

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Efex 40 mg chewable tablets for dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

### Active substance:

Marbofloxacin.....40.00 mg

### Excipient(s):

<b><u>Qualitative composition of excipients and other constituents</u></b>
Lactose monohydrate
Copovidone
Silica, colloidal anhydrous
Croscarmellose sodium
Hydrogenated castor oil
Pig liver powder
Malted yeast
Cellulose microcrystalline

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 infections caused by strains of microorganisms susceptible to marbofloxacin :

- skin and soft tissue infections (skinfold pyoderma, impetigo, folliculitis, furunculosis, cellulitis),
- urinary tract infections (UTI) associated or not with prostatitis or epididymitis,
- respiratory tract infections

### 3.3 Contraindications

Do not use in dogs aged less than 12 months, or less than 18 months for giant breeds of dogs with a longer growth period.

Do not use in cases of hypersensitivity to the active substance, other (fluoro)quinolones or any of the excipients.

### 3.4 Special warnings

A low urinary pH could have an inhibitory effect on the activity of marbofloxacin.

Cross-resistance has been shown between marbofloxacin and other fluoroquinolones. Use of the product should be carefully considered when susceptibility testing has shown resistance to other fluoroquinolones because its effectiveness may be reduced.

### 3.5 Special precautions for use

#### Special precautions for safe use in the target species:

The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

The fluoroquinolones have been shown to induce erosion of articular cartilage in juvenile dogs and care should be taken to dose accurately especially in young animals.

The fluoroquinolones are also known for their potential neurological side effects. Cautious use is recommended in dogs diagnosed as suffering from epilepsy.

Use of the product should be based on identification and susceptibility testing of the target pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.” Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

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

People with known hypersensitivity to (fluoro)quinolones or other components of the formulation should avoid 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 use.

#### Special precautions for the protection of the environment:

Not applicable.

### 3.6 Adverse events

Dogs:

<p>Very rare (&lt;1 animal / 10,000 animals treated, including isolated reports):</p>	<p>Vomiting<sup>2</sup>, Soft stool<sup>2</sup> Hyperactivity<sup>1,2</sup> Modification of thirst<sup>2,3</sup></p>
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1 Transient

2 Cease spontaneously after treatment.

3 Increase or decrease.

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:

Studies in laboratory animals (rat, rabbit) showed no teratogenicity, embryotoxicity and maternotoxicity with marbofloxacin at therapeutic doses.

The safety of marbofloxacin has not been assessed in pregnant and lactating dogs. Use only according to the benefit/risk assessment by the responsible veterinarian in pregnant and lactating animals.

### **3.8 Interaction with other medicinal products and other forms of interaction**

Fluoroquinolones are known to interact with orally administered cations (Aluminium, Calcium, Magnesium, Iron). In such cases, the bioavailability may be reduced.

Serum levels of theophylline should be carefully monitored when theophylline and marbofloxacin are used concomitantly, as fluoroquinolones may increase serum levels of theophylline.

### **3.9 Administration routes and dosage**

Oral use.

The recommended dose rate is 2 mg/kg/d (1 tablet for 20 kg per day) in single daily administration.

- in skin and soft tissue infections, treatment duration is at least 5 days. Depending on the course of the disease, it may be extended up to 40 days.

- in urinary tract infections, treatment duration is at least 10 days. Depending on the course of the disease, it may be extended up to 28 days.

- in respiratory infections, treatment duration is at least 7 days and depending on the course of the disease, it may be extended up to 21 days.

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

The chewable tablets may be accepted by dogs or can be administered directly into the mouth of the animals.

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)**

Overdosage may cause acute signs in the form of neurological disorders, which should be treated symptomatically.

### **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 ATC vet code:**

QJ01MA93

### **4.2 Pharmacodynamics**

Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the fluoroquinolone group which acts by inhibition of DNA gyrase and topoisomerase IV.. It has a broad-spectrum activity in vitro against Gram-positive bacteria (in particular staphylococci and streptococci) and, Gram-negative

bacteria (*Escherichia coli*, *Enterobacter cloacae*, *Proteus* spp., *Klebsiella* spp., *Shigella* spp., *Pasteurella* spp., *Pseudomonas* spp.) as well as *Mycoplasma* spp..

A report on microbiological susceptibility including two European field surveys covering hundreds of canine and feline pathogens sensitive to marbofloxacin was published on 2009

Micro-organisms	MIC (µg/ml)
<i>Staphylococcus intermedius</i>	0,23 - 0,25
<i>Escherichia coli</i>	0,125 - 0,25
<i>Pasteurella multocida</i>	0,04
<i>Pseudomonas aeruginosa</i>	0,94

MIC breakpoints have been determined for *Enterobacteriaceae* and *Staphylococcus spp* in dogs and cats (skin, soft tissue, UTI). CLSI, July 2013 as  $\leq 1$  µg/ml for sensitive, 2 µg/ml for intermediate and  $\geq 4$  µg/ml for resistant bacterial strains to marbofloxacin.

Marbofloxacin is not active against anaerobes, yeasts or fungi.

The activity of marbofloxacin against the target bacterial species is bactericidal concentration-dependant.

Resistance to fluoroquinolones occurs by chromosomal mutations with the following mechanisms: decrease in bacterial cell wall permeability, expression change of genes encoding for efflux pumps or mutations in genes encoding enzymes responsible for molecule binding. Plasmid-mediated resistance to fluoroquinolones, which confers reduced susceptibility, has also been described. Depending on the underlying resistance mechanism, cross-resistance to other (fluoro)quinolones and co-resistance to other antimicrobial classes can occur.

#### 4.3 Pharmacokinetics

After oral administration in dogs at the recommended dose of 2 mg/kg, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.5 µg/ml within 2 hours

Its bioavailability is close to 100%.

It is weakly bound to plasma proteins (less than 10%), extensively distributed and in most tissues (liver, kidney, skin, lung, bladder, digestive tract) it achieves higher concentrations than in plasma. Marbofloxacin is eliminated slowly ( $t_{1/2\beta} = 14$  h in dogs) predominantly in the active form in urine (2/3) and faeces (1/3).

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major Incompatibilities

Not applicable

### 5.2 Shelf life

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

Shelf-life after first opening the immediate packaging: 72 hours

### 5.3 Special precautions for storage

Blister: PVC-TE-PVDC – aluminium heat sealed: Do not store above 30°C.

Blister: PA-AL-PVC – aluminium heat sealed: This veterinary medicinal product does not require any special temperature storage conditions.

Tablet portions should be stored in the blister pack.

Any tablet portions remaining after 72 hours should be discarded.  
Keep the blister in the outer carton.

#### **5.4 Nature and composition of immediate packaging**

- (Polyvinyl chloride-Thermo-elast-Polyvinylidene chloride – aluminium heat sealed) containing 8 tablets per blister:

Cardboard box of 8 tablets containing 1 blister of 8 tablets

Cardboard box of 16 tablets containing 2 blisters of 8 tablets

Cardboard box of 120 tablets containing 15 blisters of 8 tablets

Cardboard box of 240 tablets containing 30 blisters of 8 tablets

- (Polyamide-Aluminium-Polyvinyl chloride – aluminium heat sealed) containing 6 tablets per blister:

Cardboard box of 6 tablets containing 1 blister of 6 tablets

Cardboard box of 12 tablets containing 2 blisters of 6 tablets

Cardboard box of 120 tablets containing 20 blisters of 6 tablets

Cardboard box of 240 tablets containing 40 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**

Ceva

### **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 containing 6, 8, 12, 16, 120 or 240 tablets

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Efex 40 mg chewable tablets

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each tablet contains:

Marbofloxacin.....40.00 mg

**3. PACKAGE SIZE**

6 tablets

8 tablets

12 tablets

16 tablets

120 tablets

240 tablets

**4. TARGET SPECIES**

Dogs

**5. INDICATIONS**

**6. ROUTES OF ADMINISTRATION**

Oral use.

**7. WITHDRAWAL PERIODS**

**8. EXPIRY DATE**

Exp. {mm/yyyy}

Any tablet portions remaining after 72 hours should be discarded.

**9. SPECIAL STORAGE PRECAUTIONS**

Blister: PVC-TE-PVDC – aluminium heat sealed: Do not store above 30°C

Tablet portions should be stored in the blister pack.

Keep the blister 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**



**14. MARKETING AUTHORISATION NUMBERS**

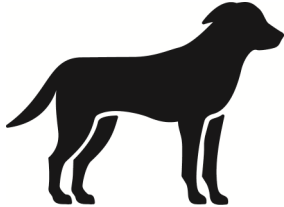
**15. BATCH NUMBER**

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**  
Blister

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Efex



**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE**

40 mg of marbofloxacin

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Efex 40 mg chewable tablets for dogs

### 2. Composition

Each tablet contains:

**Active substance:**

Marbofloxacin.....40.0 mg

Chewable tablet

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

### 3. Target species

Dogs

### 4. Indications for use

Treatment of infections caused by strains of microorganisms susceptible to marbofloxacin:

- skin and soft tissue infections (skinfold pyoderma, impetigo, folliculitis, furunculosis, cellulitis),
- urinary tract infections (UTI) associated or not with prostatitis or epididymitis.
- respiratory tract infections.

### 5. Contraindications

Do not use in dogs aged less than 12 months, or less than 18 months for giant breeds of dogs with a longer growth period.

Do not use in cases of hypersensitivity to the active substance, other (fluoro)quinolones or any of the excipients.

### 6. Special warnings

Special warnings:

A low urinary pH could have an inhibitory effect on the activity of marbofloxacin.

Cross-resistance has been shown between marbofloxacin and other fluoroquinolones. Use of the product should be carefully considered when susceptibility testing has shown resistance to other fluoroquinolones because its effectiveness may be reduced.

Special precautions for safe use in the target species:

The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

The fluoroquinolones have been shown to induce erosion of articular cartilage in juvenile dogs and care should be taken to dose accurately especially in young animals.

The fluoroquinolones are also known for their potential neurological side effects. Cautious use is recommended in dogs diagnosed as suffering from epilepsy.

Use of the product should be based on identification and susceptibility testing of the target pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.” Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

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

People with known hypersensitivity to (fluoro)quinolones or other components of the formulation should avoid 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 use.

Pregnancy and lactation:

Studies in laboratory animals (rat, rabbit) showed no teratogenicity, embryotoxicity and maternotoxicity with marbofloxacin at therapeutic doses.

The safety of marbofloxacin has not been assessed in pregnant and lactating dogs. Use only according to the benefit/risk assessment by the responsible veterinarian in pregnant and lactating animals.

Interaction with other medicinal products and other forms of interaction:

Fluoroquinolones are known to interact with orally administered cations (Aluminium, Calcium, Magnesium, Iron). In such cases, the bioavailability may be reduced.

Serum levels of theophylline should be carefully monitored when theophylline and marbofloxacin are used concomitantly, as fluoroquinolones may increase serum levels of theophylline.

Overdose:

Overdosage may cause acute signs in the form of neurological disorders, which should be treated symptomatically.

## **7. Adverse events**

Dogs:

Very rare

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

Vomiting<sup>2</sup>, Soft stool<sup>2</sup>

Hyperactivity<sup>1,2</sup>

Modification of thirst<sup>2,3</sup>

1 Transient

2 Cease spontaneously after treatment.

3 Increase or decrease.

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.

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

Oral use.

The recommended dose rate is 2 mg/kg/d (1 tablet for 20 kg per day) in single daily administration.

- in skin and soft tissue infections, treatment duration is at least 5 days. Depending on the course of the disease, it may be extended up to 40 days.
- in urinary tract infections, treatment duration is at least 10 days. Depending on the course of the disease, it may be extended up to 28 days.
- in respiratory infections, treatment duration is at least 7 days and depending on the course of the disease, it may be extended up to 21 days.

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

## **9. Advice on correct administration**

The chewable tablets may be accepted by dogs or can be administered directly into the mouth of the animals.

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.

Blister: Polyvinyl chloride-Thermo-elast-Polyvinylidene chloride – aluminium heat sealed: Do not store above 30°C

Blister: Polyamide-Aluminium-Polyvinyl chloride – aluminium heat sealed: This veterinary medicinal product does not require any special temperature storage conditions.

Tablet portions should be stored in the blister pack

Any tablet portions remaining after 72 hours should be discarded

Keep the blister in the outer carton.

Do not use after the expiry date which is stated on the carton and blister 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 authorisation numbers and pack sizes**

(MA)

##### Pack sizes:

Cardboard box with 6 tablets  
Cardboard box with 8 tablets  
Cardboard box with 12 tablets  
Cardboard box with 16 tablets  
Cardboard box with 120 tablets  
Cardboard box with 240 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: and contact details to report suspected adverse reactions:

*(Name and address to be completed nationally)*

Tel: +800 35 22 11 51

Email: [pharmacovigilance@ceva.com](mailto:pharmacovigilance@ceva.com)

Manufacturer responsible for batch release:

Ceva Santé Animale  
Boulevard de la Communication  
Zone Autoroutière  
53950 LOUVERNE  
FRANCE

#### **17. Other information**