SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Rhemox Forte, 1000 mg/g Powder for use in Drinking Water for chickens, ducks, turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:
Active substance:
Amoxicillin trihydrate 1000 mg
(equivalent to amoxicillin 871.24 mg)

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for use in Drinking Water.
White to off-white powder.

4. CLINICAL PARTICULARS

4.1 Target species

Chickens, ducks, turkeys

4.2 Indications for use, specifying the target species

Treatment of infections in chickens, ducks and turkeys caused by bacteria susceptible to amoxicillin.

4.3 Contraindications

Do not use in animals with hypersensitivity to penicillins and other ß-lactam antibiotics.
Do not use in ruminants and horses and lagomorphs and rodents such as rabbits, hamsters, gerbils and guinea pigs.
Do not administer to animals with renal disease including anuria or oliguria.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Official, national and regional antimicrobial policies should be taken into account when the product is used.
Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the amoxicillin and may 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.

People with known hypersensitivity to beta-lactam antibiotics should avoid handling the product. Handle this product with great care to avoid exposure, taking all recommended precautions:

- 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.
- Wear impervious gloves during preparation and administration of medicated water.
- Wash any exposed skin after handling the product or medicated water.
- Wash hands after use.

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)

Penicillins and cephalosporins may cause hypersensitivity reactions following administration in very rare occasions. Allergic reactions to these substances may occasionally be serious. If suspected adverse reactions do occur, treatment should be discontinued immediately.

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

Laboratory studies in rats have not produced any evidence of a teratogenic effect due to the administration of amoxicillin.
Use only accordingly to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

The product should not be administered with antibiotics that have a bacteriostatic mode of action, such as tetracyclines, macrolides, sulphonamides.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.

Dosage:

Use the following formula in order to calculate the quantity of the product (mg) that should be incorporated in the drinking water tank:

$$\frac{Dose \begin{matrix}(mg\ product\ per\ kg \\ body\ weight\ per\ day)\end{matrix} * \begin{matrix}mean\ body\ weight\ (kg) \\ of\ animals\ to\ be\ treated\end{matrix}}{mean\ daily\ water\ consumption\ (litre)\ per\ animal\ per\ day} = \_\_ mg \begin{matrix}product\ per\ litre \\ drinking\ water\end{matrix}$$

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

Suitably calibrated weighing equipment should be used for dispensing the calculated amount of the product.

Solubility in water varies depending on temperature and water quality as well as on time and intensity of stirring. Under worst case conditions (4 °C and soft water) maximum solubility is approximately 1.0 g/l but increases by raising temperature. At 20 °C and in hard water maximum solubility is increased to at least 2.1 g/l. Complete dissolution of the powder should be ensured.

For stock solutions and for use of a proportioner: Take care not to exceed maximum solubility which can be achieved under the given conditions. Adjust flow rate settings of the dosing pump according to concentration of the stock solution and water intake of the animals treated. Moderate increase of temperature and constant stirring can help to raise solubility.

<u>Chickens</u>
Recommended dosage is 15 mg amoxicillin trihydrate/kg bodyweight.
The total period of treatment should be for 3 consecutive days or in severe cases for 5 consecutive days.

Ducks
Recommended dosage is 20 mg amoxicillin trihydrate/kg bodyweight for 3 consecutive days.

Turkeys
Recommended dosage is 15-20 mg amoxicillin trihydrate/kg bodyweight for 3 consecutive days or in severe cases for 5 consecutive days.
Administration route:
The product is administered in the drinking water. Prepare the solution with fresh tap water immediately before use. Any unused medicated water should be discarded after 24 hours.
In order to ensure consumption of the medicated water, animals should not have access to other water supplies whilst being treated.
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.

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

No side effects with overdosage have been reported. Treatment should be symptomatic, no specific antidote is available.

4.11 Withdrawal period(s)

Meat and offal:
Chickens 1 day
Ducks 9 days
Turkeys 5 days

Not for use in birds producing or intended to produce eggs for human consumption.
Do not use within 3 weeks of the start of laying period.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-Lactam antibiotic, Penicillins with extended spectrum.
ATC vet code: QJ01CA04.

5.1 Pharmacodynamic properties

Amoxicillin is a time-dependent bactericidal antibiotic which acts by inhibiting the synthesis of bacterial cell walls during bacterial replication. It inhibits the formation of bridges between the chains of linear polymers constituting the peptidoglycan cell wall of gram-positive bacteria.
Amoxicillin is a broad-spectrum penicillin. It is also active against a limited range of gram-negative bacteria on which the outer layer of the bacterial cell wall is composed of lipolysaccharide and proteins.
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.
Cross-resistance is observed between amoxicillin and other penicillins, particularly with aminopenicillins.
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 is well absorbed following oral administration and it is stable in the presence of gastric acids. Excretion of amoxicillin is mainly in the unchanged form via the kidneys to give high concentration in renal tissue and urine. Amoxicillin is well distributed in body fluids.

For chickens, amoxicillin is quickly absorbed with T_{max} (=1hr) and amoxicillin concentrations < 0.25 µg/ml after 6 hours after a dose of 10 mg/kg.
For turkeys, at a dose rate of 10 mg/kg, the C_{max} was lower than seen in chickens.
For ducks, an oral dose of 20 mg/kg decreased to below a level of 0.25 µg/ml by 5 hours after administration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

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:

100 g, 200 g, 500 g:	3 months
1 kg, 5 kg:	6 months

Shelf life after dilution or reconstitution according to directions: 24 hours

6.4 Special precautions for storage

Store in a dry place.
Keep the bag tightly closed after first opening in order to protect from moisture and light.

This veterinary medicinal product does not require any special temperature storage conditions.

Any medicated water which is not consumed within 24 hours should be discarded.

6.5 Nature and composition of immediate packaging

PET/ALU/PE bag

Package sizes:
Bag of 100 g
Bag of 200 g
Bag of 500 g
Bag of 1 kg
Bag of 5 kg

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

LIVISTO Int'l, S.L.
Av. Universitat Autònoma, 29
08290 Cerdanyola del Vallès
(Barcelona) Spain

8. MARKETING AUTHORISATION NUMBER

Vm 43173/4001

9. DATE OF FIRST AUTHORISATION

14 June 2016

10. DATE OF REVISION OF THE TEXT

July 2021

PROHIBITION OF SALE, SUPPLY AND/OR USE

Veterinary prescription only.

Approved 02 July 2021