[Version 8, 10/2012]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylmasin 250 000 IU/g premix for medicated feeding stuff for pigs and chickens (ES, IT)
Pharmasin 250 000 IU/g premix for medicated feeding stuff for pigs and chickens (PT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Tylosin (as tylosin phosphate): 250 000 IU

Excipients:
Wheat meal

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff
Off white to beige granules.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs, Chickens

4.2 Indications for use, specifying the target species

Pigs: Treatment and metaphylaxis of enzootic pneumonia caused by *Mycoplasma hyopneumoniae,* atrophic rhinitis, Porcine Proliferative Enteropathy caused by *Lawsonia intracellularis.*

Chickens: Treatment and metaphylaxis of Chronic Respiratory Disease (CRD) caused by *Mycoplasma gallisepticum* or *M. synoviae*, necrotic enteritis caused by *Clostridium perfringens*, sensitive to tylosin

The presence of the disease in the group should be confirmed before metaphylactic treatment.

4.3 Contraindications

Do not use in animals with known sensitivity to the active substance and/or to any of the excipients of the veterinary medicinal product
Do not use in animals with known hyper sensitivity to tylosin and other macrolides
Do not use in horses. Danger of inflammation of the cecum.
Do not use where cross-resistance to other macrolides (MLS-resistance) is suspected,
Do not use in animals vaccinated with tylosin-sensitive vaccines either at the same time or within one week previously.
Do not use in animals with hepatic disorders.

4.4 Special warnings for each target species

Animals with acute infections may have a reduced feed intake and should be treated with a suitable injectable product first.

4.5 Special precautions for use

Special precautions for use in animals

Mix well with feed to ensure good distribution.
Whenever possible, the product should only be used based on susceptibility testing.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to Tylosin and other Macrolides.
Use of veterinary medicinal product in poultry must comply with Regulation EC 1177/2006 of the Commission and the transposing national regulations.

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

Tylosin may induce irritation. Macrolides, such a tylosin, may also cause hypersensitivity (allergy) following injection, inhalation, ingestion or contact with skin or eye. Hypersensitivity to tylosin may lead to cross reactions to other macrolides and vice versa. Allergic reactions to these substances may occasionally be serious and therefore direct contact should be avoided.
People with known hypersensitivity to macrolides or the excipients of the product should avoid contact with the veterinary medicinal product.
To avoid exposure during mixing, personal protective equipment consisting of overalls, safety glasses, impervious gloves and either a disposable half mask respirator conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 with a filter to EN143 should be worn when handling the veterinary medicinal product.
Wash hands after use.
In case of accidental skin contact, wash thoroughly with soap and water. In case of accidental eye contact, flush the eyes with plenty of clean, running water.
If you develop symptoms following exposure, such as skin rash, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

Other precautions

Tylosin is toxic for plants. The poultry litter coming from treated animals should not be used as fertilizer without being mixed with at least the same amount of litter coming from untreated animals.

4.6 Adverse reactions (frequency and seriousness)

In pigs, adverse reactions have been observed, including diarrhoea, pruritus, erythema, rectal oedema and prolapse in very rare cases.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Laboratory studies in mice and rats have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. No studies have been conducted in the target species population. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Florfenicol, lincosamides and other macrolides, which have an action similar to tylosin could interact by competing for binding to the 50S subunit, so it is not recommended for use simultaneously.

4.9 Amounts to be administered and administration route

In feed use.

Pigs:
Treatment and metaphylaxis of enzootic pneumonia caused by *Mycoplasma hyopneumoniae*, atrophic rhinitis, and Porcine Proliferative Enteropathy caused by *Lawsonia intracellularis:*
3000 – 6000 IU tylosin per kg bw (corresponding to 12-24 mg product per kg bw), used as the sole ration for 21 days. Treatment duration should not exceed 3 weeks.

Chickens :
Treatment and metaphylaxis of Chronic Respiratory Disease (CRD) caused by *Mycoplasma gallisepticum* or *M. synoviae:*
In broiler chickens and replacement pullets: 127 000 IU tylosin per kg bw (corresponding to 508 mg product per kg bw) during the first five days of age followed by a second treatment at the age of 3-5 weeks.
In laying hens: 50 000 IU tylosin per kg bw (corresponding to 200 mg product per kg bw) for 5 days.

Treatment and metaphylaxis of necrotic enteritis caused by *Clostridium perfringens*, sensitive to tylosin: 10 000 – 20 000 IU tylosin per kg bw (corresponding to 40-80 mg product per kg bw) for 7 days.

All species:
For the preparation of the medicated feed the body weight of the animals to be treated and their actual daily feed consumption should be taken into due account. Consumption may vary depending on factors like age, breed, and husbandry system. To provide the required amount of active substance in mg per kg mixed feed the following calculation should be made:

$$\frac{\text{Dose (mg/kg BW) X Average body weight (kg) of the animals to be treated}}{\text{Average daily feed intake (kg per animal) X Premix concentration (g/kg)}} = \text{kg product per ton mixed feed}$$

Instructions for mixing:
Mix the required dose of product in a small quantity of feed (20-25 kg) before incorporating into the final amount of feed.

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

Tylosin has a wide margin of tolerance in pigs and chickens when administered orally. Tylosin has been shown to produce no adverse effects when fed to pigs at 600 ppm in the feed (six times the recommended dose level) for 28 days. At high levels diarrhoea, apathy, convulsions may occur. The therapy is symptomatic.

4.11 Withdrawal period(s)

Pigs	Meat and offal: Zero days
Chickens	Meat and offal: Zero days
	Eggs: Zero days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterials for systemic use, macrolides,
ATCvet code: QJ01FA90

5.1 Pharmacodynamic properties

Tylosin is an antibiotic belonging to the macrolide family. Its antimicrobial activity is mainly bacteriostatic. The mechanism of antibacterial action of tylosin is caused by inhibition of protein synthesis at the level of the reversible binding of the drug to protein 27 of the 50S subunit of the bacterial ribosome, once it has penetrated into the bacterium by passive diffusion. Thus tylosin inhibits transpeptidation.
The antimicrobial activity of tylosin include Gram positive bacteria, such as *Clostridium perfringens* and some strains of Gram-negative bacteria such as *Pasteurella spp, Mycoplasma spp* at concentrations of 16 µg/ml or less and *Lawsonia sp*.

5.2 Pharmacokinetic particulars

Absorption
Following oral administration, absorption is around 30% .
Distribution
It is well distributed to all tissues, in the lung reaching levels several times higher than those observed in plasma at the same time.
Binding to plasma proteins is low, around 35 %.
Biotransformation and excretion
Tylosin undergoes biotransformation in the liver and is later excreted in the bile (faeces), via the kidney and also milk.
The elimination half-life in pigs after intravenous administration is about 4 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

(Wheat meal)
Dipotassium phosphate (E340)
Pregelatinised starch (potato)

6.2 Major 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: 2 years
Shelf-life after first opening the immediate packaging: 3 months
Shelf life after incorporation into meal or pelleted feed: 2 months

6.4. Special precautions for storage

Store in the original container in order to protect from light.
Store in a dry place
Store below 30°C
Do not refrigerate or freeze
Protect from frost.

6.5 Nature and composition of immediate packaging

Low density polyethylene inner lined multi-walled paper bag with sutured crimp.
Polyethylene/aluminium foil/polyethylene terephthalate sachet.

Pack sizes:
Sachet of 1 kg
Bag of 5 kg
Bag of 20 kg

Not all pack sizes may be marketed.

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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

For IT & PT:

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium

For ES:

Biovet JSC
39 Petar Rakov Str
4550 Peshtera
Bulgaria

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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

10 DATE OF REVISION OF THE TEXT

{MM/YYYY}

PROHIBITION OF SALE, SUPPLY AND/OR USE

Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.
ES only:
For animal treatment only – to be supplied only on veterinary prescription.
To be administered by the veterinarian or under veterinarian supervision.