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

Excipient:
Benzyl alcohol (E1519) 40 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A pale yellow to amber-coloured liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, goats and pigs.

4.2 Indications for use, specifying the target species

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

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

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 4.5.

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

4.3 Contraindications

Do not administer to chickens, turkeys or horses.
Do not use in cases of hypersensitivity to tylosin, other macrolides or any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

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 product is used

Use of the 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 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.

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

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

Care should be taken to avoid accidental self-injection.

If accidental self-injection occurs, seek medical attention immediately.

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.

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.

Do not handle the product if you are allergic to ingredients in the product.

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.

4.6 Adverse reactions (frequency and seriousness)

Hypersensivity reactions may occur.
Blemishes may occur at the site of injection and can persist for up to 21 days following administration.

In very rare cases the following have been observed:
- Swelling/inflammation at the site of injection
- Vulval swelling in cattle,
- Oedema of the rectal mucosa, partial anal protrusion (rosebudding), erythema and pruritus in pigs.
- Anaphylactic shock and death.

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

4.7 Use during pregnancy, lactation or lay

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.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

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.

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

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.

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

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

4.11 Withdrawal period(s)

Cattle:
Meat – 28 days
Milk – 108 hours

Goat:
Meat – 42 days
Milk – 108 hours

Pigs:
Meat and offal – 16 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, macrolides.
ATC vet code: QJ01FA90.

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

<u>Absorption:</u>

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

<u>Distribution, Biotransformation and Elimination:</u>

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.

5.3 Environmental properties

Tylosin is persistent in some soils

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Propylene glycol (E1520)
Water for injections

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: 28 days

6.4 Special precautions for storage

Do not store above 25 °C.
Do not freeze.
Keep the container in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

The product is presented in 50ml, 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.

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

Huvepharma N.V.
Uitbreidingstraat 80
2600 Antwerp
Belgium

8. MARKETING AUTHORISATION NUMBER

Vm 30282/4045

9. DATE OF FIRST AUTHORISATION

28 November 2018

10. DATE OF REVISION OF THE TEXT

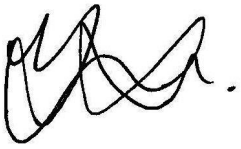
October 2020

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

Any person intending to manufacture, import, possess, sell, supply and use this veterinary medicinal product must first consult the relevant Member State's competent authority on the current vaccination policies, as these activities may be prohibited in a Member State on the whole or part of its territory pursuant to national legislation.

Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.



Approved: 20 October 2020