SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NL: Clavoral 50/12.5 mg tabletten voor katten en honden
CZ: Clavubactin 50/12.5 mg tablety pro kočky a psi
ES: Clavubactin 50/12.5 mg comprimidos para gatos y perros
FR: Clavubactin 50/12.5 mg comprimés pour chats et chiens
HU: Clavubactin 50/12.5 mg tabletta macskák és kutyák számára
IE: Clavubactin 50/12.5 mg tablets for cats and dogs
IS: Clavubactin vet. 50/12.5 mg töflur fyrir ketti og hunda
IT: Clavubactin 50/12.5 mg compresse per gatti e cani
PL: Clavubactin vet. 50/12.5 mg tabletki dla kotów i psów
SK: Clavubactin 50/12.5 mg tablety pre psov a mačky
UK: Clavubactin 50/12.5 mg tablets for cats and dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:	*quantity*
Amoxicillin (as amoxicillin trihydrate)	50 mg
Clavulanic acid (as potassium clavulanate)	12.5 mg

Excipient(s):	
Quinoline Yellow E104	0.06 mg
Titanium dioxide E171	0.10 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet
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 and cats

4.2 Indications for use, specifying the target species

Treatment of infections in cats and 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.
- Digestive 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 hypersensivity to penicillin or other substances of the beta-lactam group.
Do not use in serious dysfunction of the kidneys accompanied by anuria and oliguria.
Do not use in rabbits, guinea pigs, hamsters, chinchillas or 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 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 β-lactam antibiotics
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 reactions (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 advise 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 and cats. 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 and cats.
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).

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.

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 0.6 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 0.12 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* and *Klebsiella spp*.
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, *Staphylococcus intermedius* 0.094 µg/ml, and *Bordetella bronchiseptica* 4 µg/ml.
Bacteria with a MIC90 of $\leq$ 2 µg/ml are considered being susceptible and those with a MIC90 of $\geq$ 8 µg/ml being resistant. Resistance is shown among *Enterobacter spp, Pseudomonas aeruginosa* and 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 and cats 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	Tmax	t1/2	AUC∞

	(µg/ml)	(hour)	(hour)	h.µg/ml
Dog				
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
Cat				
Amoxicillin	12.87 ± 2.12	1.47 ± 0.44	1.24 ± 0.28	38.74 ± 4.68
Clavulanic acid	4.60 ± 1.68	0.72 ± 0.26	0.63 ± 0.16	6.18 ± 2.19

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf-life of tablet quarters: 12 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.
Carton containing 5 aluminium/aluminium blister strips each strip with 4 tablets.
Carton containing 25 aluminium/aluminium blister strips each strip with 4 tablets.
Carton containing 1 aluminium/aluminium blister strip with 10 tablets.
Carton containing 10 aluminium/aluminium blister strips each strip with 10 tablets.
Carton containing 25 aluminium/aluminium blister strips each strip with 10 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

AST Farma 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

06 October 2014

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Clavoral 50/12.5 mg tablets for cats and dogs
(Amoxicillin and Potassium clavulanate)

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each tablet contains:
Active substances

Amoxicillin (as amoxicillin trihydrate)	50 mg
Clavulanic acid (as potassium clavulanate)	12.5 mg

Excipient(s)

Quinoline Yellow E104	0.06 mg
Titanium dioxide E171	0.10 mg

3. PHARMACEUTICAL FORM

Tablet.

4. PACKAGE SIZE

Carton containing 5 aluminium/aluminium blister strips each strip with 2 tablets.
Carton containing 5 aluminium/aluminium blister strips each strip with 4 tablets.
Carton containing 25 aluminium/aluminium blister strips each strip with 4 tablets.
Carton containing 1 aluminium/aluminium blister strip with 10 tablets.
Carton containing 10 aluminium/aluminium blister strips each strip with 10 tablets.
Carton containing 25 aluminium/aluminium blister strips each strip with 10 tablets.

5. TARGET SPECIES

Dog and cat.

6. INDICATION(S)

Treatment of infections in cats and 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.
- Digestive 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.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral administration.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Penicillins and cephalosporins may occasionally cause severe allergic reactions. See package leaflet for user warnings.

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 12 hours.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, 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 will help to protect the environment.

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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight 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)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

(Aluminium/aluminium strip)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Clavoral 50/12.5 mg tablet for cats and 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 50/12.5 mg tablets for cats and 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

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

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Clavoral 50/12.5 mg tablets for cats and dogs.
(Amoxicillin and Potassium clavulanate)

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

Active substances per tablet:

Amoxicillin (as amoxicillin trihydrate)	50	mg
Clavulanic acid (as potassium clavulanate)	12.5	mg

Other ingredients

Quinoline yellow lacquer (E104)	0.06 mg
Titanium dioxide (E171)	0.10 mg

4. INDICATION(S)

Treatment of infections in cats and 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 c o l i* (including beta-lactamase producing strains), *Fusobacterium necrophorum* and *Proteus spp*.
- Respiratory tract infections associated with Staphylococci (including beta-lactamase producing strains), Streptococci and Pasteurellae.
- Digestive 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.

5. CONTRAINDICATIONS

Do not use in animals with known hypersensivity to penicillin or other substances of the betalactam group.

Do not use in serious dysfunction of the kidneys accompanied by anuria and oliguria.
Do not use in rabbits, guinea pigs, hamsters, chinchillas or gerbils.
Do not use in case of known resistance to the combination.

6. ADVERSE REACTIONS

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

7. TARGET SPECIES

Dogs and cats.

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.

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).

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.

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 container.

Keep out of the reach and sight of children.
Quarter tablets should be returned to the opened strip and stored in a refrigerator.
Quarter tablets should be used within 12 hours.
Do not use after the expiry date stated on the carton after EXP.

12. SPECIAL WARNING(S)

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 β-lactam antibiotics
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 reactions (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 advise 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 and cats. 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.

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

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15. OTHER INFORMATION

Pack sizes
Carton containing 5 aluminium/aluminium blister strips each strip with 2 tablets.
Carton containing 5 aluminium/aluminium blister strips each strip with 4 tablets.
Carton containing 25 aluminium/aluminium blister strips each strip with 4 tablets.
Carton containing 1 aluminium/aluminium blister strip with 10 tablets.
Carton containing 10 aluminium/aluminium blister strips each strip with 10 tablets.
Carton containing 25 aluminium/aluminium blister strips each strip with 10 tablets.
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.