

INCREXXA 25- tulathromycin injection

Elanco US Inc.

Elanco™ **Increxxa™ 25** **(tulathromycin injection)**

Injectable Solution **Antibiotic**

25 mg of tulathromycin/mL

For use in suckling calves, dairy calves, veal calves, and swine. Not for use in ruminating cattle.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION

Increxxa 25 Injectable Solution is a ready-to-use sterile parenteral preparation containing tulathromycin, a semi-synthetic macrolide antibiotic of the subclass triamillide. Each mL of Increxxa 25 contains 25 mg of tulathromycin as the free base in a 50% propylene glycol vehicle, monothioglycerol (5 mg/mL), citric acid (4.8 mg/mL) with hydrochloric acid and sodium hydroxide added to adjust pH. Increxxa 25 consists of an equilibrated mixture of two isomeric forms of tulathromycin in a 9:1 ratio.

The chemical names of the isomers are (2R,3S,4R,5R,8R,10R,11R,12S,13S, 14R)-13-[[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino) methyl] - α -L-ribohexopyranosyl]oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14- hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)- β -D-xylo-hexopyranosyl]- oxy]-1-oxa-6-azacyclopentadecan-15-one and (2R,3R,6R,8R,9R,10S,11S, 12R)-11-[[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino)methyl]- α -L-ribohexopyranosyl]oxy]-2-[(1R,2R)-1,2-dihydroxy-1-methylbutyl]-8- hydroxy-3,6,8,10,12-pentamethyl-9-[[3,4,6-trideoxy-3-(dimethylamino)- β -D-xylo-hexopyranosyl]oxy]-1-oxa-4-azacyclotridecan-13-one, respectively.

INDICATIONS

Swine

Increxxa 25 Injectable Solution is indicated for the treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Bordetella bronchiseptica*, *Haemophilus parasuis*, and *Mycoplasma hyopneumoniae*; and for the control of SRD associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, and *Mycoplasma hyopneumoniae* in groups of pigs where SRD has been diagnosed.

Suckling Calves, Dairy Calves, and Veal Calves

BRD - Increxxa 25 Injectable Solution is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*.

DOSAGE AND ADMINISTRATION

Swine

Inject intramuscularly as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) Body Weight (BW). Do not inject more than 4 mL per injection site.

Table 1. Increxxa 25 Swine Dosing Guide (25 mg/mL)

Animal Weight (Pounds)	Dose Volume (mL)
4	0.2
10	0.5
15	0.7
20	0.9
22	1.0
25	1.1
30	1.4
50	2.3
70	3.2
90	4.0

Calves

Inject subcutaneously as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) BW. Do not inject more than 11.5 mL per injection site.

Table 2. Increxxa 25 Calf Dosing Guide (25mg/mL)

Animal Weight (Pounds)	Dose Volume (mL)
50	2.3
75	3.4
100	4.5
150	7.0
200	9.0
250	11.5

CONTRAINDICATIONS

The use of Increxxa 25 Injectable Solution is contraindicated in animals previously found to be hypersensitive to the drug.

WARNINGS

FOR USE IN ANIMALS ONLY.

NOT FOR HUMAN USE.

KEEP OUT OF REACH OF CHILDREN.

NOT FOR USE IN CHICKENS OR TURKEYS.

RESIDUE WARNINGS

Swine

Swine intended for human consumption must not be slaughtered within 5 days from the last treatment.

Calves

Calves intended for human consumption must not be slaughtered within 22 days from the last treatment with Increxxa 25 Injectable Solution. This drug is not for use in ruminating cattle.

PRECAUTIONS

Swine

The effects of tulathromycin injection 25 mg/mL on porcine reproductive performance, pregnancy, and lactation have not been determined. Intramuscular injection can cause a transient local tissue reaction that may result in trim loss of edible tissue at slaughter.

Cattle

The effects of tulathromycin injection 25 mg/mL on bovine reproductive performance, pregnancy, and lactation have not been determined. Subcutaneous injection can cause a transient local tissue reaction that may result in trim loss of edible tissue at slaughter.

ADVERSE REACTIONS

Swine

In one field study, one out of 40 pigs treated with tulathromycin injection 100 mg/mL at 2.5 mg/kg BW exhibited mild salivation that resolved in less than four hours.

Calves

In one BRD field study, two calves treated with tulathromycin injection 100 mg/mL at 2.5 mg/kg BW exhibited transient hypersalivation. One of these calves also exhibited transient dyspnea, which may have been related to pneumonia.

Post Approval Experience

The following adverse events are based on post approval adverse drug experience reporting for tulathromycin injection 100 mg/mL. Not all adverse events are reported to the FDA CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of reporting frequency in cattle: Injection site reactions and anaphylaxis/anaphylactoid reactions. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDAVETS or <http://www.fda.gov/reportanimalae>.

CLINICAL PHARMACOLOGY

At physiological pH, tulathromycin (a weak base) is approximately 50 times more soluble in hydrophilic than lipophilic media. This solubility profile is consistent with the extracellular pathogen activity typically associated with the macrolides.¹ Markedly higher tulathromycin concentrations are observed in the lung parenchyma as compared to the plasma, and these elevated concentrations can remain in lung tissue for several days beyond that which can be measured in the plasma. However the clinical relevance of these elevated lung concentrations is undetermined.

As a class, macrolides tend to be primarily bacteriostatic, but may be bactericidal against some pathogens.² When acting as a cidal compound, they tend to exhibit concentration independent killing; the rate of bacterial eradication does not change once serum drug concentrations reach 2 to 3 times the minimum inhibitory concentration (MIC) of the targeted pathogen. Under these conditions, the time that serum concentrations remain above the MIC becomes the major determinant of antimicrobial activity.

Macrolides also exhibit a post-antibiotic effect (PAE), the duration of which tends to be both drug and pathogen dependent. In general, by increasing the macrolide concentration and the exposure time, the PAE will increase to some maximal duration.³ Tulathromycin is eliminated from the body primarily unchanged via biliary excretion.

¹ Carbon, C. 1998. *Pharmacodynamics of Macrolides, Azalides, and Streptogramins: Effect on Extracellular Pathogens. Clin. Infect. Dis., 27:28-32.*

² Nightingale, C.J. 1997. *Pharmacokinetics and Pharmacodynamics of Newer Macrolides. Pediatr. Infect. Dis. J., 16:438-443.*

³ Andes D, Anon J, Jacobs MR, Craig WA. (2004). *Application of pharmacokinetics and pharmacodynamics to antimicrobial therapy of respiratory tract infections. Clin Lab Med., 24:477-502.*

Swine

Following intramuscular (IM) administration to feeder pigs at a dosage of 2.5 mg/kg BW, tulathromycin is nearly completely absorbed, with peak plasma concentrations achieved within ~0.25 hr. The volume of distribution exceeds 15 L/kg, which is consistent with extensive tissue binding.

This large distribution volume results in a long terminal elimination half-life (60 to 90 hours) despite a rapid systemic free drug clearance (187 mL/kg/hr). There are no gender differences in swine tulathromycin pharmacokinetics.

Comparative Bioavailability Summary

Despite slightly lower peak concentrations with tulathromycin injection 25 mg/mL, a single IM dose of 2.5 mg tulathromycin/kg BW of either tulathromycin injection 100 mg/mL or tulathromycin injection 25 mg/mL resulted in comparable tulathromycin total systemic exposure.

Therefore, tulathromycin injection 25 mg/mL is to be considered therapeutically equivalent to tulathromycin injection 100 mg/mL when administered to swine by IM injection at a dose of 2.5 mg tulathromycin/kg BW.

Calves

Following subcutaneous (SC) administration into the neck of feeder calves at a dosage

of 2.5 mg/kg BW, tulathromycin is nearly completely absorbed, with peak plasma concentrations achieved within ~0.25 hr. The volume of distribution exceeds 11 L/kg⁴, which is consistent with extensive tissue binding. This large distribution volume results in a long terminal elimination half-life of more than 100 hours, despite a rapid systemic free drug clearance (170 mL/kg/hr). No pharmacokinetic differences are observed in castrated male versus female calves.

Comparative Bioavailability Summary

Despite slightly lower peak concentrations with tulathromycin injection 25 mg/mL, a single SC dose of 2.5 mg tulathromycin/kg BW of either tulathromycin injection 100 mg/mL or tulathromycin injection 25 mg/mL resulted in comparable total systematic tulathromycin exposure.

Therefore, tulathromycin injection 25 mg/mL is considered therapeutically equivalent to tulathromycin injection 100 mg/mL when administered to calves by SC injection at a dose of 2.5 mg tulathromycin/kg BW.

⁴ Clearance and volume estimates are based on intersubject comparisons of 2.5 mg/kg BW administered by either subcutaneous or intravenous injection.

MICROBIOLOGY

Swine

Tulathromycin has demonstrated *in vitro* activity against *A. pleuropneumoniae*, *P. multocida*, *B. bronchiseptica*, *H. parasuis*, and *M. hyopneumoniae*. The MICs of tulathromycin against indicated pathogens collected from field studies were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLSI, M31-A and M31-A3). MICs for *H. parasuis* were determined using Veterinary Fastidious Medium and were incubated up to 48 hours at 35 to 37°C in a CO₂-enriched atmosphere. These values are represented in Table 3, below.

Table 3. Tulathromycin minimum inhibitory concentration (MIC) values* for indicated pathogens isolated from field studies evaluating SRD in the U.S. and Canada.

Indicated Pathogen	Date Isolated	No. of Isolates	MIC ₅₀ ** (µg/mL)	MIC ₉₀ ** (µg/mL)	MIC Range (µg/mL)
<i>Actinobacillus pleuropneumoniae</i>	2000-2002	135	16	32	16 to 32
	2007-2008	88	16	16	4 to 32
<i>Haemophilus parasuis</i>	2000-2002	31	1	2	0.25 to > 64
<i>Pasteurella multocida</i>	2000-2002	55	1	2	0.5 to > 64
	2007-2008	40	1	2	≤ 0.03 to 2
<i>Bordetella bronchiseptica</i>	2000-2002	42	4	8	2 to 8

* The correlation between *in vitro* susceptibility data and clinical effectiveness is unknown.

** The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

Calves

Tulathromycin has demonstrated *in vitro* activity against *M. haemolytica*, *P. multocida*, *H. somni*, and *M. bovis*, four pathogens associated with BRD. The MICs of tulathromycin against indicated pathogens collected from field studies using tulathromycin injection 100 mg/mL were determined using methods recommended by the CLSI (M31-A2). These values are represented in Table 4, below.

Table 4. Tulathromycin minimum inhibitory concentration (MIC) values* for indicated pathogens isolated from field studies evaluating BRD in the U.S.

Indicated Pathogen	Date Isolated	No. of Isolates	MIC ₅₀ ** (µg/mL)	MIC ₉₀ ** (µg/mL)	MIC Range (µg/mL)
<i>Mannheimia haemolytica</i>	1999	642	2	2	0.5 to 64
<i>Pasteurella multocida</i>	1999	221	0.5	1	0.25 to 64
<i>Histophilus somni</i>	1999	36	4	4	1 to 4
<i>Mycoplasma bovis</i>	1999	43	0.125	1	≤ 0.063 to > 64

* The correlation between *in vitro* susceptibility data and clinical effectiveness is unknown.

** The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

EFFECTIVENESS

Swine

Plasma concentrations of tulathromycin administered as tulathromycin injection 100 mg/mL or as tulathromycin injection 25 mg/mL were demonstrated to be therapeutically equivalent (see CLINICAL PHARMACOLOGY, Comparative Bioavailability Summary). Therefore effectiveness studies conducted with tulathromycin injection 100 mg/mL support the effectiveness for tulathromycin injection 25 mg/mL.

In a multi-location field study to evaluate the treatment of naturally occurring SRD, 266 pigs were treated with tulathromycin injection 100 mg/mL. Responses to treatment were compared to saline-treated controls. Success was defined as a pig with normal attitude, normal respiration, and rectal temperature of < 104°F on Day 7. The treatment success rate was significantly greater ($P \leq 0.05$) in tulathromycin injection 100 mg/mL-treated pigs (70.5%) compared to saline-treated pigs (46.1%). *M. hyopneumoniae* was isolated from 106 saline-treated and non-treated sentinel pigs in this study.

Two induced infection model studies were conducted to confirm the effectiveness of tulathromycin injection 100 mg/mL against *M. hyopneumoniae*. Ten days after inoculation intranasally and intratracheally with a field strain of *M. hyopneumoniae*, 144 pigs were treated with either tulathromycin injection 100 mg/mL (2.5 mg/kg BW) intramuscularly or an equivalent volume of saline. Pigs were euthanized and necropsied 10 days post-treatment. The mean percentage of gross pneumonic lung lesions was statistically significantly lower ($P < 0.0001$) for tulathromycin injection 100 mg/mL-treated pigs than for saline-treated pigs in both studies (8.52% vs. 23.62% and 11.31% vs. 26.42%).

The effectiveness of tulathromycin injection 100 mg/mL for the control of SRD was evaluated in a multi-location natural infection field study. When at least 15% of the study candidates showed clinical signs of SRD, all pigs were enrolled and treated with tulathromycin injection 100 mg/mL (226 pigs) or saline (227 pigs). Responses to treatment were evaluated on Day 7. Success was defined as a pig with normal attitude, normal respiration, and rectal temperature of $< 104^{\circ}\text{F}$.

The treatment success rate was significantly greater ($P < 0.05$) in tulathromycin injection 100 mg/mL-treated pigs compared to saline-treated pigs (59.2% vs. 41.2%).

Calves

Plasma concentrations of tulathromycin administered as tulathromycin injection 100 mg/mL or as tulathromycin injection 25 mg/mL were demonstrated to be therapeutically equivalent (see CLINICAL PHARMACOLOGY, Comparative Bioavailability Summary). Therefore effectiveness studies conducted with tulathromycin injection 100 mg/mL support the effectiveness for tulathromycin injection 25 mg/mL.

BRD - In a multi-location field study, 314 calves with naturally occurring BRD were treated with tulathromycin injection 100 mg/mL. Responses to treatment were compared to saline-treated controls. A cure was defined as a calf with normal attitude/activity, normal respiration, and a rectal temperature of $\leq 104^{\circ}\text{F}$ on Day 14. The cure rate was significantly higher ($P \leq 0.05$) in tulathromycin injection 100 mg/mL-treated calves (78%) compared to saline-treated calves (24%). There were two BRD-related deaths in the tulathromycin injection 100 mg/mL-treated calves compared to nine BRD-related deaths in the saline-treated calves.

Fifty-two tulathromycin injection 100 mg/mL-treated calves and 27 saline-treated calves from the multi-location field BRD treatment study had *Mycoplasma bovis* identified in cultures from pre-treatment nasopharyngeal swabs. Of the 52 tulathromycin injection 100 mg/mL-treated calves, 37 (71.2%) calves were categorized as cures and 15 (28.8%) calves were categorized as treatment failures. Of the 27 saline-treated calves, 4 (14.8%) calves were categorized as cures and 23 (85.2%) calves were treatment failures.

A Bayesian meta-analysis was conducted to compare the BRD treatment success rate in young calves (calves weighing 250 lbs or less and fed primarily a milk-based diet) treated with tulathromycin injection 100 mg/mL to the success rate in older calves (calves weighing more than 250 lbs and fed primarily a roughage and grain-based diet) treated with tulathromycin injection 100 mg/mL. The analysis included data from four BRD treatment effectiveness studies conducted for the approval of tulathromycin injection 100 mg/mL in the U.S. and nine contemporaneous studies conducted in Europe. The analysis showed that the BRD treatment success rate in young calves was at least as good as the BRD treatment success rate in older calves. As a result, tulathromycin injection 100 mg/mL was considered effective for the treatment of BRD associated with *M. haemolytica*, *P. multocida*, *H. somni*, and *M. bovis* in suckling calves, dairy calves, and veal calves. Two induced infection model studies were conducted to confirm the effectiveness of tulathromycin injection 100 mg/mL against *Mycoplasma bovis*. A total of 166 calves were inoculated intratracheally with field strains of *Mycoplasma bovis*. When calves became pyrexemic and had abnormal respiration scores, they were treated with either tulathromycin injection 100 mg/mL (2.5 mg/kg BW) subcutaneously or an equivalent volume of saline. Calves were observed for signs of BRD for 14 days post-treatment, then were euthanized and necropsied. In both studies, mean lung lesion percentages were statistically significantly lower in the tulathromycin injection 100 mg/mL-treated calves compared with saline-treated calves (11.3% vs. 28.9%, $P =$

0.0001 and 15.0% vs. 30.7%, $P < 0.0001$).

ANIMAL SAFETY

Swine

Plasma concentrations of tulathromycin administered as tulathromycin injection 100 mg/mL or as tulathromycin injection 25 mg/mL were demonstrated to be therapeutically equivalent (see CLINICAL PHARMACOLOGY, Comparative Bioavailability Summary).

Therefore systemic target animal safety studies conducted with tulathromycin injection 100 mg/mL support the systemic safety for tulathromycin injection 25 mg/mL.

Safety studies were conducted in pigs receiving a single intramuscular dose of 25 mg/kg BW, or 3 weekly intramuscular doses of 2.5, 7.5, or 12.5 mg/kg BW (both studies utilized tulathromycin injection 100 mg/mL). In all groups, transient indications of pain after injection were seen, including restlessness and excessive vocalization. Tremors occurred briefly in one animal receiving 7.5 mg/kg BW. Discoloration and edema of injection site tissues and corresponding histopathologic changes were seen in animals at all dosages and resolved over time. No other drug-related lesions were observed macroscopically or microscopically.

Sixteen growing pigs were injected with either saline or tulathromycin injection 25 mg/mL as a single injection of 4 mL. Injection site observations included two instances of erythema in the tulathromycin injection 25 mg/mL-treated group on Day 1 post-injection. No heat, sensitivity, firmness, necrosis, drainage, or swelling was observed at any injection sites in either treatment group. The gross and microscopic findings in the tulathromycin injection 25 mg/mL-treated group were consistent with inflammatory changes induced by injections and were considered to be mild or moderate with progression to macroscopic resolution by Day 28 post-injection and microscopic resolution by Day 42 post-injection.

Calves

Plasma concentrations of tulathromycin administered as tulathromycin injection 100 mg/mL or as tulathromycin injection 25 mg/mL were demonstrated to be therapeutically equivalent (see CLINICAL PHARMACOLOGY, Comparative Bioavailability Summary).

Therefore systemic target animal safety studies conducted with tulathromycin injection 100 mg/mL support the systemic safety for tulathromycin injection 25 mg/mL. A safety study was conducted in feeder calves receiving tulathromycin injection 100 mg/mL as a single subcutaneous dose of 25 mg/kg BW, or 3 weekly subcutaneous doses of 2.5, 7.5, or 12.5 mg/kg BW. In all groups, transient indications of pain after injection were seen, including head shaking and pawing at the ground. Injection site swelling, discoloration of the subcutaneous tissues at the injection site and corresponding histopathologic changes were seen in animals in all dosage groups. These lesions showed signs of resolving over time. No other drug-related lesions were observed macroscopically or microscopically.

An exploratory study was conducted in feeder calves receiving tulathromycin injection 100 mg/mL as a single subcutaneous dose of 10, 12.5, or 15 mg/kg BW.

Macroscopically, no lesions were observed. Microscopically, minimal to mild myocardial degeneration was seen in one of six calves administered 12.5 mg/kg BW and two of six calves administered 15 mg/kg BW. A safety study was conducted in preruminant calves 13 to 27 days of age receiving tulathromycin injection 100 mg/mL at 2.5 mg/kg BW or 7.5 mg/kg BW once subcutaneously. With the exception of minimal to mild injection site

reactions, no drug-related clinical signs or other lesions were observed macroscopically or microscopically.

Sixteen growing cattle were injected with either saline (eight animals) as a single injection of 11.5 mL or tulathromycin injection 25 mg/mL (eight animals) as a single injection of either 2.5 mg/kg BW or a dose volume of 11.5 mL (whichever volume was higher). One calf in the tulathromycin injection 25 mg/mL-treated group was observed to have firmness at the injection site for a single day.

Two tulathromycin injection 25 mg/mL-treated calves exhibited injection site swelling. In one calf, the swelling resolved within 48 hours. In the other calf, the swelling was observed over a three-day period, after which the calf underwent a scheduled necropsy, preventing further injection site observations. No injection site swelling was observed in saline-treated animals. At necropsy, three of the saline-treated calves and five of the tulathromycin injection 25 mg/mL-treated calves had altered tissue present at the injection site. The gross and microscopic findings in the tulathromycin injection 25 mg/mL-treated group were consistent with inflammatory changes induced by injections, were considered to be mild to marked, and progressed to macroscopic resolution and microscopic resolution by Day 42 post-injection.

STORAGE CONDITIONS

50 mL and 100 mL vials: Store at or below 25°C (77°F) with excursions up to 40°C (104°F). Use this product within 90 days of first puncture and puncture a maximum of 9 times. If more than 9 punctures are anticipated, the use of automatic injection equipment or a repeated syringe is recommended. Puncture a maximum of 4 times with a dosage delivery device no larger than 4.75 mm in diameter. Any product remaining beyond these parameters should be discarded.

250 mL vials: Store at or below 25°C (77°F) with excursions up to 40°C (104°F). Use this product within 90 days of first puncture and puncture a maximum of 22 times. If more than 22 punctures are anticipated, the use of automatic injection equipment or a repeated syringe is recommended. Puncture a maximum of 4 times with a dosage delivery device no larger than 4.75 mm in diameter. Any product remaining beyond these parameters should be discarded.

HOW SUPPLIED

Increxxa 25 (tulathromycin injection) Injectable Solution is available in the following package sizes:

50 mL vial

100 mL vial

250 mL vial

Approved by FDA under ANADA # 200-665

Product of China.

Distributed by: Elanco US Inc.

Greenfield, IN 46140

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact **1-800-428-4441**. For additional information about adverse drug experiences reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

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TAKE TIME

OBSERVE LABEL DIRECTIONS

Elanco™

8838840 PA230414X 100342

Principal Display Panel - 100 mL Carton Label

Elanco™

Increxxa™ **25**
(tulathromycin injection)

Injectable Solution

Antibiotic

25 mg of tulathromycin/mL

For use in suckling calves, dairy calves, veal calves, and swine. Not for use in ruminating cattle.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Net Contents: 100 mL

Approved by FDA under ANADA # 200-665



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See package insert for complete product information and storage conditions. For swine and bovine respiratory disease. **Swine:** Inject intramuscularly as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) Body Weight (BW). Do not inject more than 4 mL per injection site. **Calves:** Inject subcutaneously as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) body weight (BW). Do not inject more than 11.5 mL per injection site. **WARNINGS:** FOR USE IN ANIMALS ONLY. NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. NOT FOR USE IN CHICKENS OR TURKEYS.

RESIDUE WARNINGS
Swine intended for human consumption must not be slaughtered within 5 days from the last treatment.
Calves intended for human consumption must not be slaughtered within 22 days from the last treatment with Increxxa 25 Injectable Solution. This drug is not for use in ruminating cattle.

STORAGE CONDITIONS: Store at or below 25°C (77°F). Use within 90 days of first vial puncture. To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact **1-800-428-4441**. For additional information about adverse drug experiences reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.
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8720270 YL230414B 100339

LOT:
EXP:

Principal Display Panel - 250 mL Carton Label

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Distributed by: Elanco US, Inc. Greenfield, IN 46140
Product of China.

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TAKE TIME OBSERVE LABEL DIRECTIONS



8446480 SR230414C 100335

Elanco™

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See package insert for complete product information and storage conditions.

Increxxa 25 Injectable Solution is indicated for the treatment of swine respiratory disease (SRD) and for the control of SRD in groups of pigs where SRD has been diagnosed. Increxxa 25 Injectable Solution is also indicated for the treatment of bovine respiratory disease (BRD) in suckling calves, dairy calves, and veal calves.

Swine

Inject intramuscularly as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) Body Weight (BW). Do not inject more than 4 mL per injection site.

Table 1. Increxxa 25 Swine Dosing Guide (25 mg/mL)

Animal Weight (Pounds)	Dose Volume (mL)
4	0.2
10	0.5
15	0.7
20	0.9
22	1.0
25	1.1
30	1.4
50	2.3
70	3.2
90	4.0

Calves

Inject subcutaneously as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) body weight (BW). Do not inject more than 11.5 mL per injection site.

Table 2. Increxxa 25 Calf Dosing Guide (25 mg/mL)

Animal Weight (Pounds)	Dose Volume (mL)
50	2.3
75	3.4
100	4.5
150	7.0
200	9.0
250	11.5

Each mL of Increxxa 25 contains 25 mg of tulathromycin as the free base in a 50% propylene glycol vehicle, monothioglycerol (5 mg/mL), citric acid (4.8 mg/mL) with hydrochloric acid and sodium hydroxide added to adjust pH.

LOT:
EXP:

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Net Contents: 250 mL

Approved by FDA under ANADA # 200-665

See package insert for complete product information and storage conditions. For swine and bovine respiratory disease. **Swine:** Inject intramuscularly as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) Body Weight (BW). Do not inject more than 4 mL per injection site. **Calves:** Inject subcutaneously as a single dose in the neck at a dosage of 2.5 mg/kg (1 mL/22 lb) body weight (BW). Do not inject more than 11.5 mL per injection site.

WARNINGS: FOR USE IN ANIMALS ONLY. NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. NOT FOR USE IN CHICKENS OR TURKEYS.

RESIDUE WARNINGS
Swine intended for human consumption must not be slaughtered within 5 days from the last treatment.
Calves intended for human consumption must not be slaughtered within 22 days from the last treatment with Increxxa 25 Injectable Solution. This drug is not for use in ruminating cattle.

STORAGE CONDITIONS: Store at or below 25°C (77°F). Use within 90 days of first vial puncture.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact **1-800-428-4441**. For additional information about adverse drug experiences reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae. Product of China. Distributed by: Elanco US, Inc. Greenfield, IN 46140

Elanco
Increxxa™ 25
(tulathromycin injection)

Injectable Solution
Antibiotic
 25 mg of tulathromycin/mL

For use in suckling calves, dairy calves, veal calves, and swine. Not for use in ruminating cattle.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Net Contents: 250 mL
 Approved by FDA under ANADA # 200-665

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LOT:
 EXP:

INCREXXA 25

tulathromycin injection

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:58198-7210
Route of Administration	INTRAMUSCULAR, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TULATHROMYCIN (UNII: Q839I13422) (TULATHROMYCIN - UNII:Q839I13422)	TULATHROMYCIN	25 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
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1	NDC:58198-7210-2	1 in 1 CARTON		
1		100 mL in 1 BOTTLE, GLASS		
2	NDC:58198-7210-3	1 in 1 CARTON		
2		250 mL in 1 BOTTLE, GLASS		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200665	02/07/2022	

Labeler - Elanco US Inc. (966985624)

Establishment

Name	Address	ID/FEI	Business Operations
Wisdom Pharmaceutical Co., Ltd.		527609114	API MANUFACTURE

Establishment

Name	Address	ID/FEI	Business Operations
Fareva Amboise		265825439	MANUFACTURE, PACK, LABEL

Revised: 4/2022

Elanco US Inc.