1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetmulin 20 g/kg premix for medicated feeding stuff for pigs, chickens, turkeys and rabbits (BE, BG, IE)

Vetmulin 16.2 g/kg premix for medicated feeding stuff for pigs, chickens, turkeys and rabbits (FR)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each kg contains:

Active substances:
16.2 g Tiamulin equivalent to 20 g of 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 substance or any of the excipients.
Do not use in cases of resistance to tiamulin.
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 product. In case of reduced feed intake, the inclusion levels in feed may need to be increased to achieve target dosage.
Long term or repeated use should be avoided by improving management practice and thorough cleaning and disinfection.

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 cross-resistance.

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:

People with known hypersensitivity to tiamulin should avoid contact with the veterinary medicinal product.
Direct contact with the skin, eyes and mucous membranes and inhalation of the 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 mixing or 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.
Contaminated clothing should be removed and any splashes on to the skin should be washed off immediately.

Accidental ingestion should be avoided. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or label to the physician.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Pigs:

Rare (1 to 10 animals / 10 000 animals treated):	Hypersensitivity reaction[1] (dermatitis[2], erythema[3], pruritus[4])

[1] 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, affected animals recover quickly. Symptomatic treatment such as electrolyte therapy and an anti-inflammatory therapy may be useful.
[2] Acute.
[3] Cutaneous.
[4] Intense.

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 its local representative 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 and 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 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.
For oral administration only after incorporation in medicated feed.

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 accordingly.

Based on the recommended dose and the number and weight of animals to be treated, the exact concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\text{Kg premix per tonne of feed} = \frac{\text{Dose rate (mg/kg) x average body weight (kg)}}{\text{Average feed intake (kg) x premix strength (mg/g)}}$$

To ensure a correct dosage, body weight should be determined as accurately as possible. The use of suitably calibrated measuring equipment is recommended.

The veterinary medicinal product is to be administered only for the treatment of individually fed animals or a small group of animals where the intake by individual animals can be effectively controlled.

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 infectious synovitis caused by *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 1290 mg/kg and turkeys 840 mg/kg bodyweight. The clinical signs of acute toxicity in chickens are vocalisation, 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. Consideration should be given to official guidance on the incorporation of medicated premixes in final 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 (broilers, layer hens, for reproduction and pullets):
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 (for reproduction and poults):
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 package.

5.4 Nature and composition of immediate packaging

Polyethylene/paper bag of 5 and 20kg
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

Huvepharma NV

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

<Date of first authorisation:> <{DD/MM/YYYY}> <{DD month YYYY}.>

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

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month 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. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Polyethylene/paper bag of 5 and 20kg

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetmulin 20 g/kg Premix for medicated feed (BE, BG, IE)

2. STATEMENT OF ACTIVE SUBSTANCES

Each kg contains:

16.2 g tiamulin equivalent to 20 g tiamulin hydrogen fumarate

3. PACKAGE SIZE

5 kg
20 kg

4. TARGET SPECIES

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

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In-feed use.
For oral administration only after incorporation in feed.

7. WITHDRAWAL PERIODS

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.

8. EXPIRY DATE

Exp {mm/yyyy}

Shelf life after incorporation into meal or pelleted feed: 3 months.
Once opened use within 3 months.
Once opened, use by…

9. SPECIAL STORAGE PRECAUTIONS

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

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

Huvepharma NV

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Vetmulin 20 g/kg Premix for medicated feeding stuff for pigs, chickens, turkeys and rabbits (BE, BG, IE)

2. Composition

Each kg contains:

16.2 g tiamulin equivalent to 20g tiamulin hydrogen fumarate

A yellowish free-flowing granular material.

3. Target species

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

4. Indications for use

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 (broilers, layer hens, for reproduction and pullets)
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 reproduction and poults)
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.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or any of the excipients.
Do not use in cases of resistance to tiamulin.
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

6. Special warnings

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

Long term or repeated use should be avoided by improving management practice and thorough cleansing and disinfection.

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 cross-resistance.
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:
People with known hypersensitivity to tiamulin should avoid contact with the veterinary medicinal product.
Direct contact with the skin, eyes and mucous membranes and breathing 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 when mixing or 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.
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 label to the physician.

Pregnancy and lactation:
Can be used in pigs and rabbits during pregnancy and lactation.

Laying birds:
Can be used in laying chickens.

Fertility:
Can be used in breeding chickens and turkeys.

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.

Overdose:
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 (broilers, layer hens, for reproduction and pullets)and turkeys (for reproduction and poults):
The LD_5 for chickens is 1290 mg/kg and turkeys 840 mg/kg bodyweight. The clinical signs of acute toxicity in chickens are vocalisation, 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.

Special restrictions for use and special conditions for use:
This veterinary medicinal product is intended to be used for the preparation of medicated feed.
Consideration should be given to official guidance on the incorporation of medicated premixes in final feed.

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):	Hypersensitivity reaction[1] (dermatitis (skin inflammation)[2], erythema (redness)[3], pruritus (itching)[4])

[1] 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, affected animals recover quickly. Symptomatic treatment such as electrolyte therapy and an anti-inflammatory therapy may be useful.
[2] Acute.
[3] Cutaneous.
[4] Intense.

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 its local representative> 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

In-feed use.
For oral administration only after incorporation in medicated feed.

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 infectious synovitis caused by *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.

9. Advice on correct administration

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 accordingly. Based on the recommended dose and the number and weight of animals to be treated, the exact concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\textit{Kg premix per tonne} = \frac{\textit{Dose rate (mg/kg) x average bodyweight (kg)}}{\textit{Average feed intake (kg) x premix strength (mg/g)}}$$

To ensure a correct dosage, body weight should be determined as accurately as possible.
The use of suitably calibrated measuring equipment is recommended.

The veterinary medicinal product is to be administered only for the treatment of individually fed animals or a small group of animals where the intake by individual animals can be effectively controlled.

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

10. 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.

11. Special storage precautions

Keep out of the sight and reach of children.
Store below 25 °C. Store in a dry place. Protect from direct sunlight.
Store in the original package.

Shelf life after first opening the immediate packaging: 3 months.
Shelf life after incorporation into meal or pelleted feed: 3 months.
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.

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

Polyethylene/paper bag of 5 and 20kg

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

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 events>
Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium
+32 3 288 18 49
pharmacovigilance@huvepharma.com

Manufacturer responsible for batch release:
Biovet JSC
39 Petar Rakov Str
4550 Peshtera
Bulgaria

<Local representatives and contact details to report suspected adverse events>

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

17. Other information

When the container is opened for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.