[Version 9.1,06/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylovet 1 g/g granules for oral solution for pigs, chickens and turkeys (PT)
Tylmasin 1 g/g granules for oral solution for pigs, chickens and turkeys (ES)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1.1 g of the veterinary medicinal product contains:

Active substance:
1 g of tylosin (equivalent to 1.1 g of tylosin tartrate)

Excipients:
None

White to off-white coloured granules
After reconstitution: Colourless to slightly yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Chicken (broiler and layer hen), turkey and pig.

3.2 Indications for use for each target species

Broilers and laying hens:
Treatment and metaphylaxis of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* or *M. synoviae* strains sensitive to tylosin.
Treatment of outbreaks of necrotic enteritis caused by *Clostridium perfringens* strains sensitive to tylosin.

Turkeys: Treatment and metaphylaxis of infectious sinusitis caused by *Mycoplasma gallisepticum* strains sensitive to tylosin.

Pigs: Treatment of porcine proliferative enteritis or ileitis (PIA) caused by *Lawsonia intracellularis* strains sensitive to tylosin.

The presence of the disease in the herd should be established before metaphylactic treatment.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance.
Do not use in cases of known resistance to tylosin or cross-resistance to other macrolides (MLS-resistance).
Do not use in animals vaccinated with tylosin-sensitive vaccines either at the same time or within one week previously.
Do not administer to animals with hepatic damage.
Do not use in horses.

3.4 Special warnings

None.

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 identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.
Under-dosing and/or treating for an insufficient length of time are considered to promote the development of resistance in bacteria and should be avoided.
Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to Tylosin and other Macrolides.
Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.Animals with acute infections may have a reduced water and feed consumption and should be treated with a suitable injectable veterinary medicinal product first.
Do not leave or dispose of water containing tylosin tartrate where it may be accessible to either animals not under treatment or wildlife.

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

Macrolides, such as tylosin, may 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. People with known hypersensitivity to tylosin or other macrolide antibiotics should avoid contact with the veterinary medicinal product.
Tylosin may induce irritation. Avoid direct exposure of the skin, mucous membrans and inhalation of the veterinary medicinal product. Personal protective equipment consisiting 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 and during the preparation of the medicated drinking water.
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, you should seek medical advice and show the physician this warning. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Do not eat, drink or smoke while handling the veterinary medicinal product.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Chicken (broiler and layer hen) and turkey:
None known.

Pigs:

Rare (1 to 10 animals / 10 000 animals treated):	Gastric bleeding
	Erythema, pruritus,

Please note that we didn't find a suitable LLT term for this adverse event in the VeDDRa list but we will askVery rare (<1 animal / 10 000 animals treated, including isolated reports):	Rectal prolapse, oedema
	Vaginitis
	Constipation

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> <immediate packaging> for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

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.
Use only according to the benefit/risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Lincosamides and aminoglycoside antibiotics antagonise the activity of tylosin.

3.9 Administration routes and dosage

For oral administration.

Broilers and laying hens:
Treatment and metaphylaxis of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* or *M. synoviae*.
110 mg tylosin / kg bw (equivalentto 100 mg veterinary medicinal product / kg bw/ day) for 3-5 days.

Treatment of outbreaks of necrotic enteritis caused by *Clostridium perfringens.*
22 - 44 mg tylosin / kg bw (equivalent to 20 – 40 mg veterinary medicinal product / kg bw/ day) for 5 days

Turkeys:
Treatment and metaphylaxis of infectious sinusitis caused by *Mycoplasma gallisepticum* .
110 mg tylosin / kg bw (equivalent to 100 mg veterinary medicinal product / kg bw/ day) for 5 days

Pigs:
Treatment of porcine proliferative enteritis or ileitis (PIA) caused by *Lawsonia intracellularis.*
5.5-11 mg tylosin / kg bw (equals 5-10 mg veterinary medicinal product / kg bw/ day) for 7 days.

All species:
To ensure a 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 tylosin may need to be adjusted accordingly.
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

$$\frac{\text{Dose (mg/kg bw of veterinary medicinal product/ day)}}{\text{Average daily water consumption (litre) per animal per day}} \times \frac{\text{Average body weight (kg) of the animals to be treated}}{} = \text{\_\_\_\_ mg veterinary medicinal product per litre drinking water}$$

Sufficient access to the system of water supply should be available for the animals to be treated to ensure adequate water consumption. No other source of drinking water should be available during the medication period.

Colourless to slightly yellow solution.
The medicated water must be renewed every 24 hours.

If individual animals show signs of a serious infection such as a reduced water or feed intake, then they should be treated individually, such as by injection

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

There are no known toxic effects of overdose associated with the use of the veterinary medicinal product.
Do not exceed the recommended dose.

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

For administration only by a veterinarian.

3.12 Withdrawal periods

Chickens (meat and offal): Zero days
Chicken (eggs): Zero days
Pigs (meat and offal): 1 day
Turkeys (meat and offal): 1 day

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01FA90.

4.2 Pharmacodynamics

Tylosin is a macrolide antibiotic produced by a strain of *Streptomyces fradiae.* It exerts its antimicrobial effect by inhibiting protein synthesis of susceptible micro-organisms.
The tylosin spectrum of activity includes amongst others Gram-positive bacteria and *Mycoplasma spp*.

Tylosin is a macrolide antibiotic that binds to the 50S ribosomal subunit of bacterial ribosomes, specifically near the peptidyl transferase center. This binding blocks the exit tunnel of the growing peptide chain, inhibiting translocation and elongation of the nascent polypeptide. As a result, protein synthesis is disrupted, leading to bacterial growth inhibition or cell death.

4.3 Pharmacokinetics

In most species peak plasma concentrations have been attained 1 to 2 hours after administration of tylosin. Compared to plasma levels clearly higher tissue concentrations have been observed. Tylosin was extensively metabolised.

Tylosin is primarily metabolized in pigs and chickens through demethylation, hydroxylation, and ester hydrolysis. In pigs, the main metabolites include desmycosin, macrolide aglycones, and hydroxylated derivatives, excreted mainly via bile and feces. In chickens, tylosin undergoes similar metabolic

transformations, with desmycosin and relomycin being the dominant metabolites, excreted largely in feces. The metabolism is primarily hepatic, with cytochrome P450 enzymes playing a key role in biotransformation. Excretion pathways differ slightly, with pigs showing more biliary elimination, while chickens excrete a higher proportion unchanged in feces.

Environmental properties
Most of the residues are excreted in faeces predominantly consisting of tylosin (factor A), relomycin (factor D) and dihydrodesmycosin.

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.
No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years
Shelf-life after first opening the immediate packaging: 3 months
Shelf-life after dilution or reconstitution according to directions in water: 24 hours

5.3 Special precautions for storage

Store below 30°C.
Store in the original container in order to protect from light.

5.4 Nature and composition of immediate packaging

1.1 kg resealable block bottom zipped sachet made of polyethylene /aluminium/polyethylene terephthalate laminate

110 g high density polyethylene pot with polypropylene cap

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

Portugal;
Huvepharma N.V.

Spain;
Biovet JSC.

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

<{DD/MM/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

{Resealable 1.1 kg PE-Alu-PET bag}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylovet 1 g/g granules for oral solution (PT)
Tylmasin 1 g/g granules for oral solution (ES)

2. STATEMENT OF ACTIVE SUBSTANCES

Each 1.1 g of the veterinary medicinal product contains:
1 g of tylosin (equivalent to 1.1 g of tylosin tartrate)

3. TARGET SPECIES

For chicken (broilers and layer hens), turkeys and pigs

4. ROUTES OF ADMINISTRATION

For oral administration.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:
Chickens (meat and offal): Zero days
Chicken (eggs): Zero days
Pigs (meat and offal): 1 day
Turkeys (meat and offal): 1 day

6. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life after reconstitution in water: 24 hours
Shelf life after first opening: 3 months
Once broached, use by:

7. SPECIAL STORAGE PRECAUTIONS

Store below 30° C
Store in the original container in order to protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Portugal:
Huvepharma N.V.

Spain:

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{HDPE pot of 110 g}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylovet 1 g/g granules for oral solution (PT)
Tylmasin 1 g/g granules for oral solution (ES)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Each 1.1 g of the veterianry medicinal product contains:
1 g of tylosin (equivalent to 1.1 g of tylosin tartrate)

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life after dilution or reconstitution in water: 24 hours
Shelf life after first opening: 3 months
Once broached, use by:

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Tylovet® 1 g/g granules for oral solution for pigs, chickens and turkeys (PT)
Tylmasin 1 g/g granules for oral solution for pigs, chickens and turkeys (ES)

2. Composition

Each 1.1 g of the veterinary medicinal product contains:
1 g of tylosin (equivalent to 1.1 g of tylosin tartrate)

White to off-white coloured granules
After reconstitution: Colourless to slightly yellow solution.

3. Target species

Chicken (broiler and layer hen), turkey and pig.

4. Indications for use

Broilers and laying hens:
Treatment and metaphylaxis of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* or *M. synoviae* strains sensitive to tylosin.
Treatment of outbreaks of necrotic enteritis caused by *Clostridium perfringens* strains sensitive to tylosin..

Turkeys: Treatment and metaphylaxis of infectious sinusitis caused by *Mycoplasma gallisepticum* strains sensitive to tylosin..

Pigs: Treatment of porcine proliferative enteritis or ileitis (PIA) caused by *Lawsonia intracellularis* strains sensitive to tylosin..

The presence of the disease in the herd should be established before metaphylactic treatment.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance.
Do not use in cases of known resistance to tylosin or cross-resistance to other macrolides (MLS-resistance).
Do not use in animals vaccinated with tylosin-sensitive vaccines either at the same time or within one week previously.
Do not administer to animals with hepatic damage.
Do not use in horses, danger of inflammation of the cecum.

6. Special warnings

Special warnings:
None.

Special precautions for safe use in the target species:
Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information

and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach. Under-dosing and/or treating for an insufficient length of time are considered to promote the development of resistance in bacteria and should be avoided.
Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to Tylosin and other Macrolides.
Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.Animals with acute infections may have a reduced water and feed consumption and should be treated with a suitable injectable veterinary medicinal product first.
Do not leave or dispose of water containing tylosin tartrate where it may be accessible to either animals not under treatment or wildlife.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Macrolides, such as tylosin, may 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. People with known hypersensitivity to tylosin or other macrolide antibiotics should avoid contact with the veterinary medicinal product.
Tylosin may induce irritation. Avoid direct exposure of the skin, mucous membrans and inhalation of the veterinary medicinal product. Personal protective equipment consisiting 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 and during the preparation of the medicated drinking water.
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, you should seek medical advice and show the physician this warning. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Do not eat, drink or smoke while handling the veterinary medicinal product.

Pregnancy and lactation:
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. Use only according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Lincosamides and aminoglycoside antibiotics antagonise the activity of tylosin.

Overdose:
There are no known toxic effects of overdose associated with the use of the veterinary medicinal product.
Do not exceed the recommended dose.

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.
No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water.

7. Adverse events

Chicken (broiler and layer hen) and turkey:
None known.

Pigs:

Rare (1 to 10 animals / 10 000 animals treated):	Gastric bleeding
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Erythema, pruritus,(itching)
	Rectal prolapse, oedema
	Vaginitis
	Constipation

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

For oral administration.

Broilers and laying hens:
Treatment and metaphylaxis of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* or *M. synoviae*.
110 mg tylosin / kg bw (equivalent to 100 mg veterinary medicinal product / kg bw/ day) for 3-5 days.

Treatment of outbreaks of necrotic enteritis caused by *Clostridium perfringens.*
22 - 44 mg tylosin / kg bw (equivalent to 20 - 40 mg veterinary medicinal product / kg bw/ day) for 5 days

Turkeys:
Treatment and metaphylaxis of infectious sinusitis caused by *Mycoplasma gallisepticum* .
110 mg tylosin / kg bw (equivalent to 100 mg veterinary medicinal product / kg bw/ day) for 5 days

Pigs:
Treatment of porcine proliferative enteritis or ileitis (PIA) caused by *Lawsonia intracellularis.*
5.5-11 mg tylosin / kg bw (equivalent to 5 - 10 mg veterinary medicinal product / kg bw/ day) for 7 days.

All species:
To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of the antimicrobial has to be adjusted accordingly.
To provide the required amount of active substance in mg per litre of water, the following calculation should be made:

Dose (mg/kg bw of veterinary medicinal product/ day) X Average body weight (kg) of the animals to be treated = ____ mg veterinary medicinal product per

Average daily water consumption (litre) per animal per day litre drinking water

If individual animals show signs of a serious infection such as a reduced water or feed intake, then they should be treated individually, such as by injection.

9. Advice on correct administration

Sufficient access to the system of water supply should be available for the animals to be treated to ensure adequate water consumption. No other source of drinking water should be available during the medication period.

Colourless to slightly yellow solution.
The medicated water must be renewed every 24 hours.

10. Withdrawal periods

Withdrawal period:
Chickens (meat and offal): Zero days
Chicken (eggs): Zero days
Pigs (meat and offal): 1 day
Turkeys (meat and offal): 1 day

11. Special storage precautions

Keep out of the sight and reach of children.
Store in the original container in order to protect from light.
Store below 30°C.
Shelf-life after first opening the immediate packaging: 3 months
Shelf-life after dilution or reconstitution according to directions in water: 24 hours

Do not use this veterinary medicinal product after the expiry date which is stated on the label. 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

1.1 kg resealable block bottom zipped sachet made of polyethylene /aluminium/polyethylene terephthalate laminate

110 g high density polyethylene pot with polypropylene cap
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

<{DD/MM/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:

Portugal:
Huvepharma N.V.
Uitbreidingstraat 80
2600 Antwerp
Bélgica
+32 3 288 18 49
pharmacovigilance@huvepharma.com

Spain:
Biovet JSC
Petar Rakov 39
Peshtera, 4550
Bulgaria
+32 3 288 18 49
pharmacovigilance@huvepharma.com

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