# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Clavubactin 500/125 mg tablets for dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

| **Active substances:** | *quantity* | |
|---|---|---|
| Amoxicillin (as amoxicillin trihydrate) | 500 | mg |
| Clavulanic acid (as potassium clavulanate) | 125 | mg |

| **Excipient(s):** | | |
|---|---|---|
| Quinoline Yellow E104 | 0.6 | mg |
| Titanium dioxide E171 | 1.0 | mg |

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Tablets
Yellowish-white to light yellow round tablet with a cross-shaped break mark on one side.
The tablets can be divided into 4 equal parts.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Dogs

### 4.2 Indications for use, specifying the target species

Treatment of infections in dogs caused by bacteria sensitive to amoxicillin in combination with clavulanic acid, particularly:
- Skin infections (including superficial and deep pyodermas) associated with Staphylococci (including beta-lactamase producing strains) and Streptococci.
- Urinary tract infections associated with Staphylococci (including beta-lactamase producing strains), Streptococci, *Escherichia coli* (including beta-lactamase producing strains), *Fusobacterium necrophorum* and *Proteus spp*.
- Respiratory tract infections associated with Staphylococci (including beta-lactamase producing strains), Streptococci and Pasteurellae.
- Gastrointestinal tract infections associated with *Escherichia coli* (including beta-lactamase producing strains) and Proteus spp.
- Infections of the oral cavity (mucous membrane) associated with Clostridia, Corynebacteria, Staphylococci (including beta-lactamase producing strains),

Streptococci, *Bacteroides spp* (including beta-lactamase producing strains), *Fusobacterium necrophorum* and Pasteurellae.

## 4.3 Contraindications

Do not use in animals with known hypersensitivity to penicillin or other substances of the beta-lactam group or any of the excipients.
Do not use in serious dysfunction of the kidneys accompanied by anuria and oliguria.
Do not use in rabbits, guinea pigs, hamsters, chinchillas and gerbils.
Do not use in case of known resistance to the combination.

## 4.4 Special warnings for each target species

None known.

## 4.5 Special precautions for use

### Special precautions for use in animals

Official, national and regional antimicrobial policies should be taken into account when the product is used.
Do not use in case of bacteria sensitive to narrow spectrum penicillins or to amoxicillin as single substance.
It is advised that upon initiating therapy appropriate sensitivity testing is performed and that therapy is continued only after susceptibility to the combination has been established.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the amoxicillin/clavulanate, and may decrease the effectiveness of treatment with β-lactam antibiotics due to the potential for cross-resistance.
In animals with hepatic and renal failure, the dosing regimen should be carefully evaluated.
Caution is advised in the use in small herbivores other than those in the section 4.3.

### 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 product if you know you are sensitised, or if you have been advised not to work with such preparations.
Handle this product with great care to avoid exposure, taking all recommended precautions.
If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning.
Swelling of the face, lips or eyes or difficulty with breathing, are more serious symptoms and require urgent medical attention.
Wash hands after use.

## 4.6 Adverse reactions (frequency and seriousness)

Mild gastrointestinal symptoms (diarrhoea, nausea and vomiting) may occur after administration of the product.
Allergic reactions (skin reactions, anaphylaxia) may occasionally occur. In these cases, administration should be discontinued and a symptomatic treatment given.

## 4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and mice have not produced any evidence of teratogenic or fetotoxic effects. No studies have been conducted in the pregnant and lactating dogs. Use only according to the benefit/risk assessment by the responsible veterinarian.

## 4.8 Interaction with other medicinal products and other forms of interaction

Chloramphenicol, macrolides, sulfonamides, and tetracyclines may inhibit the antibacterial effects of penicillins.
The potential for allergic cross-reactivity with other penicillins should be considered.
Penicillins may increase the effect of aminoglycosides.

## 4.9 Amounts to be administered and administration route

*Posology*
For oral administration in dogs.
To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

*Dosage*
The recommended dose is 12.5 mg of combined active substance (=10 mg amoxicillin and 2.5 mg clavulanic acid) per kg bodyweight twice daily.
The following table is intended as a guide to dispensing the product at the standard dose rate of 12.5 mg of combined actives per kg bodyweight twice daily.

| | Number of tablets twice daily | | |
|---|---|---|---|
| **Bodyweight (kg)** | **amoxicilline 50 mg/ clavulanic acid 12.5 mg** | **amoxicilline 250 mg/ clavulanic acid 62.5 mg** | **amoxicilline 500 mg/ clavulanic acid 125 mg** |
| **1 – 1.25** | | | |
| **1.25 – 2.5** | | | |
| **2.5 – 3.75** | | | |
| **3.75 – 5** | | | |
| **5 – 6.25** | | | |
| **6.25 - 12.5** | | | |
| **12.5 - 18.75** | |  | |
| **18.75 - 25** | | | |

| | | | |
|---|---|---|---|
| **25 - 31.25** | | | |
| **31.25 - 37.5** | | | |
| **37.5 - 50** | | | |
| **50 – 62.5** | | | |
| **62.5 - 75** | | | |

In refractory cases of skin infections, a double dose is recommended (25 mg per kg bodyweight, twice daily).

The majority of routine cases respond to 5 – 7 days of therapy.
In chronic cases, , a longer case of therapy is recommended. In such circumstances overall treatment length must be at the clinician's discretion, but should be long enough to ensure complete resolution of the bacterial disease.

### 4.10 Overdose (symptoms, emergency procedures, antidotes)

Mild gastrointestinal symptoms (diarrhea, nausea and vomiting) may occur more frequently after overdose of the product.

### 4.11 Withdrawal period(s)

Not applicable.

## 5. PHARMACOLOGICAL PROPERTIES

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

### 5.1 Pharmacodynamic properties

Amoxicillin is an aminobenzylpenicillin from the β-lactam penicillin family which prevents the bacterial cell wall formation by interfering with the final step of peptidoglycan synthesis.
Clavulanic acid is an irreversible inhibitor of intracellular and extracellular β-lactamases which protects amoxicillin from inactivation by many β-lactamases.
Amoxicillin/clavulanate has a wide range of activity which includes β-lactamase producing strains of both Gram-positive and Gram-negative aerobes, facultative anaerobes and obligate anaerobes.
Good susceptibility is shown with several gram-positive bacteria including Staphylococci (including beta-lactamase producing strains, MIC90 0.5 µg/ml), Clostridia (MIC90 0.5 µg/ml), Corynebacteria and Streptococci, and gram-negative bacteria including *Bacteroides spp* (including betalactamase producing strains, MIC90 0.5 µg/ml), Pasteurellae (MIC90 0.25 µg/ml), *Escherichia coli* (including beta-lactamase producing strains, MIC90 8 µg/ml) and *Proteus spp* (MIC90 0.5 µg/ml).
Variable susceptibility is found in some *E. coli*.

Susceptibility tests on bacterial pathogens from canine and feline origin revealed the following MIC50 values for a fixed combination of amoxicillin and clavulanic acid (2:1): *Proteus spp* 0.5 µg/ml and *Staphylococcus intermedius* 0.094 µg/ml.
Bacteria with a MIC90 of ≤ 2 µg/ml are considered being susceptible and those with a MIC90 of ≥ 8 µg/ml being resistant. Resistance is shown among methicillin-resistant *Staphylococcus aureus*. A trend in resistance of *E. coli* is reported.

## 5.2 Pharmacokinetic particulars

The pharmacokinetic behaviour of clavulanic acid is roughly comparable with that of amoxicillin. Amoxicillin is well absorbed after oral administration. In dogs, the systemic bioavailability is 60-70%. Amoxicillin (pKa 2.8) has a relatively small apparent distribution volume, low plasma-protein binding (34% in dogs) and a short elimination half-life period due to active tubular excretion by the kidneys. After absorption, highest concentrations are found in the kidneys (urine) and bile, followed by the liver, lungs, heart and spleen.
Distribution of amoxicillin into cerebrospinal fluid is low unless the meninges are inflamed.
Clavulanic acid (pKa 2.7) is also well absorbed after oral administration. Penetration into cerebrospinal fluid is poor. Plasma-protein binding is about 25% and the elimination halflife value is short. Clavulanic acid is largely eliminated by renal excretion (unchanged in the urine).
The pharmacokinetic parameters of the veterinary medicinal product in dogs after oral administration of a dose of 25 mg active material (= 20 mg amoxicillin + 5 mg clavulanic acid) per kg body weight are summarized in the following table.

| | Cmax (µg/ml) | Tmax (hour) | t1/2 (hour) | AUC∞ h.µg/ml |
|---|---|---|---|---|
| Amoxicillin | 11.41 ± 2.74 | 1.38 ± 0.41 | 1.52 ± 0.19 | 36.57 ± 7.31 |
| Clavulanic acid | 2.06 ± 1.05 | 0.95 ± 0.33 | 0.71 ± 0.23 | 3.14 ± 1.21 |

# 6. PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Quinoline yellow lacquer (E104)
Titanium dioxide (E171)
Microcrystalline cellulose
Hypromellose
Crospovidone
Povidone K-25
Macrogol 6000
Stearic acid
Saccharin sodium (E954)
Vanilla flavour
Colloidal anhydrous silica
Magnesium stearate.

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life of tablet quarters: 24 hours.

## 6.4. Special precautions for storage

Do not store above 25°C.
Store in the original container.
Quarter tablets should be returned to the opened strip and stored in a refrigerator.

## 6.5 Nature and composition of immediate packaging

Carton containing 5 aluminium/aluminium blister strips each strip with 2 tablets corresponding to 10 tablets per carton.
Carton containing 5 aluminium/aluminium blister strips each strip with 4 tablets corresponding to 20 tablets per carton.
Carton containing 25 aluminium/aluminium blister strips each strip with 4 tablets corresponding to 100 tablets per carton.
Carton containing 1 aluminium/aluminium blister strip with 10 tablets corresponding to 10 tablets per carton.
Carton containing 10 aluminium/aluminium blister strips each strip with 10 tablets corresponding to 100 tablets per carton.
Carton containing 25 aluminium/aluminium blister strips each strip with 10 tablets corresponding to 250 tablets per carton.
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 products should be disposed of in accordance with local requirements.

# 7. MARKETING AUTHORISATION HOLDER

Le Vet B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

# 8. MARKETING AUTHORISATION NUMBER

Vm 19994/4027

# 9. DATE OF FIRST AUTHORISATION

11 October 2010

## 10. DATE OF REVISION OF THE TEXT

February 2017

Approved 20 February 2017