

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tullavis 25 mg/ml solution for injection for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Tulathromycin 25 mg

Excipients:

| Qualitative composition of excipients and other constituents | Quantitative composition if that information is essential for proper administration of the veterinary medicinal product |
|--|---|
| Monothioglycerol | 5 mg |
| Propylene glycol | |
| Citric acid | |
| Hydrochloric acid (for pH adjustment) | |
| Sodium hydroxide (for pH adjustment) | |
| Water for injections | |

Clear colourless to yellowish solution.

3. CLINICAL INFORMATION

3.1 Target species

Pigs.

3.2 Indications for use for each 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.

3.3 Contraindications

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

3.4 Special warnings

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

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 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 veterinary medicinal product is used.

Use of the veterinary medicinal 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. 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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Pigs:

| | |
|--|--|
| Very common (>1 animal / 10 animals treated): | Injection site reaction ^{1,2} , Injection site fibrosis ¹ , Injection site haemorrhage ¹ , Injection site oedema ¹ |
|--|--|

¹ Can persist for approximately 30 days after injection.

² Reversible changes of congestion.

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:

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.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

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.

The cap may be safely punctured up to 100 times. For multiple vial entry, an aspirating needle or multi-dose syringe is recommended to avoid excessive broaching of the stopper.

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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.

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

Meat and offal: 13 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code :

QJ01FA94

4.2 Pharmacodynamics

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 triamillide.

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 ≤ 16 µg/ml susceptible and ≥ 64 µg/ml resistant. For *A. pleuropneumoniae* of swine respiratory origin the susceptible breakpoint is set at ≤ 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 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_B resistance); by enzymatic inactivation; or by macrolide efflux. MLS_B 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.

4.3 Pharmacokinetics

In pigs, the pharmacokinetic profile of tulathromycin when administered as a single intramuscular 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 0.6 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%.

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: 3 years.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Do not store above 30 °C.

5.4 Nature and composition of immediate packaging

Clear glass (Type II Ph. Eur.) vials closed with a bromobutyl rubber stopper and sealed with an aluminium cap.

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.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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

LIVISTO Int'l, S.L.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/YYYY}

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) (<https://medicines.health.europa.eu/veterinary>).

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

Tullavis 25 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Tulathromycin 25 mg/ml

3. PACKAGE SIZE

50 ml

100 ml

250 ml

4. TARGET SPECIES

Pigs

5. INDICATIONS**6. ROUTES OF ADMINISTRATION**

Intramuscular use.

7. WITHDRAWAL PERIODS

Withdrawal periods:

Meat and offal: 13 days.

8. EXPIRY DATE

Exp. {mm/yyyy}Once broached use within 28 days.

Once broached use by:

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

LIVISTO Int'l, S.L.

14. MARKETING AUTHORISATION NUMBERS**15. BATCH NUMBER**

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vial (100 ml / 250 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tullavis 25 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Tulathromycin 25 mg/ml

3. TARGET SPECIES

Pigs

4. ROUTES OF ADMINISTRATION

i.m.

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal periods:

Meat and offal: 13 days.

6. EXPIRY DATE

Exp. {mm/yyyy}Once broached use within 28 days.

Once broached use by:

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

LIVISTO Int'l, S.L.

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial (50 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tullavis Pigs

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Tulathromycin 25 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use by:

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Tullavis 25 mg/ml solution for injection for pigs

2. Composition

Each ml contains:

Active substances:

Tulathromycin 25 mg

Excipients:

Monothioglycerol 5 mg

Clear colourless to yellowish solution.

3. Target species

Pigs.

4. Indications for use

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 the active substance, macrolide antibiotics or to any of the excipients.

6. Special warnings

Special warnings:

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 safe use in the target species:

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 veterinary medicinal product is used.

Use of the veterinary medicinal 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. 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.

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.

Overdose:

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.

Major incompatibilities:

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

7. Adverse events

Pigs:

Very common (>1 animal / 10 animals treated):

Injection site reaction^{1,2}, Injection site fibrosis (scarring)¹, Injection site haemorrhage¹, Injection site oedema¹

¹ Can persist for approximately 30 days after injection.

² Reversible changes of congestion.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or its local representative using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

Intramuscular use (i.m.).

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.

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. The cap may be safely punctured up to 100 times. For multiple vial entry, an aspirating needle or multi-dose syringe is recommended to avoid excessive broaching of the stopper.

10. Withdrawal periods

Meat and offal: 13 days.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 30 °C.

Shelf life after first opening the immediate packaging: 28 days.

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.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

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.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the [Union Product Database](https://medicines.health.europa.eu/veterinary) (<https://medicines.health.europa.eu/veterinary>).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse events:

LIVISTO Int'l, S.L.
Av. Universitat Autònoma, 29
08290 Cerdanyola del Vallès (Barcelona)
Spain
Tel.: +34 934 706 270

Manufacturer responsible for batch release:

aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell
Germany

aniMedica Herstellungs GmbH
Im Südfeld 9
48308 Senden-Bösensell
Germany

Industrial Veterinaria, S.A.
Esmeralda, 19
08950 Esplugues de Llobregat (Barcelona)
Spain

Local representatives and contact details to report suspected adverse events: