SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AQUACOLI 2 000 000 IU/ml solution for use in drinking water or milk

AQUACOLI 2 000 000 IU/ml oral solution for cattle, sheep, swine and poultry (DE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution contains:

Active substance:

Colistin sulfate .....2 MIU

Excipients:

Benzyl alcohol (E1519) ..... 10 mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for use in drinking water/milk.

Clear yellow-brown solution

4. CLINICAL PARTICULARS

4.1 Target species:

Cattle (calves), sheep (lambs), pigs, chickens and turkeys.

4.2 Indications for use, specifying the target species

Treatment and metaphylaxis of enteric infections caused by non-invasive *Escherichia coli* susceptible to colistin.

The presence of the disease in the herd should be established before metaphylactic treatment.

4.3 Contra-indications

Do not use in horses, particularly in foals, since colistin, due to a shift in the gastrointestinal microflora balance could lead to the development of antimicrobial associated colitis (Colitis X), typically associated with *Clostridium difficile*, which may be fatal.

Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.
Do not use in case of resistance to the polymyxin.

4.4 Special warnings, for each target species

Colistin exerts concentration-dependent activity against Gram-negative bacteria. Following oral administration high concentrations are achieved in the gastrointestinal tract, i.e. the target site, due to the poor absorption of the substance. These factors indicate that a longer duration of treatment than the one indicated in section 4.9, leading to unnecessary exposure, is not recommended.
As an adjunct to treatment, good management and hygiene practices should be introduced in order to reduce the risk of infection and to control the potential build up of resistance.

4.5 Special precautions for use

i) Special precautions for use in animals

Do not use colistin as a substitute for good management practices.
Colistin is a last resort drug in human medicine for treatment of infections caused by certain multi-drug resistant bacteria. In order to minimise any potential risk associated with widespread use of colistin, its use should be limited to treatment or treatment and metaphylaxis of diseases, and should not be used for prophylaxis.
Whenever possible, colistin should only be used based on susceptibility testing.
Use of the product deviating from the instructions given in the SPC may lead to treatment failures and increase the prevalence of bacteria resistant to colistin.
Using the veterinary medicinal product (antimicrobials) in poultry should be in accordance with Commission Regulation EC 1177/2006 and subsequent national requirements. Whenever possible, colistin should only be used based on susceptibility testing.
In the case of newborn animals and of animals with severe gastrointestinal and renal disorders the absorption of colistin may be increased. Neuro- and nephrotoxic alterations may occur.

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

People with known hypersensitivity to polymyxins should avoid contact with the veterinary medicinal product.
Avoid direct contact with skin and eyes while handling the product. The use of gloves while handling and dosing is recommended.
Wash splashes from skin immediately with soap and plenty of water.
In case of accidental eye exposure, wash with plenty of water and seek medical attention immediately and show the label to the physician.
If you develop symptoms following exposure such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy and lactation or lay

The safety of colistin during pregnancy, lactation or lay was not investigated in target species. However, the colistin is poorly absorbed after oral administration, therefore the use of colistin during pregnancy, lactation or lay should not lead to particular problems.
Use only accordingly to the benefit-risk assessment by the responsible veterinarian during these periods.

4.8 Interactions with other medicinal products and other form of interaction

After oral administration of colistin sulphate interaction with anaesthetics and myorelaxants may not be excluded in individual cases. The combination with aminoglycosides and levamisole should be avoided. The effects of colistin sulphate may be antagonized by binary cations (iron, calcium, magnesium) and by unsaturated fatty acids and polyphosphates.

4.9 Amounts to be administered and administration route

In drinking water/milk use

For calves, lambs and pigs the recommended dose is 100 000 IU of colistin per kilogram body weight daily for 3-5 consecutive days via drinking water or milk replacer, i.e. 0.5 ml of Solution per 10 kg of body weight per day for 3 - 5 consecutive days.

The recommended daily dose should be divided into two if the product is to be administered directly into the mouth of the animal.

For chickens and turkeys the recommended dose is 75 000 IU of colistin per kilogram body weight daily for 3-5 consecutive days via drinking water, i.e. 37.5 ml of Solution per tonne of body weight per day for 3 - 5 consecutive days.

Duration of treatment should be limited to the minimum time necessary for the treatment of the disease.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. Carefully calculate the total body mass to be treated and the total daily water consumption before each treatment.
Medicated water should be made every day, immediately prior to provision. The medicated water should be the only source of drinking water for the animals for the entire duration of the treatment period.

With the following formula we can calculate an exact dosage:

$$\frac{\text{ml Veterinary medicinal product/kg bw day} \times \text{Average body weight (kg)}}{\text{Average daily water intake (l/animal)}} = \text{ml Veterinary Medicinal product per litre of drinking water}$$

If it is not possible to obtain sufficient uptake of medicated water, animals should be treated parenterally.

4.10 Overdose (symptoms, emergency procedures, antidotes)

None.

4. 11 Withdrawal period

Meat and offal: 1 day

Eggs: Zero days

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: intestinal antiinfectives, antibiotics

ATCVet Code: QA07AA10

5.1 Pharmacodynamic properties

Colistin is a polypeptide antibiotic belonging to the polymyxin class.

Colistin exerts a bactericidal action on susceptible bacteria strains by disruption of the bacterial cytoplasmic membrane leading to an alteration of cell permeability and then a leakage of intracel-lular materials.

Colistin is bactericidal and is primarily effective against a range of Gram negative bacteria, such as enterobacteriaceae and in particular Escherichia coli.

Gram-positive bacteria, as well as some species of Gram-negative bacteria, such as Proteus and Serratia, are naturally resistant to colistin.

Resistance of E.coli bacteria to colistin can result from chromosomal mutations or horizontal transfer of the mcr-1 gene.

Colistin exerts concentration-dependent activity against Gram-negative bacteria. Following oral administration high concentrations are achieved in the gastrointestinal tract, i.e. the target site, due to the poor absorption of the substance. These factors indicate that a longer duration of treat-ment leading to unnecessary exposure is not advised.

For colistin , EUCAST breakpoints are: susceptible ≤ 2 µg/ml and resistant ≥ 2 µg/ml..

5.2. Pharmacokinetic characteristics

Colistin (as sulfate) is poorly absorbed from the gastro-intestinal tract. In contrast to very low concentration of colistin in serum and tissues, high and persistent amounts are present within the different sections of the gastro-intestinal tract.

No significant metabolism is observed.

Colistin is almost exclusively eliminated via the faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol

Purified Water

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicines.

6.3 Shelf-Life

Shelf life of the veterinary medicinal product as packaged for sale: 36 months

Shelf life after first opening the immediate packaging: 3 months

Shelf life after dilution or reconstitution according to directions: 24 hours after dilution in drinking water and 6 hours after dilution in milk replacer

6.4 Special precautions for storage

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

6.5 Nature and composition of the immediate packaging

High-density polyethylene bottles of 1L and 5 L provided with polyethylene stoppers with strapping and removable polyethylene sealing disk.

Package size:

Bottle of 1 L

Bottle of 5 L

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 CALIER, S.A.

C/ Barcelonès, 26 (Pla del Ramassà)

LES FRANQUESES DEL VALLÈS, (Barcelona)

SPAIN

8. MARKETING AUTHORISATION NUMBER (S)

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

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription

Administration by a veterinary surgeon or under their direct responsibility.