

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET

{NATURE/TYPE}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Karimulina 125 mg/ml solution for use in drinking water for chickens, turkeys and pigs [ES].
Karimulina 101.2 mg/ml solution for use in drinking water for chickens, turkeys and pigs [FR].

2. COMPOSITION

Each ml contains:

Active substance:

Tiamulin hydrogen fumarate 125,0 mg
(equivalent to Tiamulin base 101.2 mg)

[FR]

Tiamulin 101.2 mg
(as hydrogen fumarate)
(equivalent to 125.0 mg of Tiamulin hydrogen fumarate)

Excipients:

Propyl parahydroxybenzoate (E-216) 0.1 mg
Methyl parahydroxybenzoate (E218) 0.9 mg

Clear and colourless solution for use in drinking water.

3. PACKAGE SIZE

1L bottle
5L bottle

4. TARGET SPECIES

Pigs, turkeys (for meat production and for reproduction) and chickens (broilers, chick for replacement, chicken for reproduction and layer hen).



5. INDICATIONS FOR USE

Indications for use

Chickens:

Treatment and metaphylaxis of chronic respiratory disease (CRD) and air sacculitis caused by *Mycoplasma gallisepticum*.

The presence of the disease in the group must be established before the product is used.

Turkeys:

Treatment and metaphylaxis of infectious sinusitis and air sacculitis caused by *Mycoplasma gallisepticum* and *Mycoplasma meleagridis*.

The presence of the disease in the group must be established before the product is used.

Pigs:

Treatment of swine dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamuline.

Treatment of pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.

Treatment of enzootic pneumonia caused by *Mycoplasma hyopneumoniae*.

Secondary infection by bacteria such as *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* can complicate enzootic pneumonia and require specific treatment.

6. CONTRAINDICATIONS

Contraindications

Do not use in cases of hypersensitivity to the active substance or to the excipients.

Do not use in animals that could receive products containing monensin, narasin or salinomycin during or for at least seven days before or after treatment with tiamulin. Severe growth depression or death may result.

See section 7 for information regarding interaction between tiamulin and ionophores.

7. SPECIAL WARNINGS

Special warnings

Special warnings:

Acute cases and seriously ill animals with reduced water intake should be treated parenterally.

The water intake of birds should be monitored at frequent intervals during treatment, especially in hot weather, because water intake may be depressed during the administration of tiamulin. This appears to be a concentration-dependent effect and does not appear to have any adverse effect on the overall performance of the birds or efficacy of the veterinary medicinal product. 500 mg tiamulin hydrogen fumarate in 4 litres of water may reduce intake by approximately 10% and 500 mg tiamulin hydrogen fumarate in 2 litres of water by 15% in chickens. In turkeys, this effect is more marked, with approximately a 20% reduction observed and therefore it is recommended not to exceed a concentration of 500 mg tiamulin hydrogen fumarate in 2 litres of the drinking water.

Cross-resistance has been shown between tiamulin and pleuromutilins but also to oxazolidinones, phenicols, streptogramins A and lincosamides notably in *Brachyspira hyodysenteriae* and in *Staphylococcus aureus* in porcine. Use of the product should be carefully considered when susceptibility testing has shown resistance to these antimicrobials because its effectiveness may be reduced. In some European regions, an increasing proportion of *Brachyspira hyodysenteriae* isolates from clinical cases demonstrate significantly reduced in vitro susceptibility to tiamulin.

Special precautions for safe use in the target species:

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

If there is no response to treatment after 5 days, diagnosis should be reviewed.

See section 7. "*Interactions with other medicinal products and other forms of interaction*" for information regarding interactions between tiamulin and ionophores.

Not for use for prophylaxis.

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

People with known hypersensitivity to tiamulin or to parabens should administer the veterinary medicinal product with caution.

This veterinary medicinal product may cause skin, mucous or ocular irritation. Direct contact with eyes, skin and mucous membranes should be avoided during the addition of the veterinary medicinal product to the drinking water and the handling of medicated water.

Personal protective equipment consisting of overalls, safety glasses and impervious gloves should be worn when handling or mixing the veterinary medicinal product or the medicated water.

Contaminated clothing should be removed and any splashes on the skin should be washed off immediately.

In case of accidental contact with eyes, rinse immediately with clean water.

Seek medical advice if irritation persists.

Do not smoke, eat or drink when mixing and handling the veterinary medicinal product.

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

Wash hands after use.

Special precautions for the protection of the environment:

The use of this veterinary medicinal product poses a risk to aquatic organisms and to terrestrial plants.

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Pregnancy and lactation:

Use only according to the benefit/risk assessment by the responsible veterinarian.

Lay:

Tiamulin can be used for laying and breeding chicken and turkeys.

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, stop both the administration of tiamulin-medicated drinking water and also the administration of ionophore-contaminated feed immediately. The feed should be removed and replaced with fresh feed not containing the anticoccidials monensin, salinomycin or narasin.

Concomitant use of tiamulin and the divalent ionophore anticoccidials lasalocid and semduramicin do not appear to cause any interaction, however the concomitant use of maduramicin may lead to a mild to moderate growth depression in chickens. The situation is transient and recovery normally occurs within 3 - 5 days following withdrawal of tiamulin treatment.

Overdose:

Single oral doses of 100 mg tiamulin hydrogen fumarate/kg body weight in pigs caused hyperpnoea and abdominal discomfort. At 150 mg tiamulin hydrogen fumarate/kg body weight no central nervous system effects were noted except for tranquillisation. At 55 mg tiamulin hydrogen fumarate/kg body weight given daily for 14 days, a transient salivation and slight gastric irritation occurred.

Tiamulin hydrogen fumarate is considered to have an adequate therapeutic index in the pig and a minimum lethal dose has not been established.

Regarding poultry, there is a relatively high therapeutic index with tiamulin hydrogen fumarate and the likelihood of an overdose is considered remote especially as water intake and hence tiamulin hydrogen fumarate intake is reduced if abnormally high concentrations are given.

The oral LD50 for hens is 1090 mg/kg bw and for turkeys 840 mg/kg bw.

The clinical signs of acute toxicity in hens are – vocalisation, clonic cramps and lying in a lateral position, and in turkeys – clonic cramps, lateral or dorsal position, salivation and ptosis.

If signs of intoxication do occur promptly remove the medicated water and replace with fresh water.

Special restrictions for use and special conditions for use:

[ES] Administración bajo control o supervisión del veterinario.

Major incompatibilities:

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

8. ADVERSE EVENTS

Adverse events

Chicken and turkeys:

Very common (>1 animal / 10 animals treated):	Decrease drinking ¹
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¹ See section 3.4

Pigs

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Erythema skin oedema ¹
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¹mild

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder, the local representative of the marketing authorisation holder using the contact details on this label, or via your national reporting system {national system details}.

9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration

For use in drinking water.

Chickens (Broilers, chick for replacement, chickens for reproduction and layer hen):

Dose: 25 mg of tiamulin hydrogen fumarate/kg b.w./day (equivalent to 0.20 ml of product/kg b.w./day) for 3-5 days.

Turkeys (for meat production and for reproduction):

Dose: 40 mg of tiamulin hydrogen fumarate/kg b.w./day (equivalent to 0.32 ml of product/kg b.w./day) for 3-5 days.

Pigs:

Treatment of swine dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamuline.

Dose: 8.8 mg of tiamulin hydrogen fumarate/kg b.w./day (equivalent to 0.07 ml of product/kg b.w./day) for 3-5 consecutive days depending on the severity of the infection and/or duration of disease.

Treatment of enzootic pneumonia caused by *M. hyopneumoniae* and treatment of pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.

Dose: 20.0 mg of tiamulin hydrogen fumarate/kg b.w./day (equivalent to 0.16 ml of product/kg b.w./day) for 5-10 consecutive days.

The weight of the animals should be determined as accurately as possible to avoid underdosing.

If there is no response to treatment after 5 days, diagnosis should be reviewed.

The intake of water depends on the clinical condition of the animals and the time of year. In order to obtain the correct dosage, the concentration of tiamulin need to be adjusted accordingly.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{ml veterinary medicinal product / kg b.w / day} \times \text{mean body weight (kg) of animals to be treated}}{\text{mean daily water intake (litre per animal)}} = \text{ml veterinary medicinal product per litre of drinking water}$$

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

When large volumes of medicated water have to be prepared, first prepare a concentrated solution and then dilute it to the required final concentration.

Prepare the medicated drinking-water solutions with tiamulin daily.

The medicated water should be the sole source of drinking water during the treatment period.

The use of suitably calibrated measuring equipment is recommended.

Any medicated drinking water remaining from the previous day should be discarded. After the end of the medication period the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance.

11. WITHDRAWAL PERIODS

Withdrawal periods

Chickens:

Meat: 6 days

Eggs: Zero days

Turkeys:

Meat: 6 days

Eggs: Not for use in birds producing or intended to produce eggs for human consumption.

Pigs:

Meat: 4 days

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp.
The expiry date refers to the last day of that month.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

The veterinary medicinal product should not enter water courses as Tiamulin may be dangerous for fish and other aquatic organisms.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Pack sizes

1 bottle of 1L

1 barrel of 5L

Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database.

17. CONTACT DETAILS

Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:

LABORATORIOS KARIZOO, S.A.

Pol. Ind. La Borda, Mas Pujades, 11-12

08140 Caldes de Montbui (Barcelona)
Spain
Tel: +34938654148

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

18. OTHER INFORMATION

Other information

Tiamulin is very persistent in soil

19. THE WORDS “FOR ANIMAL TREATMENT ONLY”
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For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

Shelf life after first opening the immediate packaging: use immediately.

Shelf life after reconstitution according to directions: 24 hours.

Once opened use immediately. discard unused product.

21. BATCH NUMBER

Lot {number}