

*[Version 8.2,01/2021]*

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Troxzan 25 mg/ml solution for injection for pigs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

### Active substance:

Tulathromycin .....25 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, free from visible particles.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Pigs

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

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.

### 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.

### 4.5 Special precautions for use

#### 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.

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)**

Pathomorphological injection site reactions (including reversible changes of congestion, oedema, fibrosis and haemorrhage) are present for approximately 30 days after injection.

#### **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**

Intramuscular use.

A single intramuscular injection of 2.5 mg tulathromycin/kg bodyweight (equivalent to 1 ml/10 kg bodyweight) in the neck.

For treatment of pigs over 40 kg bodyweight, divide the dose so that no more than 4 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.

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 cap may be safely punctured up to 25 times.

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

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.

#### **4.11 Withdrawal period(s)**

Meat and offal: 13 days.

### **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 *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Mycoplasma hyopneumoniae*, *Haemophilus parasuis* and *Bordetella bronchiseptica* the bacterial pathogens most commonly associated with swine respiratory disease. Increased minimum inhibitory concentration (MIC) values have been found in some isolates of *Actinobacillus pleuropneumoniae*.

The Clinical and Laboratory Standards Institute CLSI has set the clinical breakpoints for tulathromycin against *P. multocida* and *B. bronchiseptica* of swine respiratory origin, as  $\leq 16$   $\mu\text{g/ml}$  susceptible and  $\geq 64$   $\mu\text{g/ml}$  resistant. For *A. pleuropneumoniae* of swine respiratory origin the susceptible breakpoint is set as  $\leq 64$   $\mu\text{g/ml}$ . CLSI has also published clinical breakpoints for tulathromycin based on a disk diffusion method (CLSI document VET08, 4<sup>th</sup> ed, 2018). No clinical breakpoints have been set 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 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 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%.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Monothioglycerol  
Propylene glycol  
Citric acid  
Hydrochloric acid dilute (for pH adjustment)  
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: 30 months  
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 colourless glass vials with bromobutyl rubber stopper covered with a fluorinated polymer coating and sealed with aluminium cap.

Pack sizes:  
Cardboard box with 1 vial of 100 ml

### **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**

Laboratorios Syva, S.A.U.  
Avda. Párroco Pablo Díez, 49-57  
(24010) Trobajo del Camino – León  
Spain

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

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

Date of first authorisation:

**10. DATE OF REVISION OF THE TEXT**

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

Not applicable.

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

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

Cardboard box (100 ml)

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

Troxzan 25 mg/ml solution for injection for pigs  
Tulathromycin

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains:  
Tulathromycin ..... 25 mg

**3. PHARMACEUTICAL FORM**

Solution for injection

**4. PACKAGE SIZE**

100ml

**5. TARGET SPECIES**

Pigs

**6. INDICATION(S)**

**7. METHOD AND ROUTES OF ADMINISTRATION**

For intramuscular use.  
Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Withdrawal periods:  
Meat and offal: 13 days.

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

Read the package leaflet before use.

**10. EXPIRY DATE**

EXP {month/year}

Once opened, use within 28 days

Once opened use by:

**11. SPECIAL STORAGE CONDITIONS**

**12. SPECIFIC 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**

Laboratorios Syva, S.A.U.  
Avda. Párroco Pablo Díez, 49-57  
(24010) Trobajo del Camino – León  
Spain

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

**17. MANUFACTURER’S BATCH NUMBER**

Batch {number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

Glass vial (100 ml)

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

Troxzan 25 mg/ml solution for injection for pigs  
Tulathromycin

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains:  
Tulathromycin ..... 25 mg

**3. PHARMACEUTICAL FORM**

Solution for injection

**4. PACKAGE SIZE**

100ml

**5. TARGET SPECIES**

Pigs

**6. INDICATION(S)**

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

For intramuscular use.  
Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Withdrawal periods:  
Meat and offal: 13 days.

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

Read the package leaflet before use.

**10. EXPIRY DATE**

EXP {month/year}

Once opened, use within 28 days

Once opened use by:

**11. SPECIAL STORAGE CONDITIONS**

**12. SPECIFIC 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**

Laboratorios Syva, S.A.U.  
Avda. Párroco Pablo Díez, 49-57  
(24010) Trobajo del Camino – León  
Spain

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

**17. MANUFACTURER’S BATCH NUMBER**

Batch {number}

**B. PACKAGE LEAFLET**

**PACKAGE LEAFLET:  
TROXXAN 25 mg/ml solution for injection for pigs**

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

Marketing authorisation holder and manufacturer responsible for batch release:

Laboratorios Syva, S.A.U.  
Avda. Párroco Pablo Díez, 49-57  
(24010) Trobajo del Camino – León  
Spain

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

Troxzan 25 mg/ml solution for injection for pigs  
Tulathromycin

**3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS**

Each ml contains:

**Active substance:**

Tulathromycin ..... 25 mg

**Excipients:**

Monothioglycerol ..... 5 mg

Clear colourless to slightly yellow solution, free from visible particles.

**4. INDICATION(S)**

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.

**5. CONTRAINDICATIONS**

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

**6. ADVERSE REACTIONS**

Pathomorphological injection site reactions (including reversible changes of congestion, oedema, fibrosis and haemorrhage) are present for approximately 30 days after injection.

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.

Alternatively you can report via your national reporting system {national system details}.

## **7. TARGET SPECIES**

Pigs

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

Intramuscular use.

A single intramuscular injection of 2.5 mg tulathromycin/kg bodyweight (equivalent to 1 ml/10 kg bodyweight) in the neck.

For treatment of pigs over 40 kg bodyweight, divide the dose so that no more than 4 ml are injected at one site.

The cap may be safely punctured up to 25 times.

## **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.

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

Meat and offal: 13 days.

## **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. The expiry date refers to the last day of that month.

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.

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

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.

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 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.

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**

MM/YYYY

**15. OTHER INFORMATION**

**Pack sizes:**

Cardboard box with 1 vial of 100 ml.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.