1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav 250 mg 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)	200	mg
Clavulanic acid (as Potassium clavulanate)	50.0	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)	1.225 mg
Sodium Starch Glycollate	
Silicon Dioxide	
Copovidone	
Magnesium Stearate	
Microcrystalline Cellulose	
Calcium Carbonate	
Heavy Magnesium carbonate	
Roast Beef Flav-o-lok	

Round pink tablet with a score line and 250 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 βlactamase 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 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.

3.3 Contraindications

Do not use in cases of hypersensitivity to penicillin, other 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 the kidneys accompanied by anuria and oliguria.
Do not use where resistance to this combination is known to occur.
Do not administer to horses and ruminating animals.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for 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.
Caution is advised in the use in small herbivores other than those in 3.3.

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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Gastrointestinal disorders (Diarrhoea, Vomiting) Allergic reactions (e.g. skin reaction, anaphylaxis) [1] Hypersensitivity reaction[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 authorization holder or its local representative or the national competent authority via the national reporting system. See also 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 benefit/risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interactions

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.

3.9 Administration routes and dosage

Oral use. The dosage 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.

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

The veterinary medicinal 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 12.5 mg of the combined actives administered twice daily for 8 days did not demonstrate adverse reactions.

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 PROPERTIES

4.1 ATC Vet 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 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 ß-lactamase and therefore combination with an effective ß-lactamase inhibitor (clavulanic acid) extends the range of bacteria against which it is active to include ß-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 ß-lactamase producing strains)
Clostridia
Streptococci

Gram-negative:
Escherichia coli (including most ß-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 (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: C_{max} of 6.30 +/-0.45 μg/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 +/- 0.24 μg/ml for clavulanic acid.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
Blister packs: 2 years.
Tubs: 6 months.

5.3 Special precautions for storage

Do not store above 25 ºC.
Store in the original package in order to protect from moisture.

5.4 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.

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

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF THE 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).

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 250 mg Tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:

Active substances:

Amoxicillin (as Amoxicillin Trihydrate)	200 mg
Clavulanic Acid (as Potassium Clavulanate)	50 mg

3. PACKAGE SIZE

10 Tablets
20 Tablets
50 Tablets
100 Tablets
250 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

Not applicable

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C.

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

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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE LABEL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav 250 mg tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:

Active substances:

Amoxicillin (as Amoxicillin Trihydrate)	200mg
Clavulanic Acid (as Potassium Clavulanate)	50 mg

3. TARGET SPECIES

Dogs.

4. ROUTES OF ADMINISTRATION

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

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Not applicable.

6. EXPIRY DATE

Exp. {mm/yyyy}

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C.

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

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BLISTER PACKAGING

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav

2. QUANATIVE PARTICULARS OF THE ACTIVE SUBTANCES

Each tablet contains:

Active substances:

Amoxicillin (as Amoxicillin Trihydrate)	200 mg
Clavulanic Acid (as Potassium Clavulanate)	50 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 250 mg tablets for dogs

2. Composition

Active substance:

Amoxicillin (as Amoxicillin Trihydrate)	200 mg
Clavulanic Acid (as Potassium Clavulanate)	50 mg

Excipient:

Carmoisine Lake (E122)	1.225 mg

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

3. Target species

Dogs.

4. Indications for use

For the 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.
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 testing when initiating the treatment. The treatment should only proceed if sensitivity is proven to the combination.

5. Contraindications

Do not use in rabbits, guinea pigs, hamsters or gerbils.
Do not use in animals with known hypersensitivity to penicillin, other substances of the beta-lactam group, or to any of the excipients.
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.

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 and 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 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.

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

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

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

Penicillins may increase the effect of aminoglycosides.

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

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

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.

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

Pregnancy:

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

The potential for allergic cross-reactivity with other penicillin’s should be considered.

Special precautions for the protection of the environment:

Not applicable.

7. Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Gastrointestinal disorders (Diarrhoea, Vomiting) Allergic reactions (e.g. skin reaction, anaphylaxis) [1] Hypersensitivity reaction[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 or the local representative of 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

Dosage Rate: 12.5 mg combined actives/kg bodyweight twice daily. The recommended dose of 12.5 mg per kg bodyweight is equivalent to one 250 mg tablet per 20 kg bodyweight.

Dosage frequency: The following tables are intended as a guide to dispensing the veterinary medicinal product at the standard dose rate of 12.5 mg/kg twice daily.

	Number of tablets per dose twice daily
Bodyweight (kg)	250 mg
19-20	●
21-30	●◖
31-40	●●
41-50	●●◖
more than 50	●●●

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

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

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 25 °C.
Store in the original package in order to protect from moisture.
Do not use this veterinary medicinal product after the expiry date 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 authorization numbers and pack sizes

Tubs containing 100 or 250 tablets.
Blister strips containing 10, 20, 50, 100 or 250 tablets (5 tablets per strip).

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last approved.

{MM/YYYY}

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

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release

(IE)
Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

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

Manufacturer responsible for batch release:
Norbrook Laboratories Limited
Station Works
Newry
Co. Down
BT35 6JP

Norbrook Manufacturing Limited
Rossmore Industrial Estate
Monaghan
Ireland

Local representatives and contact details to report suspected adverse reactions:

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

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

Tel: +44 (0)28 3026 4435

E-mail: phvdept@norbrook.co.uk

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 Noroclav Tablets 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.