SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

VETMULIN 162 mg/ml Solution for Injection for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance

Tiamulin	162 mg/ml

Excipients

Butyl parahydroxybenzoate	0.324 mg/ml
Propyl gallate (E310)	0.163 mg/ml

For a full list of excipients: see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Pale yellow oily solution.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs.

4.2 Indications for use (specifying the target species)

For treatment and metaphylaxis of swine dysentery caused by *Brachyspira hyodysenteriae*.

For the treatment of enzootic pneumonia caused by tiamulin-susceptible *Mycoplasma hyopneumoniae* and mycoplasmal arthritis caused by tiamulin-susceptible *Mycoplasma hyosynoviae.*

4.3 Contraindications

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

4.4 Special warnings (for each target species)

Inflammation/scarring may occur at the site of injection. For this reason, it is recommended that the product should be administered into the muscle of the neck.

4.5 Special precautions for use

i)Special precautions for use in animals

Due to the likely variability (time, geographical) in the occurrence of resistance of bacteria for tiamulin, the use of the product should be based on bacteriological sampling and susceptibility testing taking into account official and local antimicrobial policies. Use of the 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.

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

In the absence of a satisfactory response to treatment, the diagnosis should be reconsidered

ii)Special precautions to be taken by the person administering the veterinary medicinal product to animals

People with known hypersensitivity to tiamulin should handle the product carefully.
Care should be taken to avoid self-injection.Direct contact with the skin, eyes and mucous membranes should be avoided when handling the product.
In case of accidental eye contact, irrigate the eyes thoroughly with clean running water immediately. Seek medical advice if irritation persists.
In case of skin contact, wash immediately with running water in order to minimise absorption through the skin.

Wash hands after use.

This product contains sesame oil. Accidental self injection may result in severe localised reactions, particularly if injected into a joint or finger. In case of accidental injection, seek medical advice immediately. Show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

In rare cases, hypersensitivity to tiamulin is reported in terms of acute dermatitis with cutaneous erythema and intense pruritus. The adverse reactions are usually mild and transient but in very rare cases may be serious. Symptomatic treatment such as electrolyte therapy and an anti-inflammatory therapy may be useful.

See also section 4.4.

4.7 Use during pregnancy, lactation or lay

The product can be used during pregnancy and lactation.

4.8 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, pigs should not receive products containing such compounds during or for at least seven days before or after treatment with this product. Severe growth depression or death may result.

Tiamulin may lessen the antibacterial activity of beta-lactam antibiotics, whose action is dependent on bacterial growth.

4.9 Amount(s) to be administered and administration route

For intramuscular use.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing

For the treatment of clinical swine dysentery:
8.1 mg tiamulin base per kg bodyweight (equivalent to 1 ml per 20 kg bodyweight) to be administered in a single treatment followed by tiamulin in the water or feed.

For the treatment of enzootic pneumonia or mycoplasmal arthritis:
12.1 mg tiamulin base per kg bodyweight (equivalent to 1.5 ml/20 kg bodyweight) daily for 3 consecutive days.

Depending on the severity of disease it may be necessary to continue treatment by orally administered tiamulin until 2 days after signs of disease have subsided

The closures should not be broached more than 5 times. In order to prevent excessive broaching of the stopper, a suitable multiple dosing device should be used.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

A single oral dose of 100 mg tiamulin/kg bodyweight caused hyperpnoea and abdominal discomfort in pigs. At a dose of 150 mg tiamulin /kg the only effect on the central nervous system was lethargy. A dose of 55 mg tiamulin/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.

4.11 Withdrawal period(s)

Meat and offal: 21 days

5. PHARMACOLOGICAL OR IMMUNOLOGICAL PROPERTIES

ATC Vet Code: QJ01XQ01
Pharmacotherapeutic group: Antibacterials for systemic use, Other antibacterials, Pleuromutilins

5.1 Pharmacodynamic properties

Tiamulin hydrogen fumarate is a semi-synthetic derivative of the diterpene antibiotic pleuromutilin, produced by *Pleurotus mutilis* later renamed *Clitopilus scyphoides*.
Tiamulin is active against pathogenic mycoplasmas, against most Gram-positive organisms and anaerobes. Tiamulin is bacteriostatic at therapeutic concentrations and has been shown to act at the 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.

Research has shown that resistant bacterial mutants can be created through multi step resistance. Horizontal transferable resistance has also been described (e.g. *vga* genes & *cfr* gene). In practice, resistance in mycoplasmas has been reported rarely. Resistance against *B. hyodysenteriae* has been seen and can vary geographically.
If response to treatment of dysentery with the product is poor, then the possibility of resistance must be considered. 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. Transferable resistance mechanism (*cfr*) can cause cross-resistance to lincosamides, streptogramins (A) and phenicols (florfenicol).
Resistance in *Brachyspira hyodysenteriae* can be caused by a point mutation in the 23S rRNA gene and/or the ribosomal protein L3 gene.

5.2 Pharmacokinetic particulars

Following a single intramuscular administration at a dose rate of approximately 14 mg tiamulin per kg bodyweight, mean maximum tiamulin concentration (approximately 350ng/ml) was reached after approximately 3 hours. The mean terminal half life is approximately 12 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butyl parahydroxybenzoate

Propyl gallate (E310)

Ethanol (96%),

Sesame oil, refined

6.2 Incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months

Shelf life after first opening the immediate packaging: 28 days. Discard any product remaining in the container at this time

6.4 Special precautions for storage

Store below 25 °C. Do not refrigerate or freeze.

Protect from light.

6.5 Nature and composition of immediate packaging

The product is presented in a 100 ml Type I amber glass vial, sealed with a nitrile rubber stopper supplied in a carton. One vial per carton.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with

local requirements.

7. MARKETING AUTHORISATION HOLDER

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium
Tel: +32 3 288 1849
Fax: + 32 3289 7845
E-mail: customerservice@huvepharma.com

8. MARKETING AUTHORISATION NUMBER

Vm 30282/4013

9. DATE OF FIRST AUTHORISATION

21 October 2009

10. DATE OF REVISION OF THE TEXT

August 2014

Approved: **07/08/14**