1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dophatyl-ject 200 000 IU/ml solution for injection for cattle, sheep, 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	

Clear yellow solution, practically free from visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, sheep, goats and pigs.

3.2 Indications for use for each target species

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. panaritium or foot rot.

Calves:
- Treatment of respiratory infections and necrobacillosis.

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

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

For information regarding swine dysentery see section 3.4.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance, other macrolides or to any of the excipients.
Do not use in animals with renal and/or liver failure.
Do not use in horses or other equines and poultry, as injection of tylosin may be fatal in these species.

Do not use in suspected cases of cross-resistance to other macrolides.

3.4 Special warnings

Cross-resistance has been shown between tylosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to macrolide antibiotics because its effectiveness may be reduced.
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.

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.
Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.
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.

The feeding of waste milk containing residues of antimicrobials to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

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

Macrolides, such as tylosin, can cause hypersensitivity (allergy) following injection, inhalation, ingestion or contact with skin or eyes. Hypersensitivity to tylosin may lead to cross reactions with other macrolides and vice versa. Benzyl alcohol and propylene glycol can also cause hypersensitivity reactions. Allergic reactions to these substances may occasionally be serious and therefore direct contact should be avoided. Do not handle the medication if you are allergic to any of the veterinary medicinal product ingredients.
If you develop symptoms following exposure, such as skin rash, seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.
The veterinary medicinal product may cause irritation to the eyes and skin.
Avoid contact with eyes and skin. If this occurs, wash the area thoroughly with water.
Care must 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.
Do not smoke, eat or drink while handling the medication.
Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle:

Common (1 to 10 animals / 100 animals treated):	Injection site inflammation[1] Injection site necrosis[1] Injection site haemorrhage[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reactions, anaphylactic shock Death Swollen vulva
Undetermined frequency (cannot be estimated from the available data)	Tachycardia Tachypnoea

[1] Can persist for up to 21 days following administration.

Pigs:

Common (1 to 10 animals / 100 animals treated):	Injection site inflammation[1] Injection site necrosis[1] Injection site haemorrhage[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reactions, anaphylactic shock Death Vulvar oedema, rectal oedema, rectal prolapse Diarrhoea Erythema, generalised itching Vaginitis Aggression
Undetermined frequency (cannot be estimated from the available data)	Tachycardia Tachypnoea

[1] Can persist for up to 21 days following administration.

Sheep and goats:

None known

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 and lactation
Studies in laboratory animals have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.
The safety of the veterinary medicinal product has not been established during pregnancy and lactation 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

None known.

3.9 Administration routes and dosage

Sheep, goats and pigs: intramuscular use
Cattle: intramuscular and intravenous use

Cattle: 5 000 – 10 000 IU tylosin/kg body weight per day for 3 days (corresponding to 2.5 to 5 ml solution for injection per 100 kg body weight). Maximum injection volume per injection site should not exceed 15 ml. Intravenous injections should be administered slowly.

Sheep, goats: 10 000 IU tylosin/kg body weight per day for 3 days (corresponding to 5 ml solution for injection per 100 kg body weight).
For sheep over 50 kg of body weight, the injection should be divided over 2 injection sites. Maximum injection volume per injection site should not exceed 2.5 ml.

Pigs: 5 000 – 10 000 IU tylosin/kg body weight per day for 3 days (corresponding to 2.5 to 5 ml solution for injection per 100 kg body weight). Maximum injection volume per injection site should not exceed 5 ml.

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

The closures should not be broached more than 20 times. In order to prevent excessive broaching 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 30 000 IU/kg body weight per day 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.

Sheep, goats:
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 of pKa 7.1. Tylosin is structurally related to erythromycin. It is produced by *Streptomyces fradiae*.
Tylosin exerts its antibiotic activity by a similar mechanism to other macrolides i.e. by binding 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, certain Gram-negative bacilli and *Mycoplasma* spp.
For mastitis in cattle, the susceptibility of *Staphylococcus* (coagulase-positive and coagulase negative), *Streptococcus uberis*, *Streptococcus dysgalactiae* towards tylosin remains high.
Susceptibility monitoring of *Mycoplasma hyopneumoniae* isolated in pigs from several EU countries resulted in MICs ranging from of ≤0.001–32 µg/mL with MIC50 of 0.016 µg/mL and MIC90 of 0.063 µg/mL. MICs follow a multimodal distribution revealing the existence of a resistant sub-population.
Resistance to macrolides can develop by mutations in genes encoding ribosomal RNA (rRNA) or some ribosomal proteins; by enzymatic modification (methylation) of the 23S rRNA target site, generally giving rise to cross-resistance with lincosamides and group B streptogramins (MLSB resistance); by enzymatic inactivation; or by macrolide efflux. MLSB resistance may be constitutive or inducible. Resistance may be chromosomal or plasmid-encoded and may be transferable if associated with transposons, plasmids, integrative and conjugative elements. Additionally, the genomic plasticity of Mycoplasma is enhanced by the horizontal transfer of large chromosomal fragments.

4.3 Pharmacokinetics

Following intramuscular injection, tylosin blood levels peak 3-4 hours post-injection.
The maximum concentration in the milk of cattle and sows is 3-6 times that of blood, about 6 hours after the injection.
6 to 24 hours after intramuscular injection, a peak tylosin concentration 7 to 8 times higher than the peak tylosin concentration in serum is observed in the lungs of cattle and pigs.
In cows, in heat or not, the mean residence time (MRT) of tylosin, injected at a dose of 10 000 IU/kg intravenously, is in the uterine secretions, approximately 6 to 7 times higher than that measured in serum.
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

Store below 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

Cardboard box with 1 colourless, type I glass vial of 50 ml or 100 ml, closed with a type I bromobutyl rubber stopper and sealed with an aluminium cap.
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

Dopharma Research B.V.

7. MARKETING AUTHORISATION NUMBER(S)

VPA10791/022/001

8. DATE OF FIRST AUTHORISATION

12/04/2024

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

24/04/2025

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).