Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

TYLOSIN BIOVET JSC 200 mg/ml solution for injection for cattle, sheep, goats and pigs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Tylosin 200,000 IU/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, sheep, goats, 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, i.e. panaritum or foot rot.

Calves:
- Treatment of respiratory infections and necrobacillosis.

Pigs:
- Treatment of enzootic pneumonia, haemorrhagic enteritis, erysipelas and metritis.
- Treatment of arthritis caused by *Mycoplasma* and *Staphylococcus* spp.

Sheep and goats:
- Treatment of respiratory infections, metritis caused by Gram-positive microorganisms, mastitis caused by Gram-positive microorganisms or *Mycoplasma* spp.

4.3 Contraindications

Do not administer to horses. Intramuscular injection can be fatal in chickens and turkeys.
Do not use in cases of hypersensitivity to tylosin, other macrolides or to 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.
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.
Official, national and regional antimicrobial policies should be taken into account when the product is used.
The efficacy data do not support the use of tylosin for the treatment of bovine mastitis caused by *Mycoplasma* spp.
Haemorrhagic enteritis caused by *Brachyspira hyodysenteriae* must be treated with caution due to a high rate of *in vitro* resistance in European strains.
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)

Blemishes may occur at the site of injection and can persist for up to 21 days following administration.
In very rare cases the following adverse reactions have been observed; swelling/inflammation at the site of injection, vulvar swelling in cattle, oedema of the rectal mucosa, partial anal protrusion ('rosebudding'), erythema and pruritus in pigs and anaphylactic shock and death.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reactions)
- 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

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

4.8 Interaction with other medicinal products and other forms of interactions

None known.

4.9 Amounts to be administered and administration route

Intramuscular or slow intravenous injection (only in cattle)

Cattle:
5-10 mg tylosin/kg bodyweight per day during 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.

Sheep and goats:
10 mg tylosin/kg bodyweight per day during 3 days (5 ml solution for injection per 100 kg bodyweight).
For sheep over 50 kg of bodyweight, the injection should be divided over two injection sites (maximum 2.5 ml injection volume per injection site).

Pigs:
5-10 mg tylosin/kg bodyweight per day during 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.

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

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

In pigs and calves an intramuscular injection of 30 mg/kg per day during 5 consecutive days produced no adverse effects.

4.11 Withdrawal period(s)

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

Sheep and goats:
Meat and offal: 42 days.
Milk: 108 hours

Pigs:
Meat and offal: 16 days.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, macrolides, tylosin
ATCvet code: QJ01FA90

5.1 Pharmacodynamic properties

Tylosin is a macrolide antibiotic with a pKa of 7.1. Tylosin is structurally similar to erythromycin. It is produced by *Streptomyces fradiae*. Tylosin has a low solublility 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 (like *Erysipelothrix*), certain Gram-negative bacilli 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 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.

5.2 Pharmacokinetic particulars

Absorption:
Following intramuscular injection the tylosin concentration reaches its maximum at 3-4 hours following administration.

Distribution:
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.

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.

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.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

BIOVET Joint Stock Company
39, Petar Rakov Street
4550 Peshtera
Bulgaria

8 MARKETING AUTHORISATION NUMBER(S)

VPA10464/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31st May 2013
Date of latest renewal: 29th September 2017

10 DATE OF REVISION OF THE TEXT

July 2020