SUMMARY OF PRODUCT CHARACTERISTICS

1.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetrimoxin L.A. 150 mg/ml suspension for injection for cattle and pigs [AT] [DE] [DK] [FI] [IS] [NL] [UK]
Longocilline 150 mg/ml suspension for injection for cattle and pigs [IE]
Vetrimoxin vet., 150 mg/ml suspension for injection for cattle and pigs [SE]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Amoxicillin (as trihydrate) 150 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection
Cream-beige 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 case of infection with beta-lactamase-producing bacteria.
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.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

The choice of using amoxicillin should be based on bacterial susceptibility testing and take into account 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 amoxicillin due to the potential for cross-resistance.

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 or absorption via the skin, which may be life threatening. Hypersensitivity to penicillin may lead to cross sensitivity to cephalosporins and vice versa. Avoid direct contact of the veterinary medicinal product with the skin or the mucosae.
Handle the product with great care to avoid exposure.
Wear gloves and wash hands after use of the veterinary medicinal product.
In case of contact with the skin or eyes, wash immediately with 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)

Allergic reactions, varying in severity from a light skin reaction such as urticaria to anaphylactic shock.
In rare cases local irritation may occur due to the injection of amoxicillin. The frequency of this adverse reaction may be decreased by reducing the volume of injection per injection site (see 4.9). The irritation is always of low intensity and recedes spontaneously and quickly.
In the case of allergic reactions, treatment should be discontinued and a symptomatic treatment should be initiated.

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 interaction

Do not use with antibiotics, which inhibit bacterial protein synthesis, as these can antagonise the bactericidal action of penicillins.

4.9 Amounts to be administered and administration route

Intramuscular use.
Shake well before use.

15 mg amoxicillin per kg bodyweight; corresponding to 1 ml of the veterinary medicinal product per 10 kg.
Administration should be repeated after 48 hours.

To ensure a correct dosage and to avoid underdosing, body weight should be determined as accurately as possible.
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.
As with other injectable preparations normal aseptic precautions should be observed.
If no distinct clinical response is seen after the second treatment, a check of the diagnosis and eventually a change of treatment are required.
Do not broach the vial more than 10 times: if necessary, use automatic syringes.

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

Amoxicillin has a wide safety margin.

4.11 Withdrawal period(s)

Cattle:
Meat and offal: 18 days
Milk: 3 days
Pigs:
Meat and offal: 20 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiinfectives for systemic use, amoxicillin,
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, Denmark, Germany, Italy, Czech Republic, and Spain) collected from diseased animals between 2009 to 2012:

Bacteria species	**Origin**	**Nb of strains**	**MIC of amoxicillin (µg/mL)**		
			Range	**MIC_{50}**	**MIC_{90}**
Pasteurella multocida	Cattle	76	0.0312 – 4	0.2	0.3
	Pigs	89	0.125 – 2	0.2	0.3
Mannheimia haemolytica	Cattle	59	0.125 – 0.5	0.15	0.2

The following amoxicillin breakpoints are recommended by the Comité de l'Antibiogramme of the Société Française de Microbiologie (SFM) : ≤ 4 µg/mL (Susceptible) and >16 µg/mL (Resistant).

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 ß-lactamases which inactivate the antimicrobial by hydrolysis of the ß-lactam ring. Bacterial ß-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 cattle Cmax (3.45µg/ml) is reached 2.45 hours after intramuscular administration. In pigs Cmax (3.54µg/ml) is reached 2 hours after intramuscular administration.

Amoxicillin is mainly distributed to the extra-cellular compartment. Its distribution into tissues is facilitated by its low degree of plasma protein binding (17%). Concentrations in pulmonary, pleural and bronchial tissues are similar to plasma concentrations. Amoxicillin diffuses into pleural and synovial fluid and into lymphatic tissue.
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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous colloidal silica
Sorbitan oleate
Propylene glycol dicaprylocaprate

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 broaching the bottle: 28 days

6.4. Special precautions for storage

Do not refrigerate.
Protect from frost.
Keep the vial in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Multilayer plastic vials (polypropylene / ethylene vinyl alcohol / polypropylene) with chlorobutyl rubber stoppers (type II) and aluminium and plastic flip capsule.

Pack sizes:
- 100 ml
- 12 x 100 ml
- 250 ml
- 12 x 250 ml

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE