

*[Version 8, 10/2012]*

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Clavudale 40 mg/10 mg tablets for cats and dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains:

Active substances:

Amoxicillin (as amoxicillin trihydrate)	40 mg
Clavulanic acid (as potassium clavulanate)	10 mg

Excipient:

Erythrosine (E127) 0.75 mg

For the full list of excipients see section 6.1.

## 3. PHARMACEUTICAL FORM

Tablet.

Pink, oblong, scored, meat flavoured tablets.

The tablet can be divided into halves.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Cats and dogs.

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

For the treatment of bacterial infections susceptible to amoxicillin in combination with clavulanic acid where clinical experience and/or sensitivity testing indicates the product as the drug of choice.

Uses include:

Skin infections (including deep and superficial pyodermas) associated with *Staphylococcus* spp. and *Streptococcus* spp.;

Infections of the oral cavity (mucous membrane) associated with *Clostridium* spp., *Corynebacterium* spp., *Staphylococcus* spp., *Streptococcus* spp., *Bacteroides* spp. and *Pasteurella* 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.

Gastrointestinal infections associated with *Escherichia coli* and *Proteus mirabilis*.

### 4.3 Contraindications

Do not use in rabbits, guinea pigs, hamsters and gerbils.

Do not use in animals with known hypersensitivity to penicillin or substances of the  $\beta$ -lactam group or any of the excipients.

Do not use in animals with either oliguria or anuria associated with renal dysfunction.

Do not use in cases of known resistance to the combination of amoxicillin and clavulanic acid.

#### **4.4 Special warnings for each target species**

None known.

#### **4.5 Special precautions for use**

##### Special precautions for use in animals

Caution is advised on the use of the product in small herbivores other than those listed in 4.3. In animals with hepatic and renal dysfunction, the dosing regimen should be carefully evaluated. Use of the product should be based on susceptibility testing and should take into account official national and regional policies with respect to the use of broad spectrum antibiotics. Do not use in cases of bacteria sensitive to narrow spectrum penicillins or to amoxicillin as a single substance. Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to amoxicillin and clavulanic acid, and may decrease the effectiveness of treatment with other  $\beta$ -lactam antibiotics, due to the potential for cross-resistance.

##### 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. Allergic reactions (skin reactions, anaphylaxis), blood dyscrasia and colitis may occasionally occur. In these cases, discontinue administration and give symptomatic treatment.

#### **4.7 Use during pregnancy, lactation or lay**

Laboratory studies in rats and mice have not produced any evidence of teratogenic or foetotoxic effects. No studies have been conducted in pregnant or lactating dogs or 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**

Bacteriostatic antibiotics (e.g. 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**

For oral administration only. The dosage rate is 10 mg amoxicillin/2.5 mg clavulanic acid/kg body weight twice daily. The tablets may be added to a little food.

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

The following table is intended as a guide to dispensing the product at the standard dose rate of 10 mg amoxicillin/2.5 mg clavulanic acid/kg body weight twice daily.

Body weight (kg)	Number of tablets twice daily
1 to ≤ 2	½
> 2 to ≤ 4	1
> 4 to ≤ 6	1½
> 6 to ≤ 8	2

In refractory cases the dose may be doubled to 20 mg amoxicillin/5 mg clavulanic acid/kg body weight twice daily.

Duration of therapy:

Routine cases involving all indications:

The majority of routine cases respond to between 5 and 7 days of therapy. Lack of effect after 5-7 days of treatment necessitates renewed examination.

Chronic or refractory cases:

In chronic cases, longer courses of antibacterial therapy may be required. In such circumstances, overall treatment length is at the clinician's discretion, but must be long enough to ensure complete resolution of the bacterial disease.

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

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

#### 4.11 Withdrawal period

Not applicable.

### 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins.

ATCvet code: QJ01CR02

#### 5.1 Pharmacodynamic properties

Amoxicillin is an aminobenzylpenicillin from the  $\beta$ -lactam penicillin family which prevents 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 in combination with clavulanic acid 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, including:

**Gram-positives with good susceptibility:** *Clostridium* spp., *Corynebacterium* spp., *Staphylococcus* spp., *Streptococcus* spp.

**Gram-negatives with good susceptibility:** *Pasteurella* spp., *Bacteroides* spp., *Proteus mirabilis*.

**Gram-negatives with variable susceptibility:** *Escherichia coli*.

Susceptibility and resistance patterns can vary with geographical area and bacterial strain, and may change over time.

Amoxicillin/clavulanic acid breakpoints (NCCLS/2012):

*Staphylococci*: sensitive: MIC  $\leq$  4/2  $\mu\text{g/ml}$ , resistant: MIC  $\geq$  8/4  $\mu\text{g/ml}$

Other organisms: sensitive: MIC  $\leq$  8/4  $\mu\text{g/ml}$ , resistant: MIC  $\geq$  32/16  $\mu\text{g/ml}$

The two main mechanisms of resistance to amoxicillin/clavulanic acid are:

- Inactivation by those bacterial beta-lactamases that are not themselves inhibited by clavulanic acid, including class B, C and D.
- Alteration of Penicillin-Binding Proteins (PBP), which reduce the affinity of the antibacterial agent for the target (methicillin resistant *S. aureus*, MRSA and *S. pseudintermedius*, MRSP).

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria. Resistance genes can be located on chromosomes (*mecA*, MRSA) or plasmids (LAT, MIR, ACT, FOX, CMY family beta-lactamases) and a variety of resistance mechanisms have emerged.

*Pseudomonas aeruginosa* and *Enterobacter* spp. can be regarded as intrinsically resistant to the combination.

## 5.2 Pharmacokinetic particulars

After the oral administration to dogs of the recommended dose of 10 mg amoxicillin/2.5 mg clavulanic acid/kg body weight the following parameters were observed: median  $T_{\max}$  of 1.5 hours for amoxicillin and of 1.0 hours for clavulanic acid.

After the oral administration to cats of the recommended dose of 10 mg amoxicillin/2.5 mg clavulanic acid/kg body weight the following parameters were observed: median  $T_{\max}$  of 2.0 hours for amoxicillin and of 0.75 hours for clavulanic acid.

Amoxicillin is well-absorbed following oral administration. In dogs the systemic bioavailability is 60-70%. 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).

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Erythrosine (E127)

Silica, colloidal anhydrous

Magnesium stearate

Sodium starch glycolate (Type A)

Cellulose, microcrystalline

Luctarom 31600z additive (meat flavour)

### 6.2 Incompatibilities

Not applicable.

### **6.3 Shelf life**

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf life after first opening the immediate packaging: 12 hours.

Any divided tablet portions remaining after 12 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**

Blister packs consisting of orientated Polyamide/Aluminium/Polyvinyl chloride film, heat sealed with aluminium foil (20µm) in strips of 6 tablets. Cartons containing 12, 24 or 120 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**

Dechra Regulatory B.V.

Handelsweg 25

5531 AE Bladel

Netherlands

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

IE: VPA22622/005/001

## **9. DATE OF FIRST AUTHORISATION**

IE: 28<sup>th</sup> October 2011

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

17/07/2020

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARTON**

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

Clavudale 40 mg/10 mg  
Tablets for cats and dogs

Amoxicillin 40 mg, Clavulanic acid 10 mg

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

1 tablet contains:

Active substances:

Amoxicillin (as amoxicillin trihydrate) 40 mg

Clavulanic acid (as potassium clavulanate) 10 mg

Excipient:

Erythrosine (E127) 0.75 mg

**3. PHARMACEUTICAL FORM**

Tablets

**4. PACKAGE SIZE**

12 tablets/24 tablets/120 tablets

**5. TARGET SPECIES**

Cats and dogs.

**6. INDICATIONS**

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

Read the package leaflet before use.  
For oral use.

**8. WITHDRAWAL PERIOD**

Not applicable.

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

Read the package leaflet before use.

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

**10. EXPIRY DATE**

EXP: (month/year)

**11. SPECIAL STORAGE CONDITIONS**

Do not store above 25°C.

Divided tablets should be stored in the blister pack.

Any divided tablet portions remaining after 12 hours should be discarded.

Keep the blister pack in the outer carton.

**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**

Dechra Regulatory B.V.  
Handelsweg 25  
5531 AE Bladel  
Netherlands

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

National item.

**17. MANUFACTURER’S BATCH NUMBER**

Lot: (number)

IE only:

VPA22622/005/001

DL

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**BLISTER**

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

Clavudale 40 mg/10 mg  
Tablets for cats and dogs

Amoxicillin 40 mg, Clavulanic acid 10 mg

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

Dechra Regulatory B.V.

**3. EXPIRY DATE**

EXP: (month/year)

**4. BATCH NUMBER**

Lot: (number)

**5. THE WORDS “FOR ANIMAL TREATMENT ONLY”**

For animal treatment only

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET FOR:

Clavudale 40 mg/10 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:**

Dechra Regulatory B.V.  
Handelsweg 25  
5531 AE Bladel  
Netherlands

#### **Manufacturer responsible for batch release:**

Laboratorio Reig Jofré SA  
Jarama s/n Polígono Industrial  
45007 Toledo  
Spain

Genera Inc.,  
Svetonedeljska cesta 2,  
Kalinovica,  
10436 Rakov Potok,  
Croatia

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

Clavudale 40 mg/10 mg tablets for cats and dogs

Amoxicillin 40 mg, Clavulanic acid 10 mg

### 3. **STATEMENT OF THE ACTIVE SUBSTANCES AND OTHER INGREDIENTS**

#### 1 tablet contains:

Active substances:

Amoxicillin (as amoxicillin trihydrate) 40 mg

Clavulanic acid (as potassium clavulanate) 10 mg

Excipient:

Erythrosine (E127) 0.75 mg

Pink, oblong, scored, meat flavoured tablets.

### 4. **INDICATIONS**

For the treatment of bacterial infections susceptible to amoxicillin in combination with clavulanic acid where clinical experience and/or sensitivity testing indicates the product as the drug of choice.

Uses include:

Skin infections (including deep and superficial pyodermas) associated with *Staphylococcus* spp. and *Streptococcus* spp.;

Infections of the oral cavity (mucous membrane) associated with *Clostridium* spp., *Corynebacterium* spp., *Staphylococcus* spp., *Streptococcus* spp., *Bacteroides* spp. and *Pasteurella* 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.;

Gastrointestinal infections associated with *Escherichia coli* and *Proteus mirabilis*.

## 5. CONTRAINDICATIONS

Do not use in rabbits, guinea pigs, hamsters and gerbils.

Do not use in animals with known hypersensitivity to penicillin or substances of the  $\beta$ -lactam group or any of the excipients.

Do not use in animals with either little or no urination associated with renal dysfunction.

Do not use in cases of known resistance to the combination of amoxicillin and clavulanic acid.

## 6. ADVERSE REACTIONS

Mild gastrointestinal signs (diarrhoea and vomiting) may occur after administration of the product.

Allergic reactions (skin reactions, anaphylaxis), blood dyscrasia and colitis may occasionally occur. In these cases, discontinue administration and give symptomatic treatment.

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

## 7. TARGET SPECIES

Cats and dogs.

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

Follow the dosage instructions given by your veterinary surgeon.

For oral administration only. The dosage rate is 10 mg amoxicillin/2.5 mg clavulanic acid/kg body weight twice daily. The tablet can be divided into halves.

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

The following table is intended as a guide to dispensing the product at the standard dose rate of 10 mg amoxicillin/2.5 mg clavulanic acid/kg body weight twice daily.

Body weight (kg)	Number of tablets twice daily
1 to $\leq$ 2	$\frac{1}{2}$
> 2 to $\leq$ 4	1
> 4 to $\leq$ 6	1 $\frac{1}{2}$
> 6 to $\leq$ 8	2

In refractory cases the dose may be doubled to 20 mg amoxicillin/5 mg clavulanic acid/kg body weight twice daily.

### Duration of therapy:

Routine cases involving all indications:

The majority of routine cases respond to between 5 and 7 days of therapy. Lack of effect after 5-7 days of treatment necessitates renewed examination.

Chronic or refractory cases:

In chronic cases, longer courses of antibacterial therapy may be required. In such circumstances, overall treatment length is at the clinician's discretion, but must be long enough to ensure complete resolution of the bacterial disease.

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

The tablets may be added to a little food.

## **10. WITHDRAWAL PERIOD**

Not applicable.

## **11. SPECIAL STORAGE PRECAUTIONS**

Keep out of the sight and reach of children.

Do not store above 25°C.

Divided tablets should be stored in the blister pack.

Any divided tablet portions remaining after 12 hours should be discarded.

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

## **12. SPECIAL WARNINGS**

### Special precautions for use in animals:

Caution is advised on the use of the product in small herbivores other than those listed in the section 'Contraindications'.

In animals with hepatic and renal dysfunction, the dosing regimen should be carefully evaluated. Use of the product should be based on susceptibility testing and should take into account official national and regional policies with respect to the use of broad spectrum antibiotics. Do not use in cases of bacteria sensitive to narrow spectrum penicillins or to amoxicillin as a single substance. Use of the product deviating from the instructions given in this package leaflet may increase the prevalence of bacteria resistant to amoxicillin and clavulanic acid, and may decrease the effectiveness of treatment with other  $\beta$ -lactam antibiotics, due to the potential for cross-resistance.

### User warnings:

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 or lactation:

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

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

Bacteriostatic antibiotics (e.g. 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 (symptoms, emergency procedures, antidotes):

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

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

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

11/12/2020

**15. OTHER INFORMATION**

IE only:  VPA22622/005/001 <table border="1"><tr><td>PO</td></tr></table> Prescription Only Medicine	PO
PO	

For animal treatment only.

To be supplied only on veterinary prescription.

Pack sizes: 12, 24 or 120 pack consisting of 2, 4 or 20 blisters, each containing 6 tablets per blister.

Not all pack sizes may be marketed.