SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZOOBIOTIC GLOBULIT 150 mg/g Premix for medicated feeding stuff for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Amoxicillin (trihydrate) .....150 mg

Excipient q.s. ..... 1 g

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff

Brown-beige granulated powder

4. CLINICAL PARTICULARS:

4.1 Target species

Pig (weaned pigs)

4.2 Indications for use, specifying target species

Prevention of infections due to *Streptococcus suis* susceptible to amoxicilin after weaning. The presence of disease in the herd should be established before treatment.

4.3 Contraindications

Do not administer to animals with a known hypersensitivity record to penicillins or other substances of the ß-lactam group. Do not administer to animals with serious kidney malfunction including anuria or oliguria. Do not use in case of presence of ß-lactamases producing bacteria.

Do not use in lagomorphs and rodents such as rabbits, guinea pigs, hamster or gerbil.

Do not use in ruminants nor horses.

4.4 Special warnings for each target species

In case of the occurrence of allergic reaction, the treatment should be withdrawn.

4.5 Special precautions for use

Special precautions for use in animals

Use of this 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. Inappropriate use of the product may increase the prevalence of bacteria resistant to amoxicillin. The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of feed animals should be treated parenterally.
Consideration should be given to improvement of management practice on the farm, mainly in hygiene management, ventilation and piglet and 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.

- Do not handle the product if you are allergic to penicillins and/or cephalosporins.

- Handle the 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.
  - Wear a dust mask (in compliance with EN140FFP1), gloves, overalls, and approved safety glasses.
  - Avoid contact with skin and eyes. Rinse thoroughly with water in case of exposure
  - Do not smoke, eat, or drink when handling 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)

Penicillins and cephalosporins may cause hypersensitivity following administration. Hypersensitive reactions are unrelated to dose. Allergic reactions (e.g. skin reaction, anaphylaxis) may occasionally occur and could occasionally be serious.

4.7 Use during pregnancy and lactation

Not applicable.

4.8 Interaction with other medicaments and other forms of interaction

The bactericidal effect of amoxicillin is neutralized by simultaneous use of pharmaceuticals with bacteriostatic mode of action (such as macrolides, sulfonamides and tetracyclines). It should not be used simultaneously with neomycin since it blocks the absorption of oral penicillins.

4.9 Amounts to be administered and administration route

In feed-use.

The dose of amoxicillin is 15 mg/kg b.w/day during 15 consecutive days.
For a feed intake of 50 g/kg, this dose regimen corresponds to 300 ppm of amoxicillin in medicated feed. In order to respect the dose regimen and to take into account the real food intake, the incorporation rate can be increased, which leads to a higher concentration in food.
Posology of Zoobiotic Globulit 150 mg/g Premix for medicated feeding stuff in feed can be established by the following formula:

mg Zoobiotic Globulit 150 mg/g Premix for medicated feeding stuff for pigs /kg feed= (100 mg Zoobiotic Globulit 150 mg/g Premix for medicated feeding stuff for pigs /kg b.w. / day) X (mean body weight of the animals to be treated (Kg)) / mean daily feed intake (Kg)

As a standard the incorporation rate in feed must be established in 2-3 Kg Zoobiotic Globulit 150 mg/g Premix for medicated feeding stuff for pigs in 5 Kg of not medicated feed; homogenize and incorporate the 7-8 Kg/Tn feed.

Granulation of medicated feed has to be carried out at a temperature not exceeding 55º C.

4.10 Overdose (symptoms, emergency procedures, antidotes)

No secondary effects have been detected at five times the dosage level. In case of severe allergic reactions the medication should be discontinued and corticoids and adrenaline should be administered.
In the other cases, apply symptomatic treatment.

4. 11 Withdrawal period

Meat and offals: 7 days

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: penicillins with extended spectrum

ATCVet Code: QJ01CA04

5.1 Pharmacodynamic properties

Amoxicillin is a broad-spectrum beta-lactam antibiotic belonging to the aminopenicillins group.

It is a semisynthetic penicillin sensitive to betalactamases action

It has a time-dependant bactericidal activity and acts against gram-positive and gram-negative microorganisms, inhibiting biosynthesis and restoring bacterial mucopeptide wall.

The mechanism of the antibacterial action of amoxicillin consists in the inhibition of the biochemical processes of synthesis and restoration the bacterial wall by blocking, selectively and irreversibly, several enzymes involved in these processes, mainly transpeptidases, endopeptidases and carboxypeptidases. The non-suitable formation and restoring of the bacterial wall, in the sensitive species, causes an osmotic imbalance that mainly affects on-growing bacteria (when synthesis processes of bacterial wall are especially important), which leads to the lysis of bacterial cell.

Studies carried out have shown that amoxicillin has a strong *in vitro* activity against *Streptococcus suis* isolated from porcine. The calculated MIC_{90} for sensitive species of *Streptococcus suis* isolated in clinical practices (Spain) during the period 1999-2002 was of 0.06μg/ml. Resistance cutting points according to NCCLS are $\leq$ 0.25μg/ml and $\geq$ 8 μg/ml.

There is complete cross-resistance between amoxicillin and other penicillins, in particular, other aminopenicillins (ampicillin) and in some cases cephalosporins.

The main mechanism of bacterial resistance to amoxicillin is the production of *betalactamases*, enzymes that cause the inactivation of antibacterial through

the hydrolysis of betalactam ring, leading to penicilloic acid, which is a stable and inactive compound. Bacterial betalactamases can be obtained from plasmids or be constitutive (chromosomic).

These betalactamases are ectocellular in gram-positive bacteria (ex. *Staphylococcus aureus)* while in gram-negative they are found in the periplasmic space.

Gram-positive bacteria are able to produce betalactamases in a great quantity and segregate them around. These enzymes are codified in plasmids that can be transferred by phage to other bacteria.

Gram-negative bacteria produce different types of betalactamases that remain located in the periplasmic space. These are codified in the chromosome as well as in plasmids.

5.2. Pharmacokinetic properties

Maximum plasma concentrations are reached 4 hours after product administration. Repeated administration of the product allowed determining that stationary state is reached within 2 days, with mean plasmatic concentrations of 0.28 μg/ml. The mean terminal half life was 13 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mix FL (Mixture of hydrogenated palm oil, stearic acid, and macrogol stearate)
Macrogol stearate
Liquid paraffin
Almond shell

6.2 Incompatibilities

None known

6.3 Shelf-Life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years

Shelf-life after incorporation into meal or pelleted feed: 3 months

Shelf life after first opening the immediate packaging: 6 months.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and composition of immediate packaging

Bags of 25 Kg with paper valve with the following four layers:

1. Semi-extensible Kraft
2. High density polyethylene sheet
3. Semi-extensible Kraft
4. Semi-extensible blank

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Drug containers and any residual contents should be disposed of in accordance with advice from local waste regulation authority.

7. MARKETING AUTHORISATION HOLDER

LABORATORIOS CALIER, S.A.
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8. MARKETING AUTHORISATION NUMBER (S)

9. DATE OF THE FIRST AUTHORISATION /RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

For animal treatment only. To be supplied only on veterinary prescription

Consideration should be given to official guidance on the incorporation of medical premixes in final feeds