LABEL TEXT

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nisinject Suspension for Injection

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

This product contains amoxicillin 140mg/ml as amoxicillin trihydrate and clavulanic acid 35 mg/ml as potassium clavulanate in an oily base. Excipients: Butylated hydroxyanisole 0.08mg and Butylated hydroxytoluene 0.08mg.

3. PHARMACEUTICAL FORM

Suspension for Injection

4. PACKAGE SIZE

50ml/100ml

5. TARGET SPECIES

Cattle and Dogs

6. INDICATION(S)

See package leaflet.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

The product is indicated for intramuscular administration to cattle and subcutaneous administration to dogs.

The recommended dosage rate of 8.75 mg/kg bodyweight [7mg/kg bw amoxicillin and 1.75 mg/kg bw of clavulanic acid] (equivalent to 1 ml per 20 kg bodyweight) once daily for 3 to 5 days.
Shake before use. Use a completely dry needle and syringe. Swab the septum before removing each dose. The maximum volume administered at the site of injection should not exceed 10ml.

8. WITHDRAWAL PERIOD

Meat and offal: 42 days Milk: 60 hours [5 milkings]

9. SPECIAL WARNING(S), IF NECESSARY

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.
Penicillins and cephalosporins may occasionally cause severe allergic reactions.
See the package leaflet for user warnings and all other warnings.
The potential for allergic cross-reactivity with other penicillins should be considered.
Penicillins may increase the effects of aminoglycosides.

10. EXPIRY DATE

Exp.: dd/mm/yy

11. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.
Store out of reach of children.
Shake before use.
Once a vial has been broached the contents should be used within 28 days.
Any unused product or waste material should be disposed of in accordance with national requirements.
Discard unused material.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of any unused product and empty containers in accordance with guidance from your local waste regulation authority

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

FOR ANIMAL TREATMENT ONLY

POM-V

To be supplied only on Veterinary Prescription

14. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

16. MARKETING AUTHORISATION NUMBER(S)

ManA 2000
Vm: 02000/4227

17. MANUFACTURER'S BATCH NUMBER

D.O.M.:
B.N.:
Exp.:

Once broached use by : _____

CARTON TEXT

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NISINJECT SUSPENSION FOR INJECTION

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

An off-white suspension containing amoxicillin 140mg/ml as amoxicillin trihydrate and clavulanic acid 35mg/ml as potassium clavulanate in an oily base.
Excipients: Butylated hydroxyanisole 0.08mg and Butylated hydroxytoluene 0.08mg

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

50/100ml

5. TARGET SPECIES

Cattle and Dogs

6. INDICATION(S)

See package leaflet

7. METHOD AND ROUTE(S) OF ADMINISTRATION

The product is indicated for intramuscular administration to cattle and subcutaneous administration to dogs.

The recommended dosage rate of 8.75 mg/kg bodyweight [7mg/kg bw amoxicillin and 1.75 mg/kg bw of clavulanic acid] (equivalent to 1 ml per 20 kg bodyweight) once daily for 3 to 5 days.
Shake before use. Use a completely dry sterile needle and syringe. Swab the septum before removing each dose. The suspension is not suitable for intravenous or intrathecal administration.
The maximum volume administered at the site of injection should not exceed 10ml.

8. WITHDRAWAL PERIOD

Meat and offal: 42 days
Milk: 60 hours [5 milkings]

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet for all other warnings.
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 kidneys accompanied by anuria or oliguria.
Use of product may occasionally result in pain on injection and/or local tissue reaction.
The use of the product is contra-indicated where resistance to the combination of penicillins or other substances of the beta-lactem group is known to occur.
Diarrhoea, vomiting and sweating may rarely occur after administration of the product.

USER WARNINGS

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

Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.

In case of accidental contact with eyes, rinse immediately with plenty of water.

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.

10. EXPIRY DATE

Exp.: dd/mm/yy

11. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC. Store out of the reach of children. Once a vial has been broached the contents should be used within 28 days. Any unused product or waste material should be disposed of in accordance with national requirements. Penicillins and cephalosporins may occasionally cause severe allergic reactions. See packaging text for user warnings. Discard unused material.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of any unused product and empty containers in accordance with guidance from your local waste regulation authority.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

FOR ANIMAL TREATMENT ONLY

POM-V

To be supplied only on Veterinary Prescription

14. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Manufactured by:
Norbrook Laboratories Limited
Station Works
Newry
Co. Down, BT35 6JP
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16. MARKETING AUTHORISATION NUMBER(S)

ManA 2000
Vm: 02000/4227

17. MANUFACTURER'S BATCH NUMBER

D.O.M.:
B.N.:
Exp.:

Further Information: Refer to Package Insert.

PACKAGE LEAFLET TEXT

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

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

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

NISINJECT SUSPENSION FOR INJECTION

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENTS

Nisinject Injection is an off-white suspension containing amoxicillin 140 mg/ml as amoxicillin trihydrate and clavulanic acid 35 mg/ml as potassium clavulanate in an oily base.
Excipients: Butylated hydroxyanisole 0.08mg and Butylated hydroxytoluene 0.08mg.

4. INDICATION(S)

In cattle:
Mastitis, Respiratory infections and soft tissue infections (e.g. joint/navel ill, abscesses etc.).

In dogs:
Respiratory tract infections, urinary tract infections, skin and soft tissue infections (e.g. abscesses, pyoderma, anal sacculitis and gingivitis).

5. 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 kidneys accompanied by anuria or oliguria.
The use of the product is contra-indicated where resistance to the combination of penicillins or other substances of the beta-lactam group is known to occur.

6. ADVERSE REACTIONS

Diarrhoea, vomiting and sweating may rarely occur after administration of the product. Hypersensitivity reactions unrelated to dose can occur with these agents.
Allergic reactions (e.g., skin reactions, anaphylaxis) may occasionally occur.
Local tissue reactions at the site of injection may occur following administration. These reactions are generally of mild to moderate swelling and/or hardness and can persist for up to 2 weeks following administration at the recommended dose rate in the rump or leg muscles and 4 days after administration at the recommended dose rate in the neck muscles. Pain on injection may occasionally occur.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle and Dogs

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

The product is indicated for intramuscular administration to cattle and subcutaneous administration to dogs.

The recommended dosage rate of 8.75 mg/kg bodyweight [7mg/kg bodyweight amoxicillin and 1.75 mg/kg/bodyweight of clavulanic acid] (1 ml per 20 kg bodyweight) once daily for 3-5 days.

9. ADVICE ON CORRECT ADMINISTRATION

Shake before use. Use a completely dry sterile needle and syringe. Swab the septum before removing each dose. The suspension is not suitable for intravenous or intrathecal administration.
In Cattle, the maximum volume administered at the site of injection should not exceed 10ml.
The product is well tolerated up to 2 times the recommended dose administered for up to 5 days in Cattle.

Studies in cattle at the normal dose rate and twice the normal dose rate have shown transient and dose dependent muscle damage at the injection site resulting in increased Creatine kinase and Aspartate Aminotransferase levels. Injection site reactions tended to be dose dependent and were fully resolved by 2

weeks after administration to the leg and rump and 4 days after administration to the neck even at twice the recommended dose rate. No other clinically significant abnormalities were detected.

The product is well tolerated up to 3 times the recommended dose rate administered for up to 6 days for dogs however, in dogs, reactions at the injection site may occur at 3 times the recommended dose rate resolving after 2 weeks.

Do not mix with other veterinary medicinal products.

10. WITHDRAWAL PERIOD

Meat & Offal: 42 days
Milk: 60 hours [5 milkings]

11. SPECIAL STORAGE PRECAUTIONS

Do not store above 25ºC.
Store out of the reach of children.
Once the vial has been broached the contents should be used within 28 days. Discard unused material.
When the container is broached (opened) for the first time, the date on which any product remaining in the container should be discarded should be calculated.
A statement of the in use shelf life of the product is given on the package. This discard date should be written in the space provided on the label.
Clavulanic acid is moisture sensitive. It is very important, therefore, that a completely dry syringe is used when extracting suspension for injection to avoid contaminating the remaining contents of the vial with water. Contamination will result in distinct beads of dark, brown discolouration corresponding to the introduced water droplets. Material affected in this way should not be used as it may have significantly reduced potency.

12. SPECIAL WARNINGS

Precautions for use in Animals

This product does not contain an antimicrobial preservative.

In case of the occurrence of allergic reaction, the treatment should be withdrawn. Inappropriate use of the product may increase the prevalence of bacteria resistant to amoxicllin /clavulanic acid and to other substances of the beta-lactam group. In animals with hepatic and renal failure the dosing regime 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 the likely efficacy of this approach.
Studies in laboratory animals have not produced any evidence of teratogenic effects. The safety of the product has not been assessed in pregnant and lactating cows or bitches. Use only according to a risk: benefit assessment by the responsible veterinary surgeon.

User Warnings

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. In case of accidental contact with eyes, rinse immediately with plenty of water.
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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Dispose of any unused product and empty containers in accordance with guidance from your local waste regulation authority.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

November 2019

15. OTHER INFORMATION

PACKAGE QUANTITIES
50 ml / 100 ml multidose vials.

FURTHER INFORMATION
In vitro Nisinject Injection is active against a wide range of clinically important bacteria including:
Gram-positive: Staphylococci (including beta-lactamase producing strains), Streptococci, Corynebacteria, Clostridia.

Gram-negative: *Escherichia coli, Campylobacter* spp, *Klebsiella* spp, *Proteus* spp, *Pasteurella* spp, *Bacteroides* spp. (including beta-lactamase producing strains), and *Haemophilus* spp.

The product is effective against bacteria which cause a wide range of diseases.

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 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-lactamases produced by some bacterial species, 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.

Another possible mode of resistance to beta-lactam antibiotics can be associated with chromosomal mutations in bacteria resulting in modification of the penicillin binding proteins (PBPs) or modification of the cellular permeability to β-lactam antibiotics by their nature such chromosomal mutations tend to be relatively slow in development primarily by vertical transmission. A trend in resistance of *E. coli* is reported.

The bactericidal effect of amoxicillin is neutralized by simultaneous use of bacteriostatic acting pharmaceuticals (macrolides, sulfonamides and tetracyclines). The potential for allergic cross-reactivity with other penicillins should be considered. Penicillins may increase the effects of aminoglycosides.

MARKETING AUTHORISATION NUMBER
Vm 02000/4227
ManA 2000

FOR ANIMAL TREATMENT ONLY.

Logo

POM-V

To be supplied only on veterinary prescription

Approved 19 November 2019