

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

REXXOLIDE 100 mg/ml solution for injection for cattle, pigs and sheep

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

### Active substance:

Tulathromycin 100 mg

### Excipient:

Monothioglycerol 5 mg

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection.

Clear colourless to slightly yellow solution.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Cattle, pigs and sheep

### 4.2 Indications for use, specifying the target species

#### Cattle:

Treatment and metaphylaxis of bovine 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.

#### Pigs:

Treatment and metaphylaxis of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Mycoplasma hyopneumoniae*, *Haemophilus parasuis* and *Bordetella bronchiseptica* susceptible to tulathromycin. The presence of the disease in the group must be established before the product is used. The veterinary medicinal product should only be used if pigs are expected to develop the disease within 2–3 days.

#### 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 use in animals:

Use of the veterinary medicinal 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.

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 tulathromycin and may decrease the effectiveness of treatment with other macrolides, lincosamides and group B streptogramins, due to the potential for cross resistance. If a hypersensitivity reaction occurs, appropriate treatment should be administered without delay.

#### Special precautions to be taken by the person administering the veterinary medicinal 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, vomiting) 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)**

Subcutaneous administration of the veterinary medicinal product to cattle causes very commonly transient pain reactions and local swellings at the injection site that can persist for up to 30 days. No such reactions have been observed in pigs and sheep after intramuscular administration.

Pathomorphological injection site reactions (including reversible changes of congestion, oedema, fibrosis and haemorrhage) are very common for approximately 30 days after injection in cattle and pigs.

In sheep transient signs of discomfort (head shaking, rubbing injection site, backing away) are very common after intramuscular injection. These signs resolve within a few minutes.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- 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**

Laboratory studies in rats and rabbits 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. Use only according to 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**

##### 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.

##### Pigs:

Intramuscular use.

A single intramuscular injection of 2.5 mg tulathromycin/kg bodyweight (equivalent to 1 ml/40 kg bodyweight) in the neck.

For treatment of pigs over 80 kg bodyweight, divide the dose so that no more than 2 ml are injected at one site.

For any respiratory disease, it is recommended to treat animals in the early stages of the disease and to evaluate the response to treatment within 48 hours after injection. If clinical signs of respiratory disease persist or increase, or if relapse occurs, treatment should be changed, using another antibiotic, and continued until clinical signs have resolved.

##### 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. For multiple vial entry, an aspirating needle or multi-dose syringe is recommended to avoid excessive broaching of the stopper. The stopper may be safely punctured up to 25 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 young pigs weighing approximately 10 kg given three or five times the therapeutic dose transient signs attributed to injection site discomfort were observed and included excessive vocalisation and restlessness. Lameness was also observed when the hind leg was used as the injection site.

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 Withdrawal period(s)**

Cattle (meat and offal): 22 days

Pigs (meat and offal): 13 days

Sheep (meat and offal): 16 days

Not authorised 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**

Pharmacotherapeutic group: Antibacterials for systemic use, macrolides.

ATC vet code: QJ01FA94.

#### **5.1 Pharmacodynamic 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 hyopneumoniae*, *Haemophilus parasuis* and *Bordetella bronchiseptica* the bacterial pathogens most commonly associated with bovine and swine respiratory disease, respectively. 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 and *P. multocida* and *B. bronchiseptica* of swine respiratory origin, as  $\leq 16$  µg/ml susceptible and  $\geq 64$  µg/ml resistant. For *A. pleuropneumoniae* of swine respiratory origin the susceptible breakpoint is set at  $\leq 64$  µg/ml. CLSI has also published clinical breakpoints for tulathromycin based on a disk diffusion

method (CLSI document VET08, 4th ed, 2018). 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 (MLS<sub>B</sub> resistance); by enzymatic inactivation; or by macrolide efflux. MLS<sub>B</sub> 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 both bovine and porcine 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 particulars

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 ( $C_{max}$ ) in plasma was approximately 0.5 µg/ml; this was achieved approximately 30 minutes post-dosing ( $T_{max}$ ). 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 ( $V_{ss}$ ) determined after intravenous administration was 11 l/kg. The bioavailability of tulathromycin after subcutaneous administration in cattle was approximately 90%.

In pigs, the pharmacokinetic profile of tulathromycin when administered as a single intramuscular dose of 2.5 mg/kg bodyweight, was also characterised by rapid and extensive absorption followed by high distribution and slow elimination. The maximum concentration ( $C_{max}$ ) in plasma was approximately 0.6 µg/ml; this was achieved approximately 30 minutes post-dosing ( $T_{max}$ ). 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 ( $V_{ss}$ ) determined after intravenous administration was 13.2 l/kg. The bioavailability of tulathromycin after intramuscular administration in pigs was approximately 88%.

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 ( $C_{max}$ ) of 1.19 µg/ml in approximately 15 minutes ( $T_{max}$ ) 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 ( $V_{ss}$ ) was 31.7 l/kg. The bioavailability of tulathromycin after intramuscular administration in sheep was 100%.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Monothioglycerol  
Propylene glycol  
Citric acid  
Hydrochloric acid, dilute  
Sodium hydroxide (for pH adjustment)  
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**

This veterinary medicinal product does not require any special storage conditions.

## **6.5 Nature and composition of immediate packaging**

Type I clear glass vial with a fluoropolymer coated chlorobutyl stopper and an aluminium overseal.

### Pack sizes:

Cardboard box containing 1 vial of 50 ml  
Cardboard box containing 1 vial of 100 ml  
Cardboard box containing 1 vial of 250 ml.

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**

Dechra Regulatory B.V.  
Handelsweg 25  
5531 AE Bladel  
The Netherlands

## **8. MARKETING AUTHORISATION NUMBER(S)**

EU/2/20/263/001-003

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 03/12/2020

## **10 DATE OF REVISION OF THE TEXT**

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

## **PROHIBITION OF SALE, SUPPLY AND/OR USE**

Not applicable.



## **ANNEX II**

- A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. STATEMENT OF THE MRLs**
- D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

## A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Eurovet Animal Health B.V.  
Handelsweg 25  
5531 AE Bladel  
The Netherlands

## B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

## C. STATEMENT OF THE MRLs

The active substance in REXXOLIDE is an allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010:

Pharmaco- logically active substance	Marker residue	Animal species	MRL	Target tissues	Other provisions	Therapeutic classification
Tulathromycin	(2R, 3S, 4R,5R, 8R, 10R,11R, 12S, 13S,14R)-2-ethyl-3,4,10,13-tetrahydroxy-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylohexopyranosyl]oxy]-1-oxa-6-azacyclopent-de-can-15-one expressed as tulathromycin equivalents	Ovine, caprine	450 µg/kg 250 µg/kg 5400 µg/kg 1800 µg/kg	Muscle Fat Liver Kidney	Not for use in animals from which milk is produced for human consumption.	Anti-infectious agents/ Antibiotics'
		Bovine	300 µg/kg 200 µg/kg 4500 µg/kg 3000 µg/kg	Muscle Fat Liver Kidney		
		Porcine	800 µg/kg 300 µg/kg  4000 µg/kg 8000 µg/kg	Muscle Skin and fat in natural proportions Liver Kidney		

The excipients listed in section 6.1 of the SPC are allowed substances for which table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this veterinary medicinal product.

## D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Specific pharmacovigilance requirements:

PSUR submissions shall be synchronised and submitted at the same frequency as for the reference product.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**Cardboard box (50 ml / 100 ml / 250 ml)**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

REXXOLIDE 100 mg/ml solution for injection for cattle, pigs and sheep  
tulathromycin

**2. STATEMENT OF ACTIVE SUBSTANCES**

Tulathromycin 100 mg/ml

**3. PHARMACEUTICAL FORM**

Solution for injection

**4. PACKAGE SIZE**

50 ml  
100 ml  
250 ml

**5. TARGET SPECIES**

Cattle, pigs and sheep

**6. INDICATION(S)****7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Cattle: Subcutaneous use.  
Pigs and sheep: Intramuscular use.  
  
Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Withdrawal periods:  
Meat and offal:  
Cattle: 22 days.  
Pigs: 13 days.  
Sheep: 16 days.

Not authorised for use in lactating 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.

**9. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.

**10. EXPIRY DATE**

EXP {month/year}

Once broached, use within 28 days.

**11. SPECIAL STORAGE CONDITIONS**

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

Disposal: read package leaflet.

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE**

For animal treatment only. To be supplied only on veterinary prescription.

**14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”**

Keep out of the sight and reach of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Dechra Regulatory B.V.  
Handelsweg 25  
5531 AE Bladel  
The Netherlands

**16. MARKETING AUTHORISATION NUMBER(S)**

EU/2/20/263/001 (50 ml)  
EU/2/20/263/002 (100 ml)  
EU/2/20/263/003 (250 ml)

**17. MANUFACTURER’S BATCH NUMBER**

Lot

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

Vial (glass - 100 ml / 250 ml)

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

REXXOLIDE 100 mg/ml solution for injection for cattle, pigs and sheep  
tulathromycin

**2. STATEMENT OF ACTIVE SUBSTANCES**

Tulathromycin 100 mg/ml

**3. PHARMACEUTICAL FORM**

Solution for injection

**4. PACKAGE SIZE**

100 ml

250 ml

**5. TARGET SPECIES**

Cattle, pigs and sheep

**6. INDICATION(S)****7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Cattle: SC.  
Pigs and sheep: IM.  
Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Withdrawal periods:  
Meat and offal:  
Cattle: 22 days.  
Pigs: 13 days.  
Sheep: 16 days.



Not authorised for use in lactating 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.

**9. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.

**10. EXPIRY DATE**

EXP

Once broached, use within 28 days.

**11. SPECIAL STORAGE CONDITIONS**

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE**

For animal treatment only. To be supplied only on veterinary prescription.

**14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”**

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Dechra Regulatory B.V.  
Handelsweg 25  
5531 AE Bladel  
The Netherlands

**16. MARKETING AUTHORISATION NUMBER(S)**

EU/2/20/263/002 (100 ml)  
EU/2/20/263/003 (250 ml)

**17. MANUFACTURER'S BATCH NUMBER**

Lot

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS****Vial (glass - 50 ml)****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

REXXOLIDE 100 mg/ml solution for injection for cattle, pigs and sheep  
tulathromycin

**2. QUANTITY OF THE ACTIVE SUBSTANCE(S)**

Tulathromycin 100 mg/ml

**3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES**

50 ml

**4. ROUTE(S) OF ADMINISTRATION**

Cattle: SC.  
Pigs and sheep: IM.

**5. WITHDRAWAL PERIOD(S)**

Withdrawal periods:

Meat and offal:

Cattle: 22 days.

Pigs: 13 days.

Sheep: 16 days.

Not authorised for use in lactating animals producing milk for human consumption.

**6. BATCH NUMBER**

Lot

**7. EXPIRY DATE**

EXP

Once broached use within 28 days.

**8. THE WORDS “FOR ANIMAL TREATMENT ONLY”**

For animal treatment only.

## **B. PACKAGE LEAFLET**

**PACKAGE LEAFLET:**  
**REXXOLIDE 100 mg/ml solution for injection for cattle, pigs and sheep**

**1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT**

Marketing authorisation holder:

Dechra Regulatory B.V.  
Handelsweg 25  
5531 AE Bladel  
The Netherlands

Manufacturer responsible for batch release:

Eurovet Animal Health B.V.  
Handelsweg 25  
5531 AE Bladel  
The Netherlands

**2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

REXXOLIDE 100 mg/ml solution for injection for cattle, pigs and sheep  
Tulathromycin

**3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)**

Each ml contains:

**Active substance:**

Tulathromycin 100 mg

**Excipients:**

Monothioglycerol 5 mg

Clear colourless to slightly yellow solution for injection.

**4. INDICATIONS**

Cattle:

Treatment and metaphylaxis of bovine respiratory disease 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.

Pigs:

Treatment and metaphylaxis of swine respiratory disease associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Mycoplasma hyopneumoniae*, *Haemophilus parasuis* and *Bordetella bronchiseptica* susceptible to tulathromycin. The presence of the disease in the group must be established before the product is used. The veterinary medicinal product should only be used if pigs are expected to develop the disease within 2–3 days.

Sheep:

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

## **5. CONTRAINDICATIONS**

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

## **6. ADVERSE REACTIONS**

Subcutaneous administration of the veterinary medicinal product to cattle causes very commonly transient pain reactions and local swellings at the injection site that can persist for up to 30 days. No such reactions have been observed in pigs and sheep after intramuscular administration.

Pathomorphological injection site reactions (including reversible changes of congestion, oedema, fibrosis and haemorrhage) are very common for approximately 30 days after injection in cattle and pigs.

In sheep, transient signs of discomfort (head shaking, rubbing injection site, backing away) are very common after intramuscular injection. These signs resolve within a few minutes.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- 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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

## **7. TARGET SPECIES**

Cattle, pigs and sheep

## **8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION**

### Cattle:

2.5 mg tulathromycin/kg bodyweight (equivalent to 1 ml/40 kg bodyweight).

A single subcutaneous injection. For treatment of cattle over 300 kg bodyweight, divide the dose so that no more than 7.5 ml are injected at one site.

### Pigs:

2.5 mg tulathromycin/kg bodyweight (equivalent to 1 ml/40 kg bodyweight).

A single intramuscular injection in the neck. For treatment of pigs over 80 kg bodyweight, divide the dose so that no more than 2 ml are injected at one site.

### Sheep:

2.5 mg tulathromycin/kg bodyweight (equivalent to 1 ml/40 kg bodyweight).

A single intramuscular injection in the neck.

## **9. ADVICE ON CORRECT ADMINISTRATION**

For any respiratory disease, it is recommended to treat animals in the early stages of the disease and to evaluate the response to treatment within 48 hours after injection. If clinical signs of respiratory disease persist or increase, or if relapse occurs, treatment should be changed, using another antibiotic, and continued until clinical signs have resolved.

To ensure correct dosage bodyweight should be determined as accurately as possible to avoid underdosing. For multiple vial entry, an aspirating needle or multi-dose syringe is recommended to avoid excessive broaching of the stopper. The stopper may be safely punctured up to 25 times.

## **10. WITHDRAWAL PERIOD(S)**

Cattle (meat and offal): 22 days.

Pigs (meat and offal): 13 days.

Sheep (meat and offal): 16 days.

Not authorised for use in lactating 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.

## **11. SPECIAL STORAGE PRECAUTIONS**

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP.

Shelf life after first opening the container: 28 days.

## **12. SPECIAL WARNING(S)**

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.

Special precautions for use in animals:

Use of the veterinary medicinal 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. 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 package leaflet may increase the prevalence of bacteria resistant to tulathromycin and may decrease the effectiveness of treatment with other macrolides, lincosamides and group B streptogramins, due to the potential for cross resistance.

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

Special precautions to be taken by the person administering the veterinary medicinal 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, vomiting) appropriate treatment should be administered. Seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy and lactation:

Laboratory studies in rats and rabbits 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. Use only according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

None known.

Overdose (symptoms, emergency procedures, antidotes):

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 young pigs weighing approximately 10 kg given three or five times the therapeutic dose transient signs attributed to injection site discomfort were observed and included excessive vocalisation and restlessness. Lameness was also observed when the hind leg was used as the injection site.

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.

Incompatibilities:

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

**13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY**

Medicines should not be disposed of via wastewater or household waste.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

**14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

**15. OTHER INFORMATION**



Pack sizes:

Cardboard box containing 1 vial of 50 ml.

Cardboard box containing 1 vial of 100 ml.

Cardboard box containing 1 vial of 250 ml.

Not all pack sizes may be marketed.