

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav 500 mg Palatable Tablets for Dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active Ingredients:

Amoxicillin (as amoxicillin trihydrate)	400 mg
Clavulanic acid (as potassium clavulanate)	100 mg

Colouring Agent:

Carmoisine Lake (E122)	2.45mg
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For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Tablet. Pink divisible circular tablet with score line on one face and figure 500 embossed on opposing face. The tablet can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Target Species

Dogs

4.2 Indications for Use, Specifying the Target Species

Treatment of the following infections caused by beta-lactamase producing strains of bacteria sensitive to amoxicillin in combination with clavulanic acid:

- Skin infections (including superficial and deep pyodermas) caused by susceptible *Staphylococci*.
- Urinary tract infections caused by susceptible *Staphylococci* or *Escherichia coli*.
- Respiratory infections caused by susceptible *Staphylococci*.
- Enteritis caused by susceptible *Escherichia coli*.

It is recommended to carry out suitable tests for sensitivity when initiating the treatment. The treatment should only proceed if sensitivity is proven to the combination.

4.3 Contraindications

Do not use in animals with known cases of hypersensitivity to penicillins or other substances of the beta-lactam group.

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

Do not use in animals with serious dysfunction of kidneys accompanied by anuria or oliguria.

Do not use where resistance to the combination is known to occur

4.4 Special warnings for each target species

None.

4.5 Special Precautions for Use

i. Special precautions for use in animals:

Inappropriate use of the product may increase the prevalence of bacteria resistant to amoxicillin/clavulanic acid.

In animals with hepatic and renal failure, the dosing regimen should be carefully evaluated.

Use of the product should be based on susceptibility testing and take into account official and local antimicrobial policies. Narrow spectrum antibacterial therapy should be used for first line treatment where susceptibility testing suggests likely efficacy of this approach.

Caution is advised in the use in small herbivores other than those in 4.3.

Do not administer to horses and ruminating animals.

ii. 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.

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 package leaflet or the label to the physician. 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)

Hypersensitivity unrelated to dose can occur with these agents.

Gastrointestinal symptoms (diarrhoea, vomiting) may occur after administration of the product.

Allergic reactions (e.g. skin reactions, anaphylaxia) may occasionally occur.

In case of occurrence of allergic reaction, the treatment should be withdrawn.

4.7 Use During Pregnancy, Lactation or Lay

Studies in laboratory animals have not produced any evidence of teratogenic effects. Use only according to the risk/benefit assessment by the responsible veterinarian.

4.8 Interactions with Other Medicinal Products and Other Forms of Interaction

Chloramphenicol, macrolides, sulfonamides and tetracyclines may inhibit the antibacterial effect of penicillin because of the rapid onset of bacteriostatic action. The potential for allergic cross-reactivity with other penicillins should be considered. Penicillins may increase the effects of aminoglycoside.

4.9 Amounts to be Administered and Administration

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

Administration is via the oral route. The dosage rate is 12.5 mg combined actives/kg bodyweight twice daily. The tablets may be crushed and added to a little food.

The following table is intended as a guide to dispensing the product at the standard dose rate of 12.5 mg/kg twice daily.

Bodyweight (kg)	Number of tablets (500 mg) per dose twice daily
20 kg	$\frac{1}{2}$
40 kg	1
60 kg	$1\frac{1}{2}$
80 kg	2

Duration of therapy:

Routine cases involving all indications: The majority of cases respond to between 5 and 7 days therapy.

Chronic or refractory cases: In these cases where there is considerable tissue damage, a longer course of therapy may be required in that it allows sufficient time for damaged tissue to repair.

4.10 Overdose (Symptoms, Emergency Procedures, Antidotes) if necessary

No adverse effects have been reported after the daily administration of 3 times the recommended dose for 8 days, and after the daily administration of the recommended dose for 21 days.

4.11 Withhold Period(s)

Not applicable

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-infective for systemic use: amoxicillin and enzyme inhibitor.

ATC vet code: QJ01CR02

5.1 Pharmacodynamic properties

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

Beta-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 glycopeptide polymer units 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 beta-lactamase inhibitor acting initially competitively but ultimately irreversibly. Clavulanic acid will penetrate the bacterial cell wall binding to both extracellular and intracellular beta-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: *Staphylococci* (including β -lactamase producing strains), *Clostridia*, *Streptococci*.

Gram-negative: *Escherichia coli* (including most β -lactamase producing strains), *Campylobacter* spp, *Pasteurellae*, *Proteus* spp.

Resistance is shown among *Enterobacter* spp, *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*. Dogs diagnosed with *Pseudomonas* infections should not be treated with this antibiotic combination. A trend in resistance of *E. coli* is reported.

5.2 Pharmacokinetic properties

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 heavily eliminated by renal excretion (unchanged in urine).

After oral administration of the 50mg presentation at the recommended dose of 12.5mg combined actives/kg to dogs, the following parameters were observed: C_{max} of 6.30 +/- 0.45µg/ml, T_{max} of 1.98 +/- 0.135h and AUC of 23.38 +/- 1.39 µg/ml.h for amoxicillin and C_{max} of 0.87 +/- 0.1µg/ml, T_{max} of 1.57 +/- 0.177hrs and AUC of 1.56 +/- 0.24mg/ml.h for clavulanic acid.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipient(s)

Sodium Starch Glycolate (type A)
Copolydione
Magnesium Stearate
Cellulose, microcrystalline
Silicon Dioxide
Calcium Carbonate
Magnesium Carbonate, heavy
Roast Beef Flavour
Lake Carmosine (E122)

6.2 Incompatibilities

Not applicable.

6.3 Shelf-Life

Shelf-life of veterinary product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 24 hours.
Any divided tablet portion remaining after 24 hours should be discarded.

6.4 Special Precautions for Storage

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

6.5 Nature and Composition of Immediate Packaging

The product is presented as follows:

Aluminium/aluminium blister strips, each containing 5 tablets. Cartons of 10, 20, 25 and 100 tablets. Not all pack sizes may be marketed.

6.6 Special Precautions for the Disposal of Unused Veterinary Medicinal Products or Waste Materials Derived from the Use of Such Products if appropriate

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

Norbrook Laboratories Limited
Station Works
Newry
County Down
BT35 6JP
Northern Ireland

8. MARKETING AUTHORISATION NUMBER

Vm 02000/4259

9. DATE OF FIRST AUTHORISATION

Date: 26 April 2006

10. DATE OF REVISION OF TEXT

Date: October 2012

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not Applicable

APPROVED 29/11/12

T. NASH