## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Invemox Premix 100 mg/g premix for medicated feeding stuff for pigs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

**Active substance:**
Amoxicillin base 100 mg
(as amoxicillin trihydrate 114.8 mg)

**Excipients:**

| **Qualitative composition of excipients and other constituents** |
|---|
| Non-crystallising liquid sorbitol |
| Light liquid paraffin |
| Corncob |

Light brown granules.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Pig (after weaning)

### 3.2 Indications for use for each target species

Treatment and metaphylaxis of infectious processes caused by *Streptococcus suis* susceptible to amoxicillin in pigs after weaning.

The presence of disease in the herd should be established before treatment.

### 3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance, other antimicrobials of the be-lactam group or to any of the excipients.
Do not use in the presence of beta-lactamase producing bacteria.
Do not use in animals with renal impairment.
Do not administer to rabbits, hamsters, gerbils and guinea pigs.

### 3.4 Special warnings

None.

### 3.5 Special precautions for use

Special precautions for safe use in the target species:

Use of the veterinary medicinal product should be based on susceptibility testing and take into account official and local antimicrobial policies.

Long term or repeated use should be avoided by improving management practice and thorough cleansing and disinfection. 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 veterinary medicinal product may increase the prevalence of bacteria resistant to amoxicillin.

The intake of medication by animals can be altered as a consequence of illness. In case of insufficient intake of feed, animals should be treated by the parenteral route.

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

Penicillins may cause hypersensitivity (allergy) following inhalation, ingestion and 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 veterinary medicinal product if you know you are sensitised or if you have been advised not to work with such preparations.

Avoid inhalation of dust and contact with skin.

When applying the veterinary medicinal product, wear gloves and a disposable half-mask respirator conforming to European Standard EN 140 with a filter to EN 143.

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.

Do not smoke, eat or drink while handling the veterinary medicinal product.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

**3.6 Adverse events**

Pig (after weaning):

| | |
|---|---|
| Undetermined frequency (cannot be estimated from the available data) | Hypersensitivity reaction[1] (e.g. urticarial rash and anaphylactic shock)<br>Gastrointestinal signs (e.g. vomiting and diarrhoea)<br>Opportunistic infection[2] |

[1]severity can range from a simple rash to anaphylactic shock.

[2]suprainfections caused by non-sensitive germs after prolonged use.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

**3.7 Use during pregnancy, lactation or lay**

Not applicable.

**3.8 Interactions with other medicinal products and other forms of interaction**

Do not administer together with bacteriostatic anti-infectious agents (tetracyclines, sulphamides, spectinomycin, trimethoprim, chloramphenicol, macrolides and lincosamides)

Do not use simultaneously with neomycin as it blocks the absorption of oral penicillins.

Do not use with antibiotics which inhibit bacterial protein synthesis as they can antagonise the bactericide effect of penicillins, except for aminoglycoside antibiotics which are recommended for use with penicillins.

**3.9. Administration routes and dosage**

In feed use

15 mg of amoxicillin/kg of b.w./day during 15 days.
This dose is equivalent to 0.15 g of the veterinary medicinal product/kg b.w./day

To ensure a correct dosage, body weight should be determined as accurately as possible.

The intake of medicated feed depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of amoxicillin may need to be adjusted accordingly.Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{mg veterinary medicinal product /kg body weight day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily feed consumption (kg/animal)}} = \text{mg veterinary medicinal product per kg of feed}$$

Considering that a pig consumes approximately 5% of its body weight per day, this dose corresponds to 300 mg of amoxicillin per Kg of feed which gives a rate of incorporation of 3.0 Kg/Ton (flour or granules).

Mixing instructions:
To ensure a correct dispersion, the veterinary medicinal product should first be mixed to equal parts with feed before incorporation into the final mix.
Avoid contact with water.
The veterinary medicinal product can be incorporated into pelleted feed, preconditioned at a temperature not greater than 85ºC.

**3.10. Symptoms of overdose (and where applicable, emergency procedures and antidotes)**

No adverse reactions were showed at 3X the recommended dose (45 mg/kg) for 15 days and at dose levels but twice time the period treatment (30 days).

If allergic or anaphylactic reactions were appearing, the medication will be suspended and the veterinarian will be warned. The immediate administration of epinephrine, antihistamines and/or corticoids is considered to be a suitable therapy of emergency.

**3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance.**

This veterinary medicinal product is intended to be used for the preparation of medicated feed.

### 3.12 Withdrawal periods

Meat and offal: 4 days.

## 4. PHARMACOLOGICAL INFORMATION

### 4.1 ATCvet code:

QJ01CA04.

### 4.2 Pharmacodynamics

Amoxicillin is a broad spectrum beta-lactam antibiotic belonging to the aminopenicillins group. The antibacterial mechanism of action of amoxicillin consists of the inhibition of the biochemical processes of bacterial cell wall synthesis by selectively and irreversible blocking different enzymes involved in such processes, largely transpeptidase, endopeptidase and carboxypeptidase. The inadequate synthesis of the bacterial wall in susceptible species produces an osmotic imbalance which particularly affects growing bacteria (when bacterial wall synthesis processes are especially important), finally leading to lysis of the bacterial cell.

There is cross-resistance between different beta-lactams.

It has bactericidal activity and acts against Gram-positive and Gram-negative microorganisms.

The *in vitro* sensitivity to amoxicillin has been determined against porcine strains of *Streptococcus suis* isolated during 2002-2007 resulting in $MIC_{90}$ values of 0.03 µg/ml (determination using the agar dilution method. Breakpoints according to NCCLS Document M31-A2).

### 4.3. Pharmacokinetics

Absorption of oral amoxicillin by oral route is independent from food intake and peak plasma concentrations are reached rapidly in most animal species between 1 and 2 hours after the veterinary medicinal product's administration.

Amoxicillin binds sparingly to plasma proteins and rapidly spreads to the body fluids and tissues. Amoxicillin is essentially distributed in the extracellular compartment. Its distribution to the tissues is facilitated by its low binding rate to plasma proteins.

The metabolism of amoxicillin is limited to hydrolysis of the beta-lactam ring, leading to the release of inactive penicillanic acid (20%). Biotransformation takes place in the liver.

Most amoxicillin is eliminated through the kidneys in active form. It is also excreted in small quantities in milk and bile.

<u>Pigs (after weaning)</u>

Following single dose administration, $C_{max}$ was 4.20 ± 2.90 µg/ml with a $T_{max}$ of 1.5 hours. Administration of the veterinary medicinal product according to the recommended posology results in a maximum plasmatic concentration at steady of 0.93±0.27 µg/ml. After withdrawal of medicated feeding stuff, it takes place a progressive decrease of the plasmatic concentration of amoxicillin with levels of 0.08 µg/ml at 10 h.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major Incompatibilities

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

### 5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 3 months.
Shelf life after incorporation into meal or pelleted feed: 3 months.

### 5.3 Special precautions for storage

Do not store above 25ºC.
Keep the container tightly closed.
Store in a dry place.

### 5.4 Nature and composition of immediate packaging

Thermosealed bag of a complex film made of paper/aluminium/LDPE.
Package sizes:
Bag of 3 kg.
Bag of 24 kg.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

## 6. NAME OF THE MARKETING AUTHORISATION HOLDER

Industrial Veterinaria, S.A.

## 7. MARKETING AUTHORISATION NUMBER(S)

VPA10509/027/001

## 8. DATE OF FIRST AUTHORISATION

## 9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

## 10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).