SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

APSASOL AMOXICILLIN TRIHYDRATE 500 mg/g
Powder for use in drinking water for pigs, chickens, ducks and turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Amoxicillin trihydrate …… 500 mg
(Equivalentto 435.6 mg amoxicillin)

Excipient:
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for use in drinking water.
Almost whitefine powder.

4. CLINICAL PARTICULARS

4.1. Target species

Pig, chicken broiler, duck broiler and turkey for meat production.)

4.2. Indications for use, specifying the target species

Chicken broiler, duck broiler and turkey for meat production: Treatment of pasteurellosis and colibacillosis caused by strains of *Pasteurella* spp. and *Escherichia coli* sensitive to amoxicillin
Pig: Treatment of infections caused by strains of *Streptococcus suis*sensitive to amoxicillin.

4.3. Contraindications

Do not use in case of hypersensitivity to penicillins or to any of the excipients.
Do not use in rabbits, guinea pigs and hamsters, neither in equidae, because amoxicillin, like all penicillins, has an important effect on caecal bacteria.
Do not use orally in animals with functional rumen.

4.4. Special warnings for each target species

The uptake of medicated water by animals can be altered as a consequence of illness. In case of insufficient water uptake, animals should be treated parenterally instead.
The use of the product should be combined with good management practices, i.e. good hygiene, proper ventilation, no overstocking

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 animals. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
Official, national and regional antimicrobial policies should be taken into account when the product is used.
Use of the 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 crossresistance.

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

Penicillins and cephalosporins may cause hypersensitivity (allergy) following 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 this product if you know you are sensitised, or if you have been advised not to work with such preparations.
Handle this product with great care to avoid exposure, taking all recommended precautions.
Take the necessary action to prevent the powder from spreading while the product is being added to drinking water.
Avoid inhalation of dust. Wear either a disposable half-mask respirator conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 with a filter to EN143.
Avoid contact with the skin and eyes. Wear gloves, overalls and goggles during preparation and administration of medicated water or liquid feed. In case of contact, rinse with plenty of clean water.
Wash any exposed skin after handling the product or medicated water or feed. Wash hands after use.
Do not smoke, eat or drink while handling the product.
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.

4.6. Adverse reactions (frequency and seriousness)

In very rare cases the following adverse reactions may appear:

-Hypersensitivity reactions may occur, the severity varying from skin rash to anaphylactic shock.
-Gastrointestinal symptoms(vomiting, diarrhoea).

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).

4.7. Use during pregnancy, lactation or lay

Laboratory studies in rats and mice have not produced any evidence of teratogenic, foetotoxic, maternotoxic effects.
The safety of the veterinary medicinal product has not been established during pregnancy or lactation in sows. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

Do not use in birds in lay and within 4 weeks before the onset of the laying period.

See section 4.11.

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 as they can antagonise the bactericidal effect of penicillins.
Do not administer together with bacteriostatic antibiotics.

4.9. Amounts to be administered and administration route

In drinking water use.

<u>Dosage and treatment regimen</u>

-Pigs: 20 mg of amoxicillin trihydrate/kg of bodyweight every 24 hours (corresponding to 40 mg product/kg bodyweight/day) for 4 days.

-Chicken broilers: 15 mg of amoxicillin trihydrate/kg of bodyweight every 24 hours (corresponding to 30 mg product/kg bodyweight/day) for 5 days.

-Duck broilers: 20 mg of amoxicillin trihydrate/kg of bodyweight every 24 hours (corresponding to 40 mg product/kg bodyweight/day) for 3 days.

-Turkeys for meat production: 15 to 20 mg of amoxicillin trihydrate/kg of bodyweight every 24 hours (corresponding to 30-40 mg product/kg bodyweight/day) for 5 days.

The uptake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of amoxicillin has to be adjusted taking into account the daily waterconsumption.

Based on the dose to be used, and the number and weight of the animals to be treated, the exact daily amount of product can be calculated using the following formula:

$$\text{g of product/ litre of drinking water/day} = \frac{\text{Mean bodyweight (kg) of animals x dose (mg amoxicilin trihydrate/kg bw/day)}}{\text{Mean daily water consumption (litres) x 500}}$$

To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing.

No other source of drinking water should be available during the medication period. Medicated drinking water should be refreshed every 24 hours.

After the end of the medication period the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance,

The required amount of product should be weighed as accurately as possible using suitably calibrated weighing equipment.

4.10. Overdose (symptoms, emergency procedures, antidotes)

Not described. Amoxicillin has a wide margin of safety.

4.11. Withdrawal period(s)

Meat and offal:

Pigs: 6 days
Chicken broilers: 1 day
Duck broilers: 9 days
Turkeys for meat production: 5 days

Eggs: Not authorised for use in birds producing eggs for human consumption.Do not use within 4 weeks before the onset of the laying period.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic Group: Beta-lactam antibacterials, Penicillins with extended spectrumATC vet code: QJ01CA04

Pharmacodynamic properties

Amoxicilin is abroad spectrum betalactamic antibiotic belonging to the aminopenicillins group with bactericidal activity.

Mechanism of action:

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.

Spectrum of action

The species considered to be sensitive to amoxicillin include:

- Gram-positive bacteria:
    - *Streptococcus suis*

- Gram-negative:
    - *Pasteurella* spp.
    - *Escherichia coli*

However, thebacteria which generally present resistance to amoxicillin are:
- Penicillinase-producing staphylococci.
- Some enterobacteria such as *Klebsiella* spp, *Enterobacter* spp, *Proteus* spp and other Gram-negative bacteria such as *Pseudomonas aeruginosa*.

The principal mechanism of bacterial resistance to amoxicillin is the production of β-lactamases, enzymes which inactivate the antibacterial product by hydrolysis of the β-lactam ring, thus obtaining penicillanic acid, a stable but inactive compound. Bacterial β-lactamases can be acquired via plasmids or can be constitutive (chromosomal).
These β-lactamases are exocellular in Gram-positive bacteria and found in the periplasmic space in Gram-negative bacteria.

Gram-positive bacteria are capable of producing and secreting large quantities of β-lactamases. These enzymes are encoded in plasmids which can be transferred by phages to other bacteria.

Gram-negative bacteria produce different types of β-lactamases, which remain in the periplasmic space and which are codified in the chromosome or in the plasmid.

There is complete cross-resistance between amoxicillin and other penicillins, in particular, other aminopenicillins.

Critical concentrations (breakpoints) of sensitivity (S) and resistance (R) in µg/ml (Source: CLSI 2008):

*Streptococcus*spp ≤ 0.25 (S); ≥ 8 (R)

5.1. Pharmacokinetic properties

General:
Absorption of oral amoxicillin is independent from food intake and peak plasma concentrations are reached rapidly in most animal species, from 1 to 2 hours after the product's administration.
Amoxicillin binds sparingly to plasma proteins and rapidly spreads to the body fluids and tissues. Amoxicillin is widely 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 β-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.

Chicken Broiler:
Oral bioavailability is about 67%. Maximum plasma concentration is reached in around one hour. It is well and quickly distributed in the organism, with low binding to plasma proteins (17-20%).

Pigs:
After the administration of the product at the recommended dose in drinking water, plasma concentrations ranged from 0.53 µg/ml (Cmax) to 0.27 µg/ml (Cmin). Steady state was reached 10 hours after the first administration."

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Citric acid

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: 2 years
Shelf-life after first opening the immediate packaging: 1 month
Shelf-life after reconstitutionaccording to directions: 24 hours

6.4 Special precautions for storage

Store below 25 °C.
Store in the original container.

6.5. Nature and composition of immediate packaging

Aluminium multi-layer bags with inner layer made of linear low density polyethylene and outer reinforcement polyethylene terephthalate layer. The bags are closed by heat sealing.

Pack size:
Bag of 400 g
Bag of 1 kg.

Not all pack sizes may be marketed

6.6. Special precautions for the disposal of unused veterinary medicinal product or waste materials

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Andres Pintaluba S.A.
Polígono Industrial Agro-Reus
C/ Prudenci Bertrana nº 5
43206 - Reus (Tarragona)
Spain

8. MARKETING AUTHORISATION NUMBER

Vm 32508/4001

9. DATE OF FIRST AUTHORISATION

10 April 2017

10. DATE OF REVISION OF THE TEXT

April 2017

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription
Administration by a veterinary surgeon or under their direct responsibility

Approved: 10/04/2017