TORXIN INJECTION
(Tulathromycin)

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

TORXIN INJECTION.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Tulathromycin ……. 100mg

3. PHARMACEUTICAL FORM

Solution for Injection.

4. CLINICAL INFORMATION

4.1. Target species

Cattle & Sheep.

4.2. Indications for use specifying the target species

Cattle:
Treatment and metaphylaxis of poor respiratory disease (BRD) associated with Mannheimia haemolytica, Pasteurella multocida, Histophilus somni and Mycoplasma bovis susceptible to tulathromycin. The presence of the disease in the group must be established before the product is used.
Treatment of infectious bovine keratoconjunctivitis (IBK) associated with Moraxella bovis susceptible to tulathromycin.

Sheep:
Treatment of the early stages of infectious pododermatitis (foot rot) associated with virulent Dichelobacter nodosus requiring systemic treatment.

4.3. Contraindications

Do not use in cases of hypersensitivity to macrolide antibiotics or to any of the excipients.

4.4. Special warnings for each target species

Cross resistance occurs with other macrolides. Do not administer simultaneously with antimicrobials with a similar mode of action such as other macrolides or lincosamides.

Sheep:
The efficacy of antimicrobial treatment of foot rot might be reduced by other factors, such as wet environmental conditions, as well as inappropriate farm management. Treatment of foot rot should therefore be undertaken along with other flock management tools, for example providing dry environment.
Antibiotic treatment of benign foot rot is not considered appropriate.
Tulathromycin showed limited efficacy in sheep with severe clinical signs or chronic foot rot, and should therefore only be given at an early stage of foot rot.

4.5. Special precautions for use

Special precautions for safe use in the target species:

Use of the 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 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.
If a hypersensitivity reaction occurs appropriate treatment should be administered without delay

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

Tulathromycin is irritating to eyes. In case of accidental eye exposure, flush the eyes immediately with clean water. Tulathromycin may cause sensitisation by skin contact resulting in e.g. reddening of the skin (erythema) and/or dermatitis.
In case of accidental spillage onto skin, wash the skin immediately with soap and water. Wash hands after use. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
If there is suspicion of a hypersensitivity reaction following accidental exposure (recognised by e.g. itching, difficulty in breathing, hives, swelling on the face, nausea, vomitus) appropriate treatment should be administered. Seek medical advice immediately and show the package leaflet or the label to the physician

4.6. Adverse reactions (frequency and seriousness)

Cattle:

Very common (>1 animal / 10 animals treated):	Injection site pain1 , swelling1 , erythema1 , oedema1 , fibrosis1 and haemorrhage1

Sheep:

Very common (>1 animal / 10 animals treated):	Discomfort (head shaking, rubbing injection site, backing away2)

1 Can persist for up to 30 days after injection
2 These signs resolve within a few minutes

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.

4.7. Use during pregnancy and lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
Use only according to the benefit/risk assessment by the responsible veterinarian.
Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.

4.8. Interaction with other veterinary medicinal products and other forms of interaction

None known.

4.9. Dosage and administration route

Cattle
Subcutaneous use.
A single subcutaneous injection of 2.5 mg tulathromycin/kg bodyweight (equivalent to 1 ml/40 kg bodyweight). For treatment of cattle over 300 kg bodyweight, divide the dose so that no more than 7.5 ml are injected at one site.

Sheep
Intramuscular use.
A single intramuscular injection of 2.5 mg tulathromycin/kg body weight (equivalent to 1 ml/40 kg body weight) in the neck. To ensure correct dosage bodyweight should be determined as accurately as possible to avoid underdosing. The cap may be safely punctured up to 30 times.

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

In cattle at dosages of three, five or ten times the recommended dose, transient signs attributed to injection site discomfort were observed and included restlessness, head-shaking, pawing the ground, and brief decrease in feed intake. Mild myocardial degeneration has been observed in cattle receiving five to six times the recommended dose

In lambs (approx. 6 weeks old), at dosages of three or five times the recommended dose, transient signs attributed to injection site discomfort were observed, and included walking backwards, head shaking, rubbing the injection site, lying down and getting up, bleating.

4.11. Restrictions and special conditions of use, including restrictions on the use of antimicrobial and antiparasitic veterinary drugs, in order to reduce the risk of resistance development

Medication administered under the control or supervision of the veterinarian

4.12. Withdrawal period:

Cattle:
Meat and offal: 22 days.

Sheep:
Meat and offal**:** 16 days.

Not authorized for use in animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 2 months of expected parturition.

5. PHARMACOLOGICAL PROPERTIES

ATCVet Code: **QJ01FA94**

5.1. Pharmacodynamics properties

Tulathromycin is a semi-synthetic macrolide antimicrobial agent, which originates from a fermentation product. It differs from many other macrolides in that it has a long duration of action that is, in part, due to its three amine groups; therefore, it has been given the chemical subclass designation of triamilide.

Macrolides are bacteriostatic acting antibiotics and inhibit essential protein biosynthesis by virtue of their selective binding to bacterial ribosomal RNA. They act by stimulating the dissociation of peptidyl-tRNA from the ribosome during the translocation process. Tulathromycin possesses in vitro activity against Mannheimia haemolytica, Pasteurella multocida, Histophilus somni and Mycoplasma bovis, and Actinobacillus pleuropneumoniae, Pasteurella multocida, Mycoplasma hyopneumonia, Haemophilus parasuis and Bordetella bronchiseptica the bacterial pathogens most commonly associated with bovine Increased minimum inhibitory concentration (MIC) values have been found in some isolates of Histophilus somni and Actinobacillus pleuropneumoniae. In vitro activity against Dichelobacter nodosus (vir), the bacterial pathogen most commonly associated with infectious pododermatitis (foot rot) in sheep has been demonstrated. Tulathromycin also possesses in vitro activity against Moraxella bovis, the bacterial pathogen most commonly associated with infectious bovine keratoconjunctivitis (IBK). The Clinical and Laboratory Standards Institute CLSI has set the clinical breakpoints for tulathromycin against M. haemolytica, P. multocida, and H. somni of bovine respiratory origin. CLSI has also published clinical breakpoints for tulathromycin based on a disk diffusion method (CLSI VET01S ED6:2023). No clinical breakpoints are available for H. parasuis. Neither EUCAST nor CLSI have developed standard methods for testing antibacterial agents against veterinary Mycoplasma species and thus no interpretative criteria have been set. 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. In addition to its antimicrobial properties, tulathromycin demonstrates immune-modulating and anti-inflammatory actions in experimental studies. In bovine polymorphonuclear cells (PMNs; neutrophils), tulathromycin promotes apoptosis (programmed cell death) and the clearance of apoptotic cells by macrophages. It lowers the production of the pro-inflammatory mediators leukotriene B4 and CXCL-8 and induces the production of anti-inflammatory and pro-resolving lipid lipoxin A4.

5.2. Pharmacokinetic information

In cattle, the pharmacokinetic profile of tulathromycin when administered as a single subcutaneous dose of 2.5 mg/kg bodyweight, was characterised by rapid and extensive absorption followed by high distribution and slow elimination. The maximum concentration (Cmax) in plasma was approximately 0.5 μg/ml; this was achieved approximately 30 minutes post-dosing (Tmax). Tulathromycin concentrations in lung homogenate were considerably higher than those in plasma. There is strong evidence of substantial accumulation of tulathromycin in neutrophils and alveolar macrophages. However, the in vivo concentration of tulathromycin at the infection site of the lung is not known. Peak concentrations were followed by a slow decline in systemic exposure with an apparent elimination half-life (t 1/2) of 90 hours in plasma. Plasma protein binding was low, approximately 40%. The volume of distribution at steady-state (Vss) determined after intravenous

administration was 11 l/kg. The bioavailability of tulathromycin after subcutaneous administration in cattle was approximately 90%. Tulathromycin concentrations in lung homogenate were considerably higher than those in plasma. There is strong evidence of substantial accumulation of tulathromycin in neutrophils and alveolar macrophages. However, the in vivo concentration of tulathromycin at the infection site of the lung is not known. Peak concentrations were followed by a slow decline in systemic exposure with an apparent elimination half-life (t 1/2) of approximately 91 hours in plasma. Plasma protein binding was low, approximately 40%. The volume of distribution at steady-state (Vss) determined after intravenous administration was 13.2 l/kg. In sheep, the pharmacokinetic profile of tulathromycin, when administered as a single intramuscular dose of 2.5 mg/kg bodyweight, achieved a maximum plasma concentration (Cmax) of 1.19 µg/ml in approximately 15 minutes (Tmax) post-dosing and had an elimination half-life (t 1/2) of 69.7 hours. Plasma protein binding was approximately 60-75%. Following intravenous dosing the volume of distribution at steady-state (Vss) was 31.7 l/kg. The bioavailability of tulathromycin after intramuscular administration in sheep was 100%.

6. PHARMACEUTICAL INFORMATION

6.1 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product should not be mixed with other veterinary medicinal products.

6.2. Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the container: use immediately in 28 days, do not store.

6.2. Special precautions for storage

Store below 25°C.
Protect from light and moisture
Keep out of the reach of children.
To be used as directed by the registered veterinary practitioner only.

6.3. Nature and composition of primary conditioning

Glass vial with a bromobutyl rubber stopper and aluminium flip of seal.
Pack sizes: 50 ml

SPECIAL PRECAUTIONS FOR THE DISPOSAL OF WASTE MATERIALS
UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS

Any unused veterinary medicinal products or waste materials derived from such medicinal products should be disposed of in accordance with local requirements and placed in appropriate collection and disposal systems for unused or expired medicinal products.

7. MARKETING AUTHORISATION HOLDER

Nawan Laboratories (Pvt.) Ltd.
Plots No. 136-138, Sector-15,
Korangi Industrial Area, Karachi-74900, Pakistan.

8. MARKETING AUTHORISATION NUMBER

Reg. No.: 088848

9. DATE OF FIRST AUTHORISATION

Date of Reg.: 06-04-2018

10. DATE OF REVISION OF THE TEXT

17-02-2025

MANUFACTURED BY:

NAWAN LABORATORIES (PVT) LTD.

136, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan.