ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Label for 1L bottle and 5 L carafes

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

HIDROCOL, 4000000 IU/ml solution for use in drinking water/milk
Colistin

2. STATEMENT OF THE ACTIVE SUBSTANCES

Each ml contains:

Active substance:
Colistin (sulfate) .....4000000 IU

3. PHARMACEUTICAL FORM

Solution for use in drinking water/milk

4. PACKAGE SIZE

1 L
5 L

5. TARGET SPECIES

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

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package before use.

8. WITHDRAWAL PERIOD

Withdrawal periods:

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

Chickens and turkeys
Meat and offal: 1 day
Egg: zero days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP: month/year
Once opened use within 3 months
Use by…

11. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C
Protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. 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.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

SP VETERINARIA S.A.
Crta Reus Vinyols km 4.1
Riudoms (43330)
Spain

16. MARKETING AUTHORISATION NUMBER(S)

Vm 36967/4005

17. MANUFACTURER'S BATCH NUMBER

Batch: (number)

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
HIDROCOL, 4000000 IU/ml solution for use in drinking water/milk

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:

SP VETERINARIA S.A.
Crta Reus Vinyols km 4.1
Riudoms (43330)
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

HIDROCOL, 4000000 IU/ml solution for use in drinking water/milk
Colistin

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains:

Active substance:
Colistin (sulfate) .....4000000 IU

Excipients:
Benzyl alcohol . (E1519).....0.010 ml

Brown –orange solution

4. INDICATION(S)

Treatment and metaphylaxis of enteric infections caused by non-invasive E. *Coli*, susceptible to colistin.
In the case of metaphylaxis, the presence of the disease in the group / flock must be established before the product is used.

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to colistin sulfate or to any of the excipients.
Do not use in 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.

6. ADVERSE REACTIONS

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon. Alternatively you can report via your national reporting system {national system details}.

7. TARGET SPECIES

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

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

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 0.25 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 18.75 ml of the concentrate solution per Ton of body weight per day for 3-5 days.

9. ADVICE ON CORRECT ADMINISTRATION

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 3 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 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.
Water uptake should be monitored at frequent intervals.

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:

$$\frac{\text{ml veterinary medicinal product per kg bodyweight and day} \times \text{Average bodyweight (kg) of animals to be treated}}{\text{Average daily water intake (l/animal)}} = \text{ml of veterinary medicinal product per litre of drinking water}$$

• 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.

10. WITHDRAWAL PERIOD

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

Chickens and turkeys
Meat and offal: 1 day
Egg: zero days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not store above 25 °C
Protect from light.
Shelf life after first opening the immediate packaging: 3 months
Shelf life after dilution in water according to directions: 24 hours
Shelf life after dilution in milk/milk replacer: 3 hours

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

12. SPECIAL WARNING(S)

Special warnings for each target species:

Use of the product should be based on susceptibility testing and take into account official and local antimicrobials policies. 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.
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.
There is cross-resistance between colistin sulfate and polymyxin B.

Special precautions for use in animals:

Use of the product should be based on susceptibility testing and take into account official and local antimicrobials policies.
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.
An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.
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.
In the case of newborn animals and animals with severe gastrointestinal and renal disorders, systemic exposure to colistin sulfate may be increased. As a result, neuro- and nephrotoxic effects may occur.
Do not use colistin sulfate as a substitute for good management practices.

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 must be worn while handling and dosing the product.
Do not eat, drink or smoke while handling the 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.

Pregnancy /Lactation/Lay/Fertility:
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 accordingly to the benefit-risk assessment by the responsible veterinarian.

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.

Overdose (symptoms, emergency procedures, antidotes):
None.

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

Enviromental properties

Colistin is classified as a very persistent substance in soil.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

July 2021

15. OTHER INFORMATION

Package size:
1 litre bottle
5 litre carafes

Not all pack sizes may be marketed.

Approved: 24/09/21