

## **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NL: Clavoral 500/125 mg tabletten voor honden  
CZ: Clavubactin 500/125 mg tablety pro psi  
ES: Clavubactin 500/125 mg comprimidos para perros  
FR: Clavubactin 500/125 mg comprimés pour chiens  
HU: Clavubactin 500/125 mg tableta kutyaák számára  
IE: Clavubactin 500/125 mg tablets for dogs  
IS: Clavubactin vet. 500/125 mg töflur fyrir hunda  
IT: Clavubactin 500/125 mg compresse per cani  
PL: Clavubactin vet. 500/125 mg tabletki dla psów  
SK: Clavubactin 500/125 mg tablety pre psov  
UK: Clavubactin 500/125 mg tablets for dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

<b>Active substances:</b>	<i>quantity</i>
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  $\beta$ -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.

Bodyweight (kg)	Number of tablets twice daily		
	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 course 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  $\beta$ -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  $\beta$ -lactamases which protects amoxicillin from inactivation by many  $\beta$ -lactamases.

Amoxicillin/clavulanate has a wide range of activity which includes  $\beta$ -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, MIC<sub>90</sub> 0.5  $\mu$ g/ml), Clostridia (MIC<sub>90</sub> 0.5  $\mu$ g/ml), Corynebacteria and Streptococci, and gram-negative bacteria including *Bacteroides spp* (including betalactamase producing strains, MIC<sub>90</sub> 0.5  $\mu$ g/ml), Pasteurellae (MIC<sub>90</sub> 0.25  $\mu$ g/ml), *Escherichia coli* (including beta-lactamase producing strains, MIC<sub>90</sub> 8  $\mu$ g/ml) and *Proteus spp* (MIC<sub>90</sub> 0.5  $\mu$ g/ml). Variable susceptibility is found in some *E. coli*.

Susceptibility tests on bacterial pathogens from canine and feline origin revealed the following MIC<sub>50</sub> values for a fixed combination of amoxicillin and clavulanic acid (2:1): *Proteus spp* 0.5  $\mu$ g/ml and *Staphylococcus intermedius* 0.094  $\mu$ g/ml.

Bacteria with a MIC<sub>90</sub> of  $\leq 2$   $\mu$ g/ml are considered being susceptible and those with a MIC<sub>90</sub> of  $\geq 8$   $\mu$ g/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 half-life 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.

C <sub>max</sub>	T <sub>max</sub>	t <sub>1/2</sub>	AUC <sub>∞</sub>
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	(µg/ml)	(hour)	(hour)	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**

AST Beheer B.V.  
Wilgenweg 7  
3421 TV Oudewater  
The Netherlands  
+31 (0)348 563434  
+31 (0)348 563838  
info@astfarma.nl

**8. MARKETING AUTHORISATION NUMBER(S)**

To be established nationally.

**9. DATE OF RENEWAL OF THE AUTHORISATION**

-

**10. DATE OF REVISION OF THE TEXT**

**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

Cardboard box

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Clavoral 500/125 mg tablets for dogs  
Amoxicillin/Clavulanic acid

**2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES**

Each tablet contains:  
Amoxicillin (as amoxicillin trihydrate) 500 mg  
Clavulanic acid (as potassium clavulanate) 125 mg

**3. PHARMACEUTICAL FORM**

Tablet.

**4. PACKAGE SIZE**

10 tablets  
20 tablets  
100 tablets  
10 tablets  
100 tablets  
250 tablets

**5. TARGET SPECIES**

Dog.

**6. INDICATION(S)**

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

For oral use.  
Read the package leaflet before use.

**8. WITHDRAWAL PERIOD**

**9. SPECIAL WARNING(S), IF NECESSARY**

Penicillins and cephalosporins may occasionally cause severe allergic reactions. Read the package leaflet before use.

**10. EXPIRY DATE**

EXP {month/year}

**11. SPECIAL STORAGE CONDITIONS**

Do not store above 25°C.

Store in the original package.

Quarter tablets should be returned to the opened strip and stored in a refrigerator.

Quarter tablets should be used within 24 hours.

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

Disposal: read package leaflet

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable**

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

**14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”**

Keep out of the sight and reach of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

AST Beheer B.V.  
Wilgenweg 7  
3421 TV Oudewater  
The Netherlands

**16. MARKETING AUTHORISATION NUMBER(S)**

To be established nationally.

**17. MANUFACTURER’S BATCH NUMBER**

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS**

**(Aluminium/aluminium strip)**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Clavoral 500/125 mg tablets for dogs

**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

AST Beheer B.V.

**3. EXPIRY DATE**

EXP {month/year} .....

**4. BATCH NUMBER**

LOT .....

**5. THE WORDS "FOR ANIMAL TREATMENT ONLY"**

For animal treatment only.

**B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### Clavoral 500/125 mg tablets for dogs

#### 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:

AST Beheer B.V.  
Wilgenweg 7  
3421 TV Oudewater  
The Netherlands

Manufacturer responsible for the batch release:

Lelypharma B.V.  
Zuiveringweg 42  
8243 PZ Lelystad  
The Netherlands

#### 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Clavoral 500/125 mg tablets for dogs

#### 3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

**Active substances per tablet:**

Amoxicillin (as amoxicillin trihydrate)	500 mg
Clavulanic acid (as potassium clavulanate)	125 mg

**Other ingredients**

Quinoline yellow lacquer (E104)	0.6 mg
Titanium dioxide (E171)	1.0 mg

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. INDICATION(S)

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 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.

#### 5. 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.

## 6. ADVERSE REACTIONS

Mild gastrointestinal symptoms (diarrhea, 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.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

## 7. TARGET SPECIES

Dogs.

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

### *Posology*

For oral administration only.

### *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.

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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).

#### *Duration of therapy*

The majority of routine cases respond to 5 – 7 days of therapy.

In chronic cases, a longer course 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.

### **9. ADVICE ON CORRECT ADMINISTRATION**

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

### **10. WITHDRAWAL PERIOD**

Not applicable.

### **11. SPECIAL STORAGE PRECAUTIONS**

Do not store above 25°C.

Store in the original package.

Keep out of the sight and reach of children.

Quarter tablets should be returned to the opened strip and stored in a refrigerator.

Shelf-life of tablet quarters: 24 hours.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and blister after "EXP". The expiry date refers to the last day of that month.

### **12. SPECIAL WARNING(S)**

#### **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  $\beta$ -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 5.

#### **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.

### **Use during pregnancy and lactation**

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.

### **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.

### **Overdose**

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

### **13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIAL, IF ANY**

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

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

### **14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

### **15. OTHER INFORMATION**

Pack sizes

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.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.