

ANNEX II
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Outside of tear-open leaflet

1 LITRE BOTTLE / 5 LITRE CONTAINER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tialin 125 mg/ml solution for use in drinking water for pigs, chickens and turkeys
Tiamulin

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml of solution contains:

Active substance:

Tiamulin hydrogen fumarate 125.0 mg
equivalent to 101.2 mg of tiamulin

3. PHARMACEUTICAL FORM

Solution for use in drinking water

4. PACKAGE SIZE

1 litre, 5 litres

5. TARGET SPECIES

Pigs, chickens (pullets, breeders, layer hen) and turkeys (breeders, layer hen).

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal periods:

Pigs

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate (equivalent to 0.07 ml solution)/kg body weight)

Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate (equivalent to 0.16 ml solution)/kg body weight)

Chickens

Meat and offal: 2 days

Eggs: Zero days

Turkeys

Meat and offal: 6 days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP: {month/year}

Once opened, use by: __/__/__

Shelf life after first opening the immediate packaging: 3 months.

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

11. SPECIAL STORAGE CONDITIONS

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

Disposal: Read package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.

To be supplied only on veterinary prescription.

To be completed nationally

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Dechra Limited
Snaygill Industrial Estate
Keighley Road
Skipton
North Yorkshire
BD23 2RW
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

Vm 10434/4094

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

B. PACKAGE LEAFLET

Inside of tear-open leaflet
1 LITRE BOTTLE / 5 LITRE CONTAINER

PACKAGE LEAFLET:

Tialin 125 mg/ml solution for use in drinking water for pigs, chickens and turkeys

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:

Dechra Limited
Snaygill Industrial Estate
Keighley Road
Skipton
North Yorkshire
BD23 2RW
United Kingdom

Manufacturers responsible for batch release:

Genera Inc.
Svetonedeljska cesta 2
Kalinovica
10436 Rakov Potok
Croatia

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tialin 125 mg/ml solution for use in drinking water for pigs, chickens and turkeys
Tiamulin

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

1 ml of solution contains:

Active substance:

Tiamulin hydrogen fumarate	125.0 mg
equivalent to 101.2 mg of tiamulin	

Excipients:

Methyl parahydroxybenzoate (E218)	0.9 mg
Propyl parahydroxybenzoate	0.1 mg

Clear, colourless to pale yellow solution.

4. INDICATIONS

Pigs

- Treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamulin.
- Treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli* susceptible to tiamulin.
- Treatment of Porcine Proliferative Enteropathy (ileitis) caused by *Lawsonia intracellularis* susceptible to tiamulin.
- Treatment and metaphylaxis of Enzootic Pneumonia caused by *Mycoplasma hyopneumoniae*, including infections complicated by *Pasteurella multocida* susceptible to tiamulin.
- Treatment of Pleuropneumonia caused by *Actinobacillus pleuropneumoniae* susceptible to tiamulin.

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

Chickens

Treatment and metaphylaxis of Chronic Respiratory Disease caused by *Mycoplasma gallisepticum* and Airsacculitis and Infectious Synovitis caused by *Mycoplasma synoviae* susceptible to tiamulin.

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

Turkeys

Treatment and metaphylaxis of Infectious Sinusitis and Airsacculitis caused by *Mycoplasma gallisepticum*, *Mycoplasma synoviae* and *Mycoplasma meleagridis* susceptible to tiamulin.

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

5. CONTRAINDICATIONS

Do not use in pigs and birds 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.

Do not use in cases of hypersensitivity to the active substance or to the excipient. See section 'special warnings' for information regarding interaction between tiamulin and ionophores.

6. ADVERSE REACTIONS

On very rare occasions (less than 1 animal in 10,000 animals treated, including isolated reports) erythema or mild oedema of the skin may occur in pigs following the use of tiamulin hydrogen fumarate. Apathy and death may result.

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Pigs, chickens (pullets, breeders, layer hen) and turkeys (breeders, layer hen).

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

In drinking water use.

The product should be administered using suitably calibrated equipment.

Guidance for preparing product solutions:

When medicating large volumes of water, prepare a concentrated solution first and then dilute to the required final concentration.

The product is soluble and stable from low concentration up to maximum concentration of the product of 500 ml/L (1:1 dilution) in water of at least 4° C.

Fresh solutions of tiamulin-medicated drinking water should be made up each day. Any medicated drinking water remaining from the previous day should be discarded.

To ensure the correct dosage, body weight should be determined as accurately as possible to avoid underdosing. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of tiamulin has to be adjusted accordingly.

Make sure the animals do not have access to non-medicated water during the period when the medicated water is given.

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.

The dosage of the product to be incorporated should be established according to the following formula:

$$\frac{\text{Dose (ml product per kg body weight per day)} \times \text{Mean body weight (kg) of animals to be treated}}{\text{Mean daily water consumption (litre) per animal per day}} = \text{ml product per litre of drinking water}$$

Pigs

i) For the treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae*. The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 0.07 ml solution)/kg body weight administered daily in the drinking water of pigs for 3 to 5 consecutive days depending on the severity of the infection and/or the duration of the disease.

ii) For the treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli*.

The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 0.07 ml solution)/kg body weight administered daily in the drinking water of pigs for 3 to 5 consecutive days depending on the severity of the infection and/or the duration of the disease.

iii) For the treatment of Porcine Proliferative Enteropathy (ileitis) caused by *Lawsonia intracellularis*.

The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 0.07 solution)/kg body weight administered daily in the drinking water of pigs for 5 consecutive days.

iv) For the treatment and metaphylaxis of Enzootic Pneumonia caused by *Mycoplasma hyopneumoniae*, including infections complicated by *Pasteurella multocida* susceptible to tiamulin.

The dosage is 20 mg tiamulin hydrogen fumarate (equivalent to 0.16 ml solution)/kg body weight administered daily for 5 consecutive days.

v) For the treatment of Pleuropneumonia caused by *Actinobacillus pleuropneumoniae* susceptible to tiamulin.

The dosage is 20 mg tiamulin hydrogen fumarate (equivalent to 0.16 ml solution)/kg body weight administered daily for 5 consecutive days.

Chickens

For the treatment and metaphylaxis of Chronic Respiratory Disease caused by *Mycoplasma gallisepticum* and Airsacculitis and Infectious Synovitis caused by *Mycoplasma synoviae*.

The dosage is 25 mg tiamulin hydrogen fumarate (equivalent to 0.2 ml solution)/kg body weight administered daily for the period of 3 to 5 consecutive days.

Turkeys

For the treatment and metaphylaxis of Infectious Sinusitis and Airsacculitis caused by *Mycoplasma gallisepticum*, *Mycoplasma synoviae* and *Mycoplasma meleagridis*.

The dosage is 40 mg tiamulin hydrogen fumarate (equivalent to 0.32 ml solution)/kg body weight administered daily for the period of 3 to 5 consecutive days.

9. ADVICE ON CORRECT ADMINISTRATION

In order to avoid interactions between the ionophores and tiamulin, the veterinarian and farmer should check that the feed label does not state that it contains salinomycin, monensin and narasin.

For chickens and turkeys, in order to avoid interactions between 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 anticoccidials 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 medication immediately and replace with fresh drinking water. Remove contaminated feed as soon as possible and replace with feed not containing the tiamulin-incompatible ionophores.

10. WITHDRAWAL PERIODS

Pigs

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate (equivalent to 0.07 ml solution)/kg body weight)

Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate (equivalent to 0.16 ml solution)/kg body weight)

Chickens

Meat and offal: 2 days

Eggs: Zero days

Turkeys

Meat and offal: 6 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.

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.

Shelf life after first opening the immediate packaging: 3 months

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

12. SPECIAL WARNINGS

Special warnings for each target species:

Pigs with reduced water intake and/or in a debilitated condition 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.

Special precautions for use in animals

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of target bacteria. In some European regions, an increasing proportion of *Brachyspira hyodysenteriae* isolates from clinical cases demonstrate significantly reduced in vitro susceptibility to tiamulin. Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to tiamulin.

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

This product may cause skin and eye irritation. When mixing, direct contact with the skin and eyes should be avoided by wearing impermeable rubber gloves and safety glasses.

In case of accidental eye contact, irrigate the eyes thoroughly with clean running water immediately. Seek medical advice if irritation persists.

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

Wash hands after use.

Pregnancy and lactation:

Can be used in pigs during pregnancy and lactation.

Laying birds:

Can be used in laying chickens and in breeding chickens and turkeys.

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, 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 (symptoms, emergency procedures, antidotes):

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 LD50 is 1090 mg/kg body weight for chickens and 840 mg/kg body weight for turkeys.

The clinical signs of acute toxicity in chickens 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.

Incompatibilities:

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

Other precaution:

Tiamulin is very persistent in soils.

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

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

January 2022

15. OTHER INFORMATION

Pack sizes: 1 litre and 5 litres.
Not all pack sizes may be marketed.

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