Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Noroclav 50 mg chewable flavoured tablets for cats and dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active ingredients:
Amoxicillin 40.00 mg
(as Amoxicillin Trihydrate)
Clavulanic acid 10.00 mg
(as Potassium Clavulanate)
Excipients:
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewable Tablet.
Pale brown circular tablet with a score line and embossed with '50' on opposing faces.
The tablets can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Target Species

Cats and 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 *Staphylococcus*spp.
Urinary tract infections caused by *Staphylococcus spp*or *Escherichia coli*.
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.

4.3 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.

4.4 Special warnings for each target species

None known.

4.5 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.

4.6 Adverse reactions (frequency and seriousness)

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).

4.7 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.

4.8 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.

4.9 Amounts to be administered and administration route

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
1.0 - 2.0	½
2.1 - 4.0	1
4.1 - 6.0	1 ½
6.1 - 8.0	2
> 8	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.

4.10 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.

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 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
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.

5.2 Pharmacokinetic particulars

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 12.5 mg combined actives/kg to cats, the following parameters were observed: Cmax of 9.17 µg/ml and AUC of 53.27 µg.h/ml foramoxicillin 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 12.5 mg combined actives/kg to dogs, the following parameters were observed: Cmax of 8.92 µg/ml and AUC of 46.29 µg.h/ml foramoxicillin and Cmax of 2.21 µg/ml, and AUC of 8.99 µg.h/ml for clavulanic acid.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Starch Glycolate, type A
Povidone K30
Spray Dried Pork Liver Powder
Yeast Extract
Silica Colloidal Hydrated
Magnesium Stearate
Microcrystalline Cellulose

6.2 Major incompatibilities

Not applicable.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 1 year.
Discard any unused halved tablets immediately.

6.4 Special precautions for storage

Do not store above 30°C.
Store in a dry place.

6.5 Nature and composition of immediate packaging

Blisters (aluminium/aluminium): 20, 50, 100, 200, 250 and 500 tablets in outer packages with blister strips containing 10 tablets each.
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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA22664/094/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 June 2012
Date of last renewal: 22 June 2017

10 DATE OF REVISION OF THE TEXT

January 2019