SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substance:

364.2 mg tiamulin (equivalent to 450.0 mg tiamulin hydrogen fumarate)

Excipients:

Qualitative composition of excipients and other constituents
Povidone
Lactose monohydrate

White to pale yellow granules.

3. CLINICAL INFORMATION

3.1 Target species

Pigs, chickens and turkeys.

3.2 Indications for use for each target species

Pigs
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.
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.
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.

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.

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 herd or flock must be established before use.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in pigs and birds that could receive products containing ionophoses such as 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 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 veterinary medicinal product) in 4 litres of water reducing intake by approximately 10% and 500 mg tiamulin hydrogen fumarate (equivalent to 1.11 g of veterinary medicinal 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
Repeated use should be avoided by improving management practice and thorough cleansing and disinfection.

3.5 Special precautions for use

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.
Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to tiamulin.

Special precautions for the person administering the veterinary medicinal product to animals:

Direct contact with the skin, eyes and mucous membranes and inhalation of dust should be avoided. Personal protective equipment consisting of overalls, impermeable rubber gloves, safety glasses and a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143 should be worn when handling the veterinary medicinal product.
In case of accidental eye contact, rinse the eyes thoroughly with clean running water immediately. Seek medical advice if irritation persists and show the package leaflet or the label to the physician.

Contaminated clothing should be removed and any splashes on to the skin should be washed off immediately.
Wash hands after use.
Accidental ingestion should be avoided. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
People with known hypersensitivity to tiamulin should avoid contact with the veterinary medicinal product.

Special precautions for the protection of the environment
Not applicable.

3.6 Adverse events

Pigs:

Very rare (<1 animal / 10.00000 animals treated, including isolated report(s)):	Erythema
	Skin 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.

Fertility:
Can be used 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.

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 the 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.
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:

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

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 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 veterinary medicinal product)/kg body weight administered daily for the period of 3 to 5 consecutive days.

Pigs:
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 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.
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 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.

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 veterinary medicinal 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* susceptible to tiamulin.
The dosage is 20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of veterinary medicinal product)/kg body weight administered daily for 5 consecutive days.

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 veterinary medicinal product)/kg body weight administered daily for 5 consecutive days.

The use of suitably calibrated weighing equipment is recommended.

The maximum solubility of the veterinary medicinal product is 10 gram/liter.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Chickens and turkeys:
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 LD5 is 1090 mg/kg body weight for chickens and 840 mg/kg body weight for turkeysThe clinical signs of toxicity in chickens are vocalisation, clonic cramps and lying in a lateral position. Signs in turkeys are: clonic cramps, lateral or dorsal lying position, salivation and ptosis.
Pigs:
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. If signs of intoxication do occur promptly remove the medicated water and replace 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 veterinary medicinal product)/kg body weight)
Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of veterinary medicinal 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 hydrogen fumarate is a semi-synthetic diterpene antibiotic. The mode of action is by inhibition of ribosomal protein synthesis. It is a bacteriostatic antibiotic and the spectrum of activity includes: 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. The primary binding site is on the 50S subunit and there is possibly a secondary site where the 50S and 30S subunits join. Tiamulin 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.

In vitro research has shown that resistant bacterial mutants can be created through multi step resistance. Development of resistance in mycoplasmas is slower. Resistance against *B. hyodysenteriae* has been seen, and can vary geographically.

Cross resistance between tiamulin and tylosin tartrate has been reported: micro-organisms that are resistant for tiamulin, are also resistant for tylosin tartrate, but not vice versa.
Resistance in *Brachyspirae hyodysenteriae* can be caused by a point mutation in the 23S rRNA gene.

4.3 Pharmacokinetics

Tiamulin is well absorbed from the gastrointestinal tract of chickens and turkeys.

Chicken
Tiamulin hydrogen fumarate is well absorbed in chickens (70-95%) after oral administration and reaches peak concentrations in 2-4 hours (Tmax 2.85 hours). Following a 50 mg tiamulin hydrogen fumarate/kg body weight single dose the Cmax 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.Turkey
In turkeys serum levels of tiamulin hydrogen fumarate are lower with a 50 mg tiamulin hydrogen fumarate/kg body weight single dose giving a Cmax 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%.

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 Cmax was 1.03µg/ml and 1.82 µg/ml in serum respectively by microbiological assay and the Tmax 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.

Environmental properties

Tiamulin hydrogen fumarate is persistent in soils

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Tiamulin is incompatible with ionophore antibiotics, including monensin, narasin, salinomycin. See section 3.8.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 3 months.
Feed to which the oral granules has been added should be replaced if not consumed within 24 hours.

5.3 Special precautions for storage

Do not refrigerate or freeze.
Store in original container.

5.4 Nature and composition of immediate packaging

Block bottomed zipped 1 kg bag of polyethylene terephthalate/aluminium/low density Polyethylene.

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

Medicines should not be disposed of via wastewater.

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

Huvepharma NV

7. MARKETING AUTHORISATION NUMBER

Vm 30282/4002

8. DATE OF FIRST AUTHORISATION

19 March 2009

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

March 2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

Approved 20 May 2025
Gavin Hall