

## **ANNEX I**

### **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Therios 75 mg Chewable Tablets for Cats

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

### Active substance:

Cefalexin (as cefalexin monohydrate) ..... 75 mg

### Excipient(s):

| <b><u>Qualitative composition of excipients and other constituents</u></b> |
|--|
| Pig liver powder   |
| Yeast  |
| Croscarmellose sodium  |
| Magnesium stearate   |
| Anhydrous colloidal silica   |
| Calcium hydrogen phosphate dihydrate                                       |

Oblong scored beige tablet. The tablets can be divided into two equal parts.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cats.

### 3.2 Indications for use for each target species

Infections caused by bacteria susceptible to cefalexin:

- Lower urinary tract infections due to *E. coli* and *Proteus mirabilis*,
- Treatment of cutaneous and subcutaneous infections: pyoderma due to *Staphylococcus* spp. and wounds and abscesses due to *Pasteurella* spp.

### 3.3 Contraindications

Do not use in case of severe kidney failure.

Do not use in animals which are known to be hypersensitive to cephalosporins or any other substance from the  $\beta$ -lactam group.

Do not use in rabbits, guinea pigs, hamsters, gerbils and other small rodents.

### 3.4 Special warnings

Cross-resistance has been shown between cefalexin and other substance from the  $\beta$ -lactam group in target pathogens. Use of the product should be carefully considered when susceptibility testing has shown resistance to antimicrobials of the  $\beta$ -lactam group because its effectiveness may be reduced.

### 3.5 Special precautions for use

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

As with other antibiotics which are excreted mainly by the kidneys, systemic accumulation may occur when renal function is impaired. In cases of known renal insufficiency, the dose should be reduced and/or the interval of administration increased and nephrotoxic drugs should not be administered concurrently.

This veterinary medicinal product should not be used to treat kittens less than 9 weeks of age.

Use of the veterinary medicinal product in cats weighing less than 2.5 kg should be in accordance with the benefit/risk assessment performed by the responsible veterinarian.

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

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:

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-reactions to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.

- Do not handle this veterinary medicinal product if you know you are sensitised, or if you have been advised not to be in contact with such substances.
- Handle this veterinary medicinal product with great care to avoid exposure taking all recommended precautions. Wash hands after use.
- If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
- In case of accidental ingestion, seek medical attention and show the package leaflet or the label to the doctor.

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

Not applicable.

### 3.6 Adverse events

Cats:

|   |   |
|---|---|
| Undetermined frequency (cannot be estimated from the available data): | Vomiting, Diarrhoea<br>Allergic reaction <sup>1</sup> |
|---|---|

<sup>1</sup> allergic cross-reactivity with other beta lactams may occur.

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 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:

Laboratory studies in mouse, rat and rabbit have not produced any evidence of teratogenic effects. The safety of the product has not been investigated in pregnant or lactating cats and should only be used according to the benefit-risk assessment by the responsible veterinarian.

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

The bactericidal activity of cephalosporins is reduced by concomitant administration of bacteriostatic acting compounds (macrolides, sulfonamides and tetracyclines).

Nephrotoxicity can be increased when 1<sup>st</sup> generation cephalosporins are combined with polypeptide antibiotics, aminoglycosides or some diuretics (furosemide).

Concomitant use with such active substances should be avoided.

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

Oral use.

15 mg cefalexin per kg bodyweight twice daily, equivalent to 1 tablet for 5 kg bodyweight for:

- 5 days for wounds and abscesses.
- 10 to 14 days in case of urinary tract infections.
- 14 days at least in case of pyoderma. The treatment must be continued for 10 days once the lesions have disappeared.

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

In case of use of half tablets, put the remaining quantity of the tablet back into the blister pocket and use it for the next administration.

The tablets are flavoured. They can be administered with food or directly into the mouth of the animal.

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

No other known side effects than those under section 3.6.

### **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: QJ01DB01**

## 4.2 Pharmacodynamics

Cefalexin monohydrate is a bactericidal antibiotic of the cephalosporin family, obtained by hemi-synthesis of the 7-amino cephalosporanic nucleus.

Cefalexin acts by inhibiting the nucleopeptide synthesis of the bacterial wall. Cephalosporins interfere with transpeptidation by acylating the enzyme making it unable to cross-link muramic acid-containing peptidoglycan strands. The inhibition of the biosynthesis of the material required to build the cell wall results in a defective cell wall and consequently osmotically unstable to protoplasts. The combined action results in cell lysis and filament formation. Cefalexin is active against Gram positive and Gram negative bacteria such as *Staphylococcus* spp. (including penicillin-resistant strains), *Streptococcus* spp. and *Escherichia coli*. Cefalexin is not inactivated by  $\beta$ -lactamases produced by Gram positive bacteria. However, beta-lactamases produced by gram-negative bacteria can inhibit cefalexin by hydrolysis of the beta-lactam cycle.

Resistance to cefalexin may be due to one of the following mechanisms of resistance. Firstly, the production of various beta-lactamases (cephalosporinase), that inactivate the antibiotic, is the most prevalent mechanism among gram-negative bacteria. Secondly, a decreased affinity of the PBPs (penicillin-binding proteins) for beta-lactam drugs is frequently involved for beta -lactam resistant gram-positive bacteria. Lastly, efflux pumps, extruding the antibiotic from the bacterial cell, and structural changes in porins, reducing passive diffusion of the drug through the cell wall, may contribute to improve the resistant phenotype of a bacterium.

Well-known cross-resistance (involving the same resistance mechanism) exists between antibiotics belonging to the beta -lactam group due to structural similarities. It occurs with b-lactamases enzymes, structural changes in porins or variations in efflux pumps. Co-resistance (different resistance mechanisms involved) has been described in *E. coli* due to a plasmid harbouring various resistance genes.

MICs parameters available for *Staphylococcus* spp. and *Pasteurella multocida* are:

|                              |                           |                           |
|------------------------------|---------------------------|---------------------------|
| <i>Staphylococcus</i> spp.   | MIC <sub>50</sub> 2 µg/ml | MIC <sub>90</sub> 2 µg/ml |
| <i>Pasteurella multocida</i> | MIC <sub>50</sub> 2 µg/ml | MIC <sub>90</sub> 4 µg/ml |

## 4.3 Pharmacokinetics

In cats, the bioavailability after oral administration is around 56%.

In cats, after a single oral administration of 18.5 mg/kg of cefalexin, the plasmatic peak was reached after 1.6 h with a concentration of 22 µg/mL.

Cefalexin was detected in plasma till 24 hours after administration.

The diffusion of cefalexin in tissue is high. Cefalexin is mainly eliminated by urinary route (85%) under active form, urinary concentration peaks are significantly higher than plasmatic concentration peaks.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major incompatibilities

Not applicable.

### 5.2 Shelf life

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

Polyvinylchloride / thermo-elast / polyvinylidene chloride – aluminium heat-sealed blister:  
3 years.

Polyamide / aluminium / polyvinylchloride – aluminium heat-sealed blister: 30 months.

Any divided tablet portions remaining after 24 hours should be discarded.

### **5.3 Special precautions for storage**

Do not store above 25°C.

Store in the original package.

Return any halved tablet to the opened blister pack.

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

Blister:

- Polyvinylchloride / thermo-elast / polyvinylidene chloride – aluminium heat-sealed containing 10 tablets per blister.
- Polyamide / aluminium / polyvinylchloride – aluminium heat-sealed containing 10 tablets per blister.

Cardboard box with 1 blister of 10 tablets.

Cardboard box with 2 blisters of 10 tablets.

Cardboard box with 10 blisters of 10 tablets.

Cardboard box with 15 blisters of 10 tablets.

Cardboard box with 20 blisters of 10 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**



**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

Cardboard box containing 10, 20, 100, 150 or 200 tablets

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

Therios 75 mg Chewable Tablets

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each tablet contains:

Cefalexin (as cefalexin monohydrate) ..... 75 mg

**3. PACKAGE SIZE**

Cardboard box with 1 blister of 10 tablets

Cardboard box with 2 blisters of 10 tablets

Cardboard box with 10 blisters of 10 tablets

Cardboard box with 15 blisters of 10 tablets

Cardboard box with 20 blisters of 10 tablets

**4. TARGET SPECIES**

Cats

**5. INDICATIONS****6. ROUTES OF ADMINISTRATION**

Oral use.

**7. WITHDRAWAL PERIODS**

Not applicable.

**8. EXPIRY DATE**

Exp. {mm/yyyy}

Any divided tablet portions remaining after 24 hours should be discarded.”

**9. SPECIAL STORAGE PRECAUTIONS**

Do not store above 25°C.

Store in the original package. Return any halved tablet to the opened blister pack.

**10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”**

User warnings :

Penicillins and cephalosporins may occasionally cause severe allergic reactions.

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 NUMBER(S)**

**15. BATCH NUMBER**

Lot {number}

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

{Blister}

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

Therios



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

Cefalexin 75 mg/tablet

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Therios 75 mg Chewable Tablets for Cats

### 2. Composition

Each tablet contains

Cefalexin (as cefalexin monohydrate) ..... 75 mg

Oblong scored beige tablet. The tablets can be divided into two equal parts

### 3. Target species

Cats

### 4. Indications for use

Infections caused by bacteria susceptible to cefalexin

- Lower urinary tract infections due to *E.coli* and *Proteus mirabilis*,
- Treatment of cutaneous and subcutaneous infections: pyoderma due to *Staphylococcus.spp* and wounds and abscesses due to *Pasteurella spp.*

### 5. Contraindications

Do not use in case of severe kidney failure

Do not use in animals which are known to be hypersensitive to cephalosporins or any other substance from the  $\beta$ -lactam group.

Do not use in rabbits, guinea pigs, hamsters, gerbils and other small rodents.

### 6. Special warnings

#### Special warning:

Cross-resistance has been shown between cefalexin and other substance from the  $\beta$ -lactam group in target pathogens. Use of the product should be carefully considered when susceptibility testing has shown resistance to antimicrobials of the  $\beta$ -lactam group because its effectiveness may be reduced.

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

As with other antibiotics which are excreted mainly by the kidneys, systemic accumulation may occur when renal function is impaired. In cases of known renal insufficiency, the dose should be reduced and/or the interval of administration increased and nephrotoxic drugs should not be administered concurrently.

This veterinary medicinal product should not be used to treat kittens less than 9 weeks of age.

The use of the veterinary medicinal product in cats weighing less than 2.5 kg should be in accordance with the benefit/risk assessment performed by the responsible veterinarian.

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

Wherever possible, the use of the veterinary medicinal product should only be used based on identification and susceptibility testing of 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.

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

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross reactions to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.

- Do not handle this veterinary medicinal product if you know you are sensitised, or if you have been advised not to be in contact with such substances.
- Handle this veterinary medicinal product with great care to avoid exposure taking all recommended precautions. Wash hands after use.
- If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
- In case of accidental ingestion, seek medical attention and show the package leaflet or the label to the doctor.

Use during pregnancy, lactation:

Laboratory studies in mouse, rat and rabbit have not produced any evidence of teratogenic effects. The safety of the product has not been investigated in pregnant or lactating cats and should only be used according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

The bactericidal activity of cephalosporins is reduced by concomitant administration of bacteriostatic acting compounds (macrolides, sulfonamides and tetracyclines).

Nephrotoxicity can be increased when 1<sup>st</sup> generation cephalosporins are combined with polypeptide antibiotics, aminoglycosides or some diuretics (furosemide).

Concomitant use with such active substances should be avoided.

Overdose:

No other known side effects than those under section “Adverse events”.

## **7. Adverse events**

Cats:

|   |
|---|
| Undetermined frequency (cannot be estimated from the available data): |
|---|

|   |
|---|
| Vomiting, Diarrhoea, Allergic reaction <sup>1</sup> |
|---|

<sup>1</sup> allergic cross-reactivity with other beta lactams may occur.

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 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.

15 mg cefalexin per kg bodyweight twice daily, equivalent to 1 tablet for 5 kg bodyweight for:

- 5 days for wounds and abscesses.
- 10 to 14 days in case of urinary tract infections.
- 14 days at least in case of pyoderma. The treatment must be continued for 10 days once the lesions have disappeared.

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

In case of use of half tablets: put the remaining quantity of the tablet back into the blister pocket and use it for the next administration.

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

The tablets are flavoured. They can be administered with food or directly into the mouth of the animal.

## **10. Withdrawal periods**

Not applicable.

## **11. Special storage precautions**

Keep out of the sight and reach of children.

Do not store above 25°C.

Store in the original package.

Return any halved tablet to the opened blister pack.

Any divided tablet portions remaining after 24 hours 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 1 blister of 10 tablets  
Cardboard box with 2 blisters of 10 tablets  
Cardboard box with 10 blisters of 10 tablets  
Cardboard box with 15 blisters of 10 tablets  
Cardboard box with 20 blisters of 10 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 Louverné  
France

**17. Other information**