SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tsefalen 1000 mg film-coated tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Active substance:
Cefalexin (as cefalexin monohydrate) 1000 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets
Orange coloured oblong film-coated tablets, with a break-line on one side. Engraved with U60 on the other side.
The tablets can be divided into two equal parts.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

For the treatment of infections of the respiratory system, urogenital system and skin, localised infections in soft tissue and gastrointestinal infections caused by cefalexin-sensitive bacteria.

4.3 Contraindications

Do not use in cases of known hypersensitivity to the active substance, to other cephalosporins, to other substances of the β-lactam group or to any of the excipients.
Do not use in rabbits, gerbils, guinea pigs, and hamsters.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Wherever possible, use of the product should be based on susceptibility testing of the bacteria isolated from the animal and take into account official and local antimicrobial policies.

Deviating from the instructions given in the SPC when using the product may increase the prevalence of bacteria resistant to cefalexin and may also decrease the effectiveness of other beta-lactam antimicrobial treatments, due to the potential for cross-resistance. Therefore, deviation from the instructions must only be undertaken according to a risk/benefit assessment by the responsible veterinarian.

Do not administer in cases of known resistance to cephalosporin and penicillin.

As with other antibiotics which are excreted mainly by the kidneys, systemic accumulation may occur when renal function is impaired. In case of known renal insufficiency the dose should be reduced and antimicrobials known to be nephrotoxic should not be administered concurrently.

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

Penicillins and cephalosporins may cause sensitisation (allergy) following injection, inhalation, ingestion, or skin contact. Sensitivity to penicillins may lead to cross-sensitivity 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. 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 breathing are more serious symptoms and require urgent medical attention.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, nausea, vomiting or diarrhoea may occur following administration of the product.

In rare cases hypersensitivity can occur. In cases of hypersensitivity reactions the treatment should be discontinued.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy and lactation

Laboratory studies in rats and mice have not produced any evidence of teratogenic, foetotoxic, or maternotoxic effects.

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

In order to ensure efficacy, the veterinary medicinal product should not be used in combination with bacteriostatic antibiotics.
Concurrent use of first generation cephalosporins with polypeptide antibiotics, aminoglycosides or some diuretics such as furosemide can enhance nephrotoxicity risks.

4.9 Amounts to be administered and administration route

Oral use.
The recommended dose is 15 mg of cefalexin per kg of body weight twice a day (i.e. equivalent to one tablet twice a day for a dog weighing 66 kg). In severe or acute conditions the dose may be doubled to 30 mg/kg twice daily.

The following is a guide for the use of the product:

TSEFALEN 1000mg tablets

Bodyweight min kg	Bodyweight max kg	Number of tablets per dose*
41.0	66.0	1
66.1	80.0	1.5

**Dose to be given twice per day*

Animals weighing more than 81 kg bodyweight should be administered an appropriate combination of tablets according to bodyweight.

The product must be administered for a minimum of 5 days.
- 14 days in cases of urinary tract infection,

- At least 15 days in cases of superficial infectious dermatitis,
- At least 28 days in cases of deep infectious dermatitis.

Any increase in dose or duration of treatment should be accordingly to a benefit/risk assessment by the responsible veterinarian (e.g. chronic pyoderma).

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

The veterinary medicinal product can be given as whole tablets, or crushed and added to food if necessary.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Concerning acute toxicity, an LD50 > 0.5 g/kg has been recorded following oral administration in dogs. The administration of cefalexin has been shown to produce no serious side effects at several times the recommended dose rate.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: other beta-lactam antibacterials. First-generation cephalosporins
ATCvet Code: QJ01DB01

5.1 Pharmacodynamic properties

Cefalexin is a broad spectrum cephalosporin antibiotic with bactericidal activity against a wide range of Gram-positive and Gram-negative bacteria.

Cefalexin is a semi-synthetic bactericidal broad spectrum antibiotic belonging to the cephalosporin group which acts by interfering with bacterial cell wall formation. This bactericidal activity is mediated by drug binding to bacterial enzymes known as penicillin binding proteins (PBPs). Such enzymes are located on the inner membrane of the cell wall and their transpeptidase activity is required for the terminal stages of assembling this essential structure of the bacterial cell. Inactivation of PBPs interferes with the cross-linkage of peptidoglycan chains necessary for bacterial cell wall strength and rigidity. The bactericidal effect of cefalexin is mainly "time dependent".

Cefalexin is resistant to the action of staphylococcal penicillinase and is therefore active against the strains of *Staphylococcus aureus* that are not sensitive to penicillin (or related antibiotics such as ampicillin or amoxycillin) because of production of penicillinase.

Cefalexin is also active against the majority of ampicillin-resistant *E.coli*.

The following micro-organisms have been shown to be sensitive to Cefalexin *in vitro*: C*orynebacterium* spp, *Staphylococcus* spp (including penicillin-resistant strains), *Streptococcus* spp, *Escherichia coli*, *Moraxella* spp, *Pasteurella multocida*.

MIC data collected for cefalexin in canine isolates from the European Union (EU) (Stegmann *et al*. 2006)

Bacterial species/group and origin	**No. isolates**	**MIC50**	**MIC90**
Staphyloccoccus pseudintermedius (EU)	270	1	2
Staphyloccoccus aureus (EU)	36	2	8
Coagulase-negative staphylococci (EU)	21	1	8
Coagulase-positive staphylococci (EU)	24	1	2
β-haemolytic streptococci (EU)	86	<0.5	2
Enterococcus spp. (EU)	331	>64	>64
Pasteurella multocida (EU)	193	4	4
Escherichia coli (EU)	260	8	16
Proteus spp. (EU)	71	16	16
Klebsiella spp. (EU)	11	4	4
Enterobacter spp. (EU)	39	8	>64

The three basic mechanisms of resistance to cephalosporins result from reduced permeability, enzymatic inactivation, or absence of specific penicillin-binding proteins.

5.2 Pharmacokinetic particulars

Cefalexin is rapidly and almost completely absorbed in the gastrointestinal tract following oral administration. Cefalexin binds to a limited extent (10-20%) to plasma proteins. After oral administration of 15 mg/kg in tablets, peak blood concentration (Cmax=15 µg/ml) is usually reached between 1 and 2 hours (Tmax=90 min). Bioavailability is nearly 100% of the administered dose (AUC 6279 µg min / ml). Cefalexin does not undergo biotransformation processes that are of pharmacokinetic significance.
The elimination half-life of cefalexin is about 1.5 hours ($t_{1/2}$ = 90 min).
Elimination of the microbiologically active form is almost entirely via the kidneys by tubular excretion and glomerular filtration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Titanium dioxide (E171)
Iron oxide yellow (E172)
Iron oxide red (E172)
Povidone K-90
Sodium Starch Glycolate Type A
Magnesium stearate
Glycerol

Talc
Hypromellose

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after dividing the tablet into two: 48 hours.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Return any halved tablet to the blister pack.

6.5 Nature and composition of immediate packaging

Carton box containing 1 PVC/Aluminium blister pack of 8 tablets.
Carton box containing 4 PVC/Aluminium blister pack of 8 tablets, with a total of 32 tablets.
Carton box containing 13 PVC/Aluminium blister pack of 8 tablets, with a total of 104 tablets.

Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

ICF Srl Industria Chimica Fine
Via G.B. Benzoni, 50
26020 Palazzo Pignano – Cremona
Italy

8. MARKETING AUTHORISATION NUMBER

Vm 39896/4001

9. DATE OF FIRST AUTHORISATION

8 November 2012

10. DATE OF REVISION OF THE TEXT

May 2018

Approved 10 May 2018