Norbrook Laboratories Ltd
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Noroclav 75 mg Chewable Flavoured Tablets for Cats and Dogs

Species:	Cats, Dogs
Therapeutic indication:	**Pharmaceuticals: Antimicrobials: Oral preparations:** Tablets
Active ingredient:	Amoxicillin, Clavulanic Acid
Product:	Noroclav 75 mg Chewable Flavoured Tablets for Cats and Dogs
Product index:	Noroclav 75 mg Chewable Tablets

Qualitative and quantitative composition

Each tablet contains:

Active substance(s):

Amoxicillin (as amoxicillin trihydrate)	60 mg
Clavulanic acid (as Potassium Clavulanate)	15 mg

Excipients:

For a full list of excipients, see section Pharmaceutical Particulars

Pharmaceutical form

Chewable Tablet.

Pale brown circular tablet with a score line and embossed with '75' on opposing faces.

The tablets can be divided into equal halves.

Clinical particulars

Target Species

Cats and Dogs.

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 Staphylococcus spp.

Urinary tract infections caused by Staphylococcus spp. or Escherichia coli.

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Respiratory tract infections caused by Staphylococcus spp.

Enteritis caused by Escherichia coli.

Dental infections (e.g. gingivitis)

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.

Contraindications

The product should not be given to rabbits, hamsters, guinea pigs or gerbils. Do not use in animals with known hypersensitivity to penicillin, other beta-lactams or any of the excipients.Do not use in animals with serious dysfunction of the kidneys accompanied by anuria or oliguria.

Do not use where resistance to this combination is known to occur.

Do not administer to horses and ruminating animals.

Special Warnings for Each Target Species

None known.

Special Precautions for Use

Special precautions for use in animals

Whenever possible, the product should only be used based on susceptibility testing.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to beta-lactam antimicrobials and may decrease the effectiveness of treatment with other classes of antimicrobials due to the potential for cross resistance.

Official and regional antimicrobial policies should be taken into account.

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

Caution is advised in their use in small herbivores.

The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of animals.

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.

Adverse Reactions (Frequency and Seriousness)

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Hypersensitivity reactions to penicillins may occur in treated animals.

Allergic reactions (e.g. skin reactions, anaphylaxis) may occasionally occur. In case of occurrence of allergic reaction, the treatment should be withdrawn.

Very rarely, (less than 1 animal in 10,000 animals treated, including isolated reports), use of the product may result in gastro-intestinal disorders (vomiting, diarrhoea, anorexia).

Use During Pregnancy, Lactation or Lay

Laboratory studies in rats and mice have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.

In pregnant and lactating animals, 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 effect of penicillins because of the rapid onset of bacteriostatic action. The potential for allergic cross-reactivity with other penicillins should be considered.

Penicillins may increase the effect of aminoglycosides.

Amounts to be Administered and Administration

Administration: by the oral route.

Dosage rate: total 12.5 mg of combined actives/kg bw. (equal to 10 mg of amoxicillin + 2.5 mg of clavulanate/kg bw).

Dosage frequency: The following table is intended as a guide to dispensing at the standard dose rate of 12.5 mg/kg bw, twice daily.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

Body weight (kg)	Number of tablets to be administered twice daily
≤2	Use 50 mg tablets
[2.1- 3.0]	½
[3.1- 6.0]	1
[6.1- 9.0]	1 ½
[9.1- 12.0]	2
>12	Use 250 or 500 mg tablets

If the dog or cat does not accept the tablet from hand or bowl, then the tablets may be crumbled and added to a little food.

The majority of routine cases respond after between 5 and 7 days therapy. If no improvement is observed after 5 – 7 days, the diagnosis should be re-assessed.

In chronic or refractory cases, a longer course of therapy may be required e.g. chronic skin disease 10 - 20 days, chronic cystitis 10 - 28 days, respiratory disease 8 - 10 days.

If no improvement is observed after two weeks, the diagnosis should be re-assessed.

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

Symptomatic treatment should be initiated when necessary. Mild gastrointestinal symptoms (diarrhoea, nausea and vomiting) may occur more frequently after overdose of the product.

Withdrawal Period(s)

Not applicable.

Pharmacological particulars

Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins.

ATC Vet Code: QJ01CR02.

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 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 *-lactamase and therefore combination with an effective ß-lactamase inhibitor (clavulanic acid) extends the range of bacteria against which it is active to include *-lactamase producing species.

In vitro potentiated amoxicillin is active against a wide range of clinically important aerobic and anaerobic bacteria including:

Gram-positive:

- Staphylococcus spp. (including b-lactamase producing strains)
- Streptococcus spp.

Gram-negative:

- Escherichia coli (including most b-lactamase producing strains)
- Pasteurella spp.
- Proteus spp.

Resistance is shown among Enterobacter spp., Pseudomonas aeruginosa and methicillin-resistant Staphylococcus aureus.

Dogs and cats diagnosed with Pseudomonas infections should not be treated with this antibiotic combination.

A trend in resistance of E. coli is reported.

Resistance

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Acquired resistance prevalence may be high in E. coli.

Resistance notably develops through the production of inhibitor-resistant beta-lactamases or the hyperproduction of beta-lactamases.

In some strains of Staphylococcus aureus (methicillin-resistant S. aureus, MRSA), and of Staphylococcus pseudintermedius, resistance to all beta-lactams is conferred by the alteration of the cell wall target proteins (Penicillin-Binding Proteins). This is often associated to resistance to multiple other antimicrobial compounds with cross resistance.

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

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 (pK1 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 recommended dose of 12.5mg combined actives/kg to cats, the following parameters were observed: Cmax of 9.17 µg/ml and AUC of 53.27 µg.h/ml for amoxicillin and Cmax of 2.32 µg/ml, and AUC of 13.33 µg.h/ml for clavulanic acid.

After oral administration of the recommended dose of 12.5mg combined actives/kg to dogs, the following parameters were observed: Cmax of 8.92 µg/ml and AUC of 46.29 µg.h/ml for amoxicillin and Cmax of 2.21 µg/ml, and AUC of 8.99 µg.h/ml for clavulanic acid.

Pharmaceutical particulars

List of Excipient(s)

Sodium Starch Glycolate, type A

Povidone K30

Spray Dried Pork Liver Powder

Yeast Extract

Silica Colloidal Hydrated

Magnesium Stearate

Microcrystalline Cellulose

Incompatibilities

Not applicable.

Shelf-Life

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Shelf-life of the veterinary medicinal product as packaged for sale: 15 months

Discard any unused halved tablets immediately.

Special Precautions for Storage

Do not store above 25°C.

Store in a dry place.

Nature and Composition of Immediate Packaging

Blisters (aluminium/aluminium): 28, 56, 224 and 504 tablets in outer packages with blister strips containing 14 tablets each.

Not all pack sizes may be marketed.

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 product should be disposed of in accordance with local requirements.

Marketing Authorisation Holder (if different from distributor)

Norbrook Laboratories Limited

Station Works

Camlough Road

Newry

Co. Down

BT35 6JP

Northern Ireland

Marketing Authorisation Number

Vm 02000/4380

Significant changes

Date of the first authorisation or date of renewal

05 March 2014

Date of revision of the text

August 2017

Any other information

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Nil.

Legal category

Legal category: POM-V

GTIN

GTIN description: Noroclav 75mg Chewable: 56x

GTIN: 5023534021797

GTIN description: Noroclav 75mg Chewable: 224x

GTIN: 5023534021803

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Norbrook Laboratories Ltd
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Noroclav 250 mg Tablets for Dogs

Species:	Dogs
Therapeutic indication:	**Pharmaceuticals: Antimicrobials: Oral preparations:** Tablets
Active ingredient:	Amoxicillin, Clavulanic Acid
Product:	Noroclav 250 mg Tablets for Dogs
Product index:	Noroclav 250 mg Tablets

Qualitative and quantitative composition

Each tablet contains:

Active substance(s):

Amoxicillin (as amoxicillin trihydrate)	200 mg
Clavulanic acid (as Potassium Clavulanate)	50 mg

Excipients:

Carmoisine Lake (E122)	1.225 mg

For a full list of excipients, see section Pharmaceutical Particulars

Pharmaceutical form

Tablet.

Round pink biconvex tablet with a score line and 250 embossed on opposing faces.

Clinical particulars

Target species

Dogs.

Indications for use, specifying the target species

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

- Skin infections (including superficial and deep pyodermas) caused by susceptible Staphylococci

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- Urinary tract infection 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 testing when initiating the treatment. The treatment should only proceed if sensitivity is proven to the combination.

Contraindications

Do not use in animals with known hypersensitivity to penicillin 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 the kidneys accompanied by anuria and oliguria.

Do not use where resistance to this combination is known to occur.

Special Warnings for each target species

None.

Special precautions for use

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 section, **Contraindications**.

Do not administer to horses and ruminating animals.

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.

Adverse reactions (frequency and seriousness)

Hypersensitivity reactions unrelated to dose can occur with these agents.

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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.

Use during pregnancy, lactation or lay

Studies in laboratory animals have not produced any evidence of teratogenic, effects. 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 effect of penicillins because of the rapid onset of bacteriostatic action.

The potential for allergic cross-reactivity with other penicillins should be considered.

Penicillins may increase the effect of aminoglycosides.

Amounts to be administered and administration route

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 of combined actives/kg twice daily.

Bodyweight (kg)	Number of tablets twice daily
19-20	1
21-30	1,5
31-40	2
41-50	2,5
More than 50	3

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.

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

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

In a tolerance study a tested dose of 3 times the recommended dose of 12.5mg of the combined actives administered twice daily for 8 days did not demonstrate adverse effects.

Withdrawal period

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Not applicable.

Pharmacological particulars

Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins

ATC Vet Code: QJ01CR02

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 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 ß-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.

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.

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Clavulanic acid (pK1 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 recommended dose of 12.5mg combined actives/kg to dogs, the following parameters were observed: Cmax of 6.30 +/-0.45µg/ml, Tmax of 1.98 +/- 0.135h and AUC of 23.38 +/- 1.39 µg/ml.h for amoxicillin and Cmax of 0.87 +/- 0.1µg/ml, Tmax of 1.57 +/- 0.177hrs and AUC of 1.56 +/- 0.24mg/ml.h for clavulanic acid.

Pharmaceutical particulars

List of excipients

Carmosine Lake (E122)

Sodium Starch Glycollate

Copovidone K24-36

Magnesium Stearate

Microcrystalline Cellulose

Calcium Carbonate

Heavy Magnesium carbonate

Roast Beef Flav-o-lok

Incompatibilities

Not applicable.

Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale:

- Blister packs: 2 years
- Tubs: 6 months

Special precautions for storage

Do not store above 25°C.

Store in the original package in order to protect from moisture.

Nature and composition of immediate packaging

The product is supplied in high-density polyethylene tubs with a polyethylene screw cap lid containing 100 and 250 tablets. A sachet of desiccant is included in each container. The product is also presented in packs of 2, 4, 10, 20 and 50 blister strips (aluminium-aluminium) each containing 5 tablets per strip.

Not all pack sizes may be marketed.

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Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused product or waste material should be disposed of in accordance with national requirements.

Marketing Authorisation Holder (if different from distributor)

Norbrook Laboratories Limited

Station Works

Newry

Co. Down

BT35 6JP

Northern Ireland

Marketing Authorisation Number

Vm 02000/4212

Significant changes

Date of the first authorisation or date of renewal

25 February 2009

Date of revision of the text

November 2011

Any other information

Nil.

Legal category

Legal category: POM-V

GTIN

GTIN description: Noroclav 250mg Tabs for Dogs

GTIN: 5023534009740

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Email: enquiries@norbrook.co.uk

Noroclav 500 mg Palatable Tablets for Dogs

Species:	Dogs
Therapeutic indication:	**Pharmaceuticals: Antimicrobials: Oral preparations:** Tablets
Active ingredient:	Amoxicillin, Clavulanic Acid
Product:	Noroclav 500 mg Palatable Tablets for Dogs
Product index:	Noroclav 500 mg Palatable Tablets

Qualitative and quantitative composition

Each tablet contains:

Active substance(s):

Amoxicillin (as amoxicillin trihydrate)	400 mg
Clavulanic acid (as Potassium Clavulanate)	100 mg

Colouring Agent:

Carmoisine Lake (E122)	2.45 mg

For a full list of excipients, see section Pharmaceutical Particulars

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.

Clinical particulars

Target Species

Dogs

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:

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- 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.

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.

Special warnings for each target species

None.

Special Precautions for Use

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 section, "**Containdications**".

Do not administer to horses and ruminating animals.

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.

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.

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

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

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.

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.

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	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.

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.

Withhold Period(s)

Not applicable.

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Pharmacological particulars

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

ATC vet code: QJ01CR02

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 *-lactamase and therefore combination with an effective ß-lactamase inhibitor (clavulanic acid) extends the range of bacteria against which it is active to include *-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.

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).

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

Pharmaceutical particulars

List of Excipient(s)

Sodium Starch Glycolate (type A)

Copovidone

Magnesium Stearate

Cellulose, microcrystalline

Silicon Dioxide

Calcium Carbonate

Magnesium Carbonate, heavy

Roast Beef Flavour

Lake Carmosine (E122)

Incompatibilities

Not applicable.

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.

Special Precautions for Storage

Do not store above 25°C.

Store in a dry place.

Divided tablets should be stored in the blister pack.

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.

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

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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.

Marketing Authorisation Holder (if different from distributor)

Norbrook Laboratories Limited

Station Works

Newry

County Down

BT35 6JP

Northern Ireland

Marketing Authorisation Number

Vm 02000/4259

Significant changes

Date of the first authorisation or date of renewal

26 April 2006

Date of revision of the text

October 2012

Any other information

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not Applicable

Legal category

Legal category: POM-V

GTIN

GTIN description: Noroclav 500mg: 10 Pack

GTIN: 5023534013990

GTIN description: Noroclav 500mg: 25 Pack

GTIN: 5023534012634

GTIN description: Noroclav 500mg: 100 Pack

GTIN: 5023534012641

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