"PACKAGE LEAFLET:

Colixyme 22.5 MIU/g powder for use in drinking water

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

Marketing authorisation holder:

Andersen S.L. Avda. de la Llana, 123 08191 Rubí (SPAIN)

Manufacturer responsible for batch release:

Laboratorios Maymó S.A. Polígono Industrial Can Pelegrí C/ Ferro, 9. 08755 Castellbisbal (SPAIN)

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Colixyme 22.5 MIU/g powder for use in drinking water

Colistin sulfate

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

Each g contains:

Active substance

Colistin (as sulfate) 22.5 MIU

Excipients:

None

White or almost white powder

4. INDICATIONS

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

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

5. CONTRAINDICATIONS

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

Do not use in case of resistance to polymyxins.

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.

6. ADVERSE REACTIONS

None known.

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.

7. TARGET SPECIES

Chicken, turkeys, cattle (calves) and pigs

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

In drinking water use
Calves and pigs: 100 000 IU of colistin/kg body weight daily for 3-5 consecutive days (equivalent to 4,44 mg product/kg BW/day for 3-5 days).

Chicken and turkeys: 75 000 IU of colistin/kg body weight daily for 3-5 consecutive days (equivalent to 3,33 mg product/kg BW/day for 3-5 days).
Duration of treatment should be limited to the minimum time necessary for the treatment of the disease.
The intake of medicated water depends on the physiological and clinical condition of the animals. In order to obtain the correct dosage, the concentration of colistin 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 must be renewed every 24 hours. 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:

… g of the product per kg bodyweight	x	average body weight (kg) of the animals to be treated	x	number of animals	=....g of the product/ daily consumption of drinking water
Total water consumption (L) of the herd/flock on previous day					

Administration without a dosing pump:

The treatment is distributed in a tank over a period of 24 hours, for 3 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/kg body weight for calves and pigs and 75 000 IU of colistin/kg body weight for poultry

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.

9. ADVICE ON CORRECT ADMINISTRATIONS

Medicated water mustbe renewed every 24 hours.

Remove the drinking water of animals prior to the administration medicated water to ensure rapid intake.

10. WITHDRAWAL PERIOD

Calves and pigs

Meat and offal: 1 day

Chickens and turkeys

Meat and offal: 1 day

Eggs: zero days

11. SPECIAL STORAGE PRECAUTIONS:

Keep out of the sight and reach of children.

Keep the container tightly closed in order to protect from light,

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.

Shelf-life after first opening the container:

6150 MIU bag: 28 days

615 MIU and 1020 MIU sachets: use immediately.

Shelf-life after dilution in water according to directions: 24 hours

12. SPECIAL WARNINGS:

Special precautions for use in animals

Severely diseased animals have a different drinking pattern and must consequently be treated parenterally. 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 8, leading to unnecessary exposure, is not recommended.

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
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.

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.

Special warnings for each target species

Severely diseased animals have a different drinking pattern and must consequently be treated parenterally.

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.

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

People with known hypersensitivity to polymyxins, such as colistin, should avoid contact with the product.

Personal protective equipment consisting of gloves and protective goggles should be worn when handling and dosing the veterinary medicinal product).

When handling the product, avoid all direct contact with skin and eyes, as well as inhaling the powder.

Wash hands following use. Wash your clothes daily after using the product.

Use the product in places with suitable ventilation.

Do not smoke, eat or drink while handling the product.

If symptoms such as rash appear after exposure, seek medical attention and present these warnings. Swelling of face, lips or eyes, and difficulty breathing are serious signs that require urgent medical attention.

Interaction with other medicinal products and other forms of interaction

With myorelaxants (tubocurare, suxamethonium, pancurare, galamine) the neuromuscular blocking with respiratory failure risk may be increased.

After oral administration of colistin sulfate interaction with anaesthetics and myorelaxants may not be excluded in individual cases. The neuromuscular blocking action of muscle relaxants (tubocurare, suxamethonium, pancurare, galamine) are potentiated by Colistin increasing the risk of respiratory failure. 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.

There is cross-resistance between colistin and polymyxin B.

Overdose

In case of overdose, transient digestive problems, such as soft stools and thympanites may appear. Sings of neurotoxicity and nephrotoxicity may also appear.

Major Incompatibilities

Divalent cations (calcium, magnesium, manganese). Unsaturated fatty acids. In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy or lactation.

Use only accordingly to the benefit/risk assessment by the responsible veterinarian

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

Medicines should not be disposed of via wastewater or household waste.

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

XXX

15. OTHER INFORMATION:

Pack sizes

Bag and sachets of low density polyethylene/aluminium/ polyester with thermo-sealing closing system.

Pack sizes:

Bag of 6150 MIU containing 273,06 g of product

Cardboard box with 20 sachets of 615 MIU containing 27,3 g of product

Cardboard box with 20 sachets of 1020 MIU containing 45,28 g of product

Not all pack sizes may be marketed.

To be supplied by veterinary prescription. Administration by a veterinary surgeon or under their direct responsibility.

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

Marketing authorization Nº:

COMBINED LABEL AND PACKAGE LEAFLET (6150 MIU)

Colixyme 22.5 MIU/g powder for use in drinking water

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

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

Each g contains:

Active substance

Colistin (as sulfate) 22.5 MIU

Excipients:

None

White or almost white powder

4. PHARMACEUTICAL FORM

Powder for use in drinking water

5. PACKAGE SIZES

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8. . ADVERSE REACTIONS

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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.

9. . TARGET SPECIES

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

The intake of medicated water depends on the physiological and clinical condition of the animals. In order to obtain the correct dosage, the concentration of colistin 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 must be renewed every 24 hours. The medicated water should be the only source of drinking water for the animals for the entire duration of the treatment period.

Use the following formula in order to calculate the quantity of the product (mg) that should be incorporated per litre drinking water:

$$\frac{\text{Dose (mg product per kg body weight per day)} \times \text{mean body weight (kg) of animals to be treated}}{\text{mean daily water consumption (litre) per animal per day}} = \text{\_\_\_\_ mg product per litre drinking water}$$

Administration without a dosing pump:

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12. WITHDRAWAL PERIOD

Calves and pigs

Meat and offal: 1 day

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13. SPECIAL STORAGE PRECAUTIONS:

Keep the container tightly closed in order to protect from light.

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.

14. SPECIAL WARNINGS:

Special warnings for each target species

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18. For animal treatment only.

Veterinary use – to be supplied by veterinary prescription.

19. Keep out of the sight and reach of children

20. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the container:
6150 MIU bag: 28 days
615 MIU and 1020 MIU sachets: immediate use
Shelf-life after dilution in water according to directions: 24 hours

21. Marketing authorization Nº:

22. Manufacturer's batch number: