1.B. SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Caliermutin 800 mg/g premix for medicated feeding stuff for pigs (PT)
Caliermutin 800 mg/g Premix for pigs (ES)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Tiamulin hydrogen fumarate 800 mg
(Equivalent to 647.6 mg of Tiamulin base)

Excipients:
Lactose monohydrate 190 mg
Other excipients, 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

Pig

4.2. Indications for use, specifying the target species

Pig:
Treatment and prevention of swine dysentery caused by *Brachyspira Hyodysenteriae*.
Treatment of enzootic pneumonia induced by *Mycoplasma hyopneumoniae*.
The presence of the disease in the herd should be established before treatment.

4.3. Contraindications

Do not simultaneity administer coccidiostotics of monovalent and divalent carboxylic polyether ionophore antibiotics types.

4.4. Special warnings for each target species

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 parentally.

4.5. Special precautions for use

Special precautions for use in animals

Refer to section 4.8 for information regarding interaction between tiamulin and ionophores.

It is sound clinical practice to base treatment on susceptibility testing of the bacteria isolated from the animal 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

When mixing the veterinary medicinal product and handling the medicated feed, direct contact with eyes, skin and mucous membranes should be avoided.
Personal protective equipment should be worn when mixing the veterinary medicinal product or handling the medicated feed: overalls, impervious gloves and either a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator conforming to European Standard EN 140, with a filter to European Standard EN 143. Wash contaminated skin.

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

People with known hypersensitivity to tiamulin should administer the product with caution.
Do not smoke, eat, or drink when handling the product.

4.6. Adverse reactions (frequency and seriousness)

In very rare cases cutaneous erythema and other hypersensitivity reactions may appear.
The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment).
- Common (more than 1 but less than 10 animals in 100 animals).
- Uncommon (more than 1 but less than 10 animals in 1,000 animals).
- Rare (more than 1 but less than 10 animals in 10,000 animals).
- Very rare (less than 1 animal in 10,000 animals, including isolated reports)

4.7. Use during pregnancy, lactation or lay

Can be used in pigs during pregnancy and lactation.

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

Tiamulin has been shown to interact with ionophores such as monensin, salinomycin and narasin and may result in signs indistinguishable from an ionophore toxicosis. Animals should not receive products containing monensin, salinomycin or narasin during or at least 7 days before or after treatment with tiamulin. Severe growth depression, ataxia, paralysis or death may result.

If signs of an interaction do occur, administration of contaminated feed should be stopped immediately. The feed should be removed and replaced with fresh feed not containing the anticoccidials monensin, salinomycin or narasin.

4.9. Amounts to be administrated and administration route

Oral use, in-feed use.
Mix well with the feed to assure a homogeneous distribution.

Pigs:

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

The dose is 8 mg of tiamulin base/kg bw/day (equivalent to 12.34 mg of Caliermutin 800 mg/g premix) administered in feed during 10 days.

- Prevention of swine dysentery caused by B. hyodysenteriae:

The dose is 4 mg of tiamulin base /Kg b.w /day (equivalent to 6.17 mg of Caliermutin 800 mg/g premix) administered in feed during 10 to 14 days.
The posology of Caliermutin 800 mg/g premix in feed may be established according to the following formula:

mg of Caliermutin 800 mg/g premix / kg of feed =
(6.17 or 12.34 mg of CALIERMUTIN 800 mg/g PREMIX /kg bw. and day) X (mean bodyweight of the animals to treat (Kg) / mean of feed daily intake (Kg).

To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing.

As a standard the incorporation rate in feed for treatment may be established in 250 g of Caliermutin 800 mg/g Premix in 5 Kg of feed in blank, homogenize for 3 – 6 minutes at 60 rpm and add 5, 25 Kg obtained/ Tm of feed.

As a standard the incorporation rate in feed for prevention may be established in 125 g of Caliermutin 800 mg/g Premix in 5 Kg of feed in blank, homogenize for 3 – 6 min at 60 rpm and add 5,125 Kg obtained/ Tm of feed.

Due to the administration route and as the feed intake depends on the clinical condition of the animal, concentration of antimicrobial 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

Pigs: Meat: 5 days

5. PHARMACOLOGICAL PROPERTIES

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

Pharmacotherapeutic group: Antibacterials for systemic use
ATCVet Code: QJ 01 XQ 01

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	Resistance breakpoints	
Brachyspira hyodysenteriae		> 4 (R)
Mycoplasma hyopneumoniae	≤ 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 Tmax ranged, in general, within 2 and 4 hours. It is rapidly absorbed through intestinal tract and the minimum bioavailability is of 85% in oral use.

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

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

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactose monohydrate
Carmellose sodium

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 first opening the immediate packaging: immediately used.
Shelf life after incorporation into meal or pelleted feed: 3 months.

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

Low density polyethylene bags of 25 kg capacity in a Kraft cardboard drum 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. PI El Ramassar.

08520 LES FRANQUESES DEL VALLÈS.
BARCELONA.

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

For animal treatment only-To be supplied only on veterinary description
Administration by a veterinary surgeon or under their direct responsibility
Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.

1.B.2. LABEL AND PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Caliermutin 800 mg/g premix for pigs

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

LABORATORIOS CALIER, S.A.
C/ Barcelonès, 26. PI El Ramassar.
08520 LES FRANQUESES DEL VALLÈS.
BARCELONA. SPAIN

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Caliermutin 800 mg/g premix for medicated feeding stuff for pigs
Tiamulin hydrogen fumarate
Premix for medicated feeding stuff as granulated powder

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

Each g contains

Active substance:
Tiamulin hydrogen fumarate..... 800 mg
(Equivalent to 647.6 mg of Tiamulin base)

Excipients:
Lactose..... 190 mg
Other excipient, q.s. ..... 1 g

4. INDICATIONS

Pig:
Treatment and prevention of swine dysentery caused by *Brachyspira hyodysenteriae*
Treatment of enzootic pneumonia induced by *Mycoplasma hyopneumoniae*.
The presence of the disease in the herd should be established before treatment.

5. CONTRAINDICATIONS

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

Animals should not receive products containing ionophores (monensin, narasin or salinomycin) during or for at least seven days before or after treatment with tiamulin. Severe growth depression or death may result.

Refer to section 12, for information regarding interaction between tiamulin and ionophores.

6. ADVERSE REACTIONS

Occasionally cutaneous erythema and other hypersensitivity reactions may appear.
The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment).
- Common (more than 1 but less than 10 animals in 100 animals).
- Uncommon (more than 1 but less than 10 animals in 1,000 animals).
- Rare (more than 1 but less than 10 animals in 10,000 animals).
- Very rare (less than 1 animal in 10,000 animals, including isolated reports).

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Pig

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

Oral use, in-feed use.
Mix well with the feed to assure a homogeneous distribution.

Pigs:

- Treatment of swine dysentery caused by *B. hyodysenteriae* and of enzootic pneumonia caused by *M. hyopneumoniae*.
  The dose is 8 mg of Tiamulin base / kg bw/day (equivalent to 12.34 mg of Caliermutin 800 mg/g premix) administered in feed during 10 days.
- Prevention of swine dysentery caused by *B. hyodysenteriae.*
  The dose is 4 mg of Tiamulin base / kg bw/day (equivalent to 6.17 mg of Caliermutin 800 mg/g premix) administered in feed during 10-14 days.

The posology of CALIERMUTIN 800 mg/g Premix in feed may be established according to the following formula:
mg of CALIERMUTIN 800 mg/g Premix / kg of feed =
(6.17 or 12.34 mg of CALIERMUTIN 800 mg/g Premix /kg bw. and day) X (mean bodyweight of the animals to treat (Kg) / mean of feed daily intake (Kg)

To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing

As a standard the incorporation rate in feed for treatment may be established in 250 g of Caliermutin 800 mg/g Premix in 5 Kg of feed in blank, homogenize for 3 – 6 minutes at 60 rpm and add 5, 25 Kg obtained/ Tm of feed.

As a standard the incorporation rate in feed for prevention may be established in 125 g of Caliermutin 800 mg/g Premix in 5 Kg of feed in blank, homogenize for 3 – 6 min at 60 rpm and add 5,125 Kg obtained/ Tm of feed.

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

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD

Pigs: Meat: 5 days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.
Shelf-life after first opening the container: use immediately.
Shelf-life after incorporation into meal or pelleted feed: 3 months.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after abbreviation CAD

12. SPECIAL WARNINGS

Special warnings for each target species:
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.

Special precautions for use in animals:
Do not a simultaneity dminister coccidiostotics of carboxylic polyether ionophore antibiotics types.
It is sound clinical practice to base treatment on susceptibility testing of the bacteria isolated from the animal and to take into account official and local antimicrobial policies.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
When mixing the veterinary medicinal product and handling the medicated feed, direct contact with eyes, skin and mucous membranes should be avoided.
Personal protective equipment should be worn when mixing the veterinary medicinal product or handling the medicated feed: overalls, impervious gloves and either a disposable half-mask respirator conforming to European Standard

EN 149 or a non-disposable respirator conforming to European Standard EN 140, with a filter to European Standard EN 143. Wash contaminated skin.

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

People with known hypersensitivity to tiamulin should administer the product with caution.
Do not smoke, eat, or drink when handling the product..

Use during pregnancy, lactation or lay:
Can be used in pigs during pregnancy and lactation

Interactions with other medicinal products and other forms of interaction:
Tiamulin has been shown to interact with ionophores such as monensin, salinomycin and narasin and may result in signs indistinguishable from an ionophore toxicosis. Animals should not receive products containing monensin, salinomycin or narasin during or at least 7 days before or after treatment with tiamulin. Severe growth depression, ataxia, paralysis or death may result.

If signs of an interaction do occur, administration of contaminated feed should be stopped immediately. The feed should be removed and replaced with fresh feed not containing the anticoccidials monensin, salinomycin or narasin.

Overdose (symptoms, emergency procedures, antidotes):
In case of overdose, symptoms are transitory salivation, vomit and lethargy.

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

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

15. OTHER INFORMATION

Low density polyethylene bags of 25 kg capacity in a Kraft cardboard drum of 25 kg.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder

Reg No.:

Batch:
Expires:
For animal treatment only- To be supplied only on veterinary description
Premix for medicated feeding stuff
Administration by a veterinary surgeon or under their direct responsibility