ANNEX II

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{ Outside of tear-open leaflet / 1 litre bottle or 5 litres container}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tialin 125 mg/ml solution for use in drinking water

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
101.2 mg of tiamulin equivalent to 125.0 mg of tiamulin hydrogen fumarate

3. PACKAGE SIZE

1 litre, 5 litres

4. TARGET SPECIES

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

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water use.

7. WITHDRAWAL PERIODS

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

8. EXPIRY DATE

Exp; {mm/yyyy}
Once opened, use within 3 months. Use by: __/__/__

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

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Dechra Limited

14. MARKETING AUTHORISATION NUMBERS

Vm 10434/3007

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

17. Name of the veterinary medicinal product

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

2. Composition

Each ml contains:

Active substance:
101.2 mg of tiamulin equivalent to 125.0 mg of tiamulin hydrogen fumarate.

Excipients:
Methyl parahydroxybenzoate (E218) 0.9 mg
Propyl parahydroxybenzoate 0.1 mg
Ethanol 96% 100.0 mg
Clear, colourless to pale yellow solution.

3. Target species

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

4. Indications for use

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 veterinary medicinal 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 flock must be established before the veterinary medicinal 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 flock must be established before the veterinary medicinal product is used.

5. Contraindications

Do not use in pigs and birds that could receive veterinary medicinal 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 any of the excipients.
See section 'Special warnings' for information regarding interaction between tiamulin and ionophores.

6. Special warnings

Special warnings:
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 safe use in the target species:
Use of the veterinary medicinal 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 veterinary medicinal 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.

Interactions with other medicinal products and other forms of interaction:
Tiamulin has been shown to interact with ionophores such as monensin, salinomycin or narasin and may result in signs indistinguishable from an ionophore toxicosis. Animals should not receive veterinary medicinal 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 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, lying in a 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:
Not applicable.
Major incompatibilities:
In the absence of compatibility studies this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Pigs:

Rare (1 to 10 animals / 10,000 animals treated): Erythema (redness), Skin oedema (swelling)
Very rare (<1 animal / 10,000 animals treated, including isolated reports): Death
Undetermined frequency (cannot be estimated from the available data): Apathy

Chickens and Turkeys:
None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

In drinking water use.

The veterinary medicinal product should be administered using suitably calibrated equipment.

Guidance for preparing veterinary medicinal product solutions:
When medicating large volumes of water, prepare a concentrated solution first and then dilute to the required final concentration.
The veterinary medicinal product is soluble and stable from low concentration up to maximum concentration of the veterinary medicinal product of 500 ml/L (1:2 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 a 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.

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:

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

Pigs

17) 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 ml 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 or narasin.

For chickens and turkeys, in order to avoid interactions between the incompatible ionophores monensin, narasin or 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 precautions for disposal

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

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.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Vm 10434/3007

White opaque high density polyethylene bottle of 1 litre with transparent graduated scale closed with white opaque high density polyethylene screw-cap.
White opaque high density polyethylene container of 5 litres closed with white opaque high density polyethylene screw-cap.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

June 2023

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Dechra Limited
Snaygill Industrial Estate
Keighley Road
Skipton
North Yorkshire
BD23 2RW
United Kingdom

Manufacturer responsible for batch release:
Genera Inc.
Svetonedeljska cesta 2
Kalinovica
10436 Rakov Potok
Croatia

Local representatives and contact details to report suspected adverse reactions:

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

17. Other information

Environmental properties:
Tiamulin is very persistent in soils.

Approved 19 December 2023