SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT:

CALIERMUTIN 20mg/g PREMIX (ES)

CALIERMUTIN 20 mg/g prè-mistura para alimento medicamentoso para suinos e coelhos (PT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Active substance:

Tiamulin hydrogen fumarate……..20 mg

(Equivalent to 16.2 mg of Tiamulin)

Excipients:

Excipient q.s. .....1 g

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM:

Premix for medicated feeding stuff as granulated powder

4. CLINICAL PARTICULARS:

4.1 Target species:

Pigs and rabbits

4.2 Indications for use, specifying the target species:

Pigs:

For the treatment and metaphylaxis, when the disease is present in the group, of swine dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamulin. The presence of the disease in the group must be established before the product is used.

Treatment and prevention, proliferative enteritis (ileitis), caused by *Lawsonia intracellularis*

Treatment of enzootic pneumonia caused by *M. hyopneumoniae.*

Rabbits:

Treatment and prevention of epizootic entercolitis.

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

4.3 Contraindications:

Do not administer with ionophore polyether antibiotics as salinomycin, monensin or narasin.

Do not use in case of hypersensitivity to the active substance, or to any of the excipients.

4.4 Special warnings for each target species

In pigs and rabbits do not administer with ionophore polyether antibiotics.

The uptake of medicated feed by animals can be altered as a consequence of illness. In case of insufficient feed intake, animals should be treated parenterally.

4.5. Special precautions for use

Special precautions for use in animals

In pigs and rabbits do not administer with ionophore polyether antibiotics.

Use of the product should be based on susceptibility testing and it should take into account official and local antimicrobial policies.

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

People with known hypersensitivity to tiamulin should handle the product with care.

Tiamulin may cause irritation of the respiratory tract and eyes after its inhalation or contact.

Handle the product with care to avoid contact with skin and eyes during incorporation of premix into feed, as well as when administering the medicated feed to animals, by taking specific precautions:

Avoid dust dissemination during the incorporation of the product into feed.
Wear a dust mask (in compliance with EN140FFP1), gloves, overalls, and approved safety glasses.
Avoid contact with eyes and if it occurs wash immediately with plenty of water.
Avoid contact with skin and if it occurs wash with water and soap.
Do not smoke, eat, or drink when handling the product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness):

Occasionally, cutaneous erythema and other hypersensitivity reactions may appear.

4.7. Use during pregnancy, lactation or lay:

There are no contraindications during this period

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

Administration with ionophore polyether antibiotics in pigs may produce anorexia, diarrhoea, ataxia, lethargy, dyspnoea, myoglobinuria and death.
In rabbits administration of ionophore polyether with tiamulin may produce anorexia and gastroenteritis.

4.9. Amounts to be administered and administration route

In feed-use.
In order to guarantee a homogeneous mixture, mix properly.

Pig:

- Treatment and metaphylaxis of swine dysentery caused by B. *hyodysenteriae* and treatment of enzootic pneumonia caused by *M. hyopneumoniae:*

The treatment dose of Tiamulin is 8 mg /Kg bw/day administered by feed during 10 days.

- Treatment and prevention of ileitis caused by *Lawsonia intracellularis*. The dose of Tiamulin is 8 mg /Kg bw/day administered by feed during 14 days.

Posology of CALIERMUTIN 20 mg/g PREMIX in feed may be established according to the following formula:

mg of Caliermutin 2% premix / kg of feed =
(247 or 494 mg of CALIERMUTIN 20 mg/g PREMIX /kg bw. and day) X (mean bodyweight of the animals to treat (Kg) / mean of feed daily intake (Kg)

As a standard, the incorporation rate in feed may be established in 10 kg Caliermutin 20 mg/g premix / Tn of feed for treatment, and 5 Kg of Caliermutin 20 mg/g Premix /Tn of feed for prevention.

Rabbits:

- Treatment and prevention of epizootic enterocolitis.

The dose of Tiamulin is 1.9 mg/ Kg.bw/day administered by feed. It is recommended to maintain this treatment after weaning and during the four first weeks of fattening.

Posology of Caliermutin 20 mg/g premix in feed may be established according to the following formula:

mg of Caliermutin 20 mg/g PREMIX / kg of feed =
(117,5 mg of Caliermutin 20 mg/g premix /kg bw. and day) X (mean bodyweight of the animals to treat (Kg) / mean of feed daily intake (Kg))

As a standard the incorporation rate in feed may be established in 2 Kg of Caliermutin 20 mg/g Premix /Tn of feed.

Due to the administration route and as the feed intake depends on the clinical condition of the animal, concentration of antibiotic will be fit, considering feed daily intake, in order to ensure a correct dosage.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In case of overdose, symptoms are transitory salivation, vomit and lethargy.

4.11 Withdrawal period:

Meat: Pigs: 5 days

Rabbits: Zero days.

5. PHARMACOLOGICAL PROPERTIES:

Tiamulin is a bacteriostatic semisynthetic antibiotic that belongs to the pleuromutilins group. It acts inhibiting protein synthesis on the ribosome.

Pharmacotherapeutic group: Other antibacterials. Pleuromutilins

ATCVet Code: QJ01XQ01

5.1. Pharmacodynamic properties

Mode of action

Tiamulin acts on 70S ribosome, being its primary binding site the 50S subunit and likely a secondary binding site the joint site of 50S and 30S subunits. It bio chemically inhibits the synthesis of microbial protein by producing inactive initation complexes which prevent the elongation of the polypeptidic chain. Tiamulin has a bacteriostatic effect.

Action spectrum

Tiamulin is active against:

Species	**MIC_{90} (μg/ml)**	**Resistance breakpoints**

Brachyspira hyodysenteriae	1		> 4 (R)
Micoplasma hyopneumoniae	0,05	≤ 4 (S)	≥ 32 (R)

Resistances

Cross resistances with tylosin and other macrolides have been described.

5.2. Pharmacokinetic particulars

Tiamulin behaves as a lipophilic weak base. In pigs, at therapeutics doses, plasmatic concentrations did not exceed 1 µg/ml and T_{max} ranged, in general, within 2 and 4 hours. It is rapidly absorbed through intestinal tract and the minimum bioavailability is of 85% po.

It is widely distributed (lungs, liver muscle, intestinal content). Tiamulin is extensively metabolised by several pathways (N-dealkylation, monohydroxylation, etc.) in liver to metabolites that have poor antimicrobial activity.

Elimination occurs via urine and faeces (approximately 60 % of the oral dose is excreted in bile). A small portion of the dose appears as the parent compound (up to 3%). The highest concentrations of residues in tissues were found in the liver.

Considering rabbit as the minor specie, through the residues study carried out with rabbits and from the available data in other species, it is possible to assume that the metabolism in rabbit will not be significantly different and the extrapolation to other species is a valid assumption

6. PHARMACEUTICAL PARTICULARS:

6.1. List of excipients

Sodium carboxymethylcellulose

Lactose

Soya-bean oil

Calcium carbonate

6.2. 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: 2 years.

Shelf-life after incorporation into feed: 3 months.

Shelf-life after first opening the immediate packaging: the product should be immediately used.

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

Bags of polyester-aluminium-nylon-polyethylene of low density and 25 Kg of capacity.

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.

8. MARKETING AUTHORIZATION NUMBER: 1670-ESP

9. DATE OF FIRST AUTHORISATION: 6 February 2006

10. DATE OF REVISION OF THE TEXT: 5 Juny 2009

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary description

Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.