SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT:

NICILAN 200 mg/50 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each tablet contains:
Active substances:
Amoxicillin (as trihydrate)..... 200 mg
Clavulanic acid (as potassium clavulanate). 50 mg

Excipients:
Erythrosine (E-127) 3.75mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM:

Tablet.
Uniform pink oblong divisible tablet.

4. CLINICAL PARTICULARS:

4.1. Target species:

Dogs

4.2. Indications for use, specifying target species:

The product is indicated in dogs and cats for the treatment of bacterial infections caused by beta-lactamase producing strains resistant to amoxicillin and sensitive to amoxicillin/clavulanic acid:

- Infections of the respiratory tract (*Streptococcus spp*., *Staphylococcus spp*., *Pasteurella spp*.)
- Infections of the genitourinary tract (*Streptococcus spp*., *Staphylococcus spp*., *Escherichia coli, Fusobacterium spp.*)
- Infections of the digestive tract (*Escherichia. coli* and *Proteus spp.*)
- Infections of the skin and soft tissues (*Staphylococcus spp.*, *Streptococcus spp*.)

4.3. Contraindications:

Do not use in case of hypersensitivity to penicillins, to other beta-lactams or to any of the excipients.
Do not use in rabbits, guinea pigs, hamsters, gerbils and chinchillas.

Do not use in animals with serious dysfunction of the kidneys accompanied by anuria and/or oliguria.
Do not use where resistance to this combination is known to occur.

4.4. Special warnings for each target species
None.

4.5. Special precautions for use

Special precautions for use in animals
In animals with hepatic or renal dysfunction, the dosing regimen should be carefully evaluated and the use of the product based on a risk/benefit evaluation by the veterinary surgeon. Caution is advised in the use in small herbivores other than those in the section 4.3.
Whenever possible, the antimicrobial should only be used based on susceptibility testing.
Do not use in case of bacteria sensitive to narrow-spectrum penicillins or amoxicillin as single substance.
Official, national and regional 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 amoxicillin/clavulanic acid and may decrease the effectiveness of treatment with beta-lactam antibiotics, due to the potential for crossresistance.
The potential for allergic cross-reactions with other penicillins and cephalosporins should be considered.

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

Penicillins and cephalosporins can cause hipersensitivity reactions (allergy) after injection, inhalation, ingestion or skin contact. Hipersensitivity to pencillins may lead to cross-reactions to cephalosporins and viceversa. Allergic reactions to these substances may occasionally be serious.
People with known hypersensitivity to penicillins and/or cephalosporins should avoid contact with the veterinary medicinal product.

Avoid direct contact with the veterinary medicine by taking specific precautions:
- Wash hands after handling the veterinary medicine
- Do not smoke, eat or drink while handling the veterinary medicine

If symptoms such as skin rash occur after accidental exposure, seek medical advice and show the package leaflet or the label to the physician. Face , lips or eyes swelling or difficulty with breathing are more serious symptoms that require urgent medical attention.

4.6. Adverse reactions (frequency and seriousness):
In very rare cases it has been observed:

- Digestive tract disorders as diarrhoea, vomiting and colitis
- Allergic reactions which severity may vary from urticaria to anaphylaxia. If allergic reactions occur, medication should be discontinued and symptomatic treatment should be administered.
- Blood dyscrasies
- Secondary infections by non sensitive micro-organisms after a prolonged use.

The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment).
- Common (more than 1 but less than 10 animals in 100 animals).
- Uncommon (more than 1 but less than 10 animals in 1,000 animals).
- Rare (more than 1 but less than 10 animals in 10,000 animals).
- Very rare (less than 1 animal in 10,000 animals, including isolated reports).

- Treatment may be discontinued depending on the severity of the undesirable effects and a benefit/risk evaluation by the veterinary surgeon..

4.7. Use during pregnancy and lactation

The safety of the veterinary medicinal product has not been established during pregnancy or lactation.
Use only according to the benefit/risk assessment by the veterinary responsible.
Studies in laboratory animals have not shown any evidence of teratogenic effects.

4.8. Interaction with other medicaments and other forms of interaction:

Chloramphenicol, macrolides, sulfonamides and tetracyclines may inhibit the antibacterial effect of penicillins because of the rapid onset of bacteriostatical action.

Penicillins may increase the effect of aminoglycosides.

4.9 Amounts to be administered and administration route:

Oral use.
The dose is 10 mg amoxicillin + 2.5 mg clavulanic acid / kg body weight twice daily.
The following table is intended as a guide to dispensing the product at this standard dose rate:

Body weight (kg)	Number of tablets twice daily
20	1
30	1-1/2
40	2
60	3

Duration of treatment:

It not is recommended to extend treatment beyond 5 - 7 days.
According to veterinary criteria, dosage and frequency of administration can be increased.

To minimise gastrointestinal effects, it is recommended to administer the product at the beginning of meals. Tablets may be added to food.

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

4.10 Overdose (symptoms, emergency procedures, antidotes):
In case of overdose, gastrointestinal signs (diarrhoea, vomiting) and/or allergic reactions could appear. Symptomatic treatment should be initiated when necessary.

4.11 Withdrawal period:
Not applicable

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use. Amoxicillin and enzyme inhibitor
ATCvet code: QJ01CR02

5.1. Pharmacodynamic properties

Amoxicillin is a beta-lactam antibiotic and its structure contains a beta-lactam ring and a thiazolidine ring, common to all penicillins. Amoxicillin shows activity against Gram-positive and Gram-negative bacteria.

Beta-lactam antibiotics inhibit formation of the bacterial cell wall by interfering with the final stage of peptidoglycan synthesis. They inhibit the activity of transpeptidase enzymes, which catalyse cross-linkage of the glycopeptide polymer units that form the cell wall. They exert a bactericidal action but they only cause lysis of growing cells.

Clavulanic acid is one of the naturally occurring metabolites of *Streptomyces clavuligerus.* It has a structural similarity to the penicillin nucleus, including the beta-lactam ring. Clavulanic acid is a beta-lactamase inhibitor acting initially competitively but ultimately irreversibly. Clavulanic acid penetrates across the bacterial cell wall by binding to both extracellular and intracellular beta-lactamases.

Amoxicillin is susceptible to breakdown by beta-lactamase action, therefore combination with an effective beta-lactamase inhibitor (clavulanic acid) extends the range of bacteria against which it is active to include b-lactamase producing species.

The veterinary medicinal product is active against a wide variety of micro-organisms including:

Gram-positive:

Staphylococcus spp.
Streptococcus spp.

Gram-negative: *Pasteurella* spp.
Escherichia coli
Fusobacterium spp.
Proteus spp

ß-lactamase producing strains are included.

It is not indicated for infections caused by *Pseudomonas* spp

Resistance is shown among Enterobacter spp., Pseudomonas aeruginosa and methicillin-resistant Staphylococcus aureus.

Minimal inhibitory concentration breakpoints (µg/ml) for sensitivity (S), intermediate sensitivity (I) and resistance (R) of amoxicillin/clavulanic acid against different pathogens (CLSI, 2013):"

	S	*I*	*R*
Dogs (skin, soft tissue)			
Staphylococcus spp.	≤ *0.25/0.12*	*0.5/0.25*	≥ *1/0.5*
Escherichia coli			
Cats (skin, soft tissue, urinary tract infection)			
Staphylococcus spp.	≤ *0.25/0.12*	*0.5/0.25*	≥ *1/0.5*
Streptococcus spp.			
Escherichia coli			
Pasteurella multocida			

5.2. Pharmacokinetic particulars

After oral administration of the recommended dose of 12.5 mg amoxicillin/ clavulanic acid/ kg. b.w. in dogs, the following parameters have been obtained: mean t_{max} of 1.5h for amoxicillin and 1.0h for clavulanic acid; mean Cmax of 11.132 µg/ml and of 3.159 µg/ml for amoxicillin and clavulanic acid, respectively; mean AUC obtained after the administration of the tablets were of 30.086 h.µg/ml for amoxicillin and 4.983 h.µg/ml for clavulanic acid. The apparent elimination half-lives obtained for amoxicillin and clavulanic acid after oral administration of the tablets were 1.5 hours and 0.7 hours, respectively.

Amoxicillin and clavulanic acid are widely distributed in tissues and interstitial fluids. They are not highly bound to plasma proteins (less than 35%).

Amoxicillin is only partially metabolized to inactive penicilloic acid, and is mainly excreted unchanged in urine. Clavulanic acid is extensively metabolized by liver enzymes to inactive metabolites, and excreted in urine and faeces.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Silica colloidal anhydrous
Magnesium stearate
Sodium starch glycolate type A
Erythrosine E-127
Cellulose microcrystalline

6.2. Incompatibilities

Not applicable

6.3. Shelf-life

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

6.4. Special precautions for storage:

Store below 30°C.

6.5. Nature and composition of immediate packaging

Blister of polyamide aluminium /PVC and lake thermosolderable aluminium foils containing 6 tablets
Pack sizes:

carton box containing 12 tablets (2 blisters)
carton box containing 60 tablets (10 blisters)
carton box containing 120 tablets (20 blisters)
carton box containing 240 tablets (40 blisters)

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product 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

Laboratorios Calier S.A.
Barcelonès, 26 (Pla del Ramassà)
08520 Les Franqueses del Vallès (Barcelona)
Spain

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

For animal treatment only – to be supplied only on veterinary prescription.