Australian Government

Australian Pesticides and Veterinary Medicines Authority

Trade Advice Notice

on Fluralaner in the product EXZOLT Fluralaner Oral Solution for Chickens for use in chickens.

APVMA product number 85688

NOVEMBER 2019

Comments and enquiries regarding copyright:

Assistant Director, Communications
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262, Sydney, NSW, 2001, Australia

Telephone: +61 2 6770 2300

Email: communications@apvma.gov.au.

This publication is available from the APVMA website.

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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.

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 regulatory guidance published on the APVMA website.

About this document

This Trade Advice Notice 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 assessment.

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

Making a submission

The APVMA invites any person to submit a relevant written submission as to whether the application to register EXZOLT Fluralaner Oral Solution for Chickens 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 **Thursday 5 December 2019** 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 and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

- contact name
- company or group name (if relevant)

- postal address
- email address (if available)
- submission date.

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:

Residues and Trade
Risk Assessment Capability
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262, Sydney, NSW, 2001, Australia

Phone: +61 2 6770 2300
Email: enquiries@apvma.gov.au.

Further information

Further information can be obtained via the contact details provided above.

Further information on public release summaries can be found on the APVMA website.

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

1 INTRODUCTION

The APVMA has before it an application from INTERVET AUSTRALIA PTY LIMITED for approval of a new product, EXZOLT Fluralaner Oral Solution for Chickens (containing 10 mg fluralaner/mL), for oral administration through drinking water for treatment in chickens (pullets, breeders and layer hens).

Fluralaner is currently registered for use in dogs and cats only and has not previously been registered for use in food producing animals in Australia. The proposed use therefore requires the establishment of a residue definition (marker residue) for fluralaner, MRLs for chicken tissues and eggs and the consideration of trade implications.

2 TRADE CONSIDERATIONS

2.1 Commodities exported

Poultry meat, offal and eggs are currently considered to be major export commodities[2]

2.2 Destination and value of exports

In 2017/2018, 37.4 kiloton of Australian chicken meat worth AUD66 million was exported[3]. During the 2017 financial year, 341 metric tonne of shell eggs; 282 metric tonne of egg pulp/liquid and 116 metric tonne of egg powder valued at 1.2, 0.97 and 0.15 million Australian dollars, respectively, were exported with the predominant markets for egg products being the Republic of Korea, Vanuatu, Hong Kong and New Caledonia[4].

2.3 Proposed Australian use-pattern

EXZOLT Fluralaner Oral Solution for Chickens (containing 10 mg fluralaner/mL) is proposed to be administered as a complete course requiring 2× administrations, seven days apart, to birds over three weeks of age via drinking water at a dose rate of 0.5 mg fluralaner/kg bw, in conjunction with an interval of three months between treatment courses.

Table 1: Proposed Australian use pattern

Species	Claims	Dosage
Chicken pullets, breeders and layer hens	Treatment and control of poultry red mite (*Dermanyssus gallinae*) infestation in pullets, breeders and layer hens.	For use in drinking water. A complete course of treatment consists of two doses, administered 7 days apart. One dose is 0.5 mg fluralaner per kg body weight (equivalent to 0.05 mL of product). The complete course of treatment must be administered for a full therapeutic effect. If another course of treatment is indicated, the interval between two courses of treatment should be at least 3 months.

Withholding periods:

MEAT: DO NOT USE less than 14 days before slaughter for human consumption.

[2] APVMA Guideline: Veterinary drug residues in food commodities and overseas trade: apvma.gov.au/node/669

[3] www.agriculture.gov.au/abares/research-topics/agricultural-commodities/agricultural-commodities-trade-data#2018

[4] Australian eggs: Annual report 2016/2017, www.australianeggs.org.au/who-we-are/annual-reports/#item-818

EGGS: Zero (0) days.

Restraints: Do not use on chickens less than three weeks of age

2.4 Results from residues trials presented to the APVMA

Metabolism and residue definition

In a study involving oral administration of [^{14}C]-fluralaner to laying chickens (two treatments, seven days apart), levels of total radioactive residues (TRR) and parent fluralaner were determined in edible tissues (0.5, one, two, four and seven days after last treatment) and eggs (collected daily).

For tissues, the highest TRR concentration was found in the liver, followed by skin with fat, kidneys and breast muscle across all sacrifice time-points. Over the course of the study, the TRR concentrations decreased in all tissue types. For eggs, a five to six days delay is observed between each administration and peak residues. Thereafter, the fluralaner concentrations steadily decreases over time. Parent fluralaner was found to be the predominant component in each tissue and eggs. The ratio of marker residue (parent fluralaner) to total residue calculated across sampling time-points at one, two, four and seven days post treatment for tissues and three to 17 days post treatment for eggs, is 0.71 in liver (range: 0.66–0.78), 0.66 in kidney (range: 0.60–71), 0.77 in muscle (range: 0.82–0.74), 0.79 in skin/fat (range: 0.58–0.88); and 0.80 in eggs (range: 0.75–0.87).

It is concluded that the residue definition for chicken (meat and eggs) is parent fluralaner for both the enforcement and dietary risk assessment. The recommended residue definition for chickens as ‘fluralaner’ is consistent with the residues definition established in the EU.

Analytical method

Four validated methods for the quantification of parent fluralaner residues in chicken tissues and eggs using LC-MS/MS or HPLC-MS/MS methodologies, were considered. The method LOQ for liver, kidney, muscle and skin/fat were 30, 20, five and 40 µg/kg, respectively; 2 µg/kg across tissue and eggs; or 400 µg/kg for eggs.

Residue depletion studies

Tissues

Two tissue residue depletion studies are available which address the proposed use of fluralaner in chickens (0.58–0.82 mg fluralaner/kg bw via drinking water, two treatments, seven days apart). One study included only laying female hens (n=7), while the second study included four laying hens and four males of the same breed at each sampling time-point. Both studies involved tissue collection at one, two, four, seven and 10 days after the second treatment.

At **10 days** after the second treatment, which was the final time-point included in the two depletion studies, the combined results for parent fluralaner residues in chicken tissues following the proposed treatment of fluralaner via drinking water were:

Liver: 110–510 µg/kg (mean: 235 µg/kg)

Kidney: 59–289 µg/kg (mean: 139 µg/kg)

Muscle: 13–71 µg/kg (mean: 29 µg/kg)

Skin/fat: 70–516 µg/kg (mean: 182 µg/kg)

Based on the results of the two studies and the statistical analysis at the 95 percentile of the decline profile, MRLs of: 0.6, 0.4, 0.06 and 0.6 mg/kg for liver, kidney, muscle and skin/fat are considered appropriate for the proposed use in chickens in conjunction with the proposed **14 day** meat withholding period. The proposed MRLs are similar to those established in the EU for a similar use.

Eggs

In the egg depletion study, 15 laying hens were administered 0.49–0.68 mg fluralaner/kg bw via drinking water (two treatments, seven days apart). After administration of fluralaner at Day 0, residues were <LOQ for the first three days after the first treatment. The highest residue of 1072.0 µg/kg was observed at Day 13 (six days after the final second treatment) while the highest mean residue of 828 µg/kg was observed at Day 14 (seven days after the second treatment). Residues declined to <LOQ (400 µg/kg) at the final time-point (Day 20, 13 days after the final treatment).

At Day 14 (seven days after the final second treatment) when mean residues peaked, concentrations of fluralaner in whole egg were 637–1065 µg/kg.(mean: 828 µg/kg). The upper one-sided 95 per cent confidence limit of the 95th percentile (95/95) residue calculated on this dataset for peak egg residues at Day 14 was 1245 µg/kg.

An MRL at 1.3 mg/kg for chicken eggs is considered to be appropriate for the proposed use in conjunction with a Zero (0) day withholding period. This MRL is equivalent to that established for eggs in the EU.

2.5 Overseas registration and approved label instructions

The applicant indicated that fluralaner products are registered for use on chickens in EU, Mexico, Peru, Norway and Iceland.

2.6 Codex alimentarius commission and overseas MRLs

The Codex Alimentarius Commission (Codex) is responsible for establishing Codex Maximum Residue Limits (CXLs) for pesticides. Codex CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice (GAP) employed by various countries. Some countries may accept Codex CXLs when importing foods. Fluralaner has not been considered by Codex. The following relevant international MRLs have been established for fluralaner.

Table 2: International fluralaner MRLs

Regulator	MRL (µg/kg)					
	Muscle	Fat	Liver	Kidney	Edible offal	Eggs
Australia (recommended)	60 (meat)	600 (skin/fat)	600	400	-	1300
Codex/JECFA	-					
EU	65	650 (skin/fat)	650	420	-	1300
Japan	70	700	700	400	700	1000
Taiwan	60	600	600	400	-	1000
Korea	60	600 (skin/fat)	600	400	-	1300

2.7 Current and proposed Australian MRLs for fluralaner

Table 3: Proposed MRL standard

Amendments to Table 1			
Compound		Food	MRL (mg/kg)
FLURALANER			
	ADD:		
PE	0840	Chicken eggs	1.3
		Chicken fat/skin	0.6
		Chicken kidney	0.4
		Chicken liver	0.6
PM	0840	Chicken meat	0.06

Table 4: Proposed MRL standard

Amendments to Table 3	
Compound	Residue
DELETE:	
Fluralaner	{T} Fluralaner
ADD:	

Amendments to Table 3	
Compound	**Residue**
Fluralaner	Fluralaner

2.8 Potential risk to trade

Export of treated produce containing finite (measurable) residues of fluralaner may pose a risk to Australian trade in situations where (i) no residue tolerance (import tolerance) is established in the importing country or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

The proposed MRLs are similar to those established in Korea, Taiwan, Japan and the EU and the risk to trade associated with the proposed use is considered to be low for those markets. Codex has however not established MRLs.

Given the proposed use is for laying hens (including breeders and pullets), and not for broiler chickens raised specifically for meat production, the potential risk to trade associated with fluralaner residues in chicken tissues is considered to be low.

The potential for fluralaner residues in eggs at the proposed zero day egg withholding period may potentially result in a risk to international trade to countries that accept Codex MRLs. It is however noted that residues in eggs is expected to be below the limit of quantification at 13 days after treatment.

3 CONCLUSION

Comments are sought on the potential risk to trade in chicken eggs from the proposed use and the ability of the industry to manage any potential risk.