storage.
Any divided tablets remaining after 3 days should be discarded.

5.4 Nature and composition of immediate packaging

Blister complex: PVDC-TE-PVC/Aluminium heat sealed blisters with 6 tablets / blister
Cardboard box with 2 blisters of 6 tablets
Cardboard box with 20 blisters of 6 tablets

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

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
Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Xeden 150 mg tablet

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Enrofloxacin ..... 150.0 mg

3. PACKAGE SIZE

2 x 6 tablets
20 x 6 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp.{mm/yyyy}
Shelf-life of half tablets: 3 days.

9. SPECIAL STORAGE PRECAUTIONS

Store in the original container.
Protect from light.
Any half tablets should be returned to the original blister for storage.
Any half tablets remaining after 3 days should be discarded.

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

14. MARKETING AUTHORISATION NUMBERS

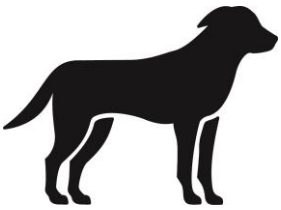
15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS {Blister}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Xeden



2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

150 mg of enrofloxacin

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Xeden 150 mg tablet for dogs

2. Composition

Each tablet contains:
Active substance:
Enrofloxacin ..... 150.0 mg

Clover-shaped scored beige tablet. The tablet can be divided into four equal parts**.**

3. Target species

Dogs.

4. Indications for use

- Treatment of lower urinary tract infections (associated or not with prostatitis) and upper urinary tract infections caused by *Escherichia coli* or *Proteus mirabilis*.
- Treatment of superficial and deep pyoderma.

5. Contraindications

Do not use in young or growing dogs (dogs aged less than 12 months (small breed) or less than 18 months (large breed)) as the veterinary medicinal product may cause epiphyseal cartilage alterations in growing puppies.
Do not use in dogs having seizure disorders, since enrofloxacin may cause CNS stimulation.
Do not use in cases of hypersensitivity to the active substance, to fluoroquinolones or to any of the excipients.Do not use in the case of resistance to quinolones, as there exists almost complete cross resistance to other quinolones and complete cross resistance to other fluoroquinolones.
See also sections “Pregnancy”, “Lactation” and “Interaction with other medicinal products and other forms of interaction”.

6. Special warnings

Special precautions for safe use in the target species:
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.
Wherever possible, fluoroquinolones should be used based on susceptibility testing.
Use of the veterinary medicinal product deviating from instructions given in the product information may increase the prevalence of bacteria resistant to fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.

Official and local antimicrobial policies should be taken into account when the veterinary medicinal product is used.
Use the veterinary medicinal product with caution in dogs with severe renal or hepatic impairment.
Pyoderma is mostly secondary to an underlying disease. It is advisable to determine the underlying cause and to treat the animal accordingly.
The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Persons with a known hypersensitivity to (fluoro)quinolones should avoid any contact with the veterinary medicinal product.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after handling the veterinary medicinal product.
In case of contact with eyes, rinse immediately with plenty of water.

Pregnancy:
Laboratory studies in rats and chinchillas have not produced any evidence of teratogenic, foetotoxic, maternotoxic effects. Use only according to the benefit/risk assessment by the responsible veterinarian.

Lactation:
As enrofloxacin passes into the maternal milk, the use is not recommended during lactation.

Interaction with other medicinal products and other forms of interaction:
Concurrent use of flunixin should be under careful veterinary monitoring, as the interactions between these drugs may lead to adverse events related to delayed elimination.
Concomitant administration of theophylline requires careful monitoring as serum levels of theophylline may increase.
Concurrent use of magnesium or aluminum containing substances (such as antacids or sucralfate) may reduce absorption of enrofloxacin. These drugs should be administered two hours apart.
Do not use with tetracyclines, phenicols or macrolides because of potential antagonistic effects.

Overdose:
Overdosing can cause vomiting and nervous signs (muscle tremor, incoordination and convulsions) which may require treatment discontinuation.
In the absence of any known antidote, apply drug elimination methods and symptomatic treatment.
If necessary, administration of aluminium- or magnesium-containing antacids or activated carbon can be used to reduce absorption of enrofloxacin.
According to literature, signs of overdosage with enrofloxacin in dogs such as inappetence and gastrointestinal disturbance were observed at approximately 10 times the recommended dose when administered for two weeks. No signs of intolerance were observed in dogs administered 5 times the recommended dose for a month.

Major incompatibilities:
None-known.

7. Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):
Vomiting Anorexia Hypersensitivity reaction[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Neurological signs (Ataxia, Tremor, Seizure, Excitation) Joint cartilage disorder[2]

[1]In this case, the administration of the product should be stopped.
[2]Possible alterations in growing puppies (see 3.3 contra-indications).

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 its local representative using the contact details at the end of this leaflet, or via your national reporting system.

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

Oral use.
5 mg of enrofloxacin/kg/day as a single daily dosing, *i.e.* one tablet for 30 kg daily for:

- 10 days in lower urinary tract infections.
- 15 days in upper urinary tract infections and lower urinary tract infections associated with prostatitis.
- Up to 21 days in superficial pyoderma depending on clinical response.
- Up to 49 days in deep pyoderma depending on clinical response.

The treatment should be reconsidered in case of lack of clinical improvement at half of the treatment duration.

The tablet is divisible and can be used as follows:

Xeden 50 mg Number of tablets per day	Xeden 150 mg Number of tablets per day	Dog weight (kg)
¼		≥ 2 - < 4
½		≥ 4 - < 6.5
¾	¼	≥ 6.5 - < 8.5
1	¼	≥ 8.5 - < 11
1 ¼	½	≥ 11 - < 13.5
1 ½	½	≥ 13.5 - < 17
	¾	≥ 17 - < 25
	1	≥ 25 - < 35
	1 ¼	≥ 35 - < 40
	1 ½	≥ 40 - < 50
	1 ¾	≥ 50 - < 55
	2	≥ 55 - < 65

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

9. Advice on correct administration

The tablets are flavoured and are well accepted by dogs. The tablets may be administered directly in the mouth of the dog or simultaneously with food if necessary.
Instruction on how to divide the tablet: Put the tablet on an even surface, with its scored side facing down (convex face up). With the tip of the forefinger, exert slight vertical pressure on the middle of the tablet to break it along its width into halves. Then, in order to obtain quarters, exert slight pressure on the middle of one half with the forefinger to break it into two parts.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store in the original container.
Protect from light.
This veterinary medicinal product does not require any special temperature storage conditions.
Any divided tablets should be returned to the original blister for storage.
Shelf-life of divided tablets: 3 days.
Any divided tablets remaining after 3 days should be discarded.
Do not use this veterinary medicinal product after the expiry date which is stated on the blister and carton after Exp. The expiry date refers to the last day of that month.

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 authorization numbers and pack sizes

(MA)

Pack sizes:
Cardboard box with 2 blisters of 6 tablets
Cardboard box with 20 blisters of 6 tablets
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{mm/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:
(Name and address to be completed nationally)
Tel: +800 35 22 11 51
Email: pharmacovigilance@ceva.com

Manufacturer responsible for batch release:
Ceva Santé Animale
Boulevard de la Communication
Zone Autoroutière
53950 Louverné
France

17. Other information