SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Amoxival 500 mg/g oral powder for pigs and chickens
Amoxival Vet (DK)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains
Active substance:
Amoxicillin500.00 mg
(as amoxicillin trihydrate 574.00 mg)
Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral powder
White or almost white powder.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs (pigs after weaning) and chickens (broilers)

4.2 Indications for use, specifying the target species

Pigs (after weaning):
Treatment of swine pleuropneumonia due to *Actinobacillus pleuropneumoniae* (susceptible to amoxicillin).

Broiler chickens:
Prevention at the group level, when disease is present, of respiratory infections caused by *Escherichia coli* (susceptible to amoxicillin).

4.3 Contraindications

Do not use in animals with known hypersensitivity to penicillins or other substances of the ß-lactam group.
Do not use in animals with serious kidney malfunction including anuria and oliguria.
Do not use in presence of β - lactamase producing bacteria.
Do not use in lagomorphs and rodents such as rabbits, guinea pigs, hamsters or gerbils.
Do not use in ruminants or horses.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of feed/ water animals should be treated parenterally.

Use of the product should be based on susceptibility testing of the bacteria isolated from animals. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Inappropriate use of the product may increase the prevalence of bacteria resistant to amoxicillin, other penicillins and may decrease its effectiveness..

Narrow spectrum antibacterial therapy should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Consideration should be given to improvement of management practice on the farm, mainly in hygiene management and ventilation avoiding stress conditions.

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.

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.

Use inhalation protection and gloves during preparation.
Wash any exposed skin thoroughly.

4.6 Adverse reactions (frequency and seriousness)

Penicillins and cephalosporins may cause hypersensitivity following administration. Allergic reactions to these substances may occasionally be serious.

4.7 Use during pregnancy, lactation or lay

Studies performed in Laboratory animals (rat, rabbit), did not show a teratogenic, embryotoxic or maternotoxic effect of amoxicillin. Safety of the product in the

pregnant and lactating sows was not demonstrated. Use only accordingly to the benefit/risk assessment by the responsible veterinarian
Laying birds: Do not use in birds in lay.

4.8 Interaction with other medicinal products and other forms of interaction

The bactericidal effect of amoxicillin is neutralized by simultaneous use of pharmaceuticals with bacteriostatic mode of action.
Not to be used simultaneously with neomycin since it blocks the absorption of oral penicillins.

4.9 Amounts to be administered and administration route

In drinking water use / in feed use.

Pigs
20 mg of amoxicillin (as trihydrate) per kg body weight daily (i.e. 400 mg of the product per 10 kg body weight per day), administered for 5 consecutive days orally in liquid feed.
In liquid feed: the pre-diluted solution must be mixed in the liquid feed until homogenous. The liquid feed should be continuously stirred during the preparation and distribution to the animals.
Preparation of medicated liquid feed should provide an amount to be consumed within the next 3 hours. Any unused medicated liquid feed should be discarded after 3 hours, and freshly medicated liquid feed for the next 3 hours should be prepared.

Chicken
20 mg of amoxicillin (as trihydrate) per kg body weight daily (i.e. 400 mg of the product per 10 kg body weight and per day) administered for 5 consecutive days in drinking water.
In drinking water: the stock solution is either mixed in the drinking water tank or used in with a dosing pump. Turn off the water supply to the tank until all the medicated solution is consumed.
When using a proportionner, adjust the pump between 2 to 5% and adapt the volume of preparation accordingly. Do not set up the dosing pump below 2%.
Preparation of medicated water should provide an amount to be consumed within the next 12 hours. Any unused medicated water should be discarded after 12 hours, and freshly medicated water for the next 12 hours should be prepared.

Recommendation for the pre-dilution:

- Add the necessary quantity of water in the container.
- Add then the product while stirring up the solution.
- Prepare the solution in ambient temperature (20°C – 25°C).
- Prepare the solution with fresh tap water (pH 5 - 9 / 20°C) immediately before use.

For a 20°C solution, respect a limit of concentration of 20g of product per liter of drinking water (equivalent to 10g of amoxicillin /L of water).

Take measures to avoid producing dust when incorporating the product into water.

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

Body weight should be determined as accurately as possible to avoid underdosing.

The intake of medicated water or liquid depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of amoxicillin has to be adjusted accordingly.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No side effects were observed after administration at 5 times the recommended dosage.

4.11 Withdrawal period(s)

Meat and offal
Pigs: 14 days
Chicken: 1 day
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: Penicillins with extended spectrum
ATCvet code: QJ01CA04

5.1 Pharmacodynamic properties

Amoxicillin is a semi-synthetic penicillin derived from the 6 APA core (6 amino-penicillic acid). It is a broad spectrum antibiotic, mainly time-dependant, bactericidal against Gram+ and Gram- bacteria, in particular *Actinobacillus pleuropneumoniae*, isolated in pigs and *Escherichia coli* isolated in broilers.

- The Amoxicillin MIC_{50}/MIC_{90} of *Actinobacillus pleuropneumoniae* is 0.25 µg/ml.

In the absence of published data for amoxicillin, the following clinical breakpoints (MIC value) for *Actinobacillus pleuropneumoniae* in pigs were set up, for ampicillin, at:

- Susceptible: ≤ 0.5 µg/L
- Intermediate: 1 µg/L
- Resistant: ≥ 2 µg/L

Mechanism of action
The antimicrobial mechanism of action consists of the inhibition of the biochemical process of bacterial wall synthesis, through a selective and irreversible blockade of several enzymes, in particular transpeptidases, endopeptidases and carboxypeptidases. In susceptible bacteria, impairment of cell wall synthesis particularly during multiplication leads to lysis of the bacteria..
Bacteria which generally present resistance to amoxicillin are:

- *Staphylococcus* species producing penicillinase,
- Enterobacteria such as *Klebsiella* spp, *Enterobacter* spp, *Proteus* spp and *Pseudomonas aeruginosa*.

Bacterial resistance towards amoxicillin is primarily mediated through β-lactamases which inactivate the antimicrobial by hydrolysis of the β-lactam ring. Bacterial β-lactamases can be codified in plasmids or in constituents of the bacterial chromosome.
These beta-lactamases are extracellular in Gram-positive bacteria (*Staphylococcus aureus*) whereas they are located in the periplasmic space in Gram-negative bacteria.
Gram-positive bacteria can produce beta-lactamases in large quantities. These enzymes are codified in plasmids, which can be transferred to other bacteria.
Gram-negative bacteria produce different types of beta-lactamases, which remain in the periplasmic space and which are codified in the chromosome or in the plasmid.
Complete cross resistance exists between amoxicillin and other penicillins, in particular other aminopenicillins.

5.2 Pharmacokinetic particulars

In pigs, after the administration of the product at a dose of 20 mg/kg in liquid feed, amoxicillin maximal plasma concentration of 2.0 µg/ml is reached 1.8 hours after the administration. The repeated administration of the drug does not lead to accumulation. The average absolute bioavailability of amoxicillin in liquid feed is estimated to be 12%.
In chickens, bioavailability after oral absorption is about 70%. Following oral administration of 20 mg/kg in chickens, Cmax is approximately 4.5 µg/ml after 15 min.. Amoxicillin is widely distributed with a Vdss of approximately 4 L/kg, with a mean residence time of approximately 3 h. After Cmax, plasma concentrations in active substance can range between 0.03 to 0.2 µg/ml during the treatment.
The repeated administration of the drug does not lead to accumulation. Amoxicillin undergoes little biotransformation. The main elimination route is renal under its active form.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica, colloidal anhydrous
Trisodium phosphate anhydrous
Pentasodium triphosphate

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: 30 months
Shelf life after first opening the immediate packaging: 1 year
Shelf life after dilution in water: 12 hours
Shelf life after incorporation in liquid feed: 3 hours

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

Polyesther / Aluminium / Polyamide / Polyethylene bags: 50 g - 100g - 500g - 1 kg - 2.5kg - 5kg

1kg white Polyethylene high density box with a yellow polypropylene screw cap.

Not all pack sizes may be marketed.

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

Ceva Animal Health Ltd
Unit 3, Anglo Office Park
White Lion Road
Amersham
Buckinghamshire
HP7 9FB

8. MARKETING AUTHORISATION NUMBER

Vm 15052/4092

9. DATE OF FIRST AUTHORISATION

29 May 2014

10. DATE OF REVISION OF THE TEXT

June 2016

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.


16 June 2016