

*[Version 9, 03/2022] corr. 11/2022*

## **ANNEX I**

### **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylovectin 200 solution for injection for cattle, goats and pigs.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

### Active substance:

Tylosin 200 000 IU

### Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Benzyl alcohol (E1519)	40 mg
Propylene glycol (E1520)	
Water for injections	

A pale yellow to amber-coloured liquid.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cattle, goats and pigs.

### 3.2 Indications for use for each target species

For the treatment of specific infections (listed below) caused by microorganisms susceptible to tylosin.

#### Cattle :

-Respiratory infections, metritis caused by Gram-positive microorganisms, mastitis caused by *Streptococcus spp*, *Staphylococcus spp* and interdigital necrobacillosis, i.e. panaritium or foot rot.

#### Cattle (calves):

-Respiratory infections and necrobacillosis.

#### Pigs:

-Enzootic pneumonia, haemorrhagic enteritis, erysipelas and metritis.  
-Arthritis caused by *Mycoplasma spp.* and *Staphylococcus spp.*

For information regarding swine dysentery see section 3.5.

#### Goats:

- Respiratory infections, metritis caused by Gram-positive microorganisms, mastitis caused by Gram-positive microorganisms or *Mycoplasma spp.*

### 3.3 Contraindications

Do not use in chickens, turkeys and horses.

Do not use in cases of hypersensitivity to the active substance, other macrolides or any of the excipients.

### 3.4 Special warnings

None.

### 3.5 Special precautions for use

#### Special precautions for safe use in the target species:

Due to likely variability (time, geographical) in susceptibility of bacteria to tylosin, bacteriological sampling and susceptibility testing are recommended. Official, national and regional antimicrobial policies should be taken into account when the veterinary medicinal product is used

Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to tylosin and may decrease the effectiveness of treatment with other macrolide antibiotics due to the potential for cross resistance.

A high rate of *in vitro* resistance has been demonstrated in European strains of *Brachyspira hyodysenteriae* implying that the veterinary medicinal product will not be sufficiently efficacious against swine dysentery.

The efficacy data do not support the use of tylosin for the treatment of bovine mastitis caused by *Mycoplasma* spp.

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

Care should be taken to avoid accidental self-injection.

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

In the event 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.

Wash hands after use.

People with known hypersensitivity to tylosin, benzylalcohol or propylene glycol should avoid contact with the veterinary medicinal product.

Tylosin may induce irritation. Macrolides, such as 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.

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.

#### Special precautions for the protection of the environment

Not applicable.

### 3.6 Adverse events

Cattle:

Very rare (<1 animal / 10,000- animals treated, including isolated reports):	<ul style="list-style-type: none"> <li>- Injection site swelling, injection site inflammation</li> <li>- Swollen vulva</li> <li>- Anaphylactic shock</li> <li>- Death</li> </ul>
Undetermined frequency (cannot be estimated from available data)	<ul style="list-style-type: none"> <li>- Hypersensitivity reaction</li> <li>- Injection site lesion<sup>1</sup></li> </ul>

<sup>1</sup> Can persist for up to 21 days following administration

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	<ul style="list-style-type: none"> <li>- Injection site swelling, Injection site inflammation</li> <li>- Anaphylactic shock</li> <li>- Rectal oedema</li> <li>- Erythema</li> <li>- Pruritus</li> <li>- Rectal prolapse (partial)</li> <li>- Death</li> </ul>
Undetermined frequency (cannot be estimated from available data)	<ul style="list-style-type: none"> <li>- Hypersensitivity reaction</li> <li>- Injection site lesion<sup>2</sup></li> </ul>

<sup>2</sup> Can persist for up to 21 days following administration

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:

Studies in laboratory animals have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. No studies have been conducted in the target species. Use only in accordance with the benefit/risk assessment by the responsible veterinarian.

### 3.8 Interaction with other medicinal products and other forms of interaction

None known.

### 3.9 Administration routes and dosage

For intramuscular or slow intravenous (cattle only) injection

Cattle and calves: 5 000 - 10 000 IU tylosin/kg bodyweight per day for 3 days (2.5 to 5 ml solution for injection per 100 kg bodyweight).

Maximum injection volume per injection site should not exceed 15 ml in cattle.

Goats: 10 000 IU tylosin/kg bodyweight per day for 3 days (5 ml solution for injection per 100 kg bodyweight).

Pigs: 5 000 IU to 10 000 IU of tylosin per kg bodyweight per day during 3 days, *i.e* 2.5 to 5 ml of solution per 100 kg bodyweight.

In pigs do not administer more than 5 ml per injection site.

Where repeat injections are to be administered, use different sites for each injection.

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

The closures should not be breached more than 15 times. In order to prevent excessive breaching of the stopper, a suitable multiple dosing device should be used.

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

Pigs and calves: Intramuscular injection of 30 mg/kg bodyweight per day (three times maximum recommended dose) for five days produced no adverse effects.

### **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**

Not applicable.

### **3.12 Withdrawal periods**

Cattle:

Meat and offal – 28 days

Milk – 108 hours

Goat:

Meat and offal – 42 days

Milk – 108 hours

Pigs:

Meat and offal – 16 days

## **4. PHARMACOLOGICAL INFORMATION**

### **4.1 ATCvet code:**

QJ01FA90.

### **4.2 Pharmacodynamics**

Tylosin is a macrolide antibiotic with a pKa of 7.1 and structurally similar to erythromycin. It is produced by *Streptomyces fradiae*. Tylosin has a low solubility in water.

Tylosin exerts its antibiotic activity by a similar mechanism to other macrolides, i.e. by binding the 50 S fraction of the ribosomes resulting, in an inhibition of the synthesis of proteins. Tylosin has mainly a bacteriostatic activity.

Tylosin has an antibiotic effect against Gram positive cocci (Staphylococci, Streptococci), Gram positive bacilli, certain Gram-negative bacilles and Mycoplasma.

Resistance to macrolides is usually plasmid-mediated but modification of ribosomes may occur through chromosomal mutation. Resistance can occur by i) decreased entry into bacteria (most common with the gram-negative bacteria), ii) synthesis of bacterial enzymes that hydrolyze the drug and, iii) modification of the target (the ribosome).

This latter resistance type may also lead to cross-resistance with other antibiotics that preferentially bind to bacterial ribosome. Gram-negative anaerobic bacteria are often resistant.

### **4.3 Pharmacokinetics**

#### Absorption:

Following intramuscular injection, tylosin blood levels peak 3-4 hours post-injection.

#### Distribution, Biotransformation and Elimination:

The maximum concentration in milk of cattle and sows is 3 -6 times higher than the blood concentration about 6 hours following injection. In bovine and porcine lungs maximum tylosin concentrations of 7-8 times higher than the maximum concentrations in serum were found at 6 -24 hours following intramuscular injection.

In cattle (whether in heat or not) the Mean Residence Time (MRT) in uterus secretions of tylosin injected by intravenous route at a dose rate of 10 mg/kg was about 6 -7 times higher than the one measured in serum. This illustrates that in uterine secretions a single tylosin injection at a dose rate of 10 mg/kg during 24 hours can result in concentrations exceeding the MIC 90 of tylosin for *Arcanobacterium pyogenes*, one of the pathogens frequently isolated when metritis is diagnosed in cattle.

#### Elimination:

Tylosin is eliminated in unchanged form in bile and urine.

#### **Environmental properties**

Tylosin is persistent in some soils

## **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: 28 days

### **5.3. Special precautions for storage**

Do not store above 25 °C.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

### **5.4 Nature and composition of immediate packaging**

The veterinary medicinal product is presented in 50 ml, 100 ml or 250 ml Type II colourless glass bottles, sealed with a bromobutyl stopper and aluminium cap supplied in a carton. One bottle per carton.

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 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 N.V.

**7. MARKETING AUTHORISATION NUMBER(S)**

**8. DATE OF FIRST AUTHORISATION**

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

**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 OUTER PACKAGE****Cardboard Box****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Tylovectin 200 solution for injection

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains:

Tylosin 200 000 IU

**3. PACKAGE SIZE**

50 ml

100 ml

250 ml

**4. TARGET SPECIES**

Cattle, goats and pigs.

**5. INDICATIONS****6. ROUTES OF ADMINISTRATION**

Intramuscular or slow intravenous (cattle only) injection

**7. WITHDRAWAL PERIODS**

Withdrawal periods:

Cattle:

Meat and offal – 28 days

Milk – 108 hours

Goat:

Meat and offal – 42 days

Milk – 108 hours

Pigs:

Meat and offal – 16 days

**8. EXPIRY DATE**

Exp {mm/yyyy}

Once broached use within 28 days.

<b>9. SPECIAL STORAGE CONDITIONS</b>
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Do not store above 25 °C.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

<b>10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”</b>
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Read the package leaflet before use.

<b>11. THE WORDS “FOR ANIMAL TREATMENT ONLY”</b>
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For animal treatment only.

<b>12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”</b>
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Keep out of the sight and reach of children.

<b>13. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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Huvepharma N.V.

<b>14. MARKETING AUTHORISATION NUMBERS</b>
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<b>15. BATCH NUMBER</b>
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Lot {number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE****Bottle****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Tylovectin 200 solution for injection

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains:

Tylosin 200 000 IU

**3. TARGET SPECIES**

Cattle, goats and pigs.

**4. ROUTES OF ADMINISTRATION**

Intramuscular or slow intravenous (cattle only) injection

Read the package leaflet before use.

**5. WITHDRAWAL PERIODS**

Withdrawal periods:

Cattle:

Meat and offal – 28 days

Milk – 108 hours

Goat:

Meat and offal – 42 days

Milk – 108 hours

Pigs:

Meat and offal – 16 days

**6. EXPIRY DATE**

Exp {mm/yyyy}

Once broached use within 28 days.

**7. SPECIAL STORAGE CONDITIONS**

Do not store above 25 °C.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

**8. NAME OF THE MARKETING AUTHORISATION HOLDER**

Huvepharma N.V.

**9. BATCH NUMBER**

Lot {number}

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Tylovectin 200 solution for injection for cattle, goats and pigs

### 2. Composition

Each ml contains:

**Active substance:**

Tylosin 200 000 IU

**Excipient:**

Benzyl alcohol (E1519) 40 mg

A pale yellow to amber-coloured liquid.

### 3. Target species

Cattle, goats and pigs.

### 4. Indications for use

For the treatment of specific infections (listed below) caused by microorganisms susceptible to tylosin.

Cattle (ruminants):

-Respiratory infections, metritis caused by Gram-positive microorganisms, mastitis caused by *Streptococcus spp*, *Staphylococcus spp* and interdigital necrobacillosis, i.e. panaritium or foot rot.

Cattle (calves):

-Respiratory infections and necrobacillosis.

Pigs:

-Enzootic pneumonia, haemorrhagic enteritis, erysipelas and metritis.  
-Arthritis caused by *Mycoplasma spp*. And *Staphylococcus spp*.

Goats:

- Respiratory infections, metritis caused by Gram-positive microorganisms, mastitis caused by Gram-positive microorganisms or *Mycoplasma spp*..

### 5. Contraindications

Do not use in chickens, turkeys and horses.

Do not use in cases of hypersensitivity to the active substance, other macrolides or any of the excipients.

### 6. Special warnings

### Special precautions for safe use in the target species:

Due to likely variability (time, geographical) in susceptibility of bacteria to tylosin, bacteriological sampling and susceptibility testing are recommended. Official, national and regional antimicrobial policies should be taken into account when the veterinary medicinal product is used.

Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to tylosin and may decrease the effectiveness of treatment with other macrolide antibiotics due to the potential for cross resistance.

A high rate of *in vitro* resistance has been demonstrated in European strains of *Brachyspira hyodysenteriae* implying that the veterinary medicinal product will not be sufficiently efficacious against swine dysentery.

The efficacy data do not support the use of tylosin for the treatment of bovine mastitis caused by *Mycoplasma* spp.

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

Care should be taken to avoid accidental self-injection.

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

In the event 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.

Wash hands after use.

People with known hypersensitivity to tylosin, benzylalcohol or propylene glycol should avoid contact with the veterinary medicinal product.

Tylosin may induce irritation. Macrolides, such as 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.

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.

### Environmental properties

Tylosin is persistent in some soils.

## **7. Adverse events**

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	- Injection site swelling, injection site inflammation - Swollen vulva - Anaphylactic shock - Death
Undetermined frequency (cannot be estimated from available data)	- Hypersensitivity reaction - Injection site lesion (blemishes) <sup>1</sup>

<sup>1</sup> Can persist for up to 21 days following administration

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	<ul style="list-style-type: none"><li>- Injection site swelling, injection site inflammation</li><li>- Anaphylactic shock</li><li>- Rectal oedema (swelling)</li><li>- Erythema</li><li>- Pruritus (itching)</li><li>- Rectal prolapse (rosebudding - partial)</li><li>- Death</li></ul>
Undetermined frequency (cannot be estimated from available data)	<ul style="list-style-type: none"><li>- Hypersensitivity reaction</li><li>- Injection site lesion (blemishes) <sup>2</sup></li></ul>

<sup>2</sup> Can persist for up to 21 days following administration

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 the local representative of the marketing authorisation holder 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 intramuscular or slow intravenous (cattle only) injection

Cattle: 5000-10 000 IU tylosin/kg bodyweight per day for 3 days (2.5 to 5 ml solution for injection per 100 kg bodyweight).

Maximum injection volume per injection site should not exceed 15 ml in cattle.

Goats: 10 000 IU tylosin/kg bodyweight per day for 3 days (5 ml solution for injection per 100 kg bodyweight).

Pigs: 5000 IU to 10 000 IU of tylosin per kg bodyweight per day during 3 days, *i.e* 2.5 to 5 ml of solution per 100 kg bodyweight.

In pigs do not administer more than 5 ml per injection site.

Where repeat injections are to be administered, use different sites for each injection.

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

The closures should not be broached more than 15 times. In order to prevent excessive broaching of the stopper, a suitable multiple dosing device should be used.

## **9. Advice on correct administration**

None.

## **10. Withdrawal periods**

Cattle:

Meat and offal – 28 days



Milk – 108 hours

Goat:

Meat and offal – 42 days

Milk – 108 hours

Pigs:

Meat and offal – 16 days

## **11. Special storage precautions**

Keep out of the sight and reach of children.

Do not store above 25 °C

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging: 28 days

## **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 system. 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**

Pack sizes:

50 ml

100 ml

250 ml

Not all pack sizes may be marketed

## **15. Date on which the package leaflet was last revised**

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 reactions

Huvepharma NV  
Uitbreidingstraat 80  
2600 Antwerpen  
Belgium

Manufacturer responsible for batch release

Biovet JSC  
39 Petar Rakov Str  
4550 Peshtera  
Bulgaria

Local representatives and contact details to report suspected adverse reactions

**17. Other information**

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