

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav 500 mg Palatable Tablets for Dogs (AT, BE, DK, ES, FR, IE, LU, NL, NO, PT, UK-NI)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:

Amoxicillin (as amoxicillin trihydrate) 400 mg

Clavulanic acid (as potassium clavulanate) 100 mg

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Carmoisine Lake (E122)	2.45 mg
Sodium Starch Glycolate (type A)	
Copovidone	
Magnesium Stearate	
Cellulose, microcrystalline	
Silicon Dioxide	
Calcium Carbonate	
Magnesium Carbonate, heavy	
Roast Beef Flavour	

Round pink tablet with a score line and 500 embossed on opposing faces.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For the 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.

3.3 Contraindications

Do not use in cases of hypersensitivity to penicillins, other active substances of the beta-lactam group or to any of the excipients.

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.

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

Do not administer to horses and ruminating animals.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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.

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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

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

¹ In these cases, treatment should be withdrawn.

² Unrelated to dose.

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:

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

3.8 Interaction 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.

3.9 Administration routes and dosage

Oral use.

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	½
40 kg	1
60 kg	1½
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.

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

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.

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.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01CR02

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 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.

5.3 Special precautions for storage

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

5.4 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.

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

{Name}

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/YYYY}

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) (<https://medicines.health.europa.eu/veterinary>).

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE**{OUTER CARTON}****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Noroclav 500 mg Palatable Tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:

Active substance:

Amoxicillin (as Amoxicillin Trihydrate) 400 mg

Clavulanic Acid (as Potassium Clavulanate) 100 mg

Excipient:

Carmosine Lake (E122) 2.45mg

3. PACKAGE SIZE

10 Tablets

20 Tablets

25 Tablets

100 Tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS**6. ROUTES OF ADMINISTRATION**

Oral use. The tablets may be crushed and added to a little food.

7. WITHDRAWAL PERIODS**8. EXPIRY DATE**

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C.

Store in a dry place.

Return any halved tablet to the open blister pack. Any divided tablet portion remaining after 24 hours should be discarded. Keep the blister in the outer carton.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

User warnings:

Penicillins and cephalosporins may occasionally cause severe allergic reactions.

See package leaflet for user warnings.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{BLISTER PACKAGE}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav 500 mg Palatable Tablets for dogs

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Each tablet contains:

Active Substances:

Amoxicillin (as amoxicillin trihydrate) 400 mg

Clavulanic acid (as potassium clavulanate) 100 mg

Excipient:

Carmoisine Lake (E122) 2.45 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Noroclav 500 mg Palatable Tablets.

2. Composition

Each tablet contains:

Active Substances:

Amoxicillin (as Amoxicillin Trihydrate)	400 mg
Clavulanic Acid	100 mg

Excipient:

Carmosine Lake (E122)	2.45 mg
-----------------------	---------

3. Target species

Dogs.

4. Indications for use

For the 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.

5. Contraindications

Do not use in cases of hypersensitivity to penicillins, other active substances of the beta-lactam group or to any of the excipients.

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.

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

Do not administer to horses and ruminating animals.

6. Special warnings

Special precautions for safe use in the target species:

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

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

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

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.

Pregnancy:

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

Interaction with other medicinal products and other forms of interaction:

The potential for allergic cross-reactivity with other penicillins should be considered. Penicillins may increase the effect of aminoglycosides.

Chloramphenicol, macrolides, sulphonamides and tetracyclines may inhibit the antibacterial effect of penicillins because of the rapid onset of bacteriostatic action.

Overdose:

The veterinary medicinal product is of a low order of toxicity and is well tolerated by the oral route.

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.

7. Adverse events

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

¹ In these cases, treatment should be withdrawn.

² Unrelated to dose.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

Oral use.

To ensure a correct dosage, bodyweight 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 veterinary medicinal 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	½
40 kg	1
60 kg	1½
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.

9. Advice on correct administration

Administration is via the oral route.

The tablets may be crushed and added to a little food.

10. Withdrawal periods

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25°C. Store in a dry place.

Return any halved tablet to the open blister pack. Any divided tablet portion remaining after 24 hours should be discarded.

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

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Aluminium/aluminium blister strips, each containing 5 tablets.
Cartons of 10, 20, 25 and 100 tablets.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland
Tel: +44 (0) 28 3026 4435
Email: phvdept@norbrook.co.uk

Manufacturer responsible for batch release:

Norbrook Laboratories Limited
Station Works
Newry
Co. Down
BT35 6JP

Norbrook Manufacturing Limited
Rossmore Industrial Estate
Monaghan
Ireland

17. Other information

Resistance to many antibiotics is caused by beta-lactamase enzymes which destroy the antibiotic before it can act on the bacteria themselves. The clavulanate in the veterinary medicinal product counteracts this defence mechanism by inactivating the beta-lactamases, thus rendering the organisms sensitive to amoxicillin's rapid bactericidal effect, at concentrations readily attainable in the body.

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*. A trend in resistance of *E. coli* is reported.