Veterinary Medicinal Product

Kesium 500 mg / 125 mg Chewable tablets for dogs

PART I B

Pharmaceutical Form

Chewable Tablet

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SUMMARY OF THE PRODUCT CHARACTERISTICS

Pharmaceutical Form

Chewable Tablet

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Kesium 500 mg / 125 mg Chewable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:

Amoxicillin (as amoxicillin trihydrate)	500.00 mg
Clavulanic acid (as potassium clavulanate)	125.00 mg

Excipient (s):
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Chewable tablet
Clover-shaped scored beige tablet. The tablets can be divided into four equal parts.

4. CLINICAL PARTICULARS

4.1. Target species:

Dogs

4.2. Indications for use, specifying the target species:

For the treatment of the following infections caused by β-lactamase producing strains of bacteria sensitive to amoxicillin in combination with clavulanic acid and where clinical experience and/or sensitivity testing indicates the product as the drug of choice:

- Skin infections (including superficial and deep pyodermas) associated with *Staphylococcus* spp..
- Urinary tract infections associated with *Staphylococcus* spp., *Streptococcus* spp.*, Escherichia coli* and *Proteus mirabilis*.
- Respiratory tract infections associated with *Staphylococcus* spp.*, Streptococcus* spp*. and Pasteurella* spp..
- Digestive tract infections associated with *Escherichia coli*.
- Infections of the oral cavity (mucous membrane) associated with *Pasteurella* spp.*, Streptococcus* spp.*, Escherichia coli.*

4.3. Contraindications

Do not use in animals with hypersensitivity to penicillins or other substances of the β-lactam group or to any excipients.
Do not use in animals with serious dysfunction of the kidneys accompanied by anuria and oliguria.

Do not administer to gerbils, guinea pigs, hamsters, rabbits and chinchillas. Do not use in horses and ruminating animals.
Do not use where resistance to this combination is known to occur.

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 with respect to the use of broad-spectrum antibiotics should be taken into account.
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 beta-lactam antibiotics
In animals with hepatic and 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.

The potential for allergic cross-reactions with other penicillin derivates and cephalosporins should be considered
The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

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 signs (diarrhoea, and vomiting) may occur after administration of the product. Treatment may be discontinued depending on the severity of the undesirable effects and a benefit/risk evaluation by the veterinary surgeon.

Allergic reactions (skin reactions, anaphylaxis) may occasionally occur. In these cases, administration should be discontinued and a symptomatic treatment given.
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, lactation or lay

Laboratory studies in rats and mice have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.
The safety of the product has not been assessed in pregnant and lactating bitches.
In pregnant and lactating animals, 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 effect of penicillins because of the rapid onset of bacteriostatic action.
Penicillins may increase the effect of aminoglycosides.

4.9. Amounts to be administered and administration route(s)

Oral use

The recommended dose of the product is 10 mg amoxicillin /2.5 mg clavulanic acid per kg body weight twice a day by the oral route in dogs, i.e. 1 tablet per 50 kg body weight every 12 h, according to the following table:

Body weight (kg)	Number of tablets to be administered twice daily
> 9 to 12.5	¼
12.6 to 20	Use the 200 mg / 50 mg
20.1 to 25	½
25.1 to 37.5	¾
37.6 to 50	1
50.1 to 62.5	1¼
62.6 to 75	1½

In refractory cases the dose may be doubled to 20 mg of amoxicillin / 5 mg clavulanic acid/kg bodyweight twice daily, at the clinician's discretion.

The chewable tablets are flavoured and are accepted by a majority of dogs. The chewable tablets can be administered directly into the mouth of the animals or added to a small quantity of food.

Duration of therapy
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.

To ensure the correct dosage, body weight should be determined as accurately as possible to avoid under-dosing.
Instruction on how to divide the tablet: Put the tablet on an even surface, with its scored side facing down (convex face up). With the tip of the forefinger, exert slight vertical pressure on the middle of the tablet to break it along its width into halves. Then, in order to obtain quarters, exert slight pressure on the middle of one half with the forefinger to break it into two parts.

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

In case of overdose diarrhoea, allergic reactions or further symptoms like central nervous excitation manifestations or cramps could appear. Symptomatic treatment should be initiated when necessary.

4.11. Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins
ATC vet code: QJ01CR02

5.1. Pharmacodynamic properties

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

β-lactam antibiotics prevent the bacterial cell wall from forming by interfering with the final stage of peptidoglycan synthesis. They inhibit the activity of transpeptidase enzymes, which catalyse cross-linkage of the peptidoglycan polymers that form the cell wall. They exert a bactericidal action but cause lysis of growing cells only.

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

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

In vitro potentiated amoxicillin is active against a wide range of clinically important aerobic and anaerobic bacteria including:

Gram-positive:
Staphylococcus spp. (including β-lactamase producing strains)
Streptococcus spp.

Gram-negative:

Escherichia coli (including most β-lactamase producing strains)

Pasteurella spp.
Proteus spp.

Resistance is shown among *Enterobacter* spp., *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*. A trend in resistance of *E. coli* is reported.
Resistance to β-lactam antibiotics is mainly mediated by β-lactamases which hydrolyze antibiotics such as amoxicillin.
According to the CLSI standard (CLSI, July 2013)., Amoxicillin-clavulanate MICs breakpoints (µg/mL) were determined for *Staphylococcus* spp*.,* and *Escherichia coli* strains in dogs (skin and soft tissue), as:
Sensitive ≤ 0.25/0.12 µg/mL; Intermediate: 0.5/0.25 µg/mL; Resistant ≥ 1/0.5µg/ml.

5.2. Pharmacokinetic particulars

After oral administration in dogs, amoxicillin and clavulanic acid are rapidly absorbed. Amoxicillin (pKa 2.8) has a relatively small apparent distribution volume, a low plasma protein binding (34% in dogs) and a short terminal half-life due to active tubular excretion via the kidneys. Following absorption the highest concentrations are found in the kidneys (urine) and the bile and then in liver, lungs, heart and spleen. The distribution of amoxicillin to the cerebrospinal fluid is low unless the meninges are inflamed.

Clavulanic acid (pKa 2.7) is also well-absorbed following oral administration. The penetration to the cerebrospinal fluid is poor. The plasma protein binding is approximately 25% and the elimination half-life is short. Clavulanic acid is mainly eliminated by renal excretion (unchanged in urine).

After single oral administration of 17 mg/kg amoxicillin and 4.3 mg/kg clavulanic acid in dogs:
- The maximal plasma concentration (Cmax) of amoxicillin (8.6 µg/mL) was observed 1.5 hour following administration.
- The maximal plasma concentration (Cmax) of clavulanic acid (4.9 µg/mL) was observed 54 minutes following administration.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipient(s):

Pig liver powder
Yeast
Crospovidone (type IA)
Povidone K 25
Hypromellose
Microcrystalline cellulose
Silica, colloidal anhydrous
Magnesium stearate

6.2. Major incompatibilities

Not applicable.

6.3. Shelf-Life

Shelf-life of the veterinary medicinal product as packaged for sale:
3 years
Any divided tablet portions remaining after 36 hours should be discarded

6.4. Special precautions for storage

Do not store above 25°C.
Divided tablets should be stored in the blister pack

6.5. Nature and composition of immediate packaging

(PA-AL-PVC – aluminium heat sealed) containing 6 tablets per blister
Cardboard box of 6 tablets
Cardboard box of 12 tablets
Cardboard box of 96 tablets
Cardboard box of 144 tablets
Cardboard box of 240 tablets
Cardboard box of 480 tablets

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

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

To be completed in accordance with national requirements