SUMMARY OF PRODUCT CHARACTERISTICS

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 (as trihydrate) 100 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

Pigs (weaned piglets).

3.2 Indications for use for each target species

Treatment 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 beta-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 orally to rabbits, guinea pigs or hamsters, given that amoxicillin, as all aminopenicillins, has an important effect on caecal bacteria.
Do not use in equidae, given that amoxicillin, as all aminopenicillins, has an important effect on caecal bacterial population.
Do not administer orally to animals with functional rumen.

3.4 Special warnings

The veterinary medicinal product is not effective against beta-lactamase producing organisms.
Cross-resistance has been shown between amoxicillin and other penicillins, in particular aminopenicillins in bacteria susceptible to amoxicillin. Use of the veterinary medicinal product/amoxicillin should be

carefully considered when susceptibility testing has shown resistance to penicillins because its effectiveness may be reduced.
The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient feed uptake, animals should be treated parenterally using a suitable injectable veterinary medicinal product prescribed by the veterinarian.

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 identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.
Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.
Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to amoxicillin and may decrease the effectiveness of treatment with other penicillins, due to the potential for cross-resistance.
Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.
The antimicrobial should not be used as part of herd health programmes.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Penicillins and cephalosporins may cause hypersensitivity reactions (allergy) after 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 the 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, skin and eye contact.
Personal protective equipment consisting of gloves and a disposable half-mask respirator conforming to European Standard EN 140 with a filter to EN 143 should be worn when handling the veterinary medicinal product.
In case of contact, it is recommended to wash the area 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 breathing difficulties 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

Pigs (weaned piglets):

Undetermined frequency (Cannot be estimated from the available data)	Hypersensitivity reaction[1] Gastrointestinal signs (e.g. vomiting and diarrhoea) 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…)
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 for 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 kg/Ton of feed (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.
The veterinary medicinal product can be incorporated into feed, preaconditioned at a temperature not greater than 85 ºC.

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

Due to the broad safety margin, is practically impossible the poisoning by accidental overdose.
If allergic or anaphylactic reactions were appearing, the medication will be suspended and the veterinarian will be warned. The immediate administration of adrenaline, 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 transpeptidases, endopeptidases and carboxypeptidases. 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 β-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 CLSI Document M31-A3).

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 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.

Pig (weaned piglet):

Following single dose administration, C_{max} was 4.20 ± 2.90 µg/ml with a T_{max} of 1.5 hours.
Administration of the 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 25 ºC.
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)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/YYYY}

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).