Australian Government

Australian Pesticides and Veterinary Medicines Authority

TRADE ADVICE NOTICE

on Tulathromycin in the Product *Draxxin Injectable Solution*

APVMA Product Number 60018

JUNE 2013

ISSN: 2200-3894 (electronic)
ISBN: 978-1-922188-35-9 (electronic)

Ownership of intellectual property rights in this publication

Unless otherwise noted, copyright (and any other intellectual property rights, if any) in this publication is owned by the Australian Pesticides and Veterinary Medicines Authority (APVMA).

Creative Commons licence

With the exception of the Coat of Arms and other elements specifically identified, this publication is licensed under a Creative Commons Attribution 3.0 Australia Licence. This is a standard form agreement that allows you to copy, distribute, transmit and adapt this publication provided that you attribute the work.

A summary of the licence terms is available from www.creativecommons.org/licenses/by/3.0/au/deed.en. The full licence terms are available from www.creativecommons.org/licenses/by/3.0/au/legalcode.

The APVMA's preference is that you attribute this publication (and any approved material sourced from it) using the following wording:

> *Source: licensed from the Australian Pesticides and Veterinary Medicines Authority (APVMA) under a Creative Commons Attribution 3.0 Australia Licence.*

In referencing this document the Australian Pesticides and Veterinary Medicines Authority should be cited as author, publisher and copyright owner.

Use of the Coat of Arms

The terms under which the Coat of Arms can be used are set out on the Department of the Prime Minister and Cabinet website (see www.dpmc.gov.au/guidelines).

Disclaimer

The material in or linking from this report may contain the views or recommendations of third parties. Third party material does not necessarily reflect the views of the APVMA, or indicate a commitment to a particular course of action.

There may be links in this document that will transfer you to external websites. The APVMA does not have responsibility for these websites, nor does linking to or from this document constitute any form of endorsement.

The APVMA is not responsible for any errors, omissions or matters of interpretation in any third-party information contained within this document.

Comments and enquiries regarding copyright:

The Manager, Public Affairs
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604 Australia

Telephone: +612 6210 4701
Email: communications@apvma.gov.au

This publication is available from the APVMA website: www.apvma.gov.au

CONTENTS

LIST OF TABLES

PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is an independent statutory authority with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Aging, Office of Chemical Safety and Environmental Health (OCSEH), Department of the Environment, Water, Heritage and the Arts (DEWHA), and State Departments of Primary Industry.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking stakeholder involvement in decision making. Part of that process is the publication of Trade Advice Notices for all proposed extensions of use for existing products where there may be trade implications.

The information and technical data required by the APVMA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the APVMA's publication *Vet MORAG: Manual of Requirements and Guidelines*.

About this document

This is a Trade Advice Notice.

It indicates that the Australian Pesticides and Veterinary Medicines Authority (APVMA) is considering an application to vary the use of an existing registered agricultural or veterinary chemical. It provides a summary of the APVMA's residue and trade consideration.

Comment is sought from industry groups and stakeholders on the information contained within this document.

Any advice the APVMA receives through this consultation which it relies on to grant this application will be noted in a subsequent Advice Summary.

Advice Summaries can be found on the APVMA website: www.apvma.gov.au.

Making a submission

The APVMA invites any person to submit a relevant written submission as to whether the application to vary the registration of ***Draxxin Injectable Solution*** should be granted. Submissions should relate only to matters that the APVMA is required by legislation to take into account in deciding whether to grant the application. These grounds relate to the **trade implications** of the extended use of the product. Submissions should state the grounds on which they are based. Comments received outside these grounds cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on **Tuesday, 16 July 2013** and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments will be taken into account by the APVMA in deciding whether to grant the application. A summary of relevant comments and the APVMA's response will be published on the APVMA website.

When making a submission please include:

- contact name
- company or group name (if relevant)
- postal address
- email address (if available)
- the date you made the submission.

All personal and ***confidential commercial information (CCI)***[1] material contained in submissions will be treated confidentially.

Written submissions on the APVMA's proposal to grant the application for registration that relate to the **grounds for registration** should be addressed in writing to:

Linden Moffatt
Veterinary Medicines Program
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Symonston ACT 2609

Phone: +612 6210 4736
Fax: +612 6210 4741
Email: vetmedicines@apvma.gov.au

Further information

Further information on trade advice notices can be found on the APVMA website: www.apvma.gov.au
.

[1] A full definition of "confidential commercial information" is contained in the Agvet Code.

1 INTRODUCTION

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has before it an application from Zoetis Australia Pty Ltd, to vary the registration of *Draxxin Injectable Solution*, which contains 100 mg/mL of tulathromycin.

The product is administered subcutaneously to cattle to treat bovine respiratory disease caused by *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma bovis*. Draxxin is also administered to pigs intramuscularly to treat swine respiratory disease caused by *Pasteurella multocida*, *Mycoplasma hyopneumoniae* and *Haemophilus parasuis*.

The application involves consideration of the proposal to extend the use of tulathromycin to dairy heifers without the establishment of a Maximum Residue Limit (MRL) for tulathromycin in milk.

2 RESIDUES IN LIVESTOCK

2.1 Proposed Australian use pattern

The proposed Australian use pattern of *Draxxin Injectable Solution* is given below.

Table 1: Proposed use pattern for Draxxin's extension of use

HOST	PURPOSE	DOSE RATE
Cattle, including dairy heifers up to the point of first mating.	For the treatment of bovine respiratory disease.	**Nominal** 2.5 mg tulathromycin/kg bodyweight by a single subcutaneous injection high on the neck.

Restraints

DO NOT USE in lactating cows which are producing milk, or dry cows that may in the future produce milk, or where milk products will be produced, for human consumption in each case.

Re-treatment interval

DO NOT RE-TREAT dairy heifers.

Withholding periods

Milk: **DO NOT USE** in lactating cows which are producing milk, or dry cows that may in the future produce milk, or where milk products will be produced, for human consumption in each case.

Trade advice

DO NOT USE less than 35 days before slaughter for export.

The ESIs on this label was correct at the time of label approval. Before using this product, confirm the current ESI from Zoetis Australia Pty Ltd on 1800 814 883 or the APVMA website (www.apvma.gov.au/residues).

2.2 Residue trials

In support of their application, Zoetis Australia Pty Ltd provided details of two residues trials conducted with *Draxxin Injectable Solution*. In one trial (Study 1531N60-09-770), dairy heifers were administered a single subcutaneous injection of 2.8 mg tulathromycin/kg bodyweight 211 to 251 days before calving. Following calving, the heifers were milked twice daily for 10 consecutive days. Tulathromycin residues in milk were quantified as the common fragment CP-60,300, expressed as tulathromycin equivalents. This study showed that tulathromycin residues in whole milk were less than 3.4 µg/L, which was the method LOD, at all sampling times after calving.

An MRL for tulathromycin in milk was not established; therefore any detection of common fragment CP-60,300 in milk will constitute a food safety and/or trade violation. The approach to not set a milk MRL for the use of Draxxin Injectable Solution in dairy heifers is consistent with that taken by regulatory agencies in the USA and the EU. When taken in conjunction with a default nine-month milk withholding period (i.e. the interval between treatment up to the point of mating to the commencement of lactation), the extension of Draxxin Injectable Solution to dairy heifers does not pose a risk to food safety or trade.

The second study (Study 1531R-60-05-477), determined the concentration of tulathromycin common fragment CP-60,300, expressed as tulathromycin equivalents, in milk of cows after freshening and in the liver of neonatal calves. The dairy cows were treated subcutaneously with *Draxxin Injectable Solution* at 2.5 mg/kg bodyweight, during the dry period. Tulathromycin common fragment CP-60,300 residues in milk from the dry cows ranged from 146–800 µg/L at first milking after freshening, compared to <3.4 µg/L in dairy heifers (see Study 1531N60-09-770). This residue depletion study did not reflect the use pattern proposed for dairy heifers. In the neonatal calf study, animals were sacrificed between 2.6–15 hours and liver samples taken at necropsy. Residues measured as the common fragment CP-60,300, expressed as tulathromycin equivalents, in liver ranged from 160–1,240 µg/kg.

In the second study, 21 to 39 days were available for the depletion of tulathromycin common fragment CP-60,300 residues from the liver of neonatal calves prior to calving and slaughter, and the resultant residues were less than the Australian MRL of 3 mg/kg for tulathromycin in cattle liver. In the case of dairy heifers treated no later than at first mating, tulathromycin common fragment CP-60,300 residues in liver from neonatal calves will be even lower since tulathromycin common fragment CP-60,300 residues will have approximately 270 days in which to deplete before first calving. Consequently, tulathromycin common fragment CP-60,300 residues in liver from calves born to treated dairy heifers are likely to comply with the Australian MRL for tulathromycin in cattle liver.

Milk MRL considerations

Milk from treated cattle, including dairy heifers treated after first mating, is prohibited from being supplied for human consumption. Heifers treated up to the point of the first mating will undergo a gestation period of about nine months (~270 days) before they begin to produce milk for human consumption. The first study described above showed that tulathromycin common fragment CP-60,300 in whole milk from heifers treated during the first trimester was below the method LOD. It was considered, therefore, that the extension of use of *Draxxin Injectable Solution* in dairy heifers up to the point of the first mating does not require an MRL for tulathromycin in milk to be established.

Withholding period Milk

As heifers do not produce milk until the first calving and since tulathromycin common fragment CP-60,300 residues in milk from heifers was less than the method LOD before calving, the following milk withholding period is recommended: ***DO NOT USE*** *in lactating cows which are producing milk, or dry cows that may in the future produce milk, or where milk products will be produced, for human consumption in each case*.

Re-treatment interval

The use pattern of *Draxxin Injectable Solution* in dairy heifer is a once only treatment prior to mating. Consequently, the following restriction on re-treating applies: **DO NOT RE-TREAT** dairy heifers.

3 RESIDUES-RELATED ASPECTS OF TRADE

3.1 Commodities exported

Australian exports of dairy produce could be affected by the use of *Draxxin Injectable Solution* in dairy cattle if residues were detected in exported products. The residue-related trade implications of the extension of use to dairy heifers must therefore be considered.

3.2 Destination and value of exports

Dairy product exports

In 2010–2011, Australia exported $AUS 2.27 billion of dairy products, including cheese, butter and butterfat, skin and whole milk powder. Details of the top export destinations, total exports and the dollar value of exports are provided in Table 2.

Table 2: Dairy Products Exported in 2010-2011 (Source: ABARE 2011)

RANK (BY $ VALUE)	IMPORTING COUNTRY	QUANTITY (KTONNE)	VALUE ($AUS MILLION)
CHEESE			
1	Japan	84.5	355.8
2	Korea, Republic of	8.8	36.8
3	Saudi Arabia	6.9	31.7
Total		**163.2**	**732.2**
BUTTER AND BUTTERFAT			
1	Singapore	5.7	27.9
2	Philippines	6.4	27.4
3	Malaysia	3.8	18.5
Total		**56.0**	**251.6**
SKIM MILK POWDER			
1	Singapore	15.7	51.6
2	Thailand	11.5	37.9
3	China	11.7	37.1
Total		**155.7**	**504.5**

RANK (BY $ VALUE)	IMPORTING COUNTRY	QUANTITY (KTONNE)	VALUE ($AUS MILLION)
CASEIN			
1	Japan	1.7	22.0
2	USA	1.4	13.1
Total		**4.7**	**52.7**
WHOLE MILK POWDER			
1	Singapore	15.5	58.4
2	China	13.7	51.6
3	Indonesia	10.2	39.7
Total		**108.4**	**402.5**
OTHER PRODUCTS			
Fresh milk		77.2 ML	96.4
Other fresh products		0.3 ML	1.3
Condensed milk		47.2	108.2
Other powders		27.8	125.0
Total			**331.0**

3.3 Overseas registrations

Draxxin Injectable Solution is currently registered in the European Union (EU), USA, Canada, Switzerland, Bulgaria, Croatia, Romania, Turkey, Ukraine, Ecuador, Mexico, Peru, Argentina, Chile, Venezuela, Korea, Japan, Vietnam and the Philippines. Its use in dairy heifers is authorised in the EU and the USA.

3.4 Comparison of the (proposed) Australian MRLs with Codex and overseas MRLs

The Codex Alimentarius Commission (Codex) is responsible for establishing CXLs for pesticides and veterinary medicines. Codex CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice employed by various countries. Some countries may accept Codex CXLs when importing foods. Codex has not considered tulathromycin. No country has established MRLs/tolerances for tulathromycin in milk.

3.5 Potential risk to trade

Export of dairy products containing measurable residues of tulathromycin may pose a risk to Australian trade in situations where: (i) no residue tolerance is established in the importing country, or (ii) where residues in Australian produce are likely to exceed a residue tolerance established in the importing country. As none of the importing countries of Australian dairy products has established an MRL/tolerance for tulathromycin in milk, any detection of tulathromycin residues in these commodities would constitute a potential trade violation.

The use pattern of *Draxxin Injectable Solution* worldwide is 2.5 mg tulathromycin/kg bodyweight by subcutaneous injection in cattle. A common fragment analytical method is validated to quantify residues in milk. This analytical method was used to quantify tulathromycin residues in Study 1531N60-09-770.

Given the results of this trial and that tulathromycin residues in milk from treated heifers are likely to deplete below the method LOD during the nine months between the time of first mating and parturition, the risk to trade is considered to be low.

3.6 Trade advice statements

A trade advice statement is already approved for edible tissues. For the extension of use to dairy heifers, a trade advice statement for milk is not required as milk from treated primiparous (first-calf) heifers is not expected to contain measurable quantities of tulathromycin residues.

4 CONCLUSIONS

The APVMA has considered whether the extension of use of *Draxxin Injectable Solution* to dairy heifers in accordance with the proposed label instructions, could potentially unduly prejudice trade and commerce between Australia and places outside Australia, as per Section 14(3)(e)(iv) of the Agvet Codes.

The risk to Australia's export trade in dairy products of allowing the use of *Draxxin Injectable Solution* up to the point of mating in dairy heifers is considered to be low when only a single treatment is permitted.

The APVMA is seeking comment from relevant industry groups and stakeholders in relation to the perceived level of risk to Australia's export trade in dairy products.