SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav 250 mg Tablets for Dogs (RMS UK)
Noroclav 250 mg Tablets for Dogs (in CMS AT, BE, IS, IT, NL, NO, PT, ES, IE except SE, FR and DK)
Noroclav Vet 200 mg/50 mg Tablets for Dogs (SE)
Noroclav P 250mg Tablets for Dogs (FR)
Noroclav Vet 250mg Tablets for Dogs (DK)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per tablet:
Active Ingredients:
Amoxicillin (as amoxicillin trihydrate) 200 mg
Clavulanic acid (as Potassium clavulanate) 50.0 mg

Excipients:
Carmoisine Lake (E122) 1.225 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

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

4. CLINICAL PARTICULARS

4.1 Target Species

Dogs.

4.2 Indications for use, specifying the target species

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.

4.3 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.

4.4 Special warnings for each target species

None.

4.5 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 4.3.
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.

4.6 Adverse reactions (frequency and seriousness)

Hypersensitivity reactions 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 benefit/risk assessment by the responsible veterinarian.

4.8 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 anminoglycosides.

4.9 Amounts to be administered and administration route

Administration is via the oral route. 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 refactory 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

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 reactions.

4.11 Withdrawal Period(s)

Not applicable.

5. PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins
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 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 betalactamase 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 _-lactamase producing strains)
Clostridia
Streptococci

Gram-negative:
Escherichia coli (including most _-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 (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 +/- 0.24 microgram/ml.h for clavulanic acid.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carmosine Lake (E122)
Sodium Starch Glycollate
Copovidone
Magnesium Sterate
Microcrystalline Cellulose
Calcium Carbonate
Silicon Dioxide
Heavy Magnesium carbonate
Roast Beef Flav-o-lok

6.2 Major Incompatibilities

Not applicable

6.3 Shelf-life

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

6.4 Special precautions for storage

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

6.5 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.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

Vm 02000/4212

9. DATE OF THE FIRST AUTHORISATION

08 March 2002

10. DATE OF REVISION OF THE TEXT

August 2019

Approved: 01 August 2019