SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Colfive 5,000,000 IU/ml Concentrate for Oral Solution for Calves, Pigs, Lambs, Chickens and Turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Colistin sulfate 5,000,000 IU

Excipients:
Benzyl alcohol (E1519) 10 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for oral solution

Clear orange-brown solution

4. CLINICAL PARTICULARS

4.1 Target species

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

4.2 Indications for use, specifying the target species

Calves, lambs, pigs, chickens, turkeys:
Treatment and metaphylaxis of enteric infections caused by non-invasive *E. coli* susceptible to colistin sulfate. The presence of the disease in the herd should be established before metaphylactic treatment.

4.3 Contraindications

Do not use in known cases of hypersensitivity to colistin sulfate or to any of the excipients.
Do not use in known cases of resistance to polymyxins.
Do not use in horses, particularly in foals, since colistin sulfate, 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.

4.4 Special warnings for each target species

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.
Colistin sulfate 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.

4.5 Special precautions for use

Special precautions for use in animals
Do not use colistin sulfate as a substitute for good management practices.
Colistin sulfate 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 sulfate, its use should be limited to treatment or treatment and metaphylaxis of diseases, and should not be used for prophylaxis.
Whenever possible, colistin sulfate 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 sulfate. There is cross-resistance between colistin sulfate and polymyxin B.
In the case of newborn animals and animals with severe gastrointestinal and renal disorders, systemic exposure to colistin sulfate may be increased. Neuro- and nephrotoxic alterations may occur.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
People with known hypersensitivity to polymyxins, such as colistin sulfate, should avoid contact with the veterinary medicinal product.
Avoid direct contact with skin and eyes while handling the product. Personal protective equipment consisting of gloves and protective goggles should be worn when handling and dosing the veterinary medicinal product.
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 physician 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, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy, lactation or lay. However, colistin sulfate is poorly absorbed after oral administration, therefore the use of colistin sulfate during pregnancy, lactation or lay should not lead to particular problems. Use only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

After oral administration of colistin sulfate interaction with anaesthetics (curarimimetic agents) and myorelaxants may not be excluded in individual cases. The combination with aminoglycosides and levamisole should be avoided. The effects of colistin sulfate 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

Oral use.
In drinking water/milk use
Calves, lambs, pigs: 100 000 IU of colistin sulfate per kg body weight daily for 3-5 consecutive days in drinking water or milk (replacer) in calves, equivalent to 0.20 ml of the concentrate solution per 10 kg body weight per day for 3-5 days.

Chickens and turkeys: 75 000 IU of colistin sulfate per kg body weight daily for 3-5 consecutive days in drinking water, equivalent to 15 ml of the concentrate solution per Ton of body weight per day for 3-5 days.

Duration of treatment should be limited to the minimum time necessary for the treatment of the disease.
Any medicated water which is not consumed within 24 hours should be discarded.
Any medicated milk which is not consumed within 6 hours should be discarded.

Direct oral administration to individual animals
The recommended daily dose should be divided into two if the product is to be administered directly into the mouth of the animal.
Prior to direct oral administration, the product should be diluted with a volume of drinking water equivalent to 2.5 x the volume of product concentrate to be administered.

Administration via drinking water
The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of colistin sulfate has to be adjusted accordingly. Carefully calculate the average body weight to be treated and the average 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.
Water uptake should be monitored at frequent intervals.

With the following formula, we can calculate an exact dosage:

$$\frac{\text{…ml of the product per kg body weight and day} \times \text{Average body weight (kg)}}{\text{Average daily water intake (l/animal)}} = \text{…ml of the product per litre of drinking water}$$

• Administration without a dosing pump:
The treatment is distributed in a tank over a period of 24 hours, for 3-5 consecutive days.
The product is added to a volume of the drinking water corresponding to the volume consumed by the animals over the treatment period (24 hours) to achieve a dose of 100 000 IU of colistin sulfate per kg body weight for pigs, lambs and calves and 75 000 IU of colistin sulfate per kg body weight for chickens and turkeys.
• Administration via a dosing pump
The treatment is distributed over a period of 24 hours, for 3-5 consecutive days.
A dosing pump is used to add a stock solution at a pre-determined concentration to the drinking water.

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

None.

4.11 Withdrawal period

Cattle (calves), sheep (lambs) and pigs
Meat and offal: 1 day

Chickens and turkeys
Meat and offal: 1 day
Eggs: Zero days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: intestinal anti-infectives, antibiotics
ATCvet code: QA07AA10

5.1 Pharmacodynamic properties

Colistin sulfate is a polypeptide antibiotic belonging to the polymyxin class.
Colistin sulfate 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 intracellular materials.
Colistin sulfate is bactericidal and is primarily effective against a range of Gram negative bacteria, such as enterobacteriaceae and in particular *Escherichia coli.*
Colistin sulfate possesses virtually no activity against Gram positive bacteria and fungi.
Gram positive bacteria are naturally resistant to colistin sulfate as are some species of Gram negative bacteria such as *Proteus* and *Serratia*. However, acquired resistance of Gram negative enteric bacteria to colistin sulfate is rare and explained by a single step mutation.

For colistin sulfate, EUCAST clinical breakpoints (01/2020) for Enterobacterales are: susceptible ≤ 2 µg/ml and resistant ≥ 2 µg/ml. It should be noted that MIC determination should be performed using the broth microdilution method.
Colistin sulfate 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 leading to unnecessary exposure is not advised.

5.2 Pharmacokinetic particulars

Colistin sulfate is poorly absorbed from the gastro-intestinal tract.
In contrast to the very low concentrations of colistin sulfate 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 sulfate is almost exclusively eliminated via the faeces.

Environmental properties
The active ingredient colistin sulfate is very persistent in soils.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Sodium acetate anhydrous
Acetic acid glacial
Purified water

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: 30 months
Shelf life after first opening the immediate packaging: 3 months
Shelf life after reconstitution in water according to directions: 24 hours
Shelf life after reconstitution in milk according to directions: 6 hours

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

High density polyethylene (HDPE) bottle heat-sealed with a polyethylene (PE) foil closed with a screw cap of HDPE equipped with a security system to give an airtight sealing. The 5 liters bottle has an integrated handle.

Package sizes:
Box with a bottle of 100 ml
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

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

8. MARKETING AUTHORISATION NUMBER

Vm 43173/4000

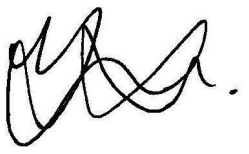
9. DATE OF FIRST AUTHORISATION

06 May 2015

10. DATE OF REVISION OF THE TEXT

October 2020

PROHIBITION OF SALE, SUPPLY AND/OR USE
Veterinary medicinal product subject to prescription



Approved: 01 October 2020