PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE
BOTTLE LABEL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliplus 2,000,000 IU/ml Concentrate for Oral Solution for use in drinking water for Cattle, Sheep, Pigs and Chickens

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml of solution for oral use contains 2 MIU (equivalent to 83.33 mg) of colistin sulfate.
Other substances: Benzyl alcohol (E1519), Disodium edetate.

3. PHARMACEUTICAL FORM

Concentrate for oral solution for use in drinking water. Clear yellow-brown solution

4. PACKAGE SIZE

250 ml, 1 litre and 5 litres.

5. TARGET SPECIES

Cattle (calves), Sheep (lambs), Pigs and Chickens

6. INDICATION(S)

Treatment and metaphylaxis of gastrointestinal infections caused by non-invasive *Escherichia coli* susceptible to colistin.
The presence of the disease in the herd should be established before metaphylactic treatment.

7. CONTRAINDICATION(S)

Do not use in case of hypersensitivity to polypeptide antibiotics or to any of the excipients.
Do not use in case of resistance to the polymyxin.
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.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

To be administered orally.

For calves, lambs and pigs the recommended dose is 100 000 IU of colistin per kilogram body weight daily 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 poultry the recommended dose is 75 000 IU of colistin per kilogram body weight daily for 3-5 consecutive days.

Administration via drinking water

The uptake of medicated water depends on the physiological and clinical conditions of the animals. In order to obtain the correct dosage, the concentration of colistin has to be adjusted accordingly. 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:

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

- Administration without a dosing pump:

The treatment is distributed in a tank over a period of 24 hours, for 3 consecutive days.
Coliplus 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 IU of colistin per kg body weight. The following sequential steps should be followed:

From the dosage regimen and the total weight of animals 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 24 hours.

The following formula can be applied:

1) Calculation of product solution volume at each day (V):
   V (ml) = (Dosage per day in IU/kg b.w. x Total weight of animals to treat) / 2,000,000 IU.

2) Calculation of the quantity of drinking water to prepare (Q_{water}):
   Q_{water} (L): (Mean individual water consumption/day) x (Number of animals to be treated)

- Administration via a dosing pump

The treatment is distributed over a period of 24 hours, for 3 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.
If the product is administered with an automated drinking water system, we have to calculate the volume and the concentration of the stock solution. The following sequential steps should be followed:

1) Calculation of product solution volume at each distribution (V):
   V (ml) = (Dosage per day in IU/kg b.w. x Total weight of animals to treat) / 2,000,000 IU

2) Calculation of the drinking water concentration (C):
   C (ml/L) = V / Total volume of water consumed by the animals in 24 hours.

3) Calculation of the stock solution volume (V_{stock})
   V_{stock} (L) = Total volume of water consumed by the animals in 24 hours x F

4) Calculation of the stock solution concentration (Cstock):
   C_{stock} (ml/L) = C / F

9. WITHDRAWAL PERIOD

Meat and offal: Calves, Lambs, Pig and Chickens: 1 day
Eggs: Zero days
Not permitted for use in animals producing milk for human consumption.

10. SPECIAL STORAGE PRECAUTIONS

Store below 25°C

11. SPECIAL WARNINGS

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.
Use of the product should be based on susceptibility testing and take into account official and local antimicrobials policies. 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.
Adverse reactions and overdose are not known for this product. If you notice any serious effects or other effects not mentioned on this label, please inform your

veterinary surgeon.Interactions: 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.
Incompatibilities: In the absence of compatibility studies this veterinary medicinal product must not be mixed with other veterinary medicinal products.

12. USER WARNINGS

People with known hypersensitivity to polymyxins, such as colistin, should avoid contact with the veterinary medicinal product.
It is recommended to wear impervious gloves when handling or administering the product.
Do not eat, drink or smoke while handling the product.
In case of accidental eye exposure, wash with plenty of water and seek medical advice immediately and show the label to the physician.
Wash hands after use.

13. USE DURING PREGNANCY, LACTATION OR LAY

The safety of the veterinarian medicinal product has not been established during pregnancy, lactation or lay in the target species. Use only accordingly to the risk/benefit of the veterinarian.
Using the veterinary medicinal product (antimicrobials) in poultry should be in accordance with Commission Regulation EC 1177/2006 and subsequent national requirements.

14. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the immediate packaging: 60 days
Shelf-life after dilution in water: 24 hours
When the container is opened for the first time, the date on which any product remaining in the container should be discarded should be worked out using the in-use shelf-life which is specified on this label. This discard date should be written in the space provided

Once opened, use by ____/____

Do not use this veterinary medicinal product after the expiry date which is stated on this label after EXP. The date refers to the last day of that month.

15. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS 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.

Other information:

Package sizes: 250 ml, 1 litre and 5 litres.
Not all pack sizes may be marketed.

16. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription.

17. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the sight and reach of children

18. MARKETING AUTHORISATION HOLDER AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

DIVASA - FARMAVIC, S.A.
Ctra. Sant Hipòlit, km 71
08503 GURB - VIC
Barcelona (Spain)

19. MARKETING AUTHORISATION NUMBER(S)

Authorisation No.

20. MANUFACTURER'S BATCH NUMBER

<Batch> <Lot> <BN> {number}