ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Denagard 450 mg/g granules for use in drinking water for pigs, chickens and turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Tiamulin hydrogen fumarate 450 mg (equivalent to tiamulin 365 mg)

Excipients:

Qualitative composition of excipients and other constituents
Lactose

White to pale yellow granules.

3. CLINICAL INFORMATION

3.1 Target species

Pigs
Chickens
Turkeys

3.2 Indications for use for each target species

Pigs
i) Treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamulin. The presence of the disease in the herd must be established before the veterinary medicinal product is used.

ii) Treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli* susceptible to tiamulin. The presence of the disease in the herd must be established before the veterinary medicinal product is used.

iii) Treatment of Porcine Proliferative Enteropathy (ileitis) caused by *Lawsonia intracellularis* susceptible to tiamulin. The presence of the disease in the herd must be established before the veterinary medicinal product is used.

iv) 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 herd must be established before the veterinary medicinal product is used.

v) 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.

3.3 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 3.8 for information regarding interaction between tiamulin and ionophores.

3.4 Special warnings

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

Water intake may be depressed during the administration of tiamulin in birds. It appears to be concentration-dependent with 500 mg tiamulin hydrogen fumarate (equivalent to 1.11 g of product) in 4 litres of water reducing intake by approximately 10 % and 500 mg tiamulin hydrogen fumarate (equivalent to 1.11 g of product) in 2 litres of water by 15 % in chickens. It does not appear to have any adverse effect on overall performance of the birds or efficacy of the veterinary medicinal product, but water intake should be monitored at frequent intervals, especially in hot weather. In turkeys, it is more marked, with approximately 20 % reduction, and therefore it is recommended not to exceed a concentration of 500 mg tiamulin hydrogen fumarate in 2 litres of the drinking water.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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.

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:

Personal protective equipment consisting of safety glasses or goggles and gloves should be worn when handling the veterinary medicinal product in order to avoid contamination of the user's eyes and topical exposure of skin. Due to the irritant properties, it is also recommended to wear a dust mask to minimise inhalation exposure.

In case of exposure or accidental spillage onto skin the affected area should be washed with soap and water. In case of accidental spillage into the eyes, the open eyes should be flushed with water.

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

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

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Pigs

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Erythema Oedema[1]

[1] Mild

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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.

3.8 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.

3.9 Administration routes and dosage

In drinking water use.

Guidance for preparing the veterinary medicinal product solutions:
When medicating large volumes of water, prepare a concentrated solution first and then dilute to the required final concentration.

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

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 has to be adjusted accordingly.

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.

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:

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

Pigs
i) For the treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae*.
The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of the veterinary medicinal 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.

ii) For the treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli*.
The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of the veterinary medicinal 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.

iii) For the treatment of Porcine Proliferative Enteropathy (ileitis) caused by *Lawsonia intracellularis*.
The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of the veterinary medicinal product)/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 44.4 mg of the veterinary medicinal product)/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 44.4 mg of the veterinary medicinal product)/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 55.6 mg of the veterinary medicinal product)/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 88.9 mg of the veterinary medicinal product)/kg body weight administered daily for the period of 3 to 5 consecutive days.

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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 LD_5 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 it with fresh water.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Pigs
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)

Chickens
Meat and offal: 2 days
Eggs: zero days

Turkeys
Meat and offal: 6 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code

QJ01XQ01

4.2 Pharmacodynamics

Tiamulin is a bacteriostatic semi-synthetic antibiotic belonging to the pleuromutilin group of antibiotics and acts at the ribosomal level to inhibit bacterial protein synthesis.

Tiamulin has shown a high level of *in vitro* activity against porcine and avian *Mycoplasma* species as well as gram-positive aerobes (streptococci and staphylococci), anaerobes (clostridia), gram-negative anaerobes (*Brachyspira hyodysenteriae*, *Brachyspira pilosicoli)*, and gram-negative aerobes (*Actinobacillus pleuropneumoniae* and *Pasteurella multocida*).

Tiamulin has been shown to act at the 70S ribosome level and the primary binding sites are on the 50S subunit. It appears to inhibit microbial protein production by producing biochemically inactive initiation complexes, which prevent elongation of the polypeptide chain.

Bactericidal concentrations can be reached but vary according to the bacterium. It can be as little as two times the MIC for *Brachyspira hyodysenteriae* and *Actinobacillus pleuropneumoniae* but as high as 50–100 times the bacteriostatic level for *Staphylococcus aureus*. The MIC distribution for tiamulin against *Brachyspira hyodysenteriae* is bimodal, suggesting reduced susceptibility of some strains to tiamulin. Due to technical constraints, the susceptibility of *Lawsonia intracellularis* is difficult to test *in vitro*.

4.3 Pharmacokinetics

Pigs
Tiamulin hydrogen fumarate is well absorbed in the pig (over 90 %) following oral administration and widely distributed through the body. Following a single oral dose of 10 mg and 25 mg tiamulin hydrogen fumarate/kg body weight, the C_{max} was 1.03 µg/ml and 1.82 µg/ml in serum respectively by microbiological assay, and the T_{max} was 2 hours for both. It has been shown to concentrate in the lung, polymorphonuclear leucocytes and also in liver, where it is metabolised and excreted (70–85 %) in the bile, the remainder is excreted via the kidney (15–30 %). Serum protein binding is approximately 30 %. Tiamulin, which has not been absorbed or metabolised, passes down the intestines to the colon. Colon contents concentrations of tiamulin have been estimated at 3.41 µg/ml following administration of tiamulin hydrogen fumarate at 8.8 mg/kg body weight.

Chickens
Tiamulin hydrogen fumarate is well absorbed in chickens (70–95 %) after oral administration and reaches peak concentrations in 2–4 hours (T_{max} 2.85 hours). Following a 50 mg tiamulin hydrogen fumarate/kg body weight single dose, the C_{max} was 4.02 µg/ml in serum by microbiological assay, and after a 25 mg/kg dose, it was 1.86 µg/ml. In drinking water, the 250 ppm (0.025 %) tiamulin hydrogen fumarate concentration provided a rolling serum level over a 48-hour medication period of 0.78 µg/ml (range 1.4–0.45 µg/ml) and at 125 ppm (0.0125 %), 0.38 µg/ml (range 0.65–0.2 µg/ml) in eight-week old chickens. Serum protein-binding was approximately 45 %. It distributes widely through the body and has been shown to concentrate in the liver and kidney (sites of excretion) and in the lung (30 times serum level). Excretion is mainly via the bile (55–65 %) and kidney (15–30 %) as mainly microbiologically inactive metabolites and is quite rapid, 99 % of the dose within 48 hours.

Turkeys
In turkeys, serum levels of tiamulin hydrogen fumarate are lower with a 50 mg tiamulin hydrogen fumarate/kg body weight single dose giving a C_{max} of 3.02 µg/ml in serum, and 25 mg/kg giving 1.46 µg/ml. These were achieved at about 2–4 hours after dosing. In breeders on 0.025 % tiamulin hydrogen fumarate, the average serum level was 0.36 µg/ml (range 0.22–0.5 µg/ml). Serum protein-binding was approximately 50 %.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 3 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.

5.3 Special precautions for storage

Do not store above 25 °C.

5.4 Nature and composition of immediate packaging

Pre-formed foil bag of 1112 g and 5000 g.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

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 national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

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

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. COMBINED LABEL-LEAFLET

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

ALUMINIUM LAMINATE BAG

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Denagard 450 mg/g granules for use in drinking water for pigs, chickens and turkeys

2. COMPOSITION

Each g contains:

Active substance:
Tiamulin hydrogen fumarate 450 mg (equivalent to tiamulin 365 mg)

White to pale yellow granules.

3. PACKAGE SIZE

1112 g
5000 g

4. TARGET SPECIES

Pigs
Chickens
Turkeys

5. INDICATIONS FOR USE

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.

6. CONTRAINDICATIONS

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 subsection 'Interactions with other medicinal products and other forms of interaction' for information regarding interaction between tiamulin and ionophores.

7. SPECIAL WARNINGS

Special warnings

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

Water intake may be depressed during the administration of tiamulin in birds. It appears to be concentration-dependent with 500 mg tiamulin hydrogen fumarate (equivalent to 1.11 g of product) in 4 litres of water reducing intake by approximately 10 % and 500 mg tiamulin hydrogen fumarate (equivalent to 1.11 g of product) in 2 litres of water by 15 % in chickens. It does not appear to have any adverse effect on overall performance of the birds or efficacy of the veterinary medicinal product, but water intake should be monitored at frequent intervals, especially in hot weather. In turkeys, it is more marked, with approximately 20 % reduction, 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 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.

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:
Personal protective equipment consisting of safety glasses or goggles and gloves should be worn when handling the veterinary medicinal product in order to avoid contamination of the user's eyes and

topical exposure of skin. Due to the irritant properties, it is also recommended to wear a dust mask to minimise inhalation exposure.

In case of exposure or accidental spillage onto skin the affected area should be washed with soap and water. In case of accidental spillage into the eyes, the open eyes should be flushed with water.

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

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

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 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 LD_5 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 it with fresh water.

Major incompatibilities:
None known.

8. ADVERSE EVENTS

Adverse events

Pigs

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Erythema (reddening of the skin) Oedema (swelling)[1]

[1] Mild

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 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

In drinking water use.

Guidance for preparing product solutions:
When medicating large volumes of water, prepare a concentrated solution first and then dilute to the required final concentration.

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

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 has 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:

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

Pigs
i) For the treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae*.
The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of the veterinary medicinal 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.

ii) For the treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli*.
The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of the veterinary medicinal 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.

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

The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of the veterinary medicinal product)/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 44.4 mg of the veterinary medicinal product)/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 44.4 mg of the veterinary medicinal product)/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 55.6 mg of the veterinary medicinal product)/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 88.9 mg of the veterinary medicinal product)/kg body weight administered daily for the period of 3 to 5 consecutive days.

10. ADVICE ON CORRECT ADMINISTRATION

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.

11. WITHDRAWAL PERIODS

Withdrawal periods

Pigs
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)

Chickens
Meat and offal: 2 days

Eggs: zero days

Turkeys
Meat and offal: 6 days

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25 °C.

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.

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
Pre-formed foil bag of 1112 g and 5000 g. Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

{MM/YYYY}

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

17. CONTACT DETAILS

Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Manufacturer responsible for batch release:
Elanco France S.A.S., 26 Rue de la Chapelle, 68330 Huningue, France

18. OTHER INFORMATION

<Other information>

19. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

Shelf life after first opening the immediate packaging: 3 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.

21. BATCH NUMBER

Lot {number}