SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sulfaprex 250/50 mg/g Premix for medicated feeding stuff for pigs and sheep (CY; EL; ES and PT)
Sulfaprex 250 mg/g+50 mg/g premix for medicated feeding stuff for pigs and sheep (PL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substances:

Sulfadiazine.....250 mg

Trimethoprim .....50 mg

Excipients:

Calcium carbonate .....q.s.1 g

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff.

Yellowish-white granulated powder

4. CLINICAL PARTICULARS

4.1 Target species

Pigs and sheep (pre-ruminant).

4.2 Indications for use, specifying target species

Pigs: For the treatment of respiratory infections caused by strains of *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis* y *Streptococcus suis* sensitive to sulfadiazine and trimethoprim.

Sheep (pre-ruminant): For the treatment of respiratory infections caused by strains of *Pasteurella multocida* sensitive to sulfadiazine and trimethoprim.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substances, to dihydrofolate reductase inhibitors or to any of the excipients.

Do not use in animals with renal or hepatic insufficiency.

Do not use in animals with blood dyscrasias.

4.4 Special warnings for each target species

The intake of medicated feed depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of antimicrobial should be adjusted accordingly and water consume should be guaranteed.

Animals with reduced feed intake and/or disturbed general condition have to be treated parenterally.

4.5 Special precautions for use

Special precautions for use in animals

Whenever possible sulfadiazine and trimethoprim association should only be used based on susceptibility testing. Official, national and regional antimicrobial policies should be taken into account when the product is used.

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

People with known hypersensitivity to active substances should avoid contact with the veterinary medicinal product.

Handle the product with careful in order to avoid its contact during feed manufacturing, as well as during medicated feed administration to animals.

Take the suitable measures to avoid dust dissemination during medicated feed manufacture.

Personal protective equipment consisting of mask (in accordance with EN140FFP1), gloves, work clothes and safety glasses should be worn when handling the veterinary medicinal product.

Avoid contact with skin and eyes. In case of contact, wash the exposed area immediately with water.

Do not smoke, eat or drink while handling this 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.

4.6 Adverse reactions (frequency and seriousness):

Alterations in the urinary tract (crystalluria, hematuria, obstruction) may occur on very rare occasions.

Allergic reactions, with possible cutaneous manifestations may occur on very rare occasions.

Signs of gastrointestinal intolerance (nausea, vomiting and diarrhea) may occur on very rare occasions.

If any of these manifestations appear, discontinue treatment.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))

- common (more than 1 but less than 10 animals in 100 animals treated)

- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)

- rare (more than 1 but less than 10 animals in 10,000 animals treated)

- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy and lactation

Do not use during the whole pregnancy or in neonates.

Do not administer to lactating females whose milk is destined for human consumption.

4.8 Interaction with other medicinal products and other forms of interaction:

Do not administer simultaneously with acid para-aminobenzoic (PABA) and derivatives (procaine, benzocaine, tetracaine,…) and in general do not administer with substances or feed that have PABA and/or folic acid.
Do not administer with oral anticoagulants or urinary acidifier.

4.9 Amounts to be administered and administration route

In-feed use.

The recommended dosage is 30 mg combined activity (25 mg sulfadiazine and 5 mg Trimethoprim) per kg bodyweight / day for 5 days. This is equivalent to 1 g of product per 10 Kg bodyweight/ day.

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

The intake of medicated feed depends on the clinical condition of the animals. In order to obtain a correct dose, the amount of premix to be administered must be adjusted to the mean daily food intake of the animals. The following formula may be used:

$$\textit{mg of product / kg of feed} = \frac{\textit{100 mg of product /kg b.w./day} \times \textit{mean body weight of animals (kg)}}{\textit{mean daily feed intake of animals (kg)}}$$

Administration method:

To mix with feed once it is manufactured. In the granulation process is recommended to prepare the mix with vapour between 5 -10 minutes at a temperature not exceeding 75ºC.

4.10 Overdose (symptoms, emergency procedures, antidotes)

In case of overdose, the following signs can be observed:

Digestive signs: nauseas, vomiting, anorexia, diarrhoea.
Urinary signs: crystaluria.
Hematopoietic alterations, such as thrombocytopenia or leukopenia.

In case of severe overdose, withdraw the treatment, give plenty of water and administer folic acid.

4. 11 Withdrawal period:

Pigs:

- Meat and offal: 3 days.

Sheep (pre-ruminant):

- Meat and offal: 4 days
- Milk: Not authorised for use in animals producing milk for human consumption

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiinfectives for systemic use, combinations of sulfonamides and trimethoprim, incl. derivates

ATCVet Code: QJ01EW10

5.1 Pharmacodynamic properties

Sulfadiazine is a bacteriostatic antibiotic that acts blocking synthesis of folic acid carriers of monocarbonated unities, essential to acid nucleic synthesis. This action is consequence of structural analogy between sulfadiazine and paraminobenzoic acid molecules (PABA).

The two compounds act sequentially on the same bacterial enzymatic pathway leading to the synthesis of tetrahydrofolic acid, a vital step in bacterial DNA synthesis. This action results in a synergistic antibacterial effect which has been demonstrated both *in vitro* and *in vivo*.

In vitro, the association is active against:

Very sensible:

Gram negative: *Pasteurella multocida, Actinobacillus pleuropneumoniae, Haemophilus parasuis*.

Gram positive: *Streptococcus suis*

5.2. Pharmacokinetic particulars

Sulfadiazine administered orally is rapidly absorbed in monogastric animals, distributed in all tissues. The rate of binding to plasma proteins is between 20 and 50% according to some sources and over 90% according to others. Levels in kidney are higher than plasma, while in the skin, liver and lungs are only slightly lower. It is metabolized in the liver to acetylated derivatives and, to a lesser extent, to hydroxylated derivatives. Its elimination half-life is 2.9 h in pigs. Excretion is mainly renal by glomerular filtration and active tubular secretion. In 24 hours urine is 50% of the dose.

Trimethoprim administered orally is rapidly absorbed (except ruminants), peak plasma concentrations at 2-4hours. All tissues and body fluids are widely distributed. Tissue concentrations are higher than plasma, especially in the lungs, liver and kidneys. The rate of binding to plasma proteins is 30 to 60%. It is metabolized in the liver by oxidation and subsequent conjugation. Excretion is mainly renal (by glomerular filtration and active tubular secretion) and less is excreted in the feces. In 24 hours urine is 75% of the dose, and 85-90% 3 days between urine and feces. Its half-life is prolonged, maintaining effective concentrations for 12 hours. Concentrations in milk are usually between 1 and 3.5 timeshigher than plasma.

In pigs, steady state between 12 and 120 h was established after the first administration, with a total duration of 108h. The maximum concentrations achieved at steady state (Cmaxss) was 11.32mg/ml and 0.656g/ml for sulfadiazine and trimethoprim, respectively, while the mean concentrations in this same period (Css) were 8,71ug/ml of sulfadiazine and 0.5mg/ml of trimethoprim. The calculated elimination half-life value was similar for the two drugs (3.26 h for sulfadiazine and 2.59 h for trimethoprim).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Paraffin, liquid

Silica, hydrophobic colloidal

Calcium carbonate

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years

Shelf-life after first opening the immediate packaging: 3 months

Shelf-life after incorporation into meal or pelleted feed for pigs: 55 days.

Shelf-life after incorporation into meal or pelleted feed for pre-ruminant sheep: 50 days.

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

25 kg multi-layer paper bag with internal low density polyethylene bag.

Bags with five layers ordered from interior to exterior:

1. Low density polyethylene sheet
2. Semi-extending kraft
3. Semi-extending kraft
4. Semi-extending kraft
5. Coated paper

Package size:

Bag of 25 kg.

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

LABORATORIOS CALIER, S.A.
C/ Barcelonès, 26 (Pla del Ramassà)
08520 LES FRANQUESES DEL VALLÈS, (Barcelona)
SPAIN

8. MARKETING AUTHORISATION NUMBER (S)

9. DATE OF THE 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.
Consideration should be given to official guidance on the incorporation of medical premixes in final feeds.
To be administered by the veterinarian or under veterinarian supervision.