SUMMARY OF PRODUCT CHARACTERISTICS

1 . NAME OF THE VETERINARY MEDICINAL PRODUCT

MACROMUTIN 125 mg/ml ORAL SOLUTION POULTRY AND PIGS (ES)
CALIERMUTIN 125 mg/ml ORAL SOLUTION POULTRY AND PIGS (PT)

2 . QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Tiamulin.....101.2 mg
Equivalent to Tiamulin hydrogen fumarate .....125.0 mg

Excipients:
Methyl parahydroxybenzoate (E219).....0.9 mg
Propyl parahydroxybenzoate (E217) .....0.1 mg

For a full list of excipients, see section 6.1.

3 . PHARMACEUTICAL FORM

Solution to be administrated in drinking water.
Clear and colourless to pale yellow solution

4 . CLINICAL PARTICULARS

4.1 Target species

Poultry (Broilers, layer hens, breeder hens and turkeys) and Porcine.

4.2 Indications for use, specifying the target species

Poultry (Broilers, laying hens, breeder hens and turkeys):
Treatment and prevention of chronic respiratory disease (CRD) caused by tiamulin sensitive strains: *Mycoplasma gallisepticum*, *Mycoplasma meleagridis.*

Porcine:

Treatment of enzootic pneumonia caused by tiamulin sensitive strains: *Mycoplasma hyopneumoniae*, *Mycoplasma hyorhinis.*

Treatment of haemorrhagic dysentery caused or complicated by tiamulin sensitive strains: *Brachyspira hyodysenteriae*

4.3 Contraindications

Do not use the product with monovalent ionophore antibiotics, 7 days before, during and 7 days after treatment of animals.

4.4 Special warnings for each target species

None

4.5 Special precautions for use

Special precautions for use in animals

Use of the product should be based on susceptibility testing.

Strategic treatment should be limited to animals where tiamulin sensitive agents have been isolated in the farm. Long term or repeated use should be avoided by improving management practice and thorough cleansing and disinfection.

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

People with known hypersensitivity to Tiamulin should avoid any contact with the product

- Avoid skin and mucous contact.
- Tiamulin can cause irritation of the respiratory tract and eyes after its inhalation or contact.
- The product should be carefully handled to avoid contact during its incorporation into drinking water.
- During product handling, use protective gloves, mask and glasses in accordance with the current normative.

- Precautions recommended to avoid a possible exposition are:
    - 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.

4.6 Adverse reactions (frequency and seriousness)

In rare cases (between 1 and 10 animals for each 10000 treated) hypersensitivity to tiamulin following oral administration has been reported, in terms of acute dermatitis with subcutaneous erythema and intense pruritus. Adverse reactions are often mild and transient but in some cases they may be serious. If these side effects occur, stop treatment immediately and clean animals and facilities with water. Normally, animals recover fast thereafter. Symptomatic treatment such as electrolyte therapy and anti-inflammatory therapy may be useful.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established in pregnant or lactating sows. Use only accordingly to the benefit/risk assessment by the responsible veterinarian

4.8 Interaction with other medicinal products and other forms of interaction

See section 4.3 Contra-Indications.

Incompatibility with certain ionophore antibiotics (see section 4.3 contraindications) may occur. Following simultaneous administration symptoms of intoxication as growth depression, paralysis and death are possible.

4.9 Amounts to be administered and administration route

Oral route in drinking water

Poultry (Broilers, laying hens, breeder hens and turkeys):

20 mg of tiamulin base/ kg b.w. per day (equivalent to 24.7 mg de tiamulin hydrogen fumarate / kg b.w./day), by oral route in drinking water, equivalent to 19.75 ml of solution per 100 kg of body weight per day, for 3 to 5 days depending on the severity of the disease.

Posology of MACROMUTIN 125 mg/ml oral solution can be established according to the following formula:

ml MACROMUTIN 125 mg/ml oral solution /l water=
(0.1975 ml MACROMUTIN 125 mg/ml oral solution /kg b.w. / day) X (animals mean body weight (kg)) / mean water intake (l)

For a water consumption of 183.1 ml/kg b.w., this dose equals to 1.079 ml of MACROMUTIN 125 mg/ml oral solution /l of water. In order to respect the dosage and taking into account the real water consumption, incorporation rate can be increased, which would mean a higher concentration in water.

Porcine:
6.48-8.10 mg tiamulin base/ kg b.w. per day (equivalent to 8-10 mg tiamulin hydrogen fumarate/ kg b.w./day) for 5 days by oral route in drinking water, equivalent to 6.40 to 8 ml of solution per 100 kg of body weight per day, for 5 days.

Posology of MACROMUTIN 125 mg/ml oral solution can be established according to the following formula:

ml MACROMUTIN 125 mg/ml oral solution /l water=
(0.064-0.08 ml MACROMUTIN 125 mg/ml oral solution /kg b.w. / day) X
(animals mean body weight (kg)) / mean water intake (l)

For a water consumption of 81 ml/kg b.w., this dose equals to 0.79 – 0.987 ml of MACROMUTIN 125 mg/ml ORAL SOLUTION /l of water. In order to respect

the dosage and taking into account the real water consumption, incorporation rate can be increased, which would mean a higher concentration in water.
Medicated drinking water should be refreshed or replaced every 24 hours
To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing

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

Not known.

4.11 Withdrawal periods

Meat and offal:
Pigs: 6 days
Broilers, laying hens and breeder hens: 6 days
Turkeys: 6 days
Eggs: zero days

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Pleuromutilins
ATCvet code: QJ01XQ01

5.1. Pharmacodynamic particulars

Tiamulin is a semi-synthetic antibiotic belonging to pleuromutilins group.
Tiamulin is a bacteriostatic antibiotic that acts by inhibiting protein synthesis by reversibly binding to the 50 S ribosome subunit.

Tiamulin is active against *Brachyspira (Brachyspira hyodysenteriae, Brachyspira pilosicoli),* Mycoplasmas *(Mycoplasma hyopneumoniae, Mycoplasma hyorhinis, Mycoplasma gallisepticum, Mycoplasma synoviae), Lawsonia intracellularis, Actinobacillus pleuropneumoniae, Clostridium perfingens*.

The mechanism of resistance is chromosomal. Appearance of resistances is slow and progressive. There is not cross resistance with macrolides and related substances.

5.2. Pharmacokinetic properties

Tiamulin is rapidly absorbed after oral administration. The biovailability is, at least, 90%. It is distributed, preferentially at intracellular level, in lungs and colon. 60-65% of tiamulin is excreted in the faeces with an entero-hepatic cycle, and 30-35% in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate

Propyl parahydroxybenzoate

Citric acid monohydrate

Ethanol, anhydrous

Disodium phosphate dodecahydrate

Purified water

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: 2 years.

Shelf-life after dilution or reconstitution according to directions: 24 hours.

After first opening the immediate packaging, discard the unused product.

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

High density polyetehylene containers of 1 L with KS-50 stopper (high density polyethylene) with strapping and welding disc.

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

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8. MARKETING AUTHORIZATION NUMBER

1732 ESP

9. DATE OF FIRST AUTHORISATION OR DATE OF RENEWAL OF THE AUTHORISATION

12 April 2007 / 18 May 2012

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE:

To be supplied only on veterinary prescription

Administration under control or supervision of a veterinary surgeon