SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliscour oral solution of colistin sulphate 2MIU/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition for 1 ml:

Active substance:
Colistin (as Colistin sulphate)…….. 2 MIU

Excipients:
Benzyl alcohol…….. 10 mg

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Oral solution.
Clear yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs: in particular suckling and post weaning.

4.2 Indications for use

Treatment and metaphylaxis of gastrointestinal infections caused by non-invasive *E.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.

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.

4.5 Special precautions for use, including special precautions to be taken by the person administering the medicinal product to the animals

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.

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

People with known hypersensitivity to polymixins should avoid contact with this product.
Accidental skin or eye contact should be avoided. Wash any splashes from skin or eyes with plenty of water.
Wash hands and exposed skin after use.

4.6 Adverse reactions

None known

4.7 Use during pregnancy, lactation or lay

The use is not recommended during pregnancy or lactation

4.8 Interaction with other medicinal products and other forms of interaction

No data available

4.9 Amounts to be administered and administration route

Oral use.
Administration via drinking water or direct application by mouth, after dilution with drinking water.
Dosage: 50 000 IU/kg of colistin per kg body weight twice a day for 5 days, i.e. 0.25 ml of Coliscour Solution per 10 kg of body weight twice a day for 5 consecutive days.

Individual administration

For suckling piglets the product should be administered only on an individual basis.
Coliscour solution should be diluted in drinking water. Take 1 ml of Coliscour solution and dilute to 40 ml with drinking water.
Administration of this diluted solution is by direct application in the mouth with a syringe: 1 ml per kg bodyweight twice a day for 5 consecutive days.
The used syringe must allow a precision of 0.2 ml.

Administration via drinking water

The medicated water should be the only source of drinking water for the animals for the entire duration of the treatment period (2 to 6 hours).
In order to ensure that the product is effectively consumed in less than 6 hours, it might be advised to:
Restrict water for one hour just before the treatment period, if the clinical condition of the animals allows this.
Or to slightly underestimate the consumption of water which will lead to a shortened treatment period.

Administration without a dosing pump:

The treatment is distributed in a tank in a pulse mode over a period of 2 to 6 hours, twice a day, for 5 consecutive days.
Coliscour solution is added to a volume of the drinking water corresponding to the volume consumed by the animals over the treatment period (2 to 6 hours) to achieve a dose rate of 50 000 IU of colistin per kg body weight.
The following sequential steps should be followed:
From the dosage regimen and the total weight of pigs to be treated, determine the necessary quantity of active ingredient, and deduce the necessary quantity of commercial product.
Determine the mean water consumption of the animals to be treated over the treatment period (2 to 6 hours), and deduce the total quantity of supplemented water to prepare.

The following formulae can be applied:
Calculation of Coliscour solution volume at each distribution (V):
V (ml) = (50 000*W)/(2 000 000) where W (kg) = total weight of pigs to treat
Or 0.025ml x W (kg) of bodyweight.
Calculation of the quantity of supplemented drinking water to prepare (Q) :
Q (L) =A x N where A = mean individual water consumption of the animals during the scheduled distribution period in litres
where N = number of animals to be treated

Administration via a dosing pump

The treatment is distributed in a pulse mode over a period of 2 to 6 hours, twice a day, for 5 consecutive days.

A dosing pump is used to add a stock solution at a pre-determined concentration to the drinking water. The pumped volume is constant, but the drinking frequency depends on the flow rate of the circuit. The flow rate (F) through the pump is a percentage.

Thus, the concentration of the stock solution corresponds to the concentration of the solution to be distributed to the animals divided by the flow rate through the pump.

If the product is administered with an automated drinking water system, the following sequential steps should be followed:

Determine the quantity of Coliscour solution to achieve a dose rate of 50 000 IU colistin per kg body weight.
Determine the mean water consumption of the animals to be treated over the scheduled treatment period (2 to 6 hours).
Calculate the concentration of the solution to be distributed to the animals
Calculate from this, the concentration of the stock solution, knowing the flow rate of the dosing pump.

1ml of Coliscour solution contains 2 000 000 IU.

The following calculation must be applied:
Calculation of Coliscour solution volume at each distribution (V) :
V (ml) = (50 000 x W)/(2 000 000) where W (kg) = total weight of pigs to treat
Or 0.025ml x W(kg) of bodyweight.

Calculation of the drinking water concentration (C) :
C (ml/L) = V/B where B = total volume of water consumed by the pigs during the scheduled distribution period (2 to 6 hours)

Calculation of the stock solution volume (V') :
V' (L) = B*F where F= flow rate through the dosing pump as a percentage

Calculation of the stock solution concentration (C') :
C' (ml/L) = C/F

The veterinary surgeon should provide suitable advice to the farmer including prevention, by vaccination of sows, and hygiene methods that might aid in prevention of the disease such as adoption of all-in-all-out procedures in farrowing units.
Duration of treatment should be limited to the minimum time necessary for the treatment of the disease.

4.10 Overdose (Symptoms, emergency procedures, antidotes)

Colistin is poorly absorbed so the therapeutic index is high.

4.11 Withdrawal periods

Meat and offal: 1 day

5. PHARMACOLOGICAL PROPERTIES

ATC vet: QA07AA10, other intestinal anti-infectives.

Colistin Sulphate is a mixture of the following sulphates of polypeptides produced by certain strains of Bacillus polymyxa var. colistinus or obtained by any other means: Colistin E1, Colistin E2, Colistin E3, Colistin E1-I, Colistin E1-7MOA.
Colistin is a polymyxin antibiotic that is used in the treatment of severe gram-negative infections, especially those due to E. coli and Salmonella spp. It is used by oral route for the treatment of gastro-intestinal infections or for selective decontamination of the gastro-intestinal tract in animals at high risk of endogenous infections. The development of resistance to colistin is rare.

5.1 Pharmacodynamic properties

Antibacterial spectrum of activity

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.

Against sensitive E. coli, colistin is bactericidal with a rapid onset of action and develops a prolonged post antibiotic action after removal of colistin.
MICs for several serotypes of E. coli range from about 0.15 to 0.5 µg/ml; susceptible strains of E. coli generally respond to concentrations below 0.5 µg/ml.

Acquired resistance

Gram-positive bacteria are naturally resistant to colistin, as are some species of gram-negative bacteria such as Proteus and Serratia. However, acquired resistance of gram-negative enteric bacteria to colistin is rare and explained by a single step mutation.

Frequency resistance

A surveillance program of resistance indicates that the susceptibility of bacterial strains of swine origin to colistin is 95% or higher.

5.2 Pharmacokinetic properties

Bioavailability

Colistin sulphate 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. In particular, there is greater persistence in the caecum and colon than in the stomach.

Linearity

The main pharmacokinetic parameter as area under the curve (AUC) and Cmax were linearly related to the administered dose.

Metabolism and Elimination

As colistin has been shown to undergo virtually no systemic absorption after oral administration, it may be stated that the colistin present in manure was actually of faecal origin. 40% of colistin is recovered as parent drug in an extractable form in manure. The 60% undetected is attributed to binding to phospholipid and liposaccharide molecules of gram-negative bacteria. No significant metabolism is observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Water Purified

6.2 Incompatibilities

None known.

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: 3 months
Shelf life after dilution according to the direction: 24 hours

6.4 Special precautions for storage

Do not store above 25 °C
Once opened use within 3 months.
Any medicated water or stock solution which is not consumed within 24 hours should be discarded.

6.5 Nature and contents of container

Nature of container:
Bottle in white, opaque, high density polyethylene.
Cap in white, opaque polypropylene with seal in poly(vinyl chloride/vinyl acetate) tamper evident, and a translucent polypropylene measuring cylinder affixed to the inside of the cap.

Package sizes:
250 ml, 500 ml, 1 litre, 2 litres and 5 litres.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused medicinal product or waste materials if any

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

Ceva Animal Health Ltd
Unit 3, Anglo Office Park
White Lion Road
Amersham
Buckinghamshire
HP7 9FB

8. MARKETING AUTHORISATION NUMBER

Vm 15052/4017

9. DATE OF FIRST AUTHORISATION

Date: 3 December 2004

10. DATE OF REVISION OF THE TEXT

Date: May 2015

APPROVED T. NASH **29/05/15**