SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NIPOXYME 22.500.000 IU/g POWDER FOR USE IN DRINKING WATER

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:

Colistin (as sulphate) 22.500.000 IU

Excipients:

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for use in drinking water.

White to almost white powder

4. CLINICAL PARTICULARS

4.1 Target species

Pig.

4.2 Indications for use, specifying the target species

Treatment and metaphylaxis of the 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.

4.3 Contraindications

Do not use in animals with kidney failure.

Do not use in case of hypersensitivity to polypeptide antibiotics.

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

Sick animals may have a reduced appetite and altered drinking pattern and should if necessary, be medicated 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 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 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 precautions to be taken by the person administering the veterinary medicinal product to animals

People with known hypersensitivity to the colistin (sulphate) should avoid contact with the veterinary medicinal product.

Personal protective equipment consisting of rubber gloves should be worn when handling the veterinary medicinal product.

Avoid the contact with the eyes and skin. In the case of accidental contact, rinse immediately with plenty of water, seek medical advice and show the package leaflet or the label to the physician.

Wash hands after using the product.

Keep the container well closed and away from the light, and always keep the product label for identification purposes.

Use the product in places with suitable ventilation.

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

If it appears symptoms after the contact, like dermal eruption seek medical advice and present these warnings. The swelling of the face, lips either eyes or respiratory difficulty are serious signs that require urgent medical attention.

4.6 Adverse reactions

None.

4.7 Use during pregnancy or lactation

The use is not recommended during pregnancy and lactation as colistin safety during these periods has not been studied in the target species.

4.8 Interaction with other medicinal products and other forms of interaction

After oral administration of colistin sulphate interaction with anaesthetics and myorelaxants may not be excluded in individual cases.

The effects of colistin sulphate may be antagonized by binary cations (iron, calcium, magnesium) and by unsaturated fatty acids.

4.9 Amounts to be administered and administration route

For administration in drinking water.

The recommended dose is 150.000 UI of colistin/kg bw/day during 5-7 days (equivalent to 5.8 mg of product/kg bw/day) to add to 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 has to be adjusted accordingly.

The quantity of product to add to the water can be calculated using the following formula:

$$\text{Quantity (mg) of product / l drinking water} = \frac{\text{5.8 mg of product/kg bw/day} \times \text{mean weight of the animal (kg)}}{\text{Mean daily consumption (litres)}}$$

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

The medicated water should be the only source of drinking water. Medicated drinking water should be refreshed or replaced every 24 hours.

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

4.10 Overdose (symptoms, emergency procedures, antidotes)

In the event of overdose, transient digestive problems such as soft stools or tympanites may appear.

Signs of neurotoxicity and nephrotoxicity may appear.

4.11 Withdrawal period

Meat and offal: 1 day.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: intestinal antiinfectives, antibiotics.

ATC vet code QA07AA10.

5.1 Pharmacodynamic properties

Colistin has a bactericidal action versus susceptible gram-negative bacteria strains such as *E. coli*. The antibacterial action is only developed against extracellular bacteria.

Colistin acts as a cationic surfactant altering the permeability of the bacteria cell membrane by combining with lipoproteins, giving rise to a loss of nutritive elements such as amino acids, inorganic ions, purines and pyrimidines. It produces an alteration in bacterial metabolism and leads to their death. It also acts by reducing the activity of bacterial endotoxins in the tissue liquids.

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. There is cross resistance between polymyxins but not with other antibiotics.

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.

5.2 Pharmacokinetic particulars

Colistin is poorly absorbed after oral administration, and its concentration in plasma is normally undetectable. It is excreted mainly in faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

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

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years
Shelf-life after first opening of the immediate packaging: 14 days
Shelf-life after dilution according to directions: 24 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

Original packaging 1 × 250 g fold-up cardboard box with an inner lining of aluminium/low-density polyethylene.
Original packaging 1 × 500 g fold-up cardboard box with an inner lining of aluminium/low-density polyethylene.
Original packaging 1 × 1 kg fold-up cardboard box with an inner lining of aluminium/low-density polyethylene.
A 250g bag of polyester/aluminium /low-density polyethylene.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

ANDERSEN S.L.
Avda. de la Llana 123
Polígono Industrial "La Llana"
08191 Rubí (Spain)

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription.

Administration by a veterinary surgeon or under their direct responsibility.