SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetmulin 100 g/kg premix for medicated feeding stuff for pigs, chickens, turkeys and rabbits

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each kg contains:

Active substance:

81 g tiamulin (equivalent to 100 g tiamulin hydrogen fumarate).

Excipients:

Qualitative composition of excipients and other constituents
Pregelatinised starch
Wheat starch

A yellowish free-flowing granular material.

3. CLINICAL INFORMATION

3.1 Target species

Pigs
Chickens (broilers, layer hens, for reproduction and pullets)
Turkeys (for reproduction and poults)
Rabbits

3.2 Indications for use for each target species

Pigs
For the treatment and metaphylaxis, when the disease is present in the group, of swine dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamulin. The presence of the disease in the group must be established before the veterinary medicinal product is used.
For the treatment of colitis caused by *Brachyspira pilosicoli.*
For the treatment of ileitis caused by *Lawsonia intracellularis.*
For the treatment of enzootic pneumonia caused by *Mycoplasma hyopneumoniae.*
Chickens
For the treatment and metaphylaxis, when the disease is present at herd level, of chronic respiratory disease (CRD) and airsacculitis caused by *Mycoplasma*

gallisepticum and *Mycoplasma synoviae* susceptible to tiamulin. The presence of the disease in the herd should be established before use.

Turkeys
For the treatment and metaphylaxis, when the disease is present at herd level, of infectious sinusitis and airsacculitis caused by *Mycoplasma gallisepticum, Mycoplasma meleagridis* and *Mycoplasma synoviae* susceptible to tiamulin. The presence of the disease in the herd should be established before use.

Rabbits
For the treatment and metaphylaxis, when the disease is present at herd level, of epizootic rabbit enterocolitis (ERE) caused by pathogens susceptible to tiamulin. The presence of the disease in the herd should be established before use.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Do not administer products containing ionophores such as monensin, salinomycin or narasin during or for at least seven days before or after treatment with the veterinary medicinal product. Severe growth depression or death may result.
See section 3.8.

3.4 Special warnings

The uptake of medication by animals can be altered as a consequence of illness. For animals with a reduced feed intake, treat parenterally using an appropriate injectable veterinary medicinal product.
Long term or repeated use should be avoided by improving management practice and thorough cleansing and disinfection.

In case of reduced feed intake, the inclusion levels in feed may need to be increased to achieve target dosage.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Do not use the veterinary medicinal product in liquid feed.

Due to the likely variability (time, geographical) in the occurrence of resistance of bacteria for tiamulin, the use of the veterinary medicinal product should be based on susceptibility testing and take into account official and local antimicrobial policies.
Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to tiamulin and may decrease the effectiveness of treatment with other pleuromutilins due to the potential for crossresistance.

If there is no response to treatment within 3 days, the diagnosis should be re-established.

Inform the feed supplier that tiamulin will be used, to avoid incorporating of ionophore products containing monensin, narasin and salinomycin products in the feed and to

avoid contamination of the feed. In case of a suspected contamination, test the feed for the presence of these ionophores before feeding. If adverse effects occur due to an interaction, stop administration of the feed immediately. Remove the contaminated feed as soon as possible and replace with uncontaminated feed.

Special precautions to be taken by 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, irrigate 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

Chickens, Turkeys, Rabbits:

None Known.

Pigs:

Rare (1 to 10 animals / 10,000 animals treated):	hypersensitivity reaction (e.g. dermatitis, erythema and pruritus)*.

* usually mild and transient but in very rare cases may be serious. If these typical side effects occur, stop treatment immediately and clean animals and pens with water. Normally, the animals recover fast thereafter. Symptomatic treatment such as electrolyte therapy and an anti-inflammatory therapy may be useful.

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.
Can be used in rabbits 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 is known to produce clinically important (often lethal) interactions with ionophore antibiotics, including monensin, narasin, salinomycin. Therefore, animals should not receive products containing such compounds during or for at least seven days before or after treatment with this veterinary medicinal product. Severe growth depression, ataxia, paralysis or death may result Tiamulin may lessen the antibacterial activity of beta-lactam antibiotics, whose action is dependent on bacterial growth.

3.9 Administration routes and dosage

In-feed use.
The intake of medicated feed depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of tiamulin may need to be adjusted using the following formula:

$$\text{Kg premix/tonne feed} = \frac{\text{Dose rate (mg/kg) x mean bodyweight (kg)}}{\text{Mean feed intake (kg) x premix strength (g/kg)}}$$

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

Pigs
Treatment and metaphylaxis of Swine Disentery caused *B. hyodysenteriae*, treatment of Porcine Colonic Spirochaetosis (colitis) caused by *B. pilosicoli*.

Dosage: 5 – 10 mg tiamulin hydrogen fumarate (equivalent to 4.05 – 8.1 mg tiamulin base) / kg bodyweight daily administered for 7 to 10 consecutive days. The dosage will normally be achieved by an inclusion level of 100 – 200 ppm tiamulin hydrogen fumarate in the finished feed providing that feed intake is unaffected.

Treatment of Porcine Proliferative Enteropathy (ileitis) caused by *L. intracellularis*

Dosage: 7.5 mg tiamulin hydrogen fumarate (equivalent to 6.075 mg tiamulin base) / kg bodyweight daily administered for 10-14 consecutive days. The dosage will normally be achieved by an inclusion level of 150 ppm tiamulin hydrogen fumarate in the finished feed providing that feed intake is unaffected.

Treatment of Enzootic Pneumonia caused by *M. hyopneumoniae.*

Dosage: 5.0 – 10.0 mg tiamulin hydrogen fumarate (equivalent to 4.05 – 8.1 mg tiamulin base) / kg bodyweight daily administered for 7 to 10 consecutive days. The dosage will normally be achieved by an inclusion level of 100 - 200 ppm tiamulin hydrogen fumarate in the finished feed, providing that feed intake is unaffected.

Secondary infection by organisms such as *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* may complicate enzootic pneumonia and require specific medication.

Chickens (broilers, layer hens, for reproduction and pullets)
Treatment and metaphylaxis of chronic respiratory disease (CRD) caused by *M. gallisepticum* and airsacculitis and *M. synoviae*.

Dosage - Treatment and metaphylaxis: 25 mg tiamulin hydrogen fumarate (equivalent to 20.25 mg tiamulin base) / kg body weight daily administered for the period of 3 to 5 consecutive days. This is normally achieved by an inclusion level of 250 - 500 ppm tiamulin hydrogen fumarate in the finished feed provided that feed intake is unaffected.

Turkeys (for reproduction and poults)
Treatment and metaphylaxis of infectious sinusitis and airsacculitis caused by *M. gallisepticum, M. synoviae and M. meleagridis*.

Dosage - Treatment and metaphylaxis: 40 mg tiamulin hydrogen fumarate (equivalent to 32.4 mg tiamulin base) / kg body weight daily administered for the period of 3 to 5 consecutive days. This is normally achieved by an inclusion level of 250 - 500 ppm tiamulin hydrogen fumarate in finished feed provided that feed intake is unaffected.

Metaphylaxis with tiamulin should only be initiated after confirmed infection with *M. gallisepticum, M. synoviae and M. meleagridis* and then as an aid in the metaphylaxis strategy to reduce the clinical signs and mortality from respiratory disease in flocks, where infection in ovum is likely because the disease is known to exist in the parent generation. The metaphylaxis strategy should include efforts to eliminate the infection from the parent generation.

Rabbits
Treatment of Epizootic Rabbit Enterocolitis (ERE) and metaphylaxis of ERE in farms with clinical signs of ERE in the previous fattening cycle as part of a programme including measures aiming to eradicate or control the infection in the farm.
Dosage: 3 mg tiamulin hydrogen fumarate (equivalent to 2.43 mg tiamulin base) / kg body weight daily. The dosage will normally be achieved by an inclusion level of 40 ppm tiamulin hydrogen fumarate in the finished feed provided that feed intake is unaffected. Treatment should be administered until 2 - 3 days after clinical signs have resolved. Metaphylaxis should be administered during 3 – 4 weeks from the first week after weaning.

Medicated feed may be pelleted using a pre-conditioning step for 5 minutes at a temperature not exceeding 75°C.

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

Pigs: A single oral dose of 100 mg/kg BW caused hyperpnoea and abdominal discomfort in pigs. At a dose of 150 mg/kg the only effect on the central nervous system was lethargy. A dose of 55 mg/kg for 14 days caused increased salivation and a mild irritation of the stomach. Tiamulin hydrogen fumarate has a relatively high therapeutic index in pigs. The minimum lethal dose has not been established in pigs.

Chickens and turkeys: The LD_5 for chickens is 1290mg/kg and turkeys 840 mg/kg bodyweight. The clinical signs of acute toxicity in chickens are - vocalization, clonic cramps and lateral recumbency. In turkeys signs of acute toxicity include clonic cramps, lateral or dorsal recumbency, salivation and ptosis.

If signs of intoxication do occur promptly remove the medicated feed, replace with fresh unmedicated feed and apply supportive, symptomatic therapy.

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

This veterinary medicinal product is intended to be used for the preparation of medicated feed.

3.12 Withdrawal periods

Pigs
Meat and offal: 6 days.

Chickens (broilers, layer hens, for reproduction and pullets)
Meat and offal: 1 day.
Eggs: Zero days.

Turkeys (for reproduction and poults)
Meat and offal: 4 days.

Rabbits
Meat and offal: Zero 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 *in-vitro* activity against a wide range of bacteria including *Brachyspira hyodysenteriae*, *Brachyspira pilosicoli*, *Lawsonia intracellularis* and *Mycoplasma* spp.

Tiamulin is bacteriostatic at therapeutic concentrations and has been shown to act at the 70S ribosome level and the primary binding site is on the 50S subunit and possibly a secondary site where the 50S and 30S subunits join. It appears to inhibit microbial protein production by producing biochemical inactive initiation complexes, which prevent elongation of the polypeptide chain.

Mechanisms responsible for resistance development in *Brachyspira* spp to the pleuromutilin class of antibiotics are considered to be based on mutations at the ribosomal target site. Clinically relevant resistance to tiamulin requires combinations of mutations around the tiamulin binding site. Resistance to tiamulin may be associated with decreased susceptibility to other pleuromutilins.

4.3 Pharmacokinetics

Pigs:
Following oral administration, tiamulin hydrogen fumarate is rapidly absorbed from the gastrointestinal tract of pigs (85-90%) and appears in the blood within 30 minutes. 2-4 hours (t_{max}) after the oral administration of 10 mg tiamulin/kg BW in the form of an oral solution, a C_{max} of 1 µg/ml was measured; an oral administration of 25 mg/kg gave a C_{max} of 1.82 µg/ml.
There is very good distribution in the tissues with accumulation in lungs and in the colon. 30-50% of tiamulin is bound to serum proteins.
Tiamulin is rapidly metabolised in the liver (hydroxylation, de-alkalysation, hydrolysis). At least 16 biologically inactive metabolites have been identified. The excretion of tiamulin and its metabolites is through the bile and faeces (70-85%). The remainder is excreted through the urine (15-30%).

Chickens
Tiamulin is well absorbed in chickens (70-95%) after oral administration.
Tiamulin 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 are similar to chickens. In breeders on 0.025% tiamulin the average serum level was 0.36µg/ml (range 0.22-0.5µg/ml).

Rabbits
There are no pharmacokinetic data available for rabbits.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

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.
Shelf life after incorporation into meal or pelleted feed: 3 months.

5.3 Special precautions for storage

Store below 25°C. Store in a dry place. Protect from direct sunlight.
Store in the original container.

5.4 Nature and composition of immediate packaging

Polyethylene/paper bag of 5kg and 20kg
Polyethylene/aluminium/polyethylene terephthalate bag of 1 kg
Not all pack sizes may be marketed.

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 30282/4011

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.

Gavin Hall
Approved: 01 May 2025