ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE VETERINARY MEDICINAL PRODUCT

SEMELCEF 1000 mg tablets for dogs (AT, BE, CY, CZ, EE, EL, ES, HR, HU, IE, PL, PT, SI, SK)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:

Cefadroxil	1000 mg
(equivalent to Cefadroxil monohydrate	1050 mg)

Excipients:
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet.
Square whitish tablet with two break-marks. The tablet can be divided in two or four equal parts.

4. CLINICAL PARTICULARS

4.1. Target species

Dogs.

4.2. Indications for use, specifying the target species

Treatment of the following infections in dogs:

- Skin and soft tissue infections caused by *Staphylococcus* spp. and *Streptococcus* spp. (pyoderma, wounds, abscesses), susceptible to cefadroxil.
- Urinary tract infections caused by *Staphylococcus* spp., *Streptococcus* spp., *Proteus mirabilis, Escherichia coli* and *Klebsiella* spp., susceptible to cefadroxil.
- Upper respiratory tract infections caused by *Staphylococcus* spp., *Streptococcus* spp., and *Pasteurella multocida*, susceptible to cefadroxil.

4.3. Contraindications

Do not use in cases of 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, Guinea pigs, hamsters, gerbils, chinchillas, equines and ruminants due to possible fatal gastrointestinal disturbances caused by e.g. *Clostridium* spp. overgrowth.

4.4. Special warnings for each target species

Pyoderma is usually secondary to an underlying disease. It is advisable to determine the underlying disease to ensure the appropriate treatment is administered.

4.5. Special precautions for use

Special precautions for use in animals

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local epidemiological information.
Official and local antimicrobial policies should be taken into account when the product is used.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cefadroxil and may decrease the effectiveness of treatment with penicillins or cephalosporins, due to the potential for cross resistance.

As with other antibiotics which are excreted mainly by the kidneys, unwanted accumulation may occur in the body when renal function is impaired. In cases of known renal insufficiency the product should be administered with caution. Antimicrobials known to be nephrotoxic should not be administered concurrently and the product should be used only according to a risk/benefit assessment by the responsible veterinarian.

The product is not appropriate for animals weighing less than 12.5 kg.

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 penicillin may lead to cross-reactions to cephalosporin 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.
Accidental ingestion may result in gastrointestinal disturbances. In order to reduce the risk of accidental ingestion by children, do not take the tablets out of the blister until ready to administer to the animal. Return part-used tablets into the blister and carton and use at the subsequent administration.
In case of accidental ingestion, particularly by children, seek medical advice immediately and show the package leaflet or the label to the physician.
Do not smoke, eat or drink while handling the medication.
Wash hands after use.

4.6. Adverse reactions (frequency and seriousness)

Allergic reactions to cephalosporins may occur in very rare cases.
Nausea, vomiting and/or diarrhea may occur in very rare cases.
The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s)) during the course of one treatment)
- 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, lactation or lay

Cephalosporins cross the placenta. However, studies conducted in laboratory animals with cefadroxil have not produced any evidence of a teratogenic effects. The safety of the veterinary medicinal product in dogs has not been established during pregnancy and lactation. Use only according 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 aminoglycoside antibiotics or some diuretics such as furosemide can enhance nephrotoxicity risks.

And see section, 4.5.i) Special precautions for use in animals.

4.9. Amounts to be administered and administration route

Oral use.

Dose: 20 mg cefadroxil/kg body weight per day (equivalent to 1/4 tablet per 12.5 kg body weight) administered once daily. The product should be administered with food.

In order to avoid under-dosing, the veterinarian should prescribe a sufficient number of tablets to ensure the animal receives at least 20 mg cefadroxil per kg bodyweight per day for the duration of the intended treatment period.

The duration of treatment depends on the nature and severity of the infection and on the response.

Infections of soft tissues and urinary tract: 10 days; pyoderma and severe infections of urinary tract may require a longer treatment period, up to 3 months.The treatment should last at least 48 hours after the disappearance of the symptoms.

The weight of the animals should be determined as accurately as possible to avoid underdosing. For dogs over 12.5 kg. The smaller tablet size should be used to achieve accurate dosing in dogs weighing less than 12.5 kg.

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

No other known side effects than those under section 4.6. In the event of overdose, treatment should be symptomatic.

4.11. Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for systemic use, first-generation cephalosporins, cefadroxil.

ATC vet code: QJ01DB05

5.1. Pharmacodynamic properties

Cefadroxil is a broad spectrum semisynthetic beta-lactam antibacterial, belonging to the family of first-generation cephalosporins.

Cefadroxil acts by inhibiting the synthesis of the bacterial cell wall by binding to PBP (penicillin binding proteins), interfering with the final phase of peptidoglycan synthesis.

Its spectrum of activity includes *Staphylococci* (including strains producing penicillinases), *Streptococci*, *Escherichia coli*, *Klebsiella* spp., *Proteus mirabilis* and *Pasteurella multocida*.

Cefadroxil is not active against MRSA (Methicillin-resistant *Staphylococcus aureus*).

In the absence of specific breakpoints for cefadroxil, the following breakpoints were established by CLSI for cephalexin (1st generation cephalosporin):

- Urinary tract infections in dogs caused by E. coli, K. pneumonia, P. mirabilis: S: ≤ 16 µg/ml, R: ≥ 32 µg/ml

Source: CLSI VET08, 4th ed. (2018).

Resistance to cephalosporins can be due to one of the following mechanisms of resistance. Firstly, the production of cephalosporinases, that inactivate the antibiotic by hydrolysis of the β-lactam ring, is the most prevalent mechanism among Gram-negative bacteria. This resistance is transmitted by plasmid or chromosomally. 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 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 as a result of the expression of beta-lactamases enzymes, structural changes in porins or in presence ofefflux pumps. Co-resistance (different resistance mechanisms involved) has been described in *E.coli* due to a plasmid harbouring various resistance genes.

5.2. Pharmacokinetic particulars

After the oral administration of the medicinal product to dogs, cefadroxil is rapidly absorbed reaching a maximum plasma concentration of approximately 20 µg/ml within 1-3 hours post-administration. Cefadroxil is excreted rapidly and completely in the urine.

An administration of 20 mg/kg bw/day for 10 days does not produce accumulation of the active substance.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Magnesium stearate

Microcrystalline cellulose

6.2. Major incompatibilities

Not applicable.

6.3. Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life of the divided tablet after first use of the primary packaging: 3 days.

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Keep every part of the divided tablet in the blister and use at time of next administration.

6.5. Nature and composition of immediate packaging

PVC/PE/PVdC/PE/PVC blisters sealed with thermoheated aluminium foil packaged into a cardboard box.

Pack-sizes:

- Box with 1 blister containing 6 tablets
- Box with 10 blister containing 6 tablets (60 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

SUPPORT PHARMA, S.L.
General Alvarez de Castro, 39
28010 Madrid, Spain

8. MARKETING AUTHORISATION NUMBERS

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AN/OR USE

For animal treatment only.
To be supplied only on veterinary prescription.