[Version 8, 10/2012]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NEUDIAVALL 150 mg/g premix for medicated feeding stuff for pigs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Amoxicillin (trihydrate) ..... 150 mg
(Equivalent to 172 mg amoxicillin trihydrate)

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff.
Fine brownish powder with a sandy feel.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs (weaned piglets).

4.2 Indications for use, specifying the target species

Treatment and metaphylaxis of infections caused by *Streptococcus suis* strains susceptible to amoxicillin in weaned piglets.
The presence of disease in the herd should be established before metaphylactic treatment.

4.3 Contraindications

Do not use in case of hypersensitivity to penicillins or cephalosporins or to any of the excipients.
Do not use in the presence of β-lactamase producing bacteria.
Do not use in animals with renal impairment.

4.4 Special warnings for each target species

Animals with reduced feed intake and/or disturbed general condition have to be treated parenterally.

4.5 Special precautions for use

Special precautions for use in animals

Use of the veterinary medicinal product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to penicillin.

Consideration should be given to improvement of management practice on the farm, mainly in hygiene management, ventilation and piglet management avoiding stress conditions.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Penicillins and cephalosporins can cause hypersensitivity reaction (allergy) after injection, inhalation, ingestion or skin contact. Crossed hypersensitivity reactions between penicillins and cephalosporins are observed.

People with known hypersensitivity to penicillins and/or cephalosporins should avoid contact with the veterinary medicinal product.

Handle the veterinary medicinal product with care to avoid dust inhalation, as well as contact with skin and eyes during incorporation of premix into feed, by taking specific precautions:

- Take the appropriate measures to avoid dust dissemination during the incorporation of the premix into feed.
- Personal protective equipment consisting of dust mask, gloves, overalls and approved safety glasses should be worn when handling the veterinary medicinal product.
- Avoid contact with skin and eyes. Rinse thoroughly with water in case of exposure.
- Do not smoke, eat or drink when handling the veterinary medicinal product.
- Wash hands after using the product.

If you develop symptoms following exposure such as skin rash, you should seek medical advice and show the present warning to the doctor. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases the following adverse reactions may occur:

Hypersensitivity reactions – seriousness may vary from a simple rash to anaphylactic shock.
Gastrointestinal symptoms (vomiting, diarrhoea).
Superinfections caused by non-sensitive germs after prolonged use.

The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment).
- Common (more than 1 but less than 10 animals in 100 animals).
- Uncommon (more than 1 but less than 10 animals in 1,000 animals).
- Rare (more than 1 but less than 10 animals in 10,000 animals).
- Very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Not applicable.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with bacteriostatic anti-infectious agents (tetracyclines, sulphamides…).

Do not use simultaneously with neomycin as it blocks the absorption of oral penicillins.
Do not use together with antibiotics which inhibit bacterial protein synthesis since they may antagonise the bactericidal action of penicillins, except for aminoglycoside antibiotics which are recommended for use with penicillins.

4.9 Amounts to be administered and administration route

Oral route, in feed use.

The premix is administered directly mixed with feed at the following dose:

15 mg of amoxicillin/kg b.w./day. This dose is equivalent to 0.1 g NEUDIAVALL 150 mg/g premix for medicated feeding stuff for pigs / kg b.w./day during 15 days.

Due to the administration form and to the fact that the water and feed consumption depend on the clinical condition of the animal, in order to assure a correct dosing, the antimicrobial concentration will be adjusted taking into account the daily consumption of feed and water. For example, the following formula may be used to calculate the medicinal product dose:

$$\frac{\text{0.1 g NEUDIAVALL 150 mg/g} \times \text{Mean weight of animals to be treated (kg)}}{\text{Mean daily feed intake by animal (kg)}} = \text{g of NEUDIAVALL 150 mg/g per kg of feed}$$

Body weight of treated animals should be determined accurately to avoid underdosing.

It is not necessary to dilute before adding to feed.

Recommendations for granulation: the temperature should not exceed 85 ºC.

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

The administration of a dose five times greater than the therapeutic dose did not cause any adverse reaction. In the case of an allergic reaction, stop the treatment and administer corticosteroids and adrenalin.

4.11 Withdrawal period(s)

Meat and offal: 7 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use. Amoxicillin.
ATCvet code: QJ01CA04.

5.1 Pharmacodynamic properties

Amoxicillin is a broad-spectrum bactericidal antibiotic belonging to the beta-lactam group. It is a semisynthetic penicillin susceptible to the action of penicillinase. Its mechanism of action consists of inhibiting bacterial wall synthesis through selective and irreversible blocking of enzymes involved in this process, mainly transpeptidases, endopeptidases and carboxypeptidases. This causes osmotic imbalance which mainly affects bacteria in the growing phase, causing lysis of the bacterial cell.

There is cross-resistance between different β-lactams.

Amoxicillin is active against Gram-positive and Gram-negative microorganisms.

Studies carried out have shown that amoxicillin has a strong *in vitro* activity against *Streptococcus suis* isolated from porcine. Resistance cutting points according to CLSI 2008, are ≤ 0.25μg/ml (S) and ≥ 8 μg/ml (R)

5.2 Pharmacokinetic particulars

Absorption of amoxicillin by oral route is independent from food intake and maximum plasma concentrations are reached rapidly in most animal species between 1 and 2 hours after administration of the veterinary medicinal product. The absolute bioavailability is 25.6 ± 14.7 %.

At the proposed dose, after reaching the state of equilibrium, pig plasma concentrations range between 0.05 and 0.15 μg/ml. The mean residence time (MRT) is about 10 hours.

Amoxicillin presents low plasma protein binding (17%) and rapidly diffuses to most body fluids and tissues. This diffusion extends to synovial effusions, expectorate fluids and lymphatic tissue. Tissue distribution indicates that levels in the lung, pleura and bronchial secretions are similar to plasma levels. Diffusion is much more satisfactory in fluids resulting from inflammatory processes. The volume of distribution at steady state (Vss) is 1.26 ± 0.52 l/Kg.

Metabolism of amoxicillin is limited to the opening of the betalactam ring by hydrolysis, releasing inactive penicilloyl acid (20%). Biotransformations occur in the liver. Plasma clearance values (CL) of 0.65 ± 0.17 l/h/Kg confirm the relatively rapid disappearance of amoxicillin from the organism.

Amoxicillin is distributed principally in the extracell compartment. Tissue distribution is facilitated by the low plasma protein binding rate. The major route of elimination for amoxicillin is active renal secretion. It is also excreted in small amounts in milk and bile.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Almond shell flour
Liquid paraffin
Dextrin
Sorbitol.

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 1 year.
Shelf life after first opening the immediate packaging: 6 months.
Shelf life after incorporation into meal or pelleted feed: 3 months.

6.4. Special precautions for storage

Store below 30ºC.

6.5 Nature and composition of immediate packaging

20 kg bags consisting of Kraft paper bag which contain an inner polyethylene bag.

Pack sizes:
20 kg bags

6.6 Special precautions for the disposal of unused veterinary medicinal product 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

MEVET S.A.U.
Polígono Industrial El Segre, p. 409-410
25191 Lleida
España

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}.
Date of last renewal: {DD/MM/YYYY}.

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Dispensation conditions: **Medicament subject to veterinary prescription.**
Administration conditions: **To be administered under the control or supervision of a veterinarian**
Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.

ANNEX III

LABELLING AND PACKAGE LEAFLET

LABELLING / PACKAGING LEAFLET / 20 kg BAG:

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

Marketing authorisation holder
MEVET S.A.U.
Polígono Industrial El Segre, p. 409-410
25191 Lleida
España

Manufacturer responsible for batch release:
LABORATORIOS HIPRA, S.A.
Avda. la Selva, 135
17170 Amer (Girona) España

MEVET S.A.U.
Polígono Industrial El Segre, p. 409-410
25191 Lleida
España

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

NEUDIAVALL 150 mg/g premix for medicated feeding stuff for pigs.
Amoxicillin (trihydrate).

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

Composition per g:

Amoxicillin (trihydrate) ..... 150 mg
(Equivalent to 172 mg amoxicillin trihydrate)

Fine brownish powder with a sandy feel.

4. INDICATION(S)

Treatment and metaphylaxis of infections caused by *Streptococcus suis* strains susceptible to amoxicillin in weaned piglets.
The presence of disease in the herd should be established before metaphylactic treatment.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to penicillins or cephalosporins or to any of the excipients.Do not use in the presence of β-lactamase producing bacteria.
Do not use in animals with renal impairment.

6. ADVERSE REACTIONS

In very rare cases the following adverse reactions may occur:

Hypersensitivity reactions – seriousness may vary from a simple rash to anaphylactic shock.
Gastrointestinal symptoms (vomiting, diarrhoea).
Suprainfections caused by non-sensitive germs after prolonged use.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

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

7. TARGET SPECIES

Pigs (weaned piglets).

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

Oral route, in feed use.

The premix is administered directly mixed with feed at the following dose:

15 mg of amoxicillin/kg b.w./day. This dose is equivalent to 0.1 g NEUDIAVALL 150 mg/g premix for medicated feeding stuff for pigs / kg b.w./day during 15 days.

Due to the administration form and to the fact that the water and feed consumption depend on the clinical condition of the animal, in order to assure a correct dosing, the antimicrobial concentration will be adjusted taking into account the daily consumption of feed and water. For example, the following formula may be used to calculate the medicinal product dose:

$$\frac{\text{0.1 g NEUDIAVALL 150 mg/g} \times \text{Mean weight of animals to be treated (kg)}}{\text{Mean daily feed intake by animal (kg)}} = \text{g of NEUDIAVALL 150 mg/g per kg of feed}$$

Body weight of treated animals should be determined accurately to avoid underdosing.

9. ADVICE ON CORRECT ADMINISTRATION

It is not necessary to dilute before adding to feed.
Recommendations for granulation: the temperature should not exceed 85 ºC.

10. WITHDRAWAL PERIOD

Meat and offal: 7 days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store below 30ºC.
Do not use after the expiry date which is stated on the packaging.
Shelf life of the veterinary medicinal product as packaged for sale: 1 year.
Shelf life after first opening the immediate packaging: 6 months.
Shelf life after incorporation into meal or pelleted feed: 3 months.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.
Once opened use by…

12. SPECIAL WARNING(S)

Special warnings for each target species:
Animals with reduced feed intake and/or disturbed general condition have to be treated parenterally.
Special precautions for use in animals:
Use of the veterinary medicinal product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to penicillin.
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Consideration should be given to improvement of management practice on the farm, mainly in hygiene management, ventilation and piglet management avoiding stress conditions.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Penicillins and cephalosporins can cause hypersensitivity reaction (allergy) after injection, inhalation, ingestion or skin contact. Crossed hypersensitivity reactions between penicillins and cephalosporins are observed.
People with known hypersensitivity to penicillins and/or cephalosporins should avoid contact with the veterinary medicinal product.
Handle the veterinary medicinal product with care to avoid dust inhalation, as well as contact with skin and eyes during incorporation of premix into feed, by taking specific precautions:

- Take the appropriate measures to avoid dust dissemination during the incorporation of the premix into feed.
- Personal protective equipment consisting of dust mask, gloves, overalls and approved safety glasses should be worn when handling the veterinary medicinal product.
- Avoid contact with skin and eyes. Rinse thoroughly with water in case of exposure.
- Do not smoke, eat or drink when handling the veterinary medicinal product.
- Wash hands after using the product.

If you develop symptoms following exposure such as skin rash, you should seek medical advice and show the present warning to the doctor. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

Pregnancy: Not applicable.

Lactation: Not applicable.

Interaction with other medicinal products and other forms of interaction:
Do not use simultaneously with bacteriostatic anti-infectious agents (tetracyclines, sulphamides…).
Do not use simultaneously with neomycin as it blocks the absorption of oral penicillins.
Do not use together with antibiotics which inhibit bacterial protein synthesis since they may antagonise the bactericidal action of penicillins, except for aminoglycoside antibiotics which are recommended for use with penicillins.

Overdose (symptoms, emergency procedures, antidotes):
The administration of a dose five times greater than the therapeutic dose did not cause any adverse reaction. In the case of an allergic reaction, stop the treatment and administer corticosteroids and adrenalin.

Incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack sizes:
20 kg bags

For animal treatment only – to be supplied on veterinary prescription.
Consideration should be given to official guidance on the incorporation of medicated premix in final feeds.

Batch:
EXP:

Reg. n^{o}: