1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Clavaseptin 750 mg palatable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:
Amoxicillin.....600 mg
(Corresponding to amoxicillin trihydrate)……688.69 mg
Clavulanic acid..... 150 mg
(Corresponding to potassium clavulanate)……. 178,69 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Brown iron oxide E172	1,43 mg
Crospovidone	
Povidone K25	
Silicon dioxide	
Microcrystalline cellulose	
Pig liver flavour	
Dried yeast	
Magnesium stearate	
Hypromellose	

Oblong, off -white to brownish speckled, scored tablets of about 24 mm. Tablet can be divided into four equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Treatment of infections caused by bacteria susceptible to amoxicillin in combination with clavulanic acid (including beta-lactamase producing strains), in particular:

- Skin infections (including deep and superficial pyodermas, wounds, abscesses) caused by *Staphylococcus* spp, *Streptococcus* spp and *Pasteurella* spp.
- Respiratory tract infections (sinusitis, rhino-tracheitis, bronchopneumonia) caused by *Staphylococcus* spp and *E. coli*.
- Infections of the oral cavity (mucous membranes) caused by *Streptococcus* spp, and *Pasteurella* spp.

- Urinary tract infections (nephritis, cystitis) caused by *E. coli*, *Klebsiella* spp and *Proteus mirabilis.*
- Digestive tract infections, especially gastroenteritis caused by *E. coli.*

3.3 Contraindications

Do not use in cases of hypersensitivity to penicillins or other substances of the β-lactam group or to any of the excipients.
Do not administer to gerbils, guinea pigs, hamsters, rabbits and chinchillas or other small herbivores.
Do not use in animals with serious dysfunction of the kidneys accompanied by anuria or oliguria.
Do not administer to horses and ruminating animals.

3.4 Special warnings

Cross-resistance has been shown between amoxicillin/clavulanic acid and β-lactam antibiotics. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to βlactam antibiotics because its effectiveness may be reduced.
Methicillin resistant *S. aureus* (MRSA) and methicillin resistant *S. pseudintermedius* (MRSP) have been isolated in cats and dogs with proportion of resistance that varies across EU countries.
Do not use in cases of known resistance to the combination of amoxicillin and clavulanic acid.
Do not use in cases of suspected or confirmed MRSA/MRSP infections, as isolates should be considered resistant to all β-lactam including amoxicillin/clavulanic acid combination.
High resistances (up to 100%) have been reported in *E. coli* isolates from skin and soft tissue infections in dogs.

3.5 Special precautions for use

<u>Special precautions for safe use in the target species:</u>

In animals with impaired liver and kidney function, the use of the veterinary medicinal product should be subject to a benefit/risk evaluation by the veterinary surgeon and the posology evaluated carefully.

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at local/regional level.
Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

Aminopenicillins in combination with beta-lactamase inhibitors are in AMEG category „C". An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.
Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.
The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.
The potential for allergic cross-reactivity with other penicillins should be considered.

<u>Special precautions to be taken by the person administering the veterinary medicinal product to animals:</u>

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 veterinary medicinal product if you know you are sensitised, or if you have been advised not to work with such preparations.

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.
Wash hands after handling the tablets.

Accidental ingestion of the veterinary medicinal product by a child may be harmful. To avoid accidental ingestion, particularly by a child, unused part-tablets should be returned to the open blister space and inserted back into the carton.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs.

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Vomiting[1], Diarrhoea.[1] Hypersensitivity reaction (Allergic skin reactions[2]), anaphylaxis[2]

[1)] Treatment may be discontinued depending on the severity of the undesirable effects and a benefit/risk evaluation by the veterinary surgeon
[2)] In these cases, administration should be discontinued and a symptomatic treatment given

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
Laboratory studies in rats have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.
Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

The bactericidal activity of amoxicillin may be reduced by the simultaneous use of bacteriostatic substances such as macrolides, tetracyclines, sulfonamides and chloramphenicol.
Penicillins may increase the effect of aminoglycosides.

3.9 Administration routes and dosage

Oral use.

To ensure the correct dosage, body weight should be determined as accurately as possible.

The recommended dose of the veterinary medicinal product is 10 mg amoxicillin / 2.5 mg clavulanic acid per kg body weight twice a day, i.e. 1 tablet per 60 kg body weight every 12 h, for 5 to 7 days, according to the following table:

Bodyweight (kg)	Number of tablets twice daily
[20.1 - 30]	½
[30.1 - 45]	¾
[45.1 - 60]	1
[60.1 - 75]	1 ¼
[75.1 - 90]	1 ½

In severe cases, the dose can be doubled at the discretion of the responsible veterinarian.

Duration of the treatment:
For all indications, a treatment of 5 to 7 days is sufficient in the majority of cases.
For chronic or recurrent cases, it may be necessary to continue treatment for 2 to 4 weeks.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

At three times the recommended dose for a period of 28 days, diarrhoea was observed in dogs. In the event of an overdose symptomatic treatment is advised.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal period

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01CR02

4.2 Pharmacodynamics

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. The antimicrobial spectrum relevant for dog's indications is summarized in the table below.

Summary of susceptibility for dog target bacteria:

Target bacteria in each indication	n	Range of MIC (µg/mL)	MIC50 (µg/mL)	MIC90 (µg/mL)	Clinical breakpoints (I/R)
Skin and soft tissues					
Staphylococcus spp	431*	0.03-32	0.12	1	0.25/1

S. aureus *S. intermedius* group Coagulase-negative *Staphylococcus* spp	38* 343* 49*	0.12-16 0.03-8 0.03-32	0.5 0.12 0.12	2 0.5 2	0.25/1 0.25/1 0.25/1
Streptococcus spp *Streptococcus canis* *Streptococcus dysgalactiae*	142* 127* 12*	0.015-0.06 0.015-0.06 0.015	≤0.015 ≤0.015 ≤0.015	≤0.015 ≤0.015 ≤0.015	- - -
Pasteurella spp	22*	0.03-0.25	0.12	0.25	-
Respiratory					
Staphylococcus spp *S. intermedius* group *S. aureus*	112* 90* 22*	0.06-8 0.06-8 0.12-8	0.12 0.12 0.25	0.5 0.25 1	- - -
Dental					
Streptococcus spp	16**	0.008 - 1	0.014	0.4	-
Pasteurella spp	68**	0.03 - 64	0.124	0.4	-
Urinary					
Escherichia coli	236*	1-32	4	16	8/-
Klebsiella spp	33*	0.5-32	2	32	8/-
Proteus spp	66*	0.5-16	1	8	8/-
Digestive					
Escherichia coli	- *	1-32	4	8	-

Breakpoints are from CLSI VET01-S7.
* MIC values determined from bacteria collected in Europe in 2021-2022 (ComPath-IV survey). Susceptibility of digestive isolates is assumed similar to that of the same bacteria in other types of infection.
** MIC values determined from bacteria collected from dog dental infections in Europe in 2002.
- Missing information.

The two main mechanisms of resistance to amoxicillin/clavulanic acid are inactivation by β-lactamases that are not inhibited by clavulanic acid, and alteration of penicillin binding proteins, which lead to co-resistance to other β-lactam antibiotics. Impermeability of bacteria or efflux pump mechanisms may also contribute to bacterial resistance, including co- and cross-resistance. Susceptibility and resistance patterns can vary with geographical area and bacterial strain, and may change over time.
Pseudomonas spp are naturally resistant to the amoxicillin – clavulanic acid combination. Methicillin resistant *S. aureus* (MRSA) and methicillin resistant *S. pseudintermedius* (MRSP) isolates have been identified in cats and dogs and should be considered resistant to all β-lactam including amoxicillin/clavulanic acid combination.
High resistances (up to 100%) have been reported in *E. coli* isolates from skin and soft tissue infections in dogs.

4.3 Pharmacokinetics

After oral administration at the recommended dose in dogs, the absorption of amoxicillin and clavulanic acid is fast. The maximum plasma concentration of amoxicillin of 8.5 µg/ml is reached in 1.4 hours and the maximum plasma concentration of clavulanic acid of 0.9 µg/ml is reached in 0.9 hours. Half-life is 1 hour in dogs for both substances.

Elimination is also fast. 12 % of the amoxicillin and 17 % of clavulanic acid is excreted in the urine. The remainder is excreted as inactive metabolites.
After repeated oral administration of the recommended dose, there is no accumulation of amoxicillin or clavulanic acid and the steady state is reached rapidly after first administration.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 48 hours.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Return any part of the tablet to the opened blister-pack and use within 48 h.

5.4 Nature and composition of immediate packaging

Aluminium/aluminium (oPA/Alu/PE) blister pack with 10 tablets/blister
Cardboard box: Pack sizes of 10, 100, 250, and 600 tablets.
Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetoquinol Ireland Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA10983/048/005

8. DATE OF FIRST AUTHORISATION

08/04/2022

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

13/11/2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).