SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PHARMASIN 200 mg/ml solution for injection for cattle and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Tylosin 200mg/ml

Excipients:
Benzyl alcohol (E1519) 40 mg/ml.

For a 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 and pigs.

4.2 Indications for use, specifying the target species

Infections caused by microorganisms susceptible to tylosin.

Cattle (adult):
- Treatment of respiratory infections, metritis caused by Gram-positive micro-organisms, mastitis caused by *Streptococcus* spp., *Staphylococcus* spp. and interdigital necrobacillosis caused by *Fusobacterium necrophorum* i.e. panaritum or foot rot

Calves:
- Treatment of respiratory infections and necrobacillosis (calf diphtheria caused by *Fusobacterium necrophorum)*.

Pigs:
- Treatment of enzootic pneumonia caused by *Mycoplasma hyopneumoniae*, haemorrhagic enteritis (Porcine proliferative haemorrhagic enteropathy due to *Lawsonia intracellularis*), erysipelas caused by *Erysipelothrix rhusiopathiae* and metritis.

- Treatment of arthritis caused by *Mycoplasma* and *Staphylococcus* spp.

4.3 Contraindications

Do not administer to chickens or turkeys in which intramuscular injection may be fatal.
Do not administer to horses or other equines in which injection of tylosin may be fatal.
Do not administer to animals with known 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

i) Special precautions for use in animals

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
The efficacy data do not support the use of tylosin for the treatment of bovine mastitis caused by *Mycoplasma* spp.

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.
For administration by the intramuscular route only.
Use different injection sites for repeated injections.

ii) 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 should avoid contact with the veterinary medicinal 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. Care should be taken to avoid accidental self-injection. If accidental self-injection occurs, seek medical attention immediately.
Tylosin may induce irritation. Avoid skin and/or eye contact. 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.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, the following adverse reactions have been observed in animals administered tylosin at the recommended rate:

- Injection site reaction
- vulval swelling in cattle,
- Oedema of the rectal mucosa, partial anal protrusion ('rosebudding'), erythema and pruritus in pigs.
- Anaphylactic shock and death.

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

The frequency of possible adverse effects is defined using the following convention:
- very common (affects more than 1 animal in 10)
- common (affects 1 to 10 animals in 100)
- uncommon (affects 1 to 10 animals in 1,000)
- rare (affects 1 to 10 animals in 10,000)
- very rare (affects less than 1 animals in 10,000)
- not known (frequency cannot be estimated from the available data)

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

Lincosamide and aminoglycoside antibiotics can antagonise the action of tylosin.

4.9 Amounts to be administered and administration route

For intramuscular injection:
Cattle: 5-10 mg 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.

Pigs: 5-10 mg tylosin/kg bodyweight per day for 3 days (2.5 to 5 ml solution for injection per 100 kg bodyweight). In pigs do not administer more than 5 ml per injection site.
To ensure the correct dosage, bodyweight should be determined as accurately as possible to avoid under dosing.
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 periods

Pigs: Meat and offal – 16 days

Cattle: Meat and offal – 28 days
Milk – 108 hours.

5. PHARMACOLOGICAL PROPERTIES

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

5.1 Pharmacodynamic properties

Tylosin is a macrolide antibiotic and exerts its antibiotic activity by a similar mechanism to other macrolides i.e. binding to the 50S 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 (*Erysipelothrix* spp.), some Gram-negative bacilli (*Pasteurella* spp., *Mannheimia* spp.) and *Mycoplasma* spp.
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 hydrolyse 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.
Resistance of *Brachyspira hyodysenteriae* to tylosin has been reported.

5.2 Pharmacokinetic properties

Absorption: Following intramuscular injection, tylosin blood levels peak 1-2 hours post-injection. Duration of activity is approximately 12 hours.

Distribution, Biotransformation and Elimination: Tylosin levels of 1.4 to 1.6 and 2.2 to 6.7µg/ml were recorded in serum and lung tissue respectively following intramuscular injection of 8.8 mg/kg bodyweight in pigs. Measurable amounts of tylosin were still present in both serum and lung tissue at 12 hours post-injection. Tylosin concentrations were greater in lung tissue than serum at all sample times.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Propylene glycol

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 of the immediate packaging: 28 days. Discard any unused material.

6.4 Special precautions for storage

Protect from light.
Store in the original container.
Do not store above 25°C.
Do not freeze.

6.5 Nature and composition of immediate packaging

The product is presented in 50ml, 100 ml or 250 ml Type II colourless glass vials, sealed with a bromobutyl stopper and aluminium cap supplied in a carton. One vial 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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Huvepharma N.V.
Uitbreidingsstraat 80
2600 Antwerpen
Belgium

8. MARKETING AUTHORISATION NUMBER

Vm 30282/4028

9. DATE OF FIRST AUTHORISATION

16 November 2016

10. DATE OF REVISION OF THE TEXT

November 2021

Approved: 02/11/21