ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
{ Low-density polyethylene-aluminium- polyethylene terephtalate laminated bags containing 1 kg or 5 kg granules.**}**

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tyawalt 450 mg/g granules for use in drinking water for pigs

2. STATEMENT OF ACTIVE SUBSTANCES

Each gram contains:

Tiamulin hydrogen fumarate	450 mg (corresponds to 364.28 mg of tiamulin base)

3. PACKAGE SIZE

1 kg
5 kg

4. TARGET SPECIES

Pigs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water use.

7. WITHDRAWAL PERIODS

Withdrawal period:

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight).
Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of product)/kg body weight).

8. EXPIRY DATE

Exp. {mm/yyyy}

Shelf-life after first opening: 4 months.
Once opened, use by……

Shelf life after dilution in water: 24 hours.

9. SPECIAL STORAGE PRECAUTIONS

After first opening, do not store above 25ºC.
Keep the original bag tightly closed after first opening.

The product after dilution in water should be stored at temperatures below 25°C.

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

KRKA UK Ltd
Thames House
Waterside Drive
Langley
Berkshire
SL3 6EZ

14. MARKETING AUTHORISATION NUMBERS

Vm 47636/3000

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Tyawalt 450 mg/g granules for use in drinking water for pigs

2. Composition

Each gram contains:

Active substance:

Tiamulin hydrogen fumarate	450 mg (corresponds to 364.28 mg of tiamulin base)

White to almost white small granules.

3. Target species

Pigs.

4. Indications for use

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. The presence of the disease in the group must be established before the product is used.
Treatment of pleuropneumonia caused by *Actinobacillus pleuropneumoniae* susceptible to tiamulin.

5. Contraindications

Do not use in animals with known hypersensitivity to the active ingredient or to any of the excipients.
Do not use in pigs 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 “Special warnings”, subsection “Interaction with other medicinal products and other forms of interaction” for information regarding interaction between tiamulin and ionophores.

6. Special warnings

Special warnings:
Animals with reduced water intake and/or in a debilitated condition should be treated parenterally.

Special precautions for safe use in the target species:

Use of the 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 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.
Not for use for prophylaxis.
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:
People with known hypersensitivity to tiamulin should avoid contact with the veterinary medicinal product.
When mixing, direct contact with the skin and mucous membranes should be avoided.
Wear safety glasses, and rubber or latex gloves when handling or mixing the product. Wash hands with soap and water after use.
If accidental contact occurs, contaminated clothing should be removed and any splashes to the skin or mucous membranes should be washed off immediately.
In case of accidental eye contact, irrigate the eyes thoroughly with clean running water immediately.
Seek medical advice if irritation persists, and show package insert or labelling to the physician.

Pregnancy and lactation:
Can be used during pregnancy and lactation.

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.

Overdose:
Single oral doses of 100 mg tiamulin hydrogen fumarate/kg body weight 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.
If signs of intoxication do occur promptly remove the medicated water and replace with fresh water.

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:

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

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 the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system <{national system details}.

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

For use in drinking water.

Guidance for preparing product solutions:
When medicating large volumes of water, prepare a concentrated solution first and then dilute to the required final concentration. Alternatively, the concentrated solution can be used in a proportional water medicator. The solubility of the product has been confirmed at the maximal concentration of 100 g of product/L in soft and hard water and at 4°C and 20°C.

Medicated drinking water should be refreshed or replaced every 24 hours.

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.

To ensure a correct dosage, body weight should be determined as accurately as possible.

The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of tiamulin may 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:

$$\frac{\textbf{x} \text{ mg veterinary medicinal product/ kg body weight per day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily water intake (l/animal)}} = \textbf{x} \text{ mg veterinary medicinal product per litre of drinking water}$$

- For the treatment of swine dysentery caused by *Brachyspira hyodysenteriae:* 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/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.
- For the treatment of porcine colonic spirochaetosis (colitis) caused by *Brachyspira pilosicoli*: 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/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.
- For the treatment of porcine proliferative enteropathy (ileitis) caused by *Lawsonia intracellularis*: 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight administered daily in the drinking water of pigs for 5 consecutive days.
- For the treatment and metaphylaxis of enzootic pneumonia caused by *Mycoplasma hyopneumoniae,* including infections complicated by *Pasteurella multocida*: 20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of product)/kg body weight administered daily for 5 consecutive days.
- For the treatment of pleuropneumonia caused by *Actinobacillus pleuropneumoniae*: 20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of product)/kg body weight administered daily for 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.
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

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight).
Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of product)/kg body weight).

11. Special storage precautions

Keep out of the sight and reach of children.

Shelf life after first opening the immediate packaging: 4 months
Shelf life after dilution in water according to directions: 24 hours.

After first opening, do not store above 25ºC.
Keep the original bag tightly closed after first opening.

The product after dilution in water should be stored at temperatures below 25°C.

Keep out of the sight and reach of children.

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

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.

Ask your veterinary surgeon 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

Low-density polyethylene-aluminium- polyethylene terephtalate laminated bags containing 1 kg or 5 kg granules.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

September 2022

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
To be completed nationally.

Manufacturer responsible for batch release:
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

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:
A transformation product of tiamulin is very persistent in soil.
Tiamulin may be toxic to plants and algae.

Approved 23 January 2023