

## **B.2. PROPOSAL FOR PACKAGING, LABELLING AND PACKAGE INSERT**

### Label-leaflet

MUTILAN 125 mg/ml ORAL SOLUTION [CZ, HU, PL, RO]  
TIAMULIN/KARIZOO 125 mg/ml ORAL SOLUTION [EL]  
Tiamulin hydrogen fumarate

#### **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 KARIZOO, S.A.  
Polígono Industrial La Borda  
Mas Pujades, 11-12  
08140 – CALDES DE MONTBUI (Barcelona)  
Spain

Manufacturer responsible for batch release:

~~LABORATORIOS KARIZOO, S.A.~~  
~~Polígono Industrial La Borda~~  
~~Mas Pujades, 11-12~~  
~~08140 – CALDES DE MONTBUI (Barcelona)~~  
~~Spain~~

#### **2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

MUTILAN 125 mg/ml Oral solution [CZ, HU, PL, RO]  
TIAMULIN/KARIZOO 125 mg/ml Oral solution [EL]  
Tiamulin hydrogen fumarate

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

Each ml contains:

~~Composition per ml:~~

#### **Active substance:**

Tiamulin hydrogen fumarate.....125.0mg

(corresponding to 101.4 mg tiamulin)

#### **Excipients:**

Propyl parahydroxybenzoate (E-216).....0.1mg

Methyl parahydroxybenzoate (E-218) .....0.9 mg

### 4. PHARMACEUTICAL FORM

Oral solution

Clear and colourless solution

### 5. PACKAGE SIZE

1-L bottles

5-L bottles

### 6. TARGET SPECIES

Pig (all categories)

Chickens (broilers, replacement pullets, layer/breeder~~laying hens and breeding birds~~)

Turkeys (poult (grower) and breeder~~and breeding turkeys~~)

### 7. INDICATIONS

#### Pigs

i) For the t~~For the t~~reatment of pig~~pig~~-swine dysentery caused by strain~~of~~ *Brachyspira hyodysenteriae* and complicated by strains~~of~~ *Fusobacterium* spp. and *Bacteroides* spp.

ii) For the t~~For the t~~reatment of porcine respiratory disease complex (PRDC) caused by *M. hyopneumoniae* and viruses such as PRRSV and Swine

~~Influenza virus~~ in pigs complicated by *P. multocida* and *A. pleuropneumoniae* bacteria.

- iii) ~~For the t~~Treatment of pleuropneumonia caused by *A. pleuropneumoniae*.

### **Chickens**

~~For the t~~Treatment and prevention of chronic respiratory diseases (CRD) and air sacculitis caused by *M. gallisepticum* and *M. synoviae*.

### **Turkeys**

~~For the t~~Treatment and prevention of infectious sinusitis and air sacculitis caused by *M. gallisepticum*, *M. synoviae* and *M. meleagridis*.

## **8. CONTRAINDICATIONS**

~~Pigs and birds should not receive products containing monensin, narasin or salinomycin during or for at least 7 days before or after treatment with tiamulin and after and during the treatment by tiamulin. Severe growth depression or death may result. Refer to section 4.8.13. for information regarding interaction between tiamulin and ionophores.~~

~~due to the fact that growth depression or fatality. Interaction of tiamulin and ionophores see section point 4.8.~~

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

~~Do not use monensin, narasin or salinomycin during or for at least seven days before or after treatment with tiamulin. This may result in severe growth depression or death. For interaction with tiamulin and ionophores see "Special Warnings".~~

~~Do not use in cases of hypersensitivity to the active substances or to any of the excipients.~~

## **9. ADVERSE REACTIONS**

~~On rare occasions~~Occasionally erythema or mild oedema of the skin may occur in pigs following the use of tiamulin and other hypersensitivity reactions can occur in pigs.

~~In these cases symptomatologic therapy is indicated.~~

~~Water intake may be depressed during the administration of tiamulin to birds. It appears to be concentration dependant with 0.025% tiamulin reducing intake by approximately 15%. It does not appear to have any~~

adverse effect on overall performance of the birds or efficacy of the product; however, the water consumption should be monitored frequently, especially during hot weather.

While administering tiamulin to poultry, the consumption of water may fall. This depends on the concentration: the 0.0125% concentration of tiamulin may result in 10% lower consumption of water, while the concentration of 0.025% may decrease the consumption by 15%. No negative effects on the overall condition of the poultry or the overall effectiveness of the product are to be expected; however, the water consumption should be monitored frequently, especially during hot weather.

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

## 10. **METHOD AND ROUTE OF ADMINISTRATION**

### **Pigs**

#### i) Treatment of swine dysentery in pigs

The dosage is 8.8 mg tiamulin hydrogen fumarate per kg bodyweight daily administered in the drinking water of pigs for 3 to 5 consecutive days. The dose is will normally be achieved at concentration of 0.006% tiamulin hydrogen fumarate (60 mg/1 litre) in drinking water.

#### ii) Additional therapy/Treatment of PRDC caused by *M. hyopneumoniae* and various viruses and complicated by *P. multocida* and *A. pleuropneumoniae*.

The dosage is 15.0-20.0 mg tiamulin hydrogen fumarate per kg bodyweight daily administered for 5 to 10 consecutive days; the dose will is normally be achieved at concentration of 0.012-0.018% tiamulin hydrogen fumarate (120-180 mg/ 1 litre) in drinking water.

#### iii) Treatment of pleuropneumonia caused by *A. pleuropneumoniae*.

The dosage is 20.0 mg tiamulin hydrogen fumarate per kg bodyweight daily administered for 5 consecutive days; the dose is will normally be achieved at concentration of 0.018% tiamulin hydrogen fumarate (180 mg/ 1 litre) in drinking water.

### **Chickens**

#### i) Treatment and prevention of chronic respiratory diseases (CRD) and air sacculitis caused by— *M. gallisepticum* and *M. synoviae* in broilers, replacement pullets and; layers/breeders with dosing: the dosage is 25—

30 mg per kilogram bodyweight daily administered for 3-5 consecutive days. The dose will normally be achieved at concentration of 0.020-0.025% tiamulin hydrogen fumarate (200-250 mg / 1 litre) in drinking water. Prevention of chronic respiratory diseases (CRD) and air sacculitis caused by *M. gallisepticum* and *M. Synoviae* in broilers, replacement pullets and laying and breeding hens: 25-30 mg tiamulin hydrogen fumarate per kg bodyweight daily administered for 3 to 5 consecutive days. The dose is normally achieved at concentration of 0.020-0.025% tiamulin hydrogen fumarate (200-250 mg / 1 litre) in drinking water.

The 0.025% concentration of tiamulin hydrogen fumarate in drinking water provides the following doses according to the age of the animals:

4-week old broiler: 30 mg tiamulin hydrogen fumarate/kg of body weight.

10-week old pullet: 30 mg tiamulin hydrogen fumarate/kg of body weight.

Laying hen: 25 mg tiamulin hydrogen fumarate/kg of body weight.

### **Turkeys**

i) For the prevention of infectious sinusitis and air sacculitis caused by *M. gallisepticum*, *M. synoviae* and *M. meleagridis*.

Turkey poults (growers): 0.025% tiamulin hydrogen fumarate (250 mg / 1 litre) in drinking water for 3 days during the first week of life and thereafter, then 1-3 days every 4-6 weeks according to the level of risk based on the assessment of the risk.

Turkey breeders: 0.025% tiamulin hydrogen fumarate (250 mg / 1 litre) in drinking water for 3-5 days every 4 weeks according to the level of risk based on the assessment of the risk.

Turkey poults (growers) — 0.025% tiamulin hydrogen fumarate (250 mg / 1 litre) in drinking water for 3 days during the first week of life and thereafter 1-3 days every 4-6 weeks according to the level of risk.

Turkeys breeders — 0.025% tiamulin hydrogen fumarate (250 mg / 1 litre) in drinking water for 3-5 days every 4 weeks according to the level of risk.

ii) For the treatment of infectious sinusitis and air sacculitis caused by *M. gallisepticum*, *M. synoviae* and *M. meleagridis*.

0.025% tiamulin hydrogen fumarate (250 mg / 1 litre) in drinking water for 3-5 consecutive days.

Tiamulin hydrogen fumarate inat 0.025% concentration 0.025% (or( 0.050%, i.e. 500 mg/1 litre,L for 20-week old male turkeysfor males of turkeys of age 20 weeks) in drinking water will provide the the following daily doses depending on the age of the turkeys for both the above indications:

corresponds to the following doses according to the age categories for of both above mentioned indications:

1-week old poultYoung turkey of age 1 week: 70 mg tiamulin hydrogen fumarate/kg body-weight

4-week old poultYoung turkey of age 4 weeks: 50 mg tiamulin hydrogen fumarate/kg body-weight

8-week old poultYoung turkey of age 8 weeks: ———25-30 mg tiamulin hydrogen fumarate/kg body-weight

20-week old poultYoung turkey of age 20 weeks: 20 mg tiamulin hydrogen fumarate/kg body-weight

For the selected categories of target animal species and indications, –a dilution can be made according to specified dosage in mg/kg bodyweight:according to the dose specifications in mg/kg b.w., as listed above, following dilutions can be prepared:

If the product will be added into large volumes of water, concentrated solution should be prepared first and then diluted to the required concentration.

Once you intend to add the veterinary medicinal product to the high volume of drinking water, prepare at first concentrated solution, which afterthat dilute to final concentration to be administered to the animals treated:

Mixing 1.0 mL of product:

With 2.1 litre of water results in 0.006% solution of tiamulin hydrogen fumarate

With 1.0 litre of water results in 0.012% solution of tiamulin hydrogen fumarate

With 0.7 litre of water results in 0.018% solution of tiamulin hydrogen fumarate

Mixing 50.0 mL of product:

With 31.3 litre of water results in 0.020% solution of tiamulin hydrogen fumarate

With 25.0 litre of water results in 0.025% solution of tiamulin hydrogen fumarate

With 12.5 litre of water results in 0.050% solution of tiamulin hydrogen fumarate

You will prepare by adding of 1 mL of product:

~~In 2.1 L of drinking water, the solution of concentration 0.006% of tiamulin hydrogen fumarate~~

~~In 1.0 L of drinking water, the solution of concentration 0.012% of tiamulin hydrogen fumarate~~

~~In 0.7 L of drinking water, the solution of concentration 0.018% of tiamulin hydrogen fumarate~~

~~You will prepare by adding of **50 ml** of product:~~

~~In 31.3 L of drinking water, the solution of concentration 0.020% of tiamulin hydrogen fumarate~~

~~In 25.0 L of drinking water, the solution of concentration 0.025% of tiamulin hydrogen fumarate~~

~~In 12.5 L of drinking water, the solution of concentration 0.050% of tiamulin hydrogen fumarate~~

~~Primarily the dose should be calculated from the dose as listed in mg/kg of body weight. It is necessary to adjust the dose according to the current water intake by animals and determine the bodyweight of the animals as accurately as possible to avoid underdosing. The exact dose should be calculated based on the actual water intake by the animals intended to be treated as well as the body weight of those animals to avoid underdosing.~~

~~Fresh solution of tiamulin-medicated drinking water should be made up each day.~~

~~Watering systems should be checked and cleaned before using the product. Fresh medicated water should be prepared each day.~~

~~Medicated water supply device should be checked and cleaned prior to use of the product.~~

~~Tiamulin hydrogen fumarate in 0.025% (0.050% or 500 mg/1litre for male turkeys 20-week old) concentration in drinking water will provide the following daily dosage depending on the age of the turkey for both the above indications:~~

~~1-week old poult: — 70 mg tiamulin hydrogen fumarate/kg of bodyweight~~

~~4-week old poult: — 50 mg tiamulin hydrogen fumarate/kg of bodyweight~~

~~8-week old poult: — 25-30 mg tiamulin hydrogen fumarate/kg of bodyweight~~

~~20-week old poult: — 20 mg tiamulin hydrogen fumarate/kg of bodyweight~~

~~For selected categories of target species and indications a dilution can be applied according to specifications of dosage to mg/kg bodyweight:~~

~~If adding the product into large volumes of water, please start by preparing a concentrated solution and then dilute it to the required concentration.~~

~~Mixing 1.0 ml of product:~~

With 2.1 litre of water results in 0.0006% solution of tiamulin hydrogen fumarate.

With 1.0 litre of water results in 0.0012% solution of tiamulin hydrogen fumarate.

With 0.7 litre of water results in 0.0018% solution of tiamulin hydrogen fumarate.

Mixing 5.0 ml of product:

With 31.3 litre of water results in 0.020% solution of tiamulin hydrogen fumarate.

With 25.0 litre of water results in 0.025% solution of tiamulin hydrogen fumarate.

With 12.5 litre of water results in 0.050% solution of tiamulin hydrogen fumarate.

This is primarily based on the dose given to mg/kg bodyweight. It is necessary to adjust the dose according to the current water intake by animals and determine the bodyweight of the animals as accurately as possible to avoid underdosing.

Fresh solution of tiamulin-medicated drinking water should be made up each day.

Water equipment should be checked and cleaned before using the veterinary medicinal product.

## 11. **ADVICE ON CORRECT ADMINISTRATION**

None

## 12. **WITHDRAWAL PERIOD**

### **Pigs**

Meat and offal ~~and offal~~: 4 days

### **Chickens**

Meat and offal ~~and offal~~: 2 days

Eggs: Zero days

### **Turkeys**

Meat and offal ~~and offal~~: 5 days

## 13. **SPECIAL WARNINGS, IF NECESSARY**

Special precautions for use in animals



Fresh drinking water must be provided to animals after drinking medicated water.

Freshly medicated water must be prepared daily.

Medicated water supply device should be checked and cleaned prior to use of the product.

Watering equipment should be inspected and cleaned prior to addition of the product.

Whenever possible, use of the product should be based on the results of susceptibility testing and information (regional, farm level) regarding current epizootological situation.

Whenever possible, use of the product should be based on the results of susceptibility testing and take into account the epidemiological information on resistance (regional, farm level) and national policies with respect to use of antimicrobials.

Use of the product deviating from the instructions information given within in the SPC may can cause increase the of prevalence of bacteria resistant to tiamulin.

If there is no response to treatment within 5 days, the diagnosis should be re-established.

Use of the product should be combined with the good farming practice, e.g. good zoohygiene, proper ventilation, avoiding of overstocking.

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

Direct contact with skin, eyes, and mucous membranes should be avoided.

Avoid contact with skin, eyes and mucous membranes.

Personal protective equipment consisting of protective goggles and rubber or latex gloves should be worn when handling the veterinary medicinal product. In case of accidental contact with skin or mucous membranes, rinse affected area immediately with plenty of water and remove contaminated clothing, which is in direct contact with the skin.

In case of accidental contact with eyes, rinse the eye immediately with plenty of fresh water. If irritation occurs seek medical advice and show the package leaflet or the label to the physician.

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

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

Wash hands after use.

### **Interaction with other medicinal products and other forms of interaction**

In order to prevent interaction of incompatible ionophores monensin, narasin and salinomycin in pigs, it should be ensured that these effective agents are not contained in the feed and that there was no contamination of the feed with these agents.

~~In~~For chickens and turkeys, in order to avoid interactions between tiamulin and the incompatible ionophores monensin, narasin and salinomycin ~~and tiamulin~~, the feed mill supplying the ~~birds~~ feed should be notified that tiamulin will be used and that these products should not be included in the feed or contaminate the feed.

The feed should be tested for the ionophores prior to use if there is any suspicion that contamination of the feed might occur.

If an interaction does occur, stop tiamulin water medication immediately and replace with fresh water. Remove contaminated feed as soon as possible and replace with feed not containing the tiamulin-incompatible ionophores.

### **Overdose (symptoms, emergency procedures, antidotes), if necessary**

Single oral doses of 100 mg/kg bodyweight ~~in pigs~~ caused hyperpnoea and abdominal discomfort in pigs. At 150 mg/kg no CNS effects were noted except for tranquillisation. At 55 mg/kg given for 14 days, a transient salivation and slight gastric irritation occurred. Tiamulin is considered to have an adequate therapeutic index in the pig and a minimum lethal dose has not been established.

Tiamulin has a relative wide therapeutic index, with a low risk of overdose mainly due to the fact that abnormally high concentrations result in decreased water consumption and hence decreased consumption of tiamulin. LD<sub>50</sub> for chicken is 1290 mg/kg bodyweight and for turkeys 840 mg/kg bodyweight.

The clinical signs of acute toxicity in chickens are – vocalization, clonic cramps and lying in a lateral position, in turkeys – clonic cramps, lateral or dorsal position, salivation and depression~~ptosis~~.

In case the symptoms of intoxication appear, remove the medicated water immediately and replace with fresh water.

~~Should the symptoms of intoxication appear, remove the medicated water immediately and replace it with fresh water.~~

### **Major ~~in~~incompatibilities**

None known

## **14. EXPIRY DATE**

EXP: {month/year}

Once opened, use by ...

Shelf life after first opening the container: 6 months.

Shelf life after dilution according to directions: 24 hours.

## **15. SPECIAL STORAGE CONDITIONS**

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

**16. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

~~Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.~~

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.

**For animal treatment only.**

**Keep out of the sight and reach of children.**

**To be supplied only on veterinary prescription.**

**Date on which the package leaflet was last approved:**

**Marketing authorization number:**

**Batch: {number}**