# Summary of Product Characteristics

## 1 NAME OF THE VETERINARY MEDICINAL PRODUCT

CITRAMOX L.A. 150 mg/ml suspension for injection for cattle and pigs

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

**Active substance:**
Amoxicillin 150.00 mg
(equivalent to 172.20 mg of amoxicillin trihydrate)

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Suspension for injection.
White to almost white suspension.

## 4 CLINICAL PARTICULARS

### 4.1 Target Species

Cattle and pigs

### 4.2 Indications for use, specifying the target species

In cattle:
Treatment of respiratory infections caused by *Mannheimia haemolytica* and *Pasteurella multocida* susceptible to amoxicillin.
In pigs:
Treatment of respiratory infections caused by *Pasteurella multocida* susceptible to amoxicillin.

### 4.3 Contraindications

Do not use in cases of known hypersensitivity to penicillins, cephalosporins or to any of the excipients.
Do not use in cases of severe renal dysfunction with anuria and oliguria.
Do not use in rabbits, hares, hamsters, guinea pigs or other small herbivores.
Do not administer to Equidae, because amoxicillin – like all aminopenicillins – may adversely affect the bacterial flora of the caecum.
Do not administer intravenously.

### 4.4 Special warnings for each target species

The product is not effective against beta-lactamase producing organisms. Complete cross-resistance has been shown between amoxicillin and other penicillins, in particular amino-penicillins. Use of the product/amoxicillin should be carefully considered when antimicrobial susceptibility testing has shown resistance to penicillins because its effectiveness may be reduced.

### 4.5 Special precautions for use

Special precautions for use in animals

Use of the product should be based on identification and susceptibility testing of the target pathogen(s) isolated from the animal. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target bacteria at farm level, or at local/regional level.
Use of the product should be in accordance with official, national and regional antimicrobial policies.

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 cross-resistance.
The feeding of waste milk containing residues of amoxicillin to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria

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

Penicillin and cephalosporin may cause an allergic reaction following accidental injection, inhalation ingestion or absorption via the skin, which may be life threatening.
Hypersensitivity to penicillin may lead to cross sensitivity to cephalosporins and vice versa. People with known hypersensitivity to penicillins or cephalosporins, should avoid contact with the veterinary medicinal product.Handle the product with great care to avoid exposure.
Wear gloves and wash hands after use of the product.
If accidental exposure to the skin or eyes occur, wash immediately with plenty of water.
Do not smoke, eat or drink during use of the product.
If you develop symptoms following exposure, such as a skin rash, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips and eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

**4.6 Adverse reactions (frequency and seriousness)**

Hypersensitivity reactions, varying in severity from a light skin reaction such as urticaria to anaphylactic shock.
Although the penicillins are not considered hepatotoxic, elevated liver enzymes have been reported.
In cattle, local reactions and swelling at the injection site may occur, but always of low intensity and recedes spontaneously and quickly. In pigs small indurations at the injection site may be observed.

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

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects of amoxicillin. However, the tolerance of the medicinal product in cattle and pigs during pregnancy and lactation has not been investigated. In these cases, use only in accordance with the benefit/risk assessment by the responsible veterinarian.

**4.8 Interaction with other medicinal products and other forms of interactions**

Do not use with antibiotics, which inhibit bacterial protein synthesis, as these can antagonise the bactericidal action of penicillins.
Because there is evidence of in vitro antagonism between beta-lactam antibiotics and bacteriostatic antibiotics (e.g. chloramphenicol, erythromycin and other macrolides, tetracyclines, sulfonamides, etc.), use together has been generally not recommended, but actual clinical importance is not clear. There is also synergic action of penicillins with aminoglycosides.
Amoxicillin may decrease the renal excretion of methotrexate causing increased levels and potential toxic effects.
Probenecid competitively blocks the tubular secretion of most penicillins, thereby increasing serum levels and serum half-lives.

**4.9 Amounts to be administered and administration route**

Intramuscular use.
To ensure a correct dosage and to avoid underdosing, body weight should be determined as accurately as possible.
15 mg amoxicillin per kg bodyweight; corresponding to 1 ml of the veterinary medicinal product per 10 kg. Administration should be repeated once after 48 hours.
In cattle, do not administer more than 20 ml of the veterinary medicinal product per injection site.
In pigs, do not administer more than 6 ml of the veterinary medicinal product per injection site.
A separate injection site should be used for each administration.
Shake the vial vigorously to achieve full resuspension before use. As with other injectable preparations normal aseptic precautions should be observed.
For 100 ml vials: Do not broach the vial more than 15 times: if necessary, use automatic syringes.
For 250 ml vials: Do not broach the vial more than 20 times: if necessary, use automatic syringes.

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

Amoxicillin has a wide safety margin. In case of overdose, treatment is symptomatic.
High doses or very prolonged use have been associated with neurotoxicity.

**4.11 Withdrawal period(s)**

Cattle:
Meat and offal: 18 days
Milk: 3 days

Pigs:
Meat and offal: 20 days

**5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES**

Pharmacotherapeutic group: Antibacterials for systemic use, penicillins with extended spectrum,
ATCvet code: QJ01CA04

**5.1 Pharmacodynamic properties**

Amoxicillin is a broad-spectrum antibiotic of the amino-penicillin family with close structural relationship to ampicillin.
Amoxicillin is a bactericide and is active against Gram-positive and Gram-negative bacteria. It inhibits the synthesis and reparation of the bacterial mucopeptide cell wall.
Amoxicillin is a semisynthetic penicillin and susceptible to the action of bacterial beta-lactamases.
Amoxicillin is a time-dependent antibiotic.
Amoxicillin is active against the following microorganisms which are involved in respiratory diseases in cattle: *Mannheimia haemolytica* and *Pasteurella multocida*.
Amoxicillin is also active against *Pasteurella multocida* that is involved in respiratory diseases in pig.

The following Minimum Inhibitory Concentrations (MIC) have been determined for amoxicillin in European isolates (France, United Kingdom, Belgium, Denmark, Germany, Italy, Czech Republic, Netherlands, Poland and Spain) collected from diseased animals between 2009 to 2012:

| Bacteria species | Origin | Nb of strains | MIC of amoxicillin (µg/mL) | | |
|---|---|---|---|---|---|
| | | | Range | MIC50 | MIC90 |
| *Pasteurella multocida* | Cattle | 134 | 0.06-8 | 0.25 | 0.5 |
| | Pigs | 152 | 0.12-128 | 0.25 | 0.5 |
| *Mannheimia haemolytica* | Cattle | 149 | 0.06-128 | 0.25 | 64 |

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. The inadequate formation of the bacterial wall, in the susceptible species, produces an osmotic imbalance that especially affects bacteria in the growth phase (during which bacterial wall synthesis processes are especially important), which ultimately leads to the lysis of the bacterial cell.

Bacteria normally resistant to amoxicillin are Penicillinase-producing staphylococci, certain *Enterobacteriaceae* such as *Klebsiella* spp., *Enterobacter* spp., *Proteus* spp. and other Gram-negative bacteria such as *Pseudomonas aeruginosa*.
There are three main mechanisms of resistance to beta-lactams: beta-lactamase production, altered expression and/or modification of penicillin binding proteins (PBP), and decreased penetration of the outer membrane. One of the most important is the inactivation of penicillin by beta-lactamase enzymes produced by certain bacteria. These enzymes are capable of cleaving the beta-lactam ring of penicillins, making them inactive. The beta-lactamase could be encoded in chromosomal or plasmidic genes.
Acquired resistances are frequent for Gram-negative bacteria such as E. coli which produce different types of β-lactamases that remain in the periplasmic space. Cross-resistance is observed between amoxicillin and other penicillins, particularly with aminopenicillins (ampicillin).

The use of extended spectrum beta-lactam drugs (e.g. aminopenicillins) might lead to the selection of multi-resistant bacterial phenotypes (e.g. those producing extended spectrum beta-lactamases (ESBLs)).

**5.2 Pharmacokinetic particulars**

Amoxicillin has low degree of plasma protein binding and so diffuses rapidly into body fluids and into tissues.
Amoxicillin is biotransformed in the liver by hydrolysis of the ß-lactam ring leading to inactive penicilloic acid (20%). Amoxicillin is mainly excreted in active form via the kidneys, and secondarily by the biliary route and through milk.

In cattle
After intramuscular administration, the maximum concentration (5.02 µg/mL) is reached at 2.0 hours. The terminal half-life time is 7.8 hours.

In pigs
After intramuscular administration, the maximum concentration (5.04 µg/mL) is reached in about 1.0 hour. The terminal half-life time is 3.7 hours.
The plasma protein binding degree is 17%.
Tissue distribution indicates that the levels in the lung, pleura and bronchial secretions are similar to plasma levels.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Silica, colloidal anhydrous
Sorbitan oleate
Propylene glycol dicaprylocaprate

**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: 28 days

**6.4 Special precautions for storage**

Do not store above 30$^{o}$C.

**6.5 Nature and composition of immediate packaging**

Multi-layer polypropylene/ethylene vinyl alcohol/ polypropylene vials closed with bromobutyl rubber stopper and aluminium and plastic flip capsule, of capacity 100 and 250 ml.
Pack size:
Cardboard box with 1 vial of 100 ml.
Cardboard box with 1 vial of 250 ml.

Not all pack sizes may be marketed.

**6.6 Special precautions for the disposal of unused veterinary medicinal products 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.
Pol. Ind. La Borda
Mas Pujades, 11-12
08140 Caldes de Montbui
Barcelona
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## 8 MARKETING AUTHORISATION NUMBER(S)

VPA10786/006/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 October 2020

## 10 DATE OF REVISION OF THE TEXT