[Version 8.2,01/2021]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CITRAMOX 100 mg/g powder for use in drinking water for pre-ruminant calves, broilers and pigs [ES, PT]
KARIMOX 100 mg/g powder for use in drinking water for pre-ruminant calves, broilers and pigs [EL]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Amoxicillin .....100 mg
(Equivalent to 114.78 mg amoxicillin trihydrate)

Excipients: q.s.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for use in drinking water.
White powder.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (pre-ruminant), chicken (broiler) and pig.

4.2 Indications for use, specifying the target species

Treatment of infections caused by bacteria sensitive to amoxicillin; colibacillosis, salmonellosis (except in broilers), streptococci, staphylococci.

4.3 Contraindications

Do not use in cases of hypersensitivity to penicillins, other beta-lactams or to any of the excipients.
Do not use in rabbits, guinea pigs, hamsters and horses, since amoxicillin, like all penicillins, has an important action on the cecal bacterial population.
Do not use in ruminants with a functional rumen.

4.4 Special warnings for each target species

The medicated water intake by animals can be modified as a consequence of the disease. In case of insufficient water intake, administer an alternative parenteral treatment.

4.5 Special precautions for use

Special precautions for use in animals

Good clinical practice requires basing treatment on susceptibility tests of bacteria isolated from sick animals. If this is not possible, the treatment should be based on local epidemiological information (regional, farm level) on the sensitivity of the different strains of the bacterial species usually involved in the infectious process.

The use of veterinary (antimicrobial) medicinal product in poultry must be in accordance with regulation (EC) 1177/2006 and subsequent national requirements.
When using this veterinary medicinal product, the official recommendations (national or regional) on the use of antimicrobials should be taken into account.
The use of the veterinary medicinal product under conditions other than those recommended in the SPC may increase the prevalence of bacteria resistant to amoxicillin and decrease the effectiveness of the treatment.

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 the product if you are allergic to penicillins and/or cephalosporins.
Handle this product with care to avoid inhaling dust and contact with skin and eyes during its incorporation into water taking all recommended precautions:
Take appropriate measures to avoid the dust spread during the product incorporation into drinking water.
Wear a disposable half mask respirator conforming to European Standard EN149 or a non-disposable respirator conforming to European Standard EN140 with a filter to EN 143 and protective gloves when handling the product.
Avoid skin and eyes contact. In case of skin and eyes contact, wash thoroughly with clear water.
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 package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

Hypersensitivity reactions may occur in very rare cases. The severity can range from simple urticaria to anaphylactic shock.
The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Pregnancy: Use only accordingly to the benefit-risk assessment by the responsible veterinarian
Laying birds: Do not use in birds in lay and within 4 weeks before the start of the laying period.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with neomycin because it blocks oral penicillin absorption.

4.9 Amounts to be administered and administration route

In drinking water use.

Dosage in drinking water: 10 mg of amoxicillin per kg b.w. every 12 hours for 5 consecutive days, equivalent to 1 g of the veterinary medicinal product / 10 kg of b.w. / every 12 hours.

If no improvement is observed in 48 hours, reconsider the diagnosis.

The uptake of medicated water depends on the clinical and physiological conditions of the animals and season. In order to obtain the correct dosage the concentration of amoxicillin has to be adjusted taking into account the daily water intake.
To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing.

According to the recommended dose and the number and weight of the animals that should receive the treatment, the exact daily dose of product should be calculated using the following formula:

x mg product per kg bodyweight per day	X	mean bodyweight (kg) of animals to be treated
Mean daily water consumption (litres) per animal		= mg of product / litre of drinking water

Medicated water should be the only source of drinking water during the treatment period.

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

In cases of several allergic reactions the treatment should be discontinued, and corticosteroids and adrenalin should be administered. In all other cases a symptomatic treatment should be established.

4.11 Withdrawal period(s)

Broilers:
- Meat and offal: 6 days
- Eggs: Not for use in birds producing or intended to produce eggs for human consumption. Do not use within 4 weeks of the start of the laying period.

Pigs:
- Meat and offal: 10 days

Pre-ruminant calves:
- Meat and offal: 2 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins.
ATCvet code: QJ01CA04

5.1 Pharmacodynamic properties

Amoxicillin has a bactericidal action and acts against Gram-positive and Gram-negative bacteria, inhibiting the biosynthesis and repair of the bacterial mucopeptide wall.
It is a semisynthetic penicillin susceptible to the action of β-lactamases.
The mechanism of antibacterial action of amoxicillin consists in the inhibition of the biochemical synthesis processes of the bacterial wall, through a selective and irreversible blockade of various enzymes involved in such processes, mainly transpeptidases, endopeptidases and carboxypeptidases. The inadequate formation of the bacterial wall, in susceptible species, produces an osmotic imbalance that especially affects bacteria in the growth phase (during which the bacterial wall synthesis processes are especially important), which finally leads to the lysis of the bacterial cell.

Bacterial species considered sensitive to amoxicillin are:

- Gram-positive bacteria:
Staphylococcus aureus, Staphylococcus spp.
Streptococcus suis

- Gram-negative bacteria:
Escherichia coli
Salmonella spp.

In contrast, the bacteria that generally show resistance to amoxicillin are:
Penicillinase-producing staphylococci.

The main mechanism of bacterial resistance to amoxicillin is the production of beta-lactamases, enzymes that cause the inactivation of the antibacterial by hydrolysis of the beta-lactam ring, thus obtaining penicilloic acid, a stable but inactive compound. Bacterial beta-lactamases can be acquired by plasmids or be constitutive (chromosomal).

These beta-lactamases are exocellular in Gram-positives (*Staphylococcus aureus*) while they are in the periplasmic space in Gram-negatives. Gram positive bacteria can produce beta-lactamases in large quantities and of secreting them to their environment. These enzymes are encoded in plasmids that can be transferred by phage to other bacteria.
Gram-negative bacteria produce different types of beta-lactamases that remain localised in the periplasmic space. These are encoded on both the chromosome and plasmids.

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

5.2 Pharmacokinetic particulars

Oral absorption of amoxicillin is independent of food intake and peak plasma concentrations are rapidly reached in most animal species within 1 to 2 hours after administration of the veterinary medicinal product.
Amoxicillin shows a low protein binding in plasma and rapidly diffuses into most body fluids and tissues. The metabolism of amoxicillin is limited to the opening of the beta-lactam ring by hydrolysis, which leads to the release of inactive penicilloic acid (20%). Metabolism takes place in the liver.
The main route of excretion is the kidney as an unchanged form. It is also excreted in small amounts in milk and bile.

In broilers:
By oral route the bioavailability is around 67%, reaching significant levels in the blood in one hour. It is well and rapidly distributed throughout the body, with little binding to plasma proteins (17-20%).

In pigs:
The plasma protein binding is 17%.
The tissue distribution indicates that the levels in the lung, pleura and bronchial secretions are similar to those in plasma.
Oral administration in drinking water made it possible to observe that equilibrium is reached in about 3 days. The mean residence time (MRT) observed was 10 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica colloidal anhydrous
Lactose monohydrate
Sucrose

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: 2 years
Shelf life after first opening the immediate packaging: 3 months
Shelf life after dilution according to directions: 24 hours

6.4. Special precautions for storage

Keep the bag tightly closed.

6.5 Nature and composition of immediate packaging

Thermosealed bags made of polyester, aluminium and low density polyethylene (LDPE) complex.
Pack sizes:
100 g bag
1 kg bag
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

LABORATORIOS KARIZOO, S.A.
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Spain

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE