

# NOTICE

## TULATHROMYCIN [in the product: Draxxin Injectable Solution]

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has before it an application from Pfizer Australia Pty Ltd for the registration of a new product, DRAXXIN INJECTABLE SOLUTION, which contains 100 mg/mL of tulathromycin. The product is an antibiotic for the treatment of bovine respiratory disease caused by *Mannheimia haemolytica* and *Pasteurella multocida* in cattle, and swine respiratory disease caused by *Mycoplasma hyopneumoniae* and *Pasteurella multocida* in pigs.

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration should be granted. Submissions should state the grounds on which the submission is based. Such grounds should relate only to matters outlined below that the APVMA is required to take into account in deciding whether to grant the application. Comments must be received by the APVMA within 28 days of the date of this notice.

### Particulars of Application

Product Name: DRAXXIN INJECTABLE SOLUTION  
Applicant Company: Pfizer Australia Pty Ltd  
Active Constituent: Tulathromycin (100mg/mL)  
Signal Heading: S4  
Statement of Claim: For the treatment of tulathromycin sensitive bacterial respiratory diseases in cattle and pigs

Pack Sizes: 20mL, 50 mL, 100mL

Maximum Residues Limits: **Table 1**

MF 0812	Cattle fat	0.1 mg/kg
MO 1280	Cattle kidney	1.0 mg/kg
MO 1281	Cattle liver	3.0 mg/kg
MM 0812	Cattle meat	0.1 mg/kg
	Pig skin/fat	0.3 mg/kg
MO 1284	Pig kidney	3.0 mg/kg
MO 1285	Pig liver	2.0 mg/kg
MM 0818	Pig meat	0.5 mg/kg

Residue Definition: **Table 3**  
Sum of tulathromycin and its metabolites that are converted by acid hydrolysis to (2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-2-ethyl-3,4,10,13-tetrahydroxy-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)- $\beta$ -D-xylohexopyranosyl]oxy]-1-oxa-6-azacyclopentadecan-15-one, expressed as tulathromycin equivalents.

Withholding Periods: Cattle meat: **DO NOT USE** less than 35 days before slaughter for human consumption.

Milk: **DO NOT USE** in cows which are producing or may in the future produce milk or milk products for human consumption.

**DO NOT USE** in bobby calves.

Pig meat: **DO NOT USE** less than 14 days before slaughter for human consumption.

Re-treatment Intervals: Cattle: **DO NOT RE-TREAT** cattle for 12 weeks after last treatment.

Pig: **DO NOT RE-TREAT** pigs for 8 weeks after last treatment.

Export Slaughter Interval: Cattle: **DO NOT SLAUGHTER** for export for 35 days after treatment.

Pig: **DO NOT SLAUGHTER** for export for 26 days after treatment.

**Summary of the APVMA's assessment of DRAXXIN INJECTABLE SOLUTION in accordance with section 14(3)(e) of the Agricultural and Veterinary Chemicals Code (the 'Agvet Code') scheduled to the Agricultural and Veterinary Chemicals Code Act 1994**

The APVMA has evaluated the application and, in its assessment in relation to human and environmental safety under section 14(3)(e) of the Agvet Code, it proposes to determine that:

- (i) The APVMA is satisfied that the use of DRAXXIN INJECTABLE SOLUTION would not present an undue hazard to the safety of people exposed to it during its handling and use.

The Department of Health and Ageing, Office of Chemical Safety (OCS) conducted an evaluation of the toxicology aspects of tulathromycin. The active constituent displays low acute oral toxicity in rats and dogs, and low dermal acute toxicity in rabbits. It is a severe eye irritant and a skin sensitizer, but is not a skin irritant. There is no evidence that tulathromycin causes teratogenicity. Tulathromycin is not genotoxic and is considered unlikely to be carcinogenic. The product DRAXXIN INJECTABLE SOLUTION is a moderate eye irritant and is likely to be a skin sensitiser.

OCS has recommended a microbiological acceptable daily intake of 0.005 mg/kg bw/day, a toxicological acceptable daily intake of 0.005 mg/kg bw/day and an acute reference dose of 0.1 mg/kg bw for tulathromycin. As DRAXXIN INJECTABLE SOLUTION is to be administered under veterinary supervision, safety directions are not required. Since the product is a moderate eye irritant, OCS has recommended that a warning statement be included on the label.

The APVMA having considered the findings and recommendations of the OCS evaluation accepts these findings and recommendations.

- (ii) The APVMA is satisfied that the proposed use of DRAXXIN INJECTABLE SOLUTION will not be an undue hazard to the safety of people using anything containing its residues. Residues data were assessed by the APVMA and Maximum Residue Limits are recommended for DRAXXIN INJECTABLE SOLUTION.

Withholding periods and re-treatment intervals have been established. The product is restricted from being used in bobby calves, dairy cows and heifers. The APVMA has conducted a dietary risk assessment and has found that the acute and chronic dietary exposures to tulathromycin residues are acceptable.

- (iii) The APVMA is satisfied that the proposed use of tulathromycin in DRAXXIN INJECTABLE SOLUTION is not likely to be harmful to human beings if used according to the product label directions.

The APVMA has evaluated and proposes to approve the active constituent, tulathromycin, and finds that the chemistry and manufacturing details of the product are acceptable. The National Drugs and Poisons Scheduling Committee has assessed DRAXXIN INJECTABLE SOLUTION and has included it in Schedule 4 of the Standard for the Uniform Scheduling of Drugs and Poisons. The signal heading that corresponds to Schedule 4 and the first aid instructions that OCS has recommended both appear on the label. Statements that warn users that tulathromycin is irritating to the eyes and may cause skin sensitisation, and the accompanying instructions are acceptable to the APVMA.

DRAXXIN INJECTABLE SOLUTION will be manufactured overseas and imported in self-contained vials. Tulathromycin is not classified as a hazardous substance, but DRAXXIN INJECTABLE SOLUTION is determined to be a hazardous substance, based on the NOHSC hazard classification of active and non-active constituents and the product toxicology information provided.

The APVMA has considered the findings of its advisors on this criterion and accepts their recommendations.

- (iv) The APVMA is satisfied that the proposed use of DRAXXIN INJECTABLE SOLUTION is not likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

The Department of the Environment and Water Resources (DEW) has evaluated the VICH Phase 1 Environment Impact Assessment of DRAXXIN INJECTABLE SOLUTION and agreed that that the Predicted Environmental Concentration<sub>soil</sub> values have met the criteria of VICH Phase 1. The Department of the Environment and Water Resources has concluded that the proposed use of DRAXXIN INJECTABLE SOLUTION on cattle and pigs will not pose an unacceptable aquatic risk and that the VICH trigger value of 100 µg/kg soil is unlikely to be exceeded.

The APVMA has considered the findings of DEW and accepts its recommendations on this criterion.

- (v) The APVMA is satisfied that the proposed use of DRAXXIN INJECTABLE SOLUTION would not adversely affect trade between Australia and places outside Australia.

Codex has not considered tulathromycin, but several countries have established MRLs/tolerances for tulathromycin. The EU MRLs for tulathromycin residues in pig liver and kidney are the same as, or higher than, the proposed Australian MRLs, but the

EU MRL for pig skin/fat (0.1 mg/kg) is significantly lower than the proposed Australia's MRL (0.3 mg/kg). The EU has not recommended an MRL for pig muscle. This implies that residues in muscle are lower than in skin/fat at any time.

The APVMA has assessed residues data and has determined that an export slaughter interval of 26 days for pigs would be required for tulathromycin residues in pig skin/fat and muscle to decline below the EU MRL of 0.1 mg/kg.

Australian MRLs for tulathromycin in edible cattle tissues are either the same as or lower than the corresponding MRLs/tolerances established by the main importers of Australian beef. Therefore observance of the domestic withholding period of 35 days will enable tulathromycin residues in edible cattle tissues to decline to below the standards of Australia's main export beef markets.

The APVMA has concluded that the overall risk to Australia's export trade in beef and pork products arising from the treatment of cattle and pigs with DRAXXIN INJECTABLE SOLUTION is considered to be low when the recommended export slaughter intervals are observed.

In relation to its assessment of efficacy under section 14(3)(f), the APVMA proposes to determine that:

The APVMA is satisfied that data from trials supporting the efficacy of DRAXXIN INJECTABLE SOLUTION adequately demonstrate that the product would be safe and effective for the proposed use in cattle and pigs.

### **Public Release Summary**

A Public Release Summary of the evaluation is available by contacting Thea Reiman on telephone (02) 6210 4726. Written submissions on the APVMA's proposal to grant the application for registration should be addressed in writing to:

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