

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. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

(UK only) Norbrook Laboratories Ltd
Station Works
Newry
Co. Down
BT35 6JP

(Rest of EU) Norbrook Laboratories (Ireland) Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

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

Pharmacologically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions	Therapeutic classification
Tulathromycin	(2R, 3S, 4R, 5R, 8R, 10R, 11R, 12S, 13S, 14R)-2-ethyl-3,4,10,13-tetrahydro-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylohexopyranosyl]oxy]-1-oxa-6-azacyclopentadecan-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.	Antiinfectious 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 4 000 µg/kg 8 000 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:

The periodic safety update report (PSUR) cycle should be restarted for submission of 6 monthly reports (covering all authorised presentations of the product) for the next two years, followed by yearly reports for the subsequent two years and thereafter at 3 yearly intervals.

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

Tulieve 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: For subcutaneous use.
Pigs and sheep: For 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

Shelf life after first opening the container: 28 days.

11. SPECIAL STORAGE CONDITIONS

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

HDPE vials: Do not store above 30°C.

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

(UK only) Norbrook Laboratories Ltd
Station Works
Newry
Co. Down
BT35 6JP

(Rest of EU) Norbrook Laboratories (Ireland) Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

Vm 02000/4441

17. MANUFACTURER'S BATCH NUMBER

Lot

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box (500ml, 1000ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tulieve 100 mg/ml solution for injection for cattle
Tulathromycin

2. STATEMENT OF ACTIVE SUBSTANCES

Tulathromycin 100 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

500 ml
1000 ml

5. TARGET SPECIES

Cattle

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period:
Meat and offal: 22 days.

Not authorised for use in lactating cattle producing milk for human consumption.
Do not use in pregnant cows or heifers, 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

Shelf life after first opening the container: 28 days.

11. SPECIAL STORAGE CONDITIONS

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

HDPE vials: Do not store above 30°C.

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

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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

(UK only) Norbrook Laboratories Ltd
Station Works
Newry
Co. Down
BT35 6JP

(Rest of EU) Norbrook Laboratories (Ireland) Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

Vm 02000/4441

17. MANUFACTURER'S BATCH NUMBER

Lot

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vial (100 ml / 250 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tulieve 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

Shelf life after first opening the container: 28 days.

Once broached use by

11. SPECIAL STORAGE CONDITIONS

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

HDPE vials: Do not store above 30°C.

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

(UK only) Norbrook Laboratories Ltd
Station Works
Newry
Co. Down
BT35 6JP

(Rest of EU) Norbrook Laboratories (Ireland) Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

Vm 02000/4441

17. MANUFACTURER'S BATCH NUMBER

Lot

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vial (500 ml/1000ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tulieve 100 mg/ml solution for injection for cattle
Tulathromycin

2. STATEMENT OF ACTIVE SUBSTANCES

Tulathromycin 100 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

500 ml
1000 ml

5. TARGET SPECIES

Cattle

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period:

Meat and offal: 22 days.

Not authorised for use in lactating cattle producing milk for human consumption. Do not use in pregnant cows or heifers, 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

Shelf life after first opening the container: 28 days.

Once broached use by

11. SPECIAL STORAGE CONDITIONS

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

HDPE vials: Do not store above 30°C.

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

(UK only) Norbrook Laboratories Ltd
Station Works
Newry
Co. Down
BT35 6JP

(Rest of EU) Norbrook Laboratories (Ireland) Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

Vm 02000/4441

17. MANUFACTURER'S BATCH NUMBER

Lot

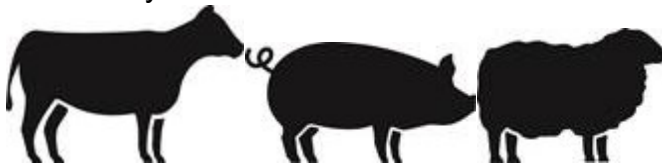
MIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial (50 ml)

Vial (50 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tulieve 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 by

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

Tulieve 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:

(UK only) Norbrook Laboratories Limited
Station Works
Camlough Road
Newry
Co. Down
BT35 6JP
Northern Ireland

(Rest of EU) Norbrook Laboratories (Ireland) Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

Manufacturer Responsible for Batch Release:

Norbrook Laboratories Ltd
Station Works
Newry
Co. Down
BT35 6JP

Norbrook Manufacturing Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

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

1 ml contains:

Active substance:

Tulathromycin 100 mg

Excipients:

Citric Acid (E330) 19.2 mg
Monothioglycerol 5 mg

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 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. Do not use simultaneously with other macrolides or lincosamides.

6. ADVERSE REACTIONS

Subcutaneous administration of the 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 (treatment and metaphylaxis)

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

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)

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.

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

HDPE vials: Do not store above 30°C.

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 sheep:

The efficacy of antimicrobial treatment of foot rot might be reduced by others 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. The product 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 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 the tulathromycin and may decrease the effectiveness of treatment with other macrolides, lincosamides and group B streptogramins due to the potential for cross resistance (MLS_B resistance).

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 skin irritation or sensitisation by skin contact. In case of accidental spillage onto skin, wash the skin immediately with soap and water.

This product may cause hypersensitivity (allergy) reactions. People with known hypersensitivity to tulathromycin should avoid contact with the product.

Wash hands after use.

Accidental self-injection may cause pain reactions and local swellings which can persist for several days. Take care to avoid self-injection. 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.

Interaction with other medicinal products and other forms of interaction:

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

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 5 to 6 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

Dispose of waste material in accordance with local requirements or ask your veterinary surgeon 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

15. OTHER INFORMATION

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).

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 or plasmids.

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.

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%.

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

Cardboard box containing 1 vial of 500 ml
Cardboard box containing 1 vial of 1 L.

The 1L vials are only available in HDPE.

The 500 ml and 1000 ml vials must not be used for pigs or sheep.

Not all pack sizes may be marketed.

Approved 16 April 2020

