I.B. SUMMARY OF PRODUCT CHARACTERISTICS AND LABEL/LEAFLET

I.B.1. SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Maymoxi 100 g/kg Premezcla medicamentosa (ES)
Maymoxi 100g/kg Premiscela per suini (IT)
Maymoxi 10 Pré-mistura medicamentosa para suínos (PT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each kg of product contains:

Active substance:
Amoxicillin (trihydrate) ..... 100 g

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff.
White powder.

4. CLINICAL PARTICULARS

4.1. Target species

Porcine (weaned piglets).

4.2. Indications for use, specifying the target species

Prevention and treatment of respiratory infections caused by *Streptococcus suis* sensible to amoxicillin in weaned piglets.
The presence of the disease in the herd should be established before the preventive 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 case resistance to penicillins or cephalosporins occurs.
Do not administer to rabbits, guinea pigs and hamsters, due to the fact that amoxicillin, as well as all other aminopenicillins, has an important action on the cecal bacterial population.
Do not use in equine, due to the fact that amoxicillin, as well as all other aminopenicillins, has an important action on the cecal bacterial population.

4.4. Special warnings for each target species

The ingestion of medication by the animal may be altered due to the illness.
In case of an insufficient feed ingestion, the animals will be treated parenterally.
Narrow spectrum antibacterial therapy should be used for first line treatment where susceptibility testing suggest the likely efficacy of this approach.
Inappropriate use of the product may increase the prevalence of bacteria resistant to penicillins.

4.5. Special precautions for use

Special precautions for use in animals

Use of the 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.

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

Penicillins and cephalosporins may produce hypersensitivity reactions (allergy) after the injection, inhalation, ingestion or skin contact. Cross hypersensitivity reactions are observed between cephalosporins and penicillins.

Do not handle the product if you are allergic to penicillins and/or cephalosporins. Handle with care to avoid contact during its addition to feed, as well during the administration of medicinal feed to the animals, taking specific precautions:

- Avoid dust dissemination during the addition of the product to feed.
- Wear an anti-dust mask (conforming to European Standard EN 140FFP1), gloves, working dress and approved safety glasses.
- Wash hands after using the product.
- If an accidental exposure of skin or eyes takes place, wash immediately with abundant water.
- Do not smoke, eat or drink while handling the product.

If symptoms appear after exposure, as cutaneous eruption, consult a doctor and show these warnings. Face, lip or eye inflammation or respiratory difficulty, are more serious signs, which require urgent medical attention.

4.6. Adverse reactions (frequency and seriousness)

The adverse reactions described for penicillins are: hypersensitivity reactions, with variable seriousness from a simple urticaria to an anaphylactic shock. Intestinal symptomatology (vomiting, diarrhoea).

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 neomycin, since it blocks the absorption of oral penicillins.
Do not use together with antibiotics which inhibit bacterial protein synthesis, since they may antagonize penicillins bactericidal action.

4.9. Amounts to be administered and administration route

Oral administration mixed with feed.
Administer 20 mg of amoxicillin/kg of bw/day (equivalent to 2 g of Maymoxi 10 Premix*/10 bw/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:

$$\frac{\text{200 mg “Maymoxi 10 Premix*” per kg bw./day} \times \text{Mean weight of animals to be treated (kg)}}{\text{Mean daily feed ingestion by animal (kg)}} = \text{mg “Maymoxi 10 Premix*”/ kg of feed}$$

Body weight of treated animals should be determined accurately to avoid underdosing.
The standard rate of addition to feed would be 4 kg of Maymoxi 10 Premix* per tonne of feed.
Temperature, pressure and humidity conditions to which the granulated feed medicated with the premix, may be subjected, are that common for the granulation: use of humid head at 150ºC, at a steam pressure of 3.6 bar for 3 minutes and a mechanical pressure of 10 bars. These conditions inside the room provide a maximum temperature of 65-70ºC, 15% of humidity and 10 bars of pressure.

4.10. Overdose (symptoms, emergency procedures, antidotes), if necessary
The administration of five times the therapeutic dose during 30 consecutive days did not produce any adverse reaction.

In case of intense allergic reactions, the treatment must be discontinued and corticoids and antihistaminics administered. In other cases administer symptomatic treatment.

4.11. Withdrawal period
Meat and offal: 8 days.

5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: Antibacterials for systemic use.
ATCvet Code: QJ01CA04

5.1. Pharmacodynamic properties
Amoxicillin is a wide spectrum beta-lactamic antibiotic, which belongs to the group of aminopenicillins. It is chemically similar to ampicillin.

It is a beta-lactamase susceptible semisynthetic penicillin.

Amoxicillin shows a time dependent bactericidal activity and acts against gram-positive and gram-negative bacteria, inhibiting the biosynthesis and the reparation of mucopeptide cell wall.

The mechanism of the antibacterial action of amoxicillin consists in the inhibition of biochemical processes of synthesis of the bacterial wall, by means of a selective and irreversible blockage of different enzymes involved, mainly transpeptidases, endopeptidases and carboxypeptidases. The inappropriate formation of bacterial wall in the susceptible species produces osmotic imbalance, which affects specially to bacteria in growth phase (during which the processes of bacterial wall synthesis are specially important), leading finally to the lysis of the bacterial cell.

Studies performed with amoxicillin have revealed that it has a remarkable *in vitro* activity against *Streptococcus suis* isolated from porcine. According to NCCLS, the breakpoints of resistance for the involved bacteria are $\leq$ 0.25 µg/ml (S) y $\geq$ 8 µg/ml (R).

There is full cross-resistance between amoxicillin and other penicillins, in particular, other aminopelicillins (ampicillin).

The main mechanism of bacterial resistance to amoxicillin is the production of beta-lactamase enzymes that lead to the inactivation of the antibacterial, by means of the hydrolysis the beta-lactam ring, thus obtaining penicilloic acid, which is stable but inactive. The bacterial beta-lactamases may be acquired by means of plasmids or be chromosomic constitutive.

These beta-lactamases are secreted outside the cell in gram-positives (*Staphylococcus aureus*), while they are found in the periplasmic space in gram-negatives.

Gram-positive bacteria may produce great amounts of beta-lactamases and secrete them to their environment. These enzymes are codified in plasmids than may be transferred by phags to other bacteria.

Gram-negative bacteria produce different types of beta-lactamases, which remain located in the periplasmic space. These are codified either in the chromosome or in plasmids.

5.2. Pharmacokinetic particulars

The amoxicillin absorption by oral administration is independent of food ingestion and the maximum plasmatic concentrations are achieved rapidly in most animal species, between 1 and 2 hours after product administration.

Amoxicillin shows a low binding to plasmatic proteins and is rapidly distributed to the main body liquids and tissues. The diffusion is extended to synovial and expectoration fluids and lymphatic tissue. The diffusion is more satisfactory in liquids resulting of an inflammatory process.

Amoxicillin is distributed essentially in extracellular fluids of the body. Its distribution to tissues is favoured by the weak index of plasmatic protein binding.

Amoxicillin is almost entirely eliminated by the kidney, in active form. Low amounts are excreted through milk and bile. Amoxicillin metabolism is limited to beta-lactam ring opening by hydrolysis, what leads to the delivery of inactive penicilloic acid (20%). Biotransformations take place in liver.

Porcine

After the administration of 20 mg/kg bw/day, through feed, the maximum plasmatic concentration of amoxicillin reached is 2.8 ± 0.2 µg/ml 2 hours later, followed by a falling phase of the concentration and a slower elimination phase with a half-life of 5.76 ± 0.82 h.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Calcium stearate
Hydrogenated vegetal oil.

6.2. Major 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: 3 years.
Shelf-life after first opening the immediate packaging: 6 months.
Shelf-life after incorporation into medicated feed: 3 months.

6.4. Special precautions for storage
This veterinary medicinal product does not require any special storage conditions.

6.5. Nature and composition of immediate packaging
Multi-layer bag of kraft paper with inner bag of low-density polyethylene, sealed with a plastic clamp. The outer bag is sewn with double thread and a tape of kraft paper.

Bag of 25 Kg.

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
Laboratorios Maymó, S.A. Vía Augusta, 302. 08017. Barcelona.

8. MARKETING AUTHORISATION NUMBER
ES: 1748 ESP
IT: 104026012
PT: 092/01/08RFVPT

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION
Date of first authorisation: 29 May 2007
Date of last renewal: DD month YYYY

10. DATE OF REVISION OF THE TEXT
DD month YYYY

PROHIBITION OF SALE, SUPPLY AND/OR USE
To be supplied only on veterinary prescription.

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