



Australian Government
**Australian Pesticides and
Veterinary Medicines Authority**



Public Release Summary

on the evaluation of the new active famoxadone in the product Zorvec Encantia
Fungicide

APVMA product number 92729

September 2024

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Assistant Director, Communications
Australian Pesticides and Veterinary Medicines Authority
PO Box 574
Canberra ACT 2601 Australia

Telephone: +61 2 6770 2300

Email: communications@apvma.gov.au

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Preface

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator responsible for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia. Before approving an active constituent and/or registering a product, the APVMA must be satisfied that the statutory criteria, including the safety, efficacy, trade, and labelling criteria, have been met. The information and technical data required by the APVMA to assess the statutory criteria of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined on the [APVMA website](#).

The APVMA has a policy of encouraging transparency in its activities and seeking community involvement in decision making. Part of that process is the publication of Public Release Summaries for products containing new active constituents. This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from advisory agencies, including other Australian Government agencies and State departments of primary industries. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience to encourage public comment.

About this document

This Public Release Summary indicates that the APVMA is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested stakeholders on the information contained within this document.

Making a submission

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 of Zorvec Encantia Fungicide 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 matters include aspects of public health, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade, and efficacy and target crop or animal safety. Submissions should state the grounds on which they are based. Comments received that address issues outside the relevant matters cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on 29 October 2024 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 the product should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

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

Please note: submissions will be published on the APVMA website unless you have asked for the submission to remain confidential, or if the APVMA chooses at its discretion not to publish any submissions received (refer to the [public consultation coversheet](#)).

Please lodge your submission using the [public consultation coversheet](#), which provides options for how your submission will be published.

Note that all APVMA documents are subject to the access provisions of the *Freedom of Information Act 1982* and may be required to be released under that Act should a request for access be made.

Unless you request for your submission to remain confidential, the APVMA may release your submission to the applicant for comment.

Written submissions should be addressed to:

Case Management Team – Pesticides
Australian Pesticides and Veterinary Medicines Authority
PO Box 574
Canberra ACT 2601

Phone: +61 2 6770 2300

Email: casemanagement@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](#).

Introduction

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Zorvec Encantia Fungicide and approval of the new active constituent, famoxadone.

Applicant

Corteva Agriscience Australia Pty Ltd.

Purpose of application

Corteva Agriscience Australia Pty Ltd has applied to the APVMA for registration of the new product Zorvec Encantia Fungicide, containing 300 g/L famoxadone and 30 g/L oxathiapiprolin as active constituents as an aqueous suspo-emulsion (SC) formulation of the new active constituent, famoxadone.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product, Zorvec Encantia Fungicide and approval of the new active constituent famoxadone.

Proposed claims and use pattern

Zorvec Encantia Fungicide is intended for the control of certain fungal diseases in spinach and rocket.

Products containing oxathiapiprolin are currently registered as a fungicide for control of downy mildew in bulb, brassica, cucurbit and leafy vegetables, and oilseed poppies.

The product will be applied by ground boom, with label restraints restricting application by aircraft and equipment carried on the back of the user or by other manual application methods (e.g., handwand/handgun).

Mode of action

Famoxadone acts via inhibition of fungal mitochondrial respiration (at complex III), resulting in decreased ATP production. It is active against zoospore germination and mycelial growth.

Oxathiapiprolin acts via inhibition of an oxysterol binding protein (OSBP) in fungal cells, which inhibits zoospore release and motility and sporangia germination.

Overseas registrations

Zorvec Encantia Fungicide is currently registered in Central and South America, South-east Asia and Africa as well as China, Japan and the US.

Chemistry and manufacture

Active constituent

The active constituent famoxadone is manufactured overseas. Details of the chemical name, structure, and physicochemical properties of famoxadone are listed below in Tables 1 to 2.

Table 1: Nomenclature and structural formula of the active constituent famoxadone

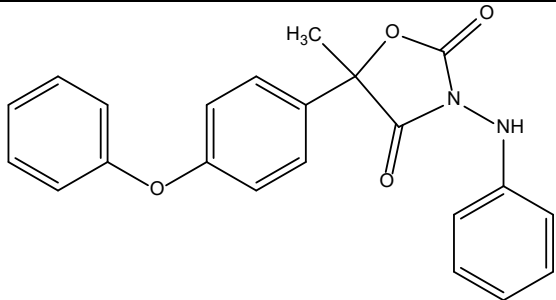
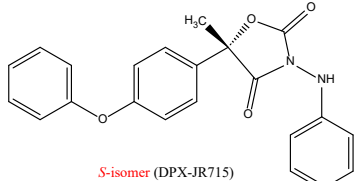
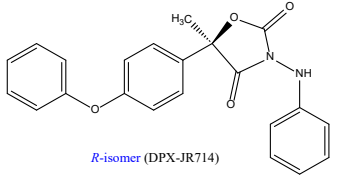
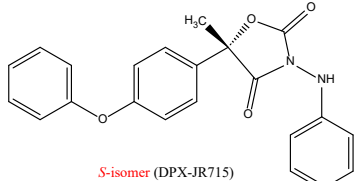
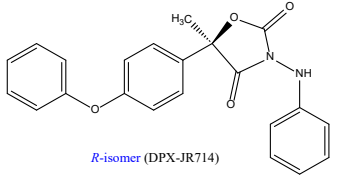
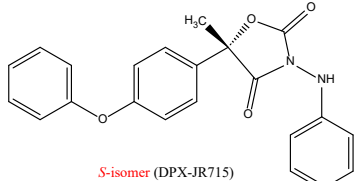
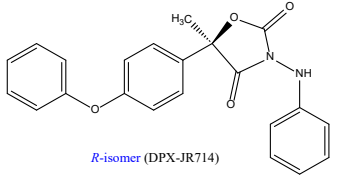
Common name (ISO):	Famoxadone		
IUPAC name:	(<i>RS</i>)-3-Anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione		
CAS registry number:	131807-57-3		
Molecular formula:	C ₂₂ H ₁₈ N ₂ O ₄		
Molecular weight:	374.4 g/mol		
Structural formula:	 <p>The chemical structure of famoxadone is shown as a 2D skeletal structure. It features a central 1,3-oxazolidine-2,4-dione ring system. The 5-position of this ring is substituted with a methyl group (H₃C) and a 4-phenoxyphenyl group (a benzene ring connected to another benzene ring via an oxygen atom). The 3-position of the ring is substituted with an anilino group (a benzene ring connected to the nitrogen atom of the oxazolidine ring via an NH group).</p>		
<p>Famoxadone consists of a racemic mixture of enantiomers (<i>S</i>-isomer to <i>R</i>-isomer ratio is about 1:1)</p> <table border="1"><tr><td><p><i>S</i>-isomer (DPX-JR715)</p></td><td><p><i>R</i>-isomer (DPX-JR714)</p></td></tr></table>		 <p><i>S</i>-isomer (DPX-JR715)</p>	 <p><i>R</i>-isomer (DPX-JR714)</p>
 <p><i>S</i>-isomer (DPX-JR715)</p>	 <p><i>R</i>-isomer (DPX-JR714)</p>		

Table 2: Key physicochemical properties of the active constituent famoxadone

Physical form:	Off-white powders
Colour:	Off-white to pale cream coloured
Odour:	Odourless
Melting point:	141.3 – 142.3°C
Boiling point:	n/a (decomposes at 275°C)
Relative density:	1.310
Stability:	Famoxadone is expected to remain in compliance with its specifications under normal conditions and is unlikely to be adversely affected by the presence of metals or metal ions.
Safety properties:	Famoxadone is not considered flammable, auto-flammable, or explosive (after testing under friction, thermal and shock conditions), and it has also no oxidising properties, indicating that it is a relatively safe chemical during transport and storage.
Solubility in water:	Essentially water insoluble 138 µg/L at pH 4 and 20°C 59 µg/L at pH 7 and 20°C 43 µg/L in unbuffered milli Q water at 20°C
Organic solvent solubility:	Acetone: 274 g/L (20°C) Dichloromethane: 239 g/L (20°C) Acetonitrile: 125 g/L (20°C) Ethyl acetate: 125 g/L (20°C) Toluene: 13 g/L (20°C) Octanol: 1.8 g/L (20°C) Hexane: 0.048 g/L (20°C)
PH (1% in water):	6.56 at 25°C
Octanol/water partition coefficient:	Log Kow = 4.59 at 20°C and pH 3 Log Kow = 4.8 at 20°C and pH 5 Log Kow = 4.65 at 20°C and pH 7 Log Kow = 5.55 at 20°C and pH 9
Vapour pressure:	6.4×10^{-7} Pa at 20°C
Henry's law constant:	5.57×10^{-3} Pa m ³ mol ⁻¹ in Milli-Q-water 1.74×10^{-3} Pa m ³ mol ⁻¹ at pH 4 4.06×10^{-3} Pa m ³ mol ⁻¹ at pH 7
UV/VIS absorption spectra:	$\epsilon = 533$ L mol ⁻¹ cm ⁻¹ at $\lambda_{\text{max}} = 231$ nm

Famoxadone is an off-white powder with a melting point at ~141-142°C. Above that, temperature thermal decomposition occurs, starting from 235°C and completely decomposing at 275°C. It is essentially water-insoluble (59 µg/L at pH 7 at 20°C), but it is readily soluble in polar organic solvents (ranged from 125 g/L in ethyl acetate and acetonitrile, to > 239 g/L in dichloromethane and acetone) and can dissolve to some extent in non-polar solvents (ranged from 0.048 g/L in *n*-hexane to 13 g/L in toluene). It has low vapour pressure (6.4×10^{-7} Pa at 20°C), while the Henry's law constants ($\sim 10^{-3}$ Pa m³ mol⁻¹) indicate a moderate volatility from water. Famoxadone has a high octanol-water partition coefficient ($\log P_{ow} = 4.65$ at pH 7 and 20°C), indicating potential for fat solubility and bioaccumulation. Famoxadone is not considered flammable, auto-flammable, or explosive, and it has also no oxidising properties, indicating that it is a relatively safe chemical during transport and storage.

Formulated product

The product *Zorvec Encantia Fungicide* will be manufactured overseas. Tables 3 and 4 outline some key aspects of the formulation and physicochemical properties of the product.

Table 3: Key aspects of the formulation of *Zorvec Encantia Fungicide*

Distinguishing name:	<i>Zorvec Encantia Fungicide</i>
Formulation type:	Suspension concentrate (SC)
Active constituent concentrations:	300 g/L famoxadone and 30 g/L oxathiapiprolin

Table 4: Physicochemical properties of *Zorvec Encantia Fungicide*

Physical form:	Milky beige liquid, with sharp to mild odour after opening vial.
PH:	4.1 (neat); 4.6 – 5.2 (1% aqueous dilution)
Relative density:	1.071
Viscosity:	923 mPa s at 25 rpm; 374 mPa s at 100 rpm using Brookfield DV-III Ultra
Pourability	Residue:< 4.8%; Rinsed residue: 0.25%
Wet sieve test	< 0.1% retained on a 75 µm sieve
Particle size	D50 <2.0 µm; D90 < 8.0 µm
Persistent foaming	< 2 mL foam after 1 minute
Safety properties:	Not thermally explosive under the test conditions Not oxidising under the test conditions Flammability: flash point > 77°C (i.e. flash point not observed below the boiling point at 77°C) Auto-ignition temperature: 422°C Zorvec Encantia Fungicide is not explosive or oxidising. It would not be classified as a flammable liquid under the Australian Dangerous Goods Code.
Storage stability:	The product should remain within specifications for at least 2 years when stored under normal conditions.

Recommendations

The APVMA has evaluated the chemistry and manufacturing aspects of the active constituent famoxadone and the associated product, *Zorvec Encantia Fungicide*, including the formulation, physicochemical properties, specifications, manufacturing process, quality control procedures, stability, batch analysis results and analytical methods, and found them to be acceptable. The available storage stability data indicate that the formulated product is expected to remain stable for at least 2 years when stored under normal conditions.

Based on a review of the chemistry and manufacturing details, the registration of *Zorvec Encantia Fungicide* and approval of the active constituent famoxadone, are supported from a chemistry perspective.

Toxicological assessment

The applicant submitted international evaluations on famoxadone undertaken by JMPR¹, EU²/EFSA³ and US EPA⁴, together with all underlying studies. In addition, acute toxicity studies and *in vitro* and *in vivo* genotoxicity studies were submitted for the product Zorvec Encantia Fungicide.

Evaluation of toxicology

While famoxadone has low acute toxicity, it is cataractogenic in dogs following repeat dosing. Although cataracts were not induced in mice, rats, or cynomolgus monkeys indicating a species-specific phenomenon, the mode of action of cataractogenesis has not been fully elucidated, and thus the human relevance of this effect cannot be excluded. Furthermore, the form and severity of the cataractogenesis observed in dogs is unlikely to be reversible.

Chemical class

Famoxadone is a QoI fungicide (FRAC group 11).

Pharmacokinetics

Orally administered famoxadone was readily absorbed from the GI tract in mice, rats, and dogs. In general, maximum concentrations (C_{max}) of radiolabel in plasma from all test species occurred between 1 and 4 hours following dosing. Elimination was relatively slow in dogs, with approximately 65% of the administered dose eliminated in faeces and urine by 24h. Excretion was faster in rats, with almost all administered doses being recovered in faeces and urine (>75% and 10%, respectively) within 24 hours. In rats, biliary excretion accounted for 30–39% of the dose, 56–65% in faeces with 2–6% in urine. In dogs, 70% of the administered dose was recovered from faeces with 8% from urine. Unmetabolised famoxadone was the major component recovered in faeces (50–60%), with hydroxylated metabolites found at up to 13% of the administered dose. In urine, only hydrolytic cleavage products, such as 4-acetoxylaniline, were detected.

Low residue levels were found in tissue of rats and dogs ranging between 0.45% to 3% of the administered dose. In dogs, the highest concentrations were found in the liver (1.34 $\mu\text{g/g}$) followed by mesenteric fat (0.95 $\mu\text{g/g}$). Residues in the whole eye and aqueous humour averaged 0.106 and 0.061 μg equivalents/g,

¹ JMPR, 2003, Joint Meeting on Pesticide Residues. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment. Geneva, Switzerland, 15–24 September 2003. <https://www.fao.org/4/y5221e/y5221e00.htm>

² EU, 2014, Famoxadone – European Commission Renewal Assessment Report (RAR). Annex B (volume 3). B6a Toxicology & Metabolism.

³ EFSA, 2015, Conclusion on the peer review of the pesticide risk assessment of the active substance famoxadone. European Food Safety Authority, Parma, Italy. EFSA Journal 2015:13(7):4194. <https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2015.4194>

⁴ US EPA, 2020, Famoxadone: Human Health Draft Risk Assessment in Support of Registration Review. Report No. D449290. 14 December 2020.

respectively, 2 h after dosing. However, low residue levels were still present in the eyes at 36 h (residue study termination).

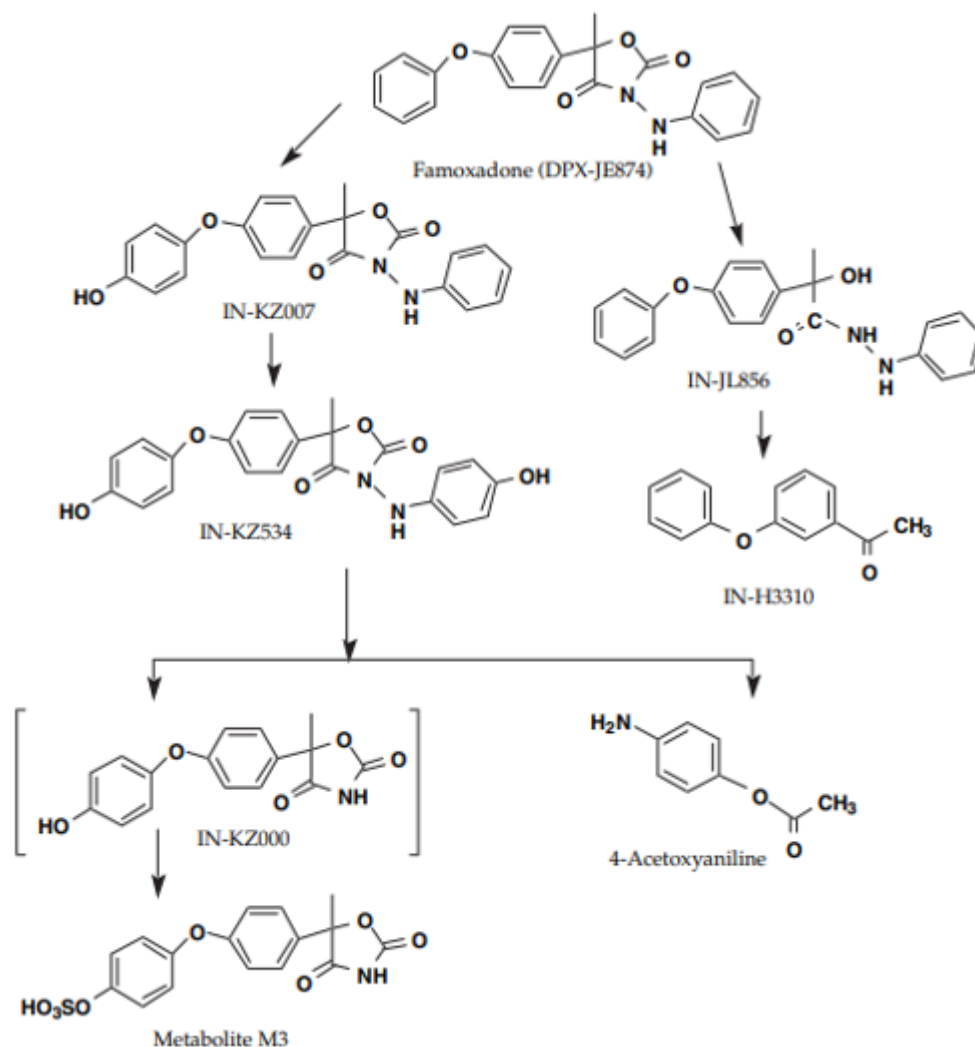
No dermal or inhalation absorption studies were provided for assessment. In the absence of inhalation absorption data, a default value of 100% for inhalation absorption was used (EFSA 2014⁵). In regard to dermal absorption, the APVMA used a default value of 5% for the concentrate (US EPA 2021⁶) and 14% for the spray dilution (pro rata EFSA default value⁷).

⁵ EFSA, 2014, Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 12(10):3874.
(<https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2014.3874>)

⁶ US EPA, 2021a, Occupational Pesticide Handler Exposure Calculator (OPHEC) (version date: May 2021). Occupational Pesticide Handler Exposure Data | Pesticide Science and Assessing Pesticide Risks | US EPA
(<https://www.epa.gov/sites/production/files/2021-05/opp-hed-occupational-handler-exposure-may-2021.xlsx>)

⁷ EFSA, 2017, EFSA Guidance on Dermal Absorption. EFSA Journal 15(6):4873.
(<https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.4873>)

Figure 1: Proposed metabolic pathways for famoxadone in rats



Acute toxicity (active constituent)

Results of acute studies indicate that famoxadone has low toxicity by the oral, dermal and inhalation routes; is a slight skin and eye irritant; but is not a skin sensitiser (As per the Guinea Pig Maximisation Test).

Acute toxicity (product)

Results of acute studies indicate that the product, Zorvec Encantia Fungicide, has low toxicity by oral, dermal, and inhalation routes; is a slight skin and eye irritant; a possible respiratory irritant; and is a skin sensitiser (Buehler test).

Repeat-dose toxicity

In short-term oral studies (14–28 days) in rodents, the predominant effect was hepatotoxicity (hypertrophy, degeneration, and single-cell necrosis) seen at >550 mg/kg bw/d in mice and >430 mg/kg bw/d in rats.

In a 28 day rat dermal study, the NOAEL was 250 mg/kg bw/d, based on increased liver enzyme levels, suggestive of minimal hepatotoxicity at 250 mg/kg bw/d. Similar hepatic effects were seen in a 4 week rat inhalation study together with effects on RBC mass and spleen weight. The NOAEL for famoxadone was 16 mg/m³ based on these effects at 110 mg/m³.

In a 90 day studies in rodents, similar effects were seen on haematology, liver, and spleen, as in short-term studies, with NOAELs of ~70 mg/kg bw/d in mice and ~15 mg/kg bw/d in rats.

In dogs, there were no effects on liver pathology or microscopic eye lesions up to 64 mg/kg bw/d famoxadone in a 5 week feeding study.

In a 13 week dog study, the main clinical sign of toxicity was myotonic twitch (proposed to be caused by increased serum hyperkalaemia). Histopathological examination of high dose animals revealed microscopic eye lesions in 7/8 animals; increased pigment (hemosiderin) in the liver; and bilateral seminiferous tubule immaturity (associated the lower body, testes, and epididymis weights). At the lowest dose of 1.3 mg/kg bw/d, eye lesions were seen in 1/8 females and therefore a NOAEL was not established.

In a one year dog study, famoxadone administration had no adverse effect on survival, clinical pathology, or histopathology. Statistically significant changes were observed in a few haematology and organ weight parameters but were not considered treatment related as they were not associated with microscopic changes and were within historical control ranges. Ophthalmoscopic examination revealed ocular lesions in males and females in high dose groups. These lesions were observed clinically as equatorial and posterior subcapsular lens opacities, and microscopically as lenticular degeneration. Partial regression of these lesions was seen in some dogs when exposure to the test substance ended (recovery group). Under the conditions of this study, the NAOEL was 1.2 mg/kg bw/d for both male and female dogs, based on ocular lesions observed at 9 mg/kg bw/d.

In a 52 week monkey study (four/sex/dose), famoxadone administration was associated with lower RBC count, haemoglobin, and haematocrit with microscopic changes in the spleen, liver, and kidney in both sexes at 1000 mg/kg bw/d. No treatment-related ophthalmic changes or changes in absolute organ weights, organ-to-body weight percentages and organ-to-brain weight ratios were found. Based on the effects seen in both sexes at 1000 mg/kg bw/d, the NOAEL was established at 100 mg/kg bw/d.

Chronic toxicity and carcinogenicity

In an 18 month feeding study in male and female mice, famoxadone was not carcinogenic. The NOAEL was established at 50 ppm (equivalent to 7 mg/kg bw/d in males), based on an increased incidence of hepatocellular hypertrophy with eosinophilic foci of cellular alteration and increased beta-oxidation activity at 96 mg/kg bw/d.

In a 2 year feeding study in male and female rats, famoxadone was not carcinogenic. Ophthalmologic evaluations were carried out on all surviving animals at 12 months and end of study. No ophthalmoscopic abnormalities were seen at 12 months, however, the incidence of lenticular degeneration was increased in mid and high dose males at 24 months. The APVMA agrees with the consensus of international agencies that eye lesions in rats were unlikely to be treatment-related as they were neither statistically significant nor

dose-related. The NOAEL was established at 8.5 mg/kg bw/d in males, based on an increased incidence of microscopic lesions indicative of hepatotoxicity and haemolysis at 17 mg/kg bw/d.

Reproductive and developmental toxicity

In a two-generation reproduction study in rats, reproductive indices, including mating, fertility, and gestation as well as pup viability at parturition were unaffected by famoxadone treatment. A slight reduction in mean pup weight was seen throughout lactation in F1 and F2 litters at maternally toxic doses.

No treatment-related effects were observed in any developmental endpoints in rats and rabbits. Maternal and foetal NOAELs in both species were 1000 mg/kg bw/d, the highest dose tested.

Famoxadone is neither a reproductive nor developmental toxicant.

Genotoxicity

Famoxadone was evaluated for genotoxic potential in a comprehensive battery of *in vitro* and *in vivo* tests. *In vitro*, famoxadone tested negative in the bacterial mutagenicity in *Salmonella typhimurium* and *E. coli* (Ames assay), mammalian cell mutagenicity (CHO/HGPRT), and equivocal in unscheduled DNA synthesis in rat primary hepatocytes and chromosome aberrations in human lymphocytes. *In vivo*, famoxadone tested negative for unscheduled DNA synthesis (UDS), and bone marrow micronucleus tests in mice and rats. In addition, *in vitro* and *in vivo* genotoxicity studies with Zorvec Encantia Fungicide were also negative.

The weight-of-evidence indicates neither famoxadone nor the Zorvec Encantia Fungicide are genotoxic.

Neurotoxicity/immunotoxicity

In acute and 90 day neurotoxicity studies in rats, there were no adverse effects in motor activity or in functional observational battery (FOB) tests or nervous system tissue morphology at any dose up to 2000 mg/kg bw (acute study) and 60 mg/kg bw/d (90-day study).

Dietary administration of famoxadone to mice and rats for 28 days did not suppress the primary humoral immune response to sheep red blood cells (SRBC) at doses up to 1662 mg/kg bw/d in mice and 56 mg/kg bw/d in rats.

Mode of action (toxicology)

The APVMA concurred with other international agencies that cataractogenicity in dogs is the most sensitive repeat-dose toxicological endpoint for famoxadone. Although lenticular degeneration was also seen in rats, it was only seen in males and did not exhibit a dose-response relationship. The APVMA agreed with international consensus that eye lesions in rats were unlikely to be treatment related. Although the available evidence indicates that famoxadone induced cataractogenicity may be species-specific, there is currently insufficient Mode of Action (MoA) data to determine the relevance of cataracts in dogs to humans. Although a number of MoA have been associated with substance-induced cataract formation in animal studies, the vast majority are of unknown mechanistic aetiology.

Toxicity of metabolites and/or impurities

The APVMA is satisfied that impurities identified in the TGAC are present below the level of toxicological concern.

No toxicity data was available for any animal metabolites. It is assumed that the toxicological profile of famoxadone reflects any specific effects due to a metabolite(s). Of note, it was not possible to extract and identify radioactive metabolites from the aqueous humour of dogs, owing to very low concentrations and small sample size.

Reports related to human toxicity

No data on adverse health effects in humans exposed to famoxadone was provided in the submitted data or PubMed online search by the APVMA.

Health-based guidance values and poisons scheduling

Poisons Standard

Famoxadone is in Schedule 6 of the SUSMP, without any exceptions.

Zorvec Encantia Fungicide requires a 'POISON' label signal header.

Health-based guidance values

Acceptable daily intake

An ADI of 0.006 mg/kg bw/d was established from a NOAEL of 1.2 mg/kg bw/d in a 52 week dog study, based on ophthalmological and histopathological changes in the lens at the next highest dose. A total uncertainty factor of 200 was used to account for the steep dose response relationship for these effects in dog studies. The APVMA notes that the ADI established by all international agencies is based on the one year dog study, and the most sensitive effect: eye lens damage.

Acute reference dose

Based on the available data, no demonstrable adverse effects occurred following a single exposure to famoxadone at doses far exceeding those to which humans would likely be exposed. Accordingly, an ARfD is not required. No evidence of famoxadone-induced neurotoxicity occurred in acute studies in rats or dogs, and there was no evidence of developmental toxicity in rats or rabbits at doses up to 1000 mg/kg bw/d.

Recommendations

There are no objections on human health grounds to the approval of the active constituent, famoxadone, when complying with the declaration of composition (DoC) provided by the applicant.

There are no objections on human health grounds to the registration of the product Zorvec Encantia Fungicide, containing 300 g/L famoxadone and 30 g/L oxathiapiprolin in an aqueous suspo-emulsion formulation, when used in accordance with the directions for use (DFU) and adhering to the recommended label safety directions and restraints (see WHS assessment).

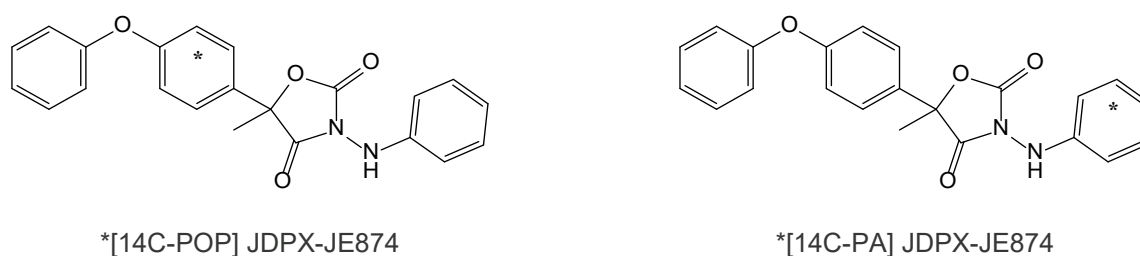
Residues assessment

The applicant has submitted metabolism, residue trial data, analytical methodology, fate in storage, processing data, and residues in trade information, which are considered here.

Metabolism

Good Laboratory Practice (GLP) studies on the metabolism and distribution of famoxadone (JDPX-JE874) were provided for both plants and animals. These studies were performed using one or 2 radio-labelled test materials with [¹⁴C]famoxadone uniformly labelled in the phenoxyphenyl or phenylamino ring. Plant metabolism studies across several crop types were considered, including fruit (grapes), fruiting vegetables (tomato), pulses and oilseeds (soybean), cereals (wheat) and root and tuber vegetables (potato) as well as in rotational crop representatives for root and tuber vegetables (sugar beet), leafy vegetables (lettuce) and cereals (wheat). For animals, metabolism studies in lactating goats and laying hens were considered.

Figure 2: The position of the ¹⁴C radio-label



* Denotes position of ¹⁴C- label

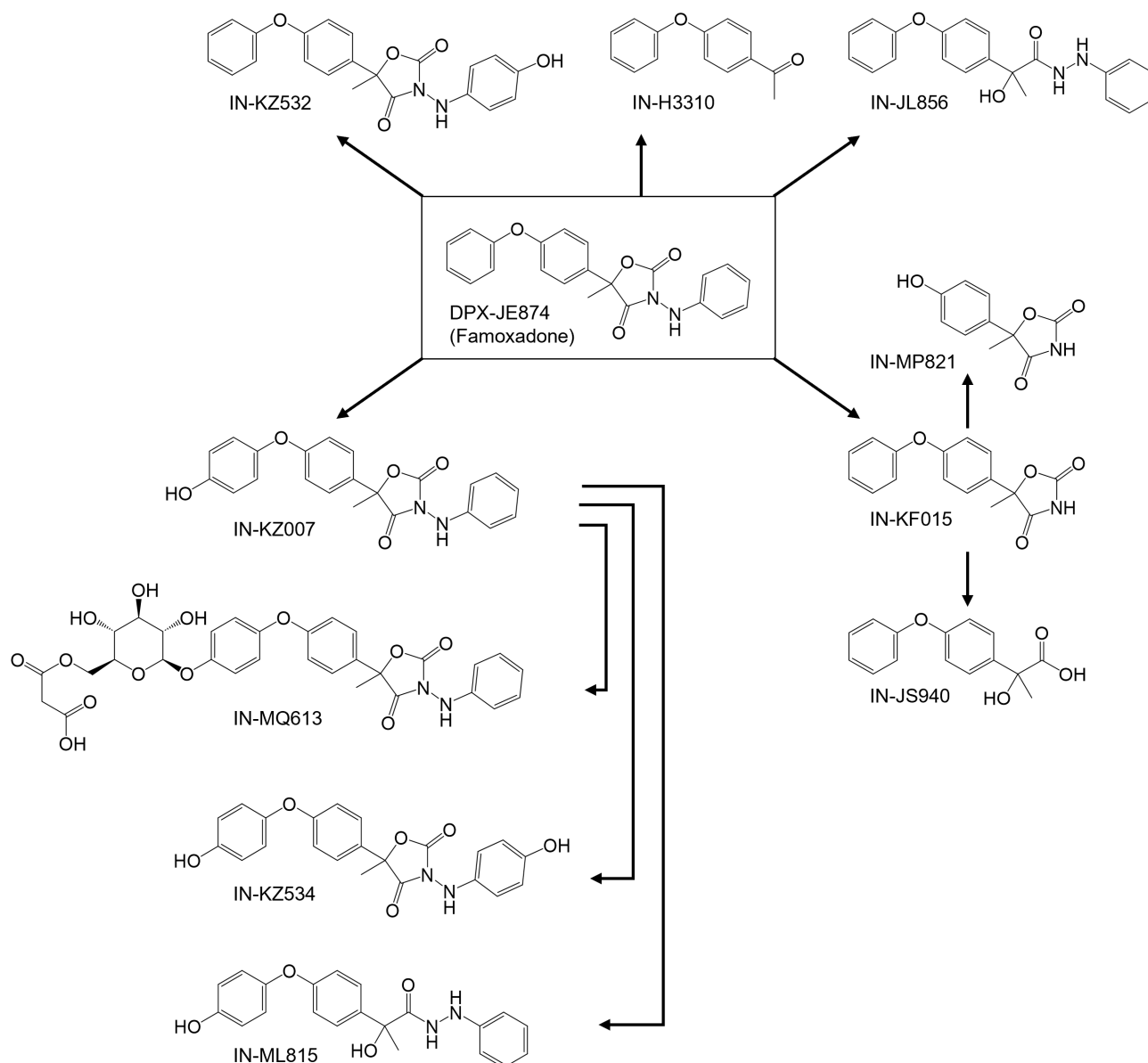
Plant commodities

Metabolism was observed to be similar between all crop types investigated, including grapes, potatoes, tomatoes, wheat, and soyabeans. At harvest, the Total Radioactive Residues (TRRs, expressed as parent equivalent) were 0.01–0.02 mg/kg for wheat grain and 2.5–4.2 mg/kg for wheat straw; less than 0.01 mg/kg in potatoes; 0.25–0.34 mg/kg in grapes; 0.03–0.08 mg/kg in soybean and 0.66–0.81 mg/kg in soya bean straw; and 0.07–0.1 mg/kg in tomatoes. Parent famoxadone was the major component of total radiolabelled residues in the majority of all plant matrices, except wheat foliage and straw, and soyabean seeds at commercial harvest. Famoxadone made up >95% TRR in grape leaves and fruit, 76–95% of potato foliage (with <0.01 mg eq. famoxadone/kg in the tuber), >90% TRR in tomatoes, 14–16% TRR in wheat foliage, 9–10% TRR in wheat straw, 20–74% TRR across soyabean straw and pods, and 11–13% TRR in soyabean seeds.

Up to 12 minor metabolites were identified across crop groups which were generally observed at <0.01 mg eq/kg (or <10% TRR) with the exception of metabolite IN-H3310 which was observed at 0.94 mg eq/kg (1.4%) in grape foliage and 0.43 mg eq/kg (4.9%) in potato foliage, IN-JL856 observed at 0.19 mg eq/kg (2.2%) in potato foliage, and IN-KZ007, IN-MQ613 and IN-KZ534 which were observed at 0.27 (7.0%), 0.31 (11%) and 0.43 mg eq/kg (15% TRR) in wheat, respectively. In soybeans, other

metabolites were identified, plus several unknowns comprised of 2–20 additional minor components individually ranging from 0.001 to 0.063 mg eq/kg (0.06–8.5% TRR).

Figure 3: Proposed metabolic pathway of famoxadone in plants



Animal commodities

In lactating goats dosed orally at the equivalent of 10 ppm in feed for 7 days with either [^{14}C -POP] or [^{14}C -PA], the majority of radioactivity (>80% of the administered radioactive dose) was excreted via faeces. Radioactive residues in milk reached a plateau between days 6 and 7, at an average of 0.018 mg/kg ^{14}C famoxadone equivalents. The majority of extractable radioactive residues were found in the aqueous acetonitrile fraction for all tissue and milk samples. The hexane fraction contained minimal amounts of radioactive residues, and only the acetonitrile fraction was analysed for radioactivity distribution.

Famoxadone was the major detectable radioactive component of residues in milk (34–49%) and tissues (11–62%). The metabolic pathway of famoxadone involved hydroxylation of the phenoxyphenyl or phenylamino rings, followed by cleavage of the hydrazine bond. In milk, no individual radioactive components were present at greater than 0.01 mg/kg, with famoxadone representing, on average, 42% TRR. IN-KZ007 and IN-KZ000 were detected in liver tissue and IN-KZ534 and IN-KZ007 were detected in faeces. The unextractable fraction of residues in liver tissues was partly released by protease digestion. The individual components released and the remaining unextractable residues were at levels <0.05 mg/kg.

In laying hens dosed orally at the equivalent of 10 ppm in the feed for 7 days with either [¹⁴C-POP] or [¹⁴C-PA], the majority of radioactivity (88–92% of the administered radioactive dose) was excreted with <0.05% TRR found in the egg and <0.1% in the tissues. Famoxadone was the major residue component in excreta at 11–18% TRR with 15 metabolites also identified. With the exception of the polar metabolite, IN-MP821 (15.4% TRR), all other metabolites were present at <5% of the administered dose in faeces. Metabolite IN-KZ007, resulting from the hydroxylation of the phenyl phenoxy ring, was the major detectable radioactive component in both eggs and liver with <0.01 mg famoxadone eq./kg detected across fat, muscle and skin (0.02 mg eq./kg from the [¹⁴C-PA] label. Across both the [¹⁴C-POP] or [¹⁴C-PA] labelled active, IN-KZ007 made up 23–27% TRR in egg yolk and 15–27% TRR in liver. Parent famoxadone made up 3.5–4.4% TRR in egg yolk and was not detected in the liver (<0.002 mg eq./kg).

Figure 4: Proposed metabolic pathway of famoxadone in lactating goats

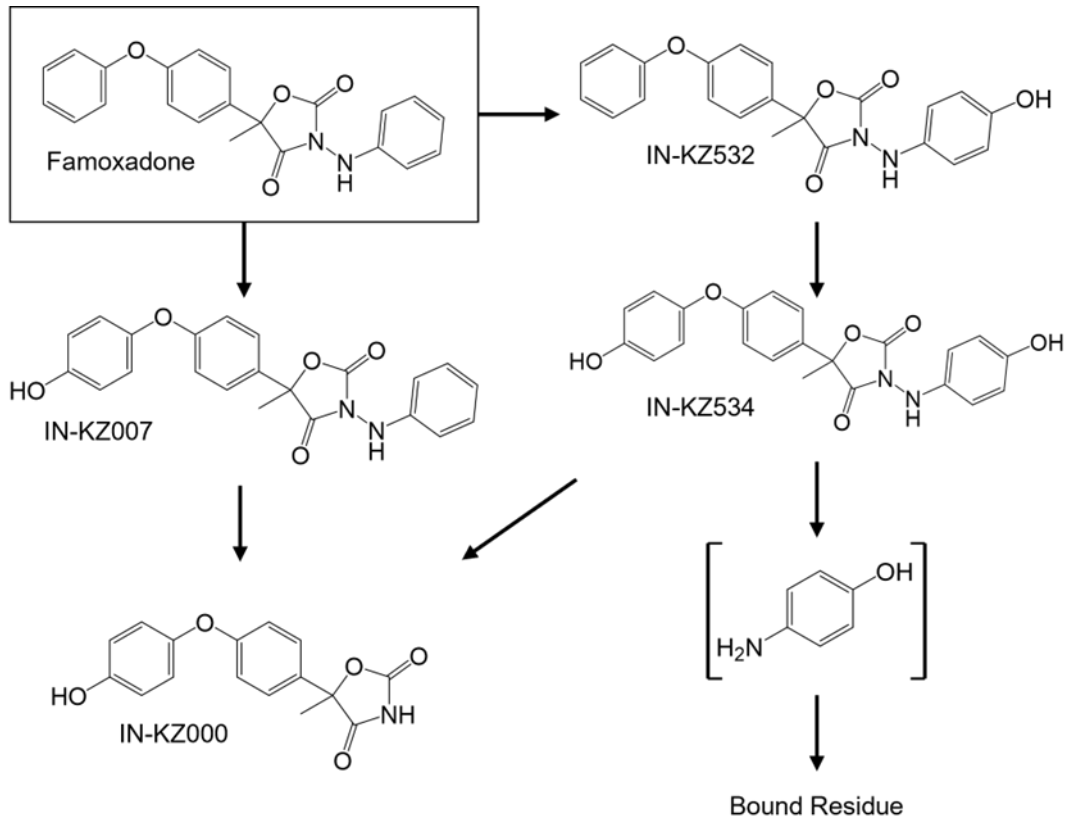
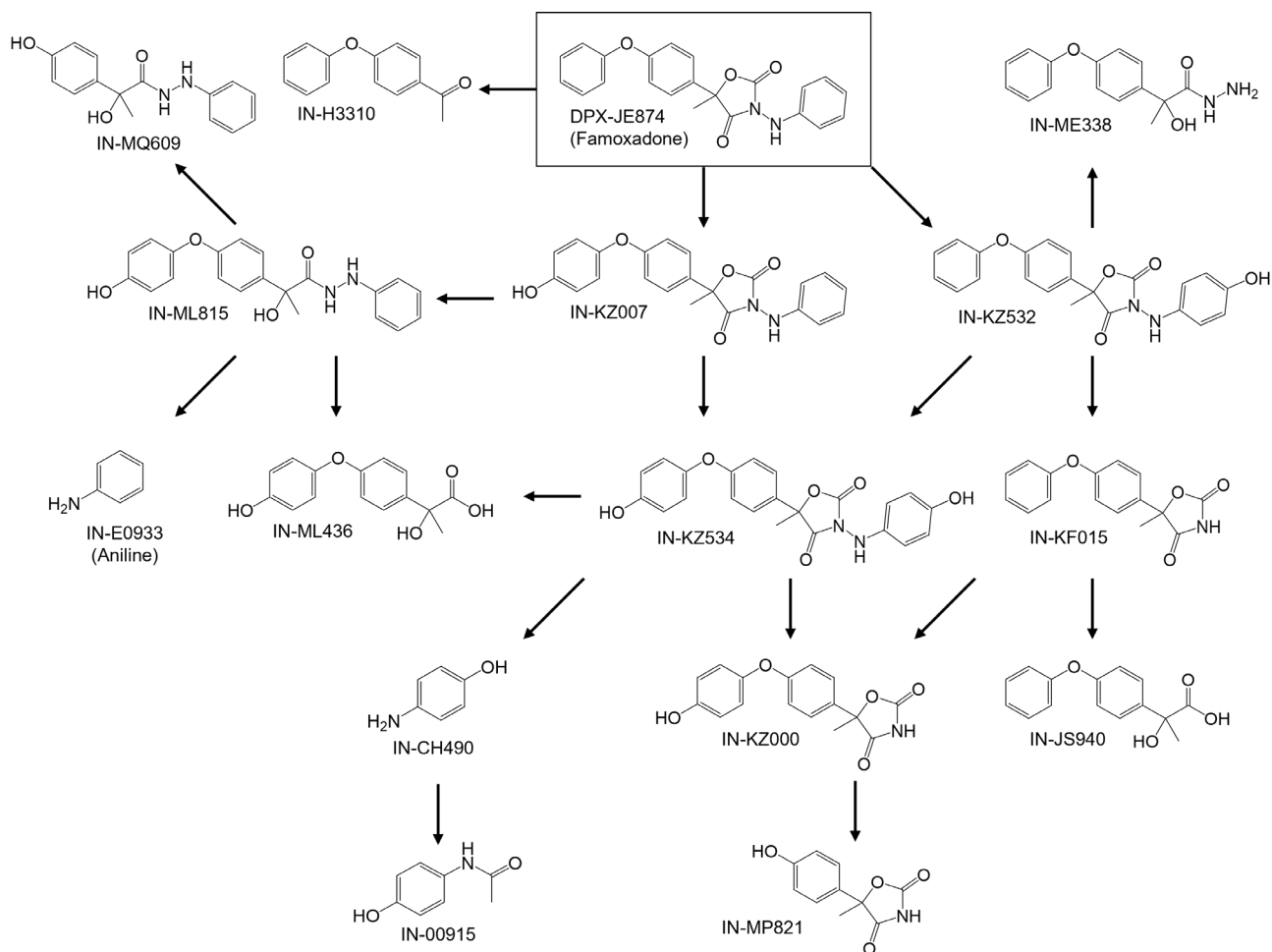


Figure 5: Proposed metabolic pathway of famoxadone in laying hens



Analytical methods and storage stability

In Australian leafy vegetable trials, residues of famoxadone and oxathiapiprolin were determined according to the analytical procedure “DuPont-30422: Analytical Method for the Determination of DPX-QGU42 and Metabolites in Crops Using LC/MS/MS.” This was either run in tandem, or with modifications from, the analytical procedure “DuPont-13908: Analytical Method for the Determination of Famoxadone in Spinach (Leafy Vegetables) using LC/MS/MS.” The Limit of Quantification (LOQ) of the method was demonstrated to be 0.010 mg/kg across head and leafy lettuce, spinach and Chinese cabbage and is summarised as follows:

Famoxadone residues are extracted from blended homogenous samples with a mixture of acetonitrile and water. Sample clean-up consists of a hexane liquid/liquid partition, followed by a salting out step. Sodium chloride is added to an aliquot of the extract to separate the aqueous phase from the organic phase. The aqueous phase is discarded and the acetonitrile layer containing famoxadone is concentrated to dryness. The residue is dissolved in 10% ethyl ether/90% hexane (v/v) and passed through a Florisil column retaining famoxadone. Famoxadone is then eluted from the column with a 20/80 ethyl acetate/hexane solution. The eluate is evaporated to dryness, reconstituted in acetonitrile and water and analysed by LC-MS/MS.

The method was validated with mean recoveries within the range of 80–120% with relative standard deviations (RSD) below 20% for each matrix, which is considered acceptable.

In US field trials, residues of famoxadone were determined in head lettuce, leafy lettuce and mustard greens according to a modified version of “*Analytical Method for the Determination of DPX-JE874 and Cymoxanil Residues in Various Matrices. Laboratory Project ID AMR 3705-95.*” The LOQ of the method was demonstrated to be 0.02 mg/kg across all three commodities. This procedure was also used for the rotational field cropping study to determine famoxadone residues in both plant and soil samples. As a superseded method, the dissolution, extraction, portioning, and clean-up are identical as above with quantification using GC/Nitrogen Phosphorous detection. The method was validated with mean recoveries in the range 80–120% and RSDs below 20% for each matrix, except for one RSD at 21% in Mustard greens, which is considered acceptable.

Residues of famoxadone were determined in spinach according to “*Analytical Method for the Determination of Cymoxanil and IN-KQ960 in Spinach (Leafy Vegetables) Using LC/MS.*” The LOQ of the method was demonstrated to be 0.02 mg/kg for spinach. Extraction consists as above with the salted acetonitrile fraction taken for purification by strong anion exchange (SAX) solid phase extraction (SPE) chromatography. The eluant is then concentrated under nitrogen stream, partitioned against hexane, and further purified by carbon (Envi-carb) SPE chromatography. The cleaned extract is then evaporated under nitrogen stream, reconstituted with methanol and 0.02% aqueous formic acid, and then analysed for residues of famoxadone (and cymoxanil and its metabolite IN-KQ960 not considered here) using high performance liquid chromatography with dual spectrometric (HPLC-MS/MS) detection. The method was validated with mean recoveries in the range 70–120% and RSDs below 20% for each matrix, which is considered acceptable.

The frozen storage stability of famoxadone residues was demonstrated for at least 18 months in an independent storage stability trial conducted in grapes, potato, wheat forage, straw and grain when stored at about -20°C . Concurrently run storage stability samples in head and leafy lettuce, spinach and mustard greens demonstrated that famoxadone residues were stable for up to 8 months in head lettuce, 11 months in mustard greens, <14 months in leafy lettuce and 25 months in spinach when stored at about -20°C . In the Australian leafy vegetable trials, samples were maintained under freezer conditions prior to analysis and tested within 6–12 months after collection. In the US trials, samples of head lettuce, leafy lettuce, spinach and mustard greens were maintained under freezer conditions prior to analysis and tested with 6–8 months, <12 months, <24 months, and <14 months after collection, respectively.

For animal commodities, analytical methods were provided for the determination of famoxadone in bovine muscle, fat, liver, and milk, as well as in poultry eggs. The first method “*Analytical Method for the Determination of Famoxadone in Milk and Bovine Tissues Using Column-Switching Liquid Chromatography with Ultraviolet Detection*” had validated LOQs of 0.01 mg/kg for bovine milk, cream, muscle, and fat and 0.05 mg/kg for liver. The method is summarised as follows: Animal tissue samples were mixed with C-18 packing and allowed to air-dry. The mixture is then packed into an SPE reservoir, eluted with hexane and then the famoxadone was eluted with acetonitrile. The eluate was filtered through a bed of basic alumina and the extract was passed through a graphitised-carbon SPE cartridge. The resulting solution that passed through the cartridge was collected and the cartridge then eluted with methanol/dichloromethane (10:90, v/v). The 2 eluates were combined and evaporated to dryness. A final clean-up was made by means of a silica cartridge, to remove additional lipid material. The final extract was analysed by column-switching HPLC (phenyl and C-18 columns) and UV detection at 245 nm. The method was validated with mean

recoveries in the range 80–100% and RSDs below 20% for each matrix, which is considered acceptable. This method was proposed for regulatory use.

A second validated method, “*Determination of Residues of Famoxadone in Animal Tissues using Multi-Residue Method DFG S 19 (LC-MS/MS Module)*” was also provide demonstrating an LOQ of 0.01 mg/kg in egg, milk, meat and liver. The method is summarised as follows:

For egg, milk, meat and liver, samples are homogenised with water and acetone 2/1 (v/v). For liquid-liquid portioning, sodium chloride and dichloromethane are added and after repeated mixing the phases are separated. Otherwise, sodium chloride and ethyl acetate/cyclohexane (1/1, v/v) are added and, following repeated homogenisation, the organic layer containing famoxadone is allowed to separate from the aqueous layer. The evaporated residue of an aliquot of the organic phase is cleaned up by gel permeation chromatography (GPC) on Bio Beads S-X3 (polystyrene gel) using a mixture of ethyl acetate/cyclohexane (1/1, v/v) as eluant. For fat, samples are dissolved in a mixture of ethyl acetate and cyclohexane (1/1, v/v) with clean up as described above. Residue-containing GPC fractions are concentrated, re-dissolved in the HPLC solvent and analysed by liquid chromatography using tandem mass spectrometric detection (LC-MS/MS). The method was validated with mean recoveries in the range 70–120% and RSDs below 20% for each matrix, which is considered acceptable.

Analytical methods for the determination of oxathiapiprolin across both plant and animal commodities have previously been assessed and require no further evaluation for this application.

Residue definition

In the primary plant metabolism studies, parent famoxadone was the major component of total radiolabelled residues in the majority of plant matrices. Famoxadone made up >95% TRR in grape leaves and fruit, 76–95% of potato foliage (with <0.01 mg eq. famoxadone/kg in the tuber), >90% TRR in tomatoes, 14–16% TRR in wheat foliage, 9–10% TRR in wheat straw, 20–74% TRR across soyabean straw and pods, and 11–13% TRR in soyabean seeds. For plants, based on famoxadone being the major component of the radioactively identified in the majority of plant matrices and the capability of the analytical methods (which analysed for parent famoxadone only), the residue definition for enforcement and risk assessment is recommended to be famoxadone. This is in line with definitions recommended by Codex and overseas.

From the lactating goat metabolism study, famoxadone was the major detectable radioactive component of residues in milk and tissues. Across both the [¹⁴C-POP] or [¹⁴C-PA] labelled active, parent famoxadone made up 34–49% TRR in whole milk, 11–26% TRR in liver, 14–42% in kidney, 40–59% in muscle and 51–62% in fat. Metabolites IN-KZ007, IN-KZ532 and IN-KZ000 were observed in liver tissue at <10% TRR.

From the laying hen metabolism study, metabolite IN-KZ007, resulting from the hydroxylation of the phenyl phenoxy ring, was the major detectable radioactive component in both eggs and liver with <0.01 mg famoxadone eq./kg detected across fat, muscle and skin (0.02 mg eq./kg from the [¹⁴C-PA] label. Across both the [¹⁴C-POP] or [¹⁴C-PA] labelled active, IN-KZ007 made up 23–27% TRR in egg yolk and 15–27% TRR in liver. Parent famoxadone made up 3.5–4.4% TRR in egg yolk and was not detected in the liver (<0.002 mg eq./kg).

For animals, the residue definition for enforcement and risk assessment is recommended to be famoxadone. This is in line with definitions recommended by Codex and overseas.

Residues in food and animal feeds

The proposed use of *Zorvec Encantia Fungicide* (SC) on spinach and rocket is for up to 3 applications, each at 210 g famoxadone/ha + 21 g oxathiapiprolin starting from the 7 to 10 days apart with a harvest withholding period of 3 days. Application can occur up to the 8 true leaf stage for baby leaves of spinach and rocket.

In support of the proposed use, the applicant has provided 2 Australian GLP residues studies conducted on leafy vegetables which include 3 trials on leafy lettuce, 3 trials on head lettuce, one trial on spinach, one trial on rocket, and one trial on Chinese cabbage. These studies were conducted with a suspoemulsion (SC) containing 310 g/L *famoxadone* and 31 g/L *oxathiapiprolin*. One study included use of adjuvants in side-by-side trials noting the proposed label states *Zorvec Encantia Fungicide* should always be applied with an adjuvant. When famoxadone and oxathiapiprolin was applied at the proposed Good Agricultural Practice (GAP) in combination with, and without, a non-ionic spray adjuvant (AGRAL Spray Adjuvant, APVMA no. 54116) or an organosilicone surfactant (MAXX Organosilicone Surfactant, APVMA no. 54348), no changes in the residues potential across treatments was observed.

Additionally, the full details of five international GLP studies (USA) conducted on leafy vegetables have been provided in support of the proposed use and include: 15 trials on head lettuce, 7 trials on leafy lettuce, 7 trials on spinach and 9 trials on Mustard greens. These studies were conducted with DPX-KP481 or Tanos 50 WG, both formulated as a water dispersible granule (WG) containing 25% *cymoxanil* and 25% *famoxadone* by weight (50% active by weight). It is noted the product formulation of the US trials differs to that of the proposed product, WG to SC; however, as the withholding period or pre-harvest interval (PHI) is ≤ 7 days, Organisation for Economic Cooperation and Development (OECD) guidance suggest residue data can be extrapolated for all formulations diluted in water in this case⁸.

The highest residues of famoxadone across leafy vegetables including brassica leafy vegetables were as follows:

In head lettuce (including wrapper leaves) at 3 days (one at 5 days) after the last of 3–7 foliar applications at 210 g a.c./ha residues were 0.23, 0.80, 1.2, 1.3, 1.6, 1.9, 2.1, 2.2, 2.6, 2.7, 2.8, 3.6, 5.3, 7.6, 8.4, 9.1, 11, and 14 mg/kg (n=18). In leafy lettuce (washed or unwashed) at 2–3 days after the last of 3–4 foliar applications at 210 g a.c./ha residues were <0.02, 2.3, 2.7, 3.8, 5.0, 6.6, 7.2 (2), 11 and 30 mg/kg (n=10). In spinach (washed or unwashed) at 2–3 days after the last of 3–4 foliar applications at 210 g a.c./ha residues were 4.6, 5.0, 11 (2), 13, 14, 22, 29 mg/kg (n=8). In brassica leafy vegetables (Mustard greens, rocket and Chinese cabbage) at 2–4 days after the last of 3–4 applications at 210 g a.c./ha residues were 2.4, 3.6, 6.0, 6.8, 10, 12, 14, 16, 17, 19, 31 mg/kg (n=11).

The combined dataset suitable for Maximum Residue Limit (MRL) estimation is, in rank order; <0.02, 0.23, 0.80, 1.2, 1.3, 1.6, 1.9, 2.1, 2.2, 2.3, 2.4, 2.6, 2.7 (2), 2.8, 3.6 (2), 3.8, 4.6, 5.0 (2), 5.3, 6.0, 6.6, 6.8, 7.2 (2), 7.6, 8.4, 9.1, 10, 11 (4), 12, 13, 14 (3), 16, 17, 19, 22, 29, 30, and 31 mg/kg (n=47). The STMR was

⁸ OECD Test Guideline 509 Crop Field Trial – June 2021 – [Link](#) – Accessed July 2024

6.60 mg/kg. The OECD MRL calculator estimates an MRL of 40 mg/kg. A famoxadone MRL of 40 mg/kg for 'VL 0053 Leafy vegetables' in conjunction with a 3 day withholding period is recommended.

Oxathiapiprolin-based products are currently registered for use on leafy vegetables for up to 3 applications, with a maximum of 2 consecutive, at 35 g a.c./ha [1.7× that proposed] and minimum re-treatment interval of 7 days with a 3 day PHI (Product number 68375).

From the Australian residue studies, residues of *oxathiapiprolin* at the proposed GAP are as follows: 0.20, 0.22, and 0.30 mg/kg in head lettuce, 0.17, 0.33, and 1.6 mg/kg in leafy lettuce, 0.37 mg/kg in spinach, 0.34 in Chinese cabbage, and 2.0 mg/kg in rocket. These remain 7.5× below the current MRL of 15 mg/kg for 'VL 0053 Leafy vegetables {except Lettuce, head}' and 6.7× below the current MRL of 2 mg/kg for 'VL 0482 Lettuce, head'. No changes to oxathiapiprolin MRLs are recommended at this time.

Crop rotation

For famoxadone, 2 GLP rotational crop studies, one confined and one field study, were provided in support of this registration application.

The confined study used radio-labelled famoxadone, either [¹⁴C-POP] or [¹⁴C-PA], applied to soil in one or 3 applications at 400 g a.c./ha aged under greenhouse conditions for 30, 120 or 365 days before planting of lettuce, sugar beet or wheat. Famoxadone residues were detected in lettuce, sugar beet roots, wheat forage and straw (0.02 to 0.06 mg/kg equivalents) but not in sugar beet tops or wheat grain (<0.01 mg/kg eq). Average residues in treated soils were 0.26 and 0.04 mg/kg famoxadone equivalents at days 30 and 120, respectively. No famoxadone was detected in crops or soil after 365 days.

The field study used a WG formulation containing 25% cymoxanil and 25% famoxadone by weight applied 6 times to growing tomatoes as a foliar broadcast spray. Each application was made at a rate of 210 g a.c./ha [1×proposed rate per application, 2× proposed seasonal rate] with applications approximately 5 days apart. Three days after the last application, mature tomatoes and tomato plants were ploughed into the soil in each treated plot and subplots were prepared for planting of rotational crops (radish, spinach and wheat) for 3 plant-back intervals 14, 30, and 60 days. Crop samples consisted of tomato foliage (primary crop) and immature samples of radish, spinach, and wheat plants harvested immediately after emergence of each crop. Radish tops (leaves) and roots, spinach leaves, and wheat forage, hay, straw and grain were also harvested at normal crop maturity. These samples were taken from each of 3 rotational planting intervals after treating tomatoes.

In the field study, the majority of residues of famoxadone were below the LOQ of the analytical method in radish tops or root samples, spinach leaves, or wheat forage, hay, grain, or straw at normal harvest after a rotational interval of 14, 30, or 60 days (residues <0.010 ppm). Finite residues were found in a single sample of radish tops (leaves) after a rotational interval of 60 days but were <0.01 mg/kg in radish tops for the shorter plant back intervals, suggesting these detections may be an anomaly. It is noted finite famoxadone residues were also found in immature radish plants sampled from the 14 and 60 day rotational interval plots, respectively, but these would be estimated to be <0.01 mg/kg when scaled for the proposed seasonal application rate. Based on the weight of evidence from all results plant back intervals are not required and an 'All other foods' famoxadone MRL is not recommended at this time.

Residues in animal commodities

Leafy vegetables, including kale forage can be fed at 40% of the diet to dairy cattle and turnip leaves or tops fed at 80% of the diet for beef cattle. As a grazing restraint has been proposed, no further consideration for mammalian livestock burden was required.

An animal transfer study was provided where famoxadone was given in gelatine capsules to lactating Holstein dairy cows twice daily for 28 days, at feeding levels of 9.0, 27, or 90 ppm. Famoxadone residues were found at all doses in the tissues analysed, with higher concentrations in liver and fat. Residues in milk reached a plateau of 0.14, 0.43, and 1.5 mg/kg after 10 days, for the 9, 27, and 90 mg/kg feeding groups respectively. Residues of famoxadone were shown to preferentially partition into the milk fat as compared to whole milk and into fat tissue as opposed to muscle by a factor of 10 to 17. As analytical methods are available and found to be valid for the determination of famoxadone in animal matrices with LOQs of 0.01 mg/kg for animal tissues (0.01 to 0.05 mg/kg for liver) and milk, it is considered appropriate to established famoxadone mammalian commodity MRLs for 'MO 0105 Edible offal (mammalian)', 'MM 0095 Meat (mammalian) [in the fat]' and 'ML 0106 Milks' at *0.01 mg/kg.

No poultry feeding study was provided and is not considered necessary for the proposed use on spinach and rocket noting they are not a significant poultry feed. The expected famoxadone dietary burden for poultry is effectively zero. As a poultry metabolism study was provided and the analytical method is available and found to be valid for the determination of famoxadone in animal matrices with LOQs of 0.01 mg/kg for animal tissue and eggs, it is considered appropriate to established famoxadone poultry commodity MRLs for 'PE 0112 Eggs', 'PM 0110 Poultry meat [in the fat]' and 'PO 0111 Poultry, edible offal of' at *0.01 mg/kg.

No changes to animal commodity oxathiapiprolin MRLs are recommended at this time.

Dietary risk assessment

The chronic dietary exposure to famoxadone and oxathiapiprolin is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and the mean daily dietary consumption data derived primarily from the 2011–12 National Nutritional and Physical Activity Survey. The NEDI calculation is made in accordance with World Health Organisation (WHO) Guidelines and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for *famoxadone* is equivalent to < 46% of the ADI. It is concluded the chronic dietary exposure of *famoxadone* is acceptable. The NEDI for *oxathiapiprolin* is equivalent to < 1% of the ADI. It is concluded the chronic dietary exposure of *oxathiapiprolin* is acceptable.

The acute dietary exposure is estimated by the National Estimated Short-Term Intake (NESTI) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR with 97.5th percentile food consumption data derived primarily from the 2011–12 National Nutritional and Physical Activity Survey. NESTI calculations are conservative estimates of short-term exposure (24 hour period) to chemical residues in food. For both *famoxadone* and *oxathiapiprolin*, as noted in the previous section, an ARfD to be unnecessary due to low oral toxicity and the absence of any developmental toxicity after a single dose; therefore, an acute dietary exposure assessment is not required.

Recommendations

The following amendments are required to be made to the APVMA MRL Standard Tables 1 and 3.

Table 5: Amendments to the APVMA MRL Standard

Amendments to Table 1			
Compound		Food	MRL (mg/kg)
Add:			
Famoxadone			
MO	0105	Edible offal (mammalian)	*0.05
PE	0112	Eggs	*0.01
VL	0053	Leafy vegetables	40
MM	0095	Meat (mammalian) [in the fat]	*0.01
ML	0106	Milks	*0.01
PM	0110	Poultry meat [in the fat]	*0.01
PO	0111	Poultry, edible offal of	*0.01
Amendments to Table 3			
Compound		Residue	
Add:			
Famoxadone		Famoxadone	

Assessment of overseas trade aspects of residues in food

The proposed use does not involve treatment of major trade commodities and significant residues are not expected to arise in livestock feeds as the applicant has proposed a “DO NOT graze or cut for sock food” restraint on the label. The following risk mitigation statement which is considered appropriate and acceptable has been proposed:

Trade advice information: EXPORT STATEMENT: Growers should note that suitable Maximum Residue Levels (MRLs) or import tolerances may not be established in all markets for produce treated with Zorvec Encantia Fungicide. If you are growing produce for export, please check with Corteva Agriscience for the latest information on MRLs and export tolerances before using this product.

The risk to trade resulting from the proposed use of *Zorvec Encantia Fungicide (SC)* is expected to be low.

Work health and safety (WHS) assessment

Occupational risk assessment is based on both acute exposure to the product and repeat exposure to the active constituent. Workers may be exposed repeatedly to the product from dermal and/or inhalation routes during mixing, loading, and application (M/L/A), and from dermal exposure during post-application activities. Minor or accidental ocular exposure may also occur.

Health hazards

Acute hazards from exposure to Zorvec Encantia Fungicide include potential skin and eye irritation and skin sensitisation. For the assessment of risk from repeated exposure to the product, an appropriate NOAEL from the available toxicological studies on famoxadone was used to estimate a margin of exposure (MOE) for different workplace activities e.g., mixing and loading, application, and crop maintenance.

Although 28-d rat dermal and inhalation NOAELs are available in the famoxadone database, the APVMA concurs with available international assessments (EU RAR (2014)⁹; EFSA (2015)¹⁰; JMPR (2003)¹¹; US EPA (2020)¹²) regarding cataractogenicity in dogs being the critical (most sensitive) endpoint for establishing MOEs.

The APVMA discounted using the 5 week dog oral study, based on the fact that; i) cataracts in dogs were not observed until around 2–3 months exposure, and ii) professional applicators could potentially use the product for longer than a 5 week period. Therefore, for mixing/loading and application (M/L/A) risks, the APVMA used a NOAEL of 1.2 mg/kg bw/d from a one year dog study, based on clinical and microscopic evidence of posterior subcortical cataracts seen at a LOAEL of 9 mg/kg bw/d.

For estimating risks to re-entry workers, the APVMA also used the NOAEL for one year dog study. Although post-application crop handling activities are usually considered to occur over a shorter period than M/L/A, hand harvesting of brassica vegetables is often carried out by professional pickers that work across multiple farms during the harvesting season therefore, a conservative approach was considered appropriate.

⁹ EU (2014). Famoxadone – European Commission Renewal Assessment Report (RAR). Annex B (volume 3). B6a Toxicology & Metabolism.

¹⁰ EFSA (2015). Conclusion on the peer review of the pesticide risk assessment of the active substance famoxadone. European Food Safety Authority, Parma, Italy. EFSA Journal 2015:13(7):4194.

¹¹ JMPR (2003). Joint Meeting on Pesticide Residues. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment. Geneva, Switzerland, 15–24 September 2003.

¹² US EPA (2020). Famoxadone: Human Health Draft Risk Assessment in Support of Registration Review. Report No. D449290. 14 December 2020.

Occupational exposure and risks

Risks during use

In the absence of worker exposure data, the US EPA Occupational Pesticide Handler Exposure Calculator (OPHEC) was used to estimate exposure from M/L/A of Zorvec Encantia Fungicide at a product application rate of 0.75 kg/ha.

To estimate risks from dermal exposure, the APVMA used the US EPA dermal absorption factor (DAF) of 5% for the suspo-emulsion concentrate.¹³ Spray dilution was modelled at 14% (pro rata EFSA default value¹⁴) in the risk assessment. These values are less conservative than EFSA defaults.

Results from OPHEC indicate acceptable risk (MOEs > 100) for M/L/A with single layer clothing and gloves for all exposure scenarios modelled. A washable hat was included in safety directions as the product is a skin sensitiser.

Risks during re-entry

Workers performing maintenance (re-entry) activities in vegetable crops may be exposed to product residues from dermal contact with foliage. Re-entry exposure and risks to workers were estimated by the APVMA using the US EPA Occupational Pesticide Re-entry Calculator (OPREC) for all label crops at the product application rate of 0.75 kg/ha with a DAF of 5%.

Re-entry intervals (REI) of zero days (day of product application) were determined for all activities except detasseling corn, which requires a 6 day REI.

Public health risk assessment

The product is intended for professional use only. Therefore, risks from handling the product are not relevant for the general public.

Exposure to residues derived from famoxadone is possible from ingestion of vegetables treated with Zorvec Encantia Fungicide. Maximum residue limits (MRLs) have been established for all label crops to ensure the Acceptable Daily Intakes (ADIs) for both famoxadone and oxathiapiprolin are not exceeded.

Recommendations

The following first aid instructions, safety directions, precautionary and re-entry statements are recommended for the product label.

¹³ LOAEL for 28-day rat oral / LOAEL for 28-day rat dermal x 100 = 25/500 x 100 = 5%

¹⁴ 70% x 5% (EPA DAF) / 25% (EFSA default DAF)

First aid instructions

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26, New Zealand 0800 764 766.

Safety directions

May irritate the eyes, nose and throat and skin. Repeated exposure may cause allergic disorders. Avoid contact with eyes and skin. Avoid inhaling vapour. When using together with other products, consult their safety directions. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and a washable hat and elbow length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

Precautionary statements

DO NOT apply by equipment carried on the back of the user or by other manual application methods (e.g., handwand/handgun)

DO NOT apply by aerial application

DO NOT apply in nursery production of transplanted crops

DO NOT use on hydroponic crops

DO NOT apply by boom sprayer unless spray droplets are MEDIUM size or larger

DO NOT allow bystanders to come into contact with the spray cloud

Re-entry statement

DO NOT enter treated areas until spray has dried

If prior entry is necessary, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

Environmental assessment

Fate and behaviour in the environment

Soil

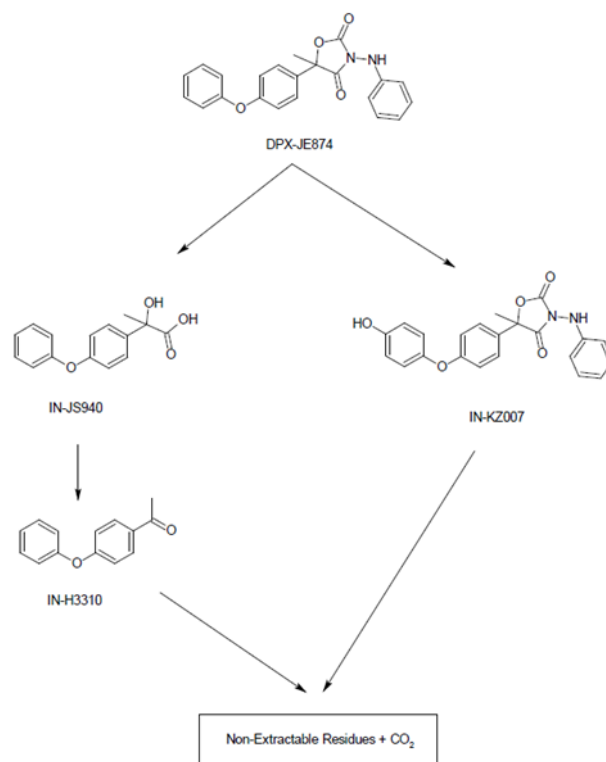
Famoxadone quickly degraded in a soil photolysis experiment under irradiated conditions with a calculated average first-order half-life of 4.1 days (11.5 days correlated to natural sunlight) forming 4 major degradation products (>10%), IN-H3310, IN-KF015, IN-MN467 and IN-MN468. Under non-irradiated conditions, the average half-life was greater than 30 days.

Famoxadone was applied to 5 soils in 2 laboratory studies and its degradation rate was evaluated under aerobic conditions at 20°C in darkness. In the first aerobic soil study using a Speyer sandy loam soil, famoxadone was labelled separately with C¹⁴ in the phenoxyphenyl ring and in the phenylamino ring, where degradation followed the first-order in multi-compartment (FOMC) kinetics with a soil half-life of 22 days. In the second aerobic soil metabolism study using four soils from representative agricultural regions of France, the United Kingdom and the United States (loamy sand, sandy loam and two silt loam soils), famoxadone was labelled with C¹⁴ in the phenoxyphenyl ring, where degradation followed the double first-order in parallel (DFOP) kinetics, and soil half-lives ranged 8.0 to 104 days. Combining data from all 5 soils, the geometric mean aerobic soil DT₅₀ was 41 days. Mineralisation was 12–32% in all soils and non-extractable residues ranged from 30 to 54% AR after 90 days. The degradation of famoxadone resulted in the formation of 2 major metabolites, IN-KZ007 (maximum 16%, formed through hydroxylation of famoxadone) and IN-JS940 (maximum 11%, formed through cleavage of the oxazolindinedione ring), and 2 minor metabolites (IN-MN467 and IN-MN468; formed at up to 9%).

Laboratory soil metabolism studies were provided for the soil metabolites of famoxadone. Geomean DT₅₀ values for IN-KZ007, IN-JS940, IN-KF015, IN-MN467, IN-MN468 and IN-H3310 were 14, 0.41, 0.63, 11, 13, and 0.60 days, respectively.

Famoxadone was applied as the active constituent to 4 soils under anaerobic conditions in 2 laboratory studies and its degradation rate was evaluated under dark conditions at 20°C. In the first study using a Speyer sandy loam soil, famoxadone was labelled separately with C¹⁴ in the phenoxyphenyl ring and in the phenylamino ring; degradation followed single first-order (SFO) kinetics and the soil half-life was 37 days. In the second study using three soils (silty clay loam and 2 sandy loam soils), degradation followed biphasic hockey-stick (HS) kinetics, where famoxadone dissipated slowly from an acidic soil (DT₅₀ >365 days) and more rapidly from slightly acidic (DT₅₀ 3.5 days) and alkaline (DT₅₀ 7.9 days) soils. As a result, the geometric mean anaerobic soil DT₅₀ was 25 days. Mineralisation was 4.5–35% in all soils and non-extractable residues ranged from 9.6–71% AR after 105–136 days. In the first anaerobic soil study, degradation of famoxadone via hydrolysis formed the major metabolite IN-JS940 (maximum 23%), while in the second study, the transformation products were IN-KZ007, IN-JS940, and IN-H3310 (no more than 6% AR) and carbon dioxide as shown below.

Figure 6: Proposed route of degradation in soil under anaerobic conditions



Four field dissipation studies were provided including 9 soils (7 sites from the United States and 2 sites from Canada) and a water-dispersible granule formulation containing 25% famoxadone and 25% cymoxanil applied to bare soil. The applications were made either as a single spray at 1620 g famoxadone/ha, 3 sprays of 270 g famoxadone/ha (809 g famoxadone/ha), or 3 sprays of 539 g famoxadone/ha/spray (1620 g famoxadone/ha) at 14 day intervals. Famoxadone dissipated rapidly in all soils; measured half-lives ranged from 5.0 to 28 days (geometric mean 14 days) and modelled half-lives (first order kinetics for the US soils and non-linear least squares for Canadian soils) ranged from 2.1 to 28 days (geometric mean 10 days). Famoxadone residues were not detected below the 0-15 cm soil depth at any site.

The mobility of famoxadone and its major soil metabolites were tested in standard batch equilibrium studies. Freundlich K_F values for famoxadone (4 soils) ranged 4.5 to 127 mL/g with a mean value of 41 mL/g (K_{FOC} 587 to 3401 mL/g, mean 1538 mL/g) indicating famoxadone could be slightly mobile in the soil environment. A positive relationship between K_F and soil organic carbon was apparent and regression-derived K_F values for 1% and 5% soil organic carbon are 5.9 and 173 mL/g, respectively. The average $1/n$ was 0.83. Metabolites were tested on 4 or 5 soils, and mean K_F values for IN-KZ007, IN-JS940, IN-MN467, IN-MN468 and IN-H3310 were 1.6, 1.6, 520, 281, and 30 L/kg, respectively. The mean K_{OC} value for IN-JL856 was 412 mL/g (HPLC method) and mean K_d value for IN-KF015 was 6.5 mL/g. All metabolites are expected to be mobile to slightly mobile in soil.

In a soil column leaching study (sandy loam soil, 1.1% organic carbon), famoxadone was applied to soil at ~240 g a.c./ha and incubated for five days at 20°C. After 5 day ageing, soil residues contained 81% famoxadone and 2 soil metabolites, IN-KZ007 (10%), and IN-JS940 (2.5%) as detected by HPLC coelution.

Mineralisation was 3.9% and non-extractable residues were 18%. After elution (160 mm) over 2 days, 85% of total radioactivity residues (TRR) were retained in the top 5 cm, while <0.1% TRR were detected in the leachate. On the basis of these data, leaching of famoxadone and its metabolites in soil is expected to be minimal.

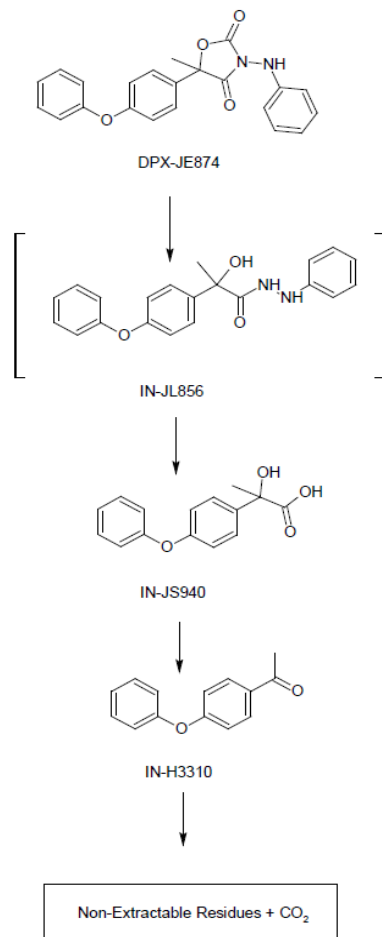
Water

Hydrolysis of famoxadone is pH-dependent with DT₅₀ values of 41 days at pH 5.0, 2.0 days at pH 7.0, and 0.065 days at pH 9.0, determined at 25°C. The major intermediate products of hydrolysis were IN-JL856 and IN-MN968 with DT₅₀ of 0.54 and 0.29 days, respectively at pH 7.0. The major degradates IN-JS940 and IN-H3310 were hydrolytically stable at pH 7.0. Photolysis is not expected to be an important route of degradation of famoxadone in natural waters. In an aqueous photolysis study, famoxadone degraded rapidly with a DT₅₀ of 1.9 days in sterile buffer solution at pH 5.0 under simulated sunlight (25°C), and DT₅₀ values of 0.16 days (light) and 0.21 days (dark) in natural water. The quantum yield calculation for famoxadone resulted in a value of 0.98 mol Einstein⁻¹ at >290 nm.

Famoxadone was non-persistent in 3 aerobic water/sediment systems at pH 7.1 and 7.7 and DT₅₀ values in whole systems ranged from 1.2 to 3.1 days (geometric mean DT₅₀ 1.7 days, SFO) with up to 76% partitioning to sediment. Major aquatic metabolites were IN-JS940 (maximum 20% in water and 6.2% in sediment) with a geometric mean DT₅₀ of 5.7 days and IN-H3310 (maximum 2.4% in water and 11% in sediment) with a geometric mean of DT₅₀ 15 days.

In anaerobic conditions, famoxadone was non-persistent in 2 water/sediment systems and DT₅₀ values were 1.5 and 1.8 days (geometric mean 1.6 days, SFO kinetics). IN-JS940 was the primary metabolite formed in water (70% in water, 15% in sediment) with a low persistence (geometric mean DT₅₀ 5.7 days). The proposed degradation pathway in water is shown below.

Figure 7: Proposed route of degradation in water



Air

Standard modelling was undertaken to predict the atmospheric half-life of famoxadone through reaction with hydroxyl radicals. The DT₅₀ from reaction with hydroxyl radicals is 0.19 days (12h-day). Famoxadone is not volatile (vapour pressure 6.4×10^{-7} Pa at 20°C), so is not expected to partition to the atmospheric compartment and will not be subject to long-range transport though the air.

Effects and associated risks to non-target species

Terrestrial vertebrates

Famoxadone has low toxicity to mammals (LD₅₀ >5000 mg a.c./kg bw, 2 species tested) and birds (LD₅₀ >2250 mg a.c./kg bw/d, *Colinus virginianus*). Following dietary administration in reproductive toxicity tests in mammals, effects in adults such as body weight changes and food consumption changes, and reduced pup weight, were observed at 45 mg a.c./kg bw/d (NOAEC 11 mg a.c./kg bw/d, *Rattus norvegicus*). Following dietary administration in reproductive toxicity tests in birds, no effects were observed at the highest test concentration (NOEC 129 mg a.c./kg bw/d, *Colinus virginianus*).

Acute risks of famoxadone to terrestrial vertebrates were determined to be acceptable under realistic, worst-case scenarios of dietary exposure within a treatment area at the maximum exposure rate. Chronic risks to mammals were determined to be acceptable for generic focal species of mammals in leafy vegetable scenarios under a Tier 1 assessment. No protection statements are therefore required.

The octanol-water partition coefficient (log K_{ow} of 4.65 at pH 7.0) for famoxadone indicates a potential for bioaccumulation. A food chain assessment indicated that any accumulated residues in earthworms or fish are not expected to reach levels harmful to predators under the proposed conditions of use. As there was no evidence of accumulation in the toxicokinetic studies it is expected that there will be no biomagnification of famoxadone in the food chain. Further, based on available data, famoxadone is not expected to be an endocrine disrupting agent.

The combination product Zorvec Encantia Fungicide is also considered to have low toxicity to mammals (LD_{50} 1551 mg a.c./kg bw, *Rattus norvegicus*) and birds (LD_{50} >774 mg a.c./kg bw, *Colinus virginianus*), and risks to terrestrial vertebrates are therefore determined to be acceptable.

Aquatic species

Famoxadone has high toxicity to fish (lowest LC_{50} 0.011 mg a.c./L, *Oncorhynchus mykiss*), aquatic invertebrates (EC_{50} 0.0014 mg a.c./L, *Crassostrea virginica*), algae (ErC_{50} 0.0067 mg a.c./L, *Raphidocelis subcapitata*) and aquatic plants (EC_{50} >0.0081 mg a.c./L, *Lemna gibba*). Sediment dwellers did not show any effects at the highest concentrations tested (EC_{50} >0.025 mg a.c./L, *Lumbriculus variegatus*).

Following long-term exposure to famoxadone, abnormalities and reduced length were observed in fish fry at concentrations as low as 0.0041 mg a.c./L (NOEC 0.0014 mg a.c./L, *Oncorhynchus mykiss*), reduced reproduction was observed in aquatic invertebrates at concentrations as low as 0.0017 mg a.c./L (NOEC 0.00083 mg a.c./L, *Mysidopsis bahia*), and decreased survival was observed in sediment dwelling species at concentrations as low as 0.032 mg a.c./L (NOEC 0.01 mg a.c./L, *Chironomus riparius*) or 14 mg a.c./kg dry sediment (NOEC 5.5 mg a.c./kg dry sediment, *Chironomus dilutus*).

Zorvec Encantia Fungicide (combined residues) is considered to have high toxicity to fish (LC_{50} 0.021 mg a.c./L, *Oncorhynchus mykiss*), aquatic invertebrates (EC_{50} 0.044 mg a.c./L, *Daphnia magna*), and algae (ErC_{50} 0.012 mg a.c./L, *Raphidocelis subcapitata*).

Because famoxadone and Zorvec Encantia Fungicide are very toxic to some aquatic species, a protection statement is required to identify the hazard on the label.

Spray drift risks to aquatic species are driven by the high toxicity of famoxadone. Based on a spray drift assessment of famoxadone, a buffer zone of 300 metres is advised for a MEDIUM spray quality and low boom height.

A runoff assessment of famoxadone was performed which considered seasonal rainfall and site characteristics that are typical of horticultural growing regions of Australia. Acceptable risks could be concluded in most regions, provided that the product is not applied when a runoff event can be expected soon after application. Timing restrictions are required in Victoria and South Australia from December to February, Burdekin region in October, and Mackay/Whitsunday region from May to December.

Bees

Famoxadone has low acute toxicity to adult bees by contact exposure ($LD_{50} >100 \mu\text{g a.c./bee}$, *Apis mellifera*). The oral acute toxicity test for famoxadone concluded no adverse effects at the highest tested dose at the maximum solubility limit ($LD_{50} >1.0 \mu\text{g a.c./bee}$, *Apis mellifera*), and a low toxicity for an EC formulation ($LD_{50} >63 \mu\text{g a.c./bee}$, *Apis mellifera*). The combination product Zorvec Encantia Fungicide is also considered to have low toxicity to bees (contact $LD_{50} >61 \mu\text{g a.c./bee}$ and oral $LD_{50} >68 \mu\text{g a.c./bee}$, *Apis mellifera*).

Following long-term dietary exposure to famoxadone, there were no effects on mortality at the highest daily dietary doses after exposure for 10 days (NOED $7.2 \mu\text{g a.c./bee/d}$, *Apis mellifera*). However, famoxadone has high acute toxicity to bee larvae based on mortality after exposure for 120 hours ($LD_{40} 0.43 \mu\text{g a.c./larva/day}$) and high chronic toxicity after 120 hours (NOED $0.25 \mu\text{g a.c./larva/day}$, *Apis mellifera*).

Risks of famoxadone and Zorvec Encantia Fungicide to adult bees were determined to be acceptable assuming direct dietary and/or contact exposure following application to blooming plants within the treatment area at the maximum rate. However acceptable risks could not be concluded to bee larvae, and protection statements are required to mitigate risks to bee brood.

Other non-target arthropods

No data was provided regarding the toxicity of famoxadone to other non-target arthropods. Zorvec Encantia Fungicide showed low toxicity to the indicator species of predatory arthropods (Tier1 and 2 $LR_{50} >446 \text{ g a.c./ha}$, *Typhlodromus pyri*) and parasitic arthropods (Tier 1 $LR_{50} >446 \text{ g a.c./ha}$, *Aphidius rhopalosiphi*), as well as for other predatory arthropods (Tier 2 $LR_{50} >446 \text{ g a.c./ha}$, *Chrysoperla carnea* and *Coccinella septempunctata*).

Risks of Zorvec Encantia Fungicide to beneficial arthropods were determined to be acceptable assuming direct contact exposure to fresh-dried residues on foliage or soil within the treatment area at the maximum rate. No protection statements are required for beneficial arthropods.

Soil organisms

Famoxadone has low toxicity to soil macro-organisms such as earthworms ($LC_{50\text{corr}} 235 \text{ mg a.c./kg dry soil}$, *Eisenia andrei*). Following long-term exposure to famoxadone, reproduction and food consumption were inhibited at 29 mg a.c./kg ds (NOEC $16 \text{ mg a.c./kg dry soil}$, *Eisenia fetida andrei*). No adverse effects of famoxadone were observed on soil processes such as nitrogen and carbon mineralisation at exaggerated soil concentrations (NOEC $2.5 \text{ mg a.c./kg dry soil}$).

Following long-term exposure to Zorvec Encantia Fungicide, reproduction of earthworms was inhibited at $11 \text{ mg a.c./kg dry soil}$ (NOEC_{corr} $6.0 \text{ mg a.c./kg dry soil}$, *Eisenia fetida*), but no effects were observed at the highest tested dose in springtails and soil mites (NOEC $>307 \text{ mg a.c./kg dry soil}$, *Folsomia candida* and *Hypoaspis aculeifer*).

Risks of famoxadone and Zorvec Encantia Fungicide to soil organisms were determined to be acceptable assuming direct exposure to maximum predicted residues in the top 5 cm of soil without interception by the crop. No protection statements are therefore required for soil organisms.

Non-target terrestrial plants

Famoxadone had low toxicity following pre-emergent exposure (seedling emergence test) and post-emergent exposure (vegetative vigour test) at the highest rate tested on a standard suite of 10 test plants ($ER_{25} > 210$ g a.c./ha, $ER_{50} > 210$ g a.c./ha). Based on available data, an oil-based suspension concentrate formulation of oxathiapiprolin had low toxicity on pre- and post-emergent exposure ($ER_{50} > 600$ g a.c./ha). As a result, risks of Zorvec Encantia Fungicide to non-target terrestrial plants for the proposed uses are considered to be acceptable, and no protection statements are required.

Recommendations

In considering the environmental safety of the proposed use of the product Zorvec Encantia Fungicide, the APVMA had regard to the toxicity of the new and existing active constituents and their residues, including metabolites and degradation products, in relation to relevant organisms and ecosystems. Based on the outcome of the risk assessment, the APVMA can be satisfied that the proposed use of the product meets the environmental safety criteria when used according to the label directions.

Efficacy and safety assessment

Proposed product use pattern of Zorvec Encantia Fungicide

The purpose of the application is to register Zorvec Encantia Fungicide, an aqueous suspo-emulsion (SC formulation that contains 300 g/L famoxadone and 30 g/L oxathiapiprolin as the active constituents, for the control of downy mildew caused by *Peronospora spp.* in spinach and rocket. This product is proposed to be applied in a regularly scheduled protective spray program in rotation with other fungicides at 700mL/ha.

The active constituent famoxadone inhibits mitochondrial respiration at complex III (bc₁) affecting the respiration enzyme ubiquinol: cytochrome c oxidoreductase. The disruption of electron transfer in the respiration chain prevents oxidative phosphorylation, depriving the fungus of any source of energy (ATP). Famoxadone is a quinone outside inhibitor (QoI) fungicide belonging to FRAC group 11. Famoxadone does not exhibit any systemic or translaminar properties.

The active constituent oxathiapiprolin inhibits an Oxysterol Binding Protein (OSBP) homologue. OSBPs are implicated in the movement of lipids between membranes, among other processes. Inhibiting OSBP may disrupt other processes in the fungal cell, such as signalling, maintaining cell membranes, and the formation of more complex lipids that are essential for the cell to survive. Oxathiapiprolin is capable of translaminar movement when applied to a leaf surface and is translocated upward via the xylem which contributes to overall protection of newly emerging growth.

Efficacy and target crop safety of Zorvec Encantia Fungicide

Corteva Agriscience Australia Pty Ltd, the applicant, provided 18 Australian trial reports to support the efficacy and crop safety of Zorvec Encantia Fungicide. The data provided was considered in conjunction with the proposed label to determine whether the use of Zorvec Encantia Fungicide as proposed controls downy mildew in spinach and rocket. The proposed label states Zorvec should be applied to spinach and rocket at 700mL/ha as up to 3 applications, 7 to 10 days apart.

The trials were conducted in Tasmania, Queensland, Western Australia, South Australia, and Victoria between 2015 and 2020. They included a nil treatment group and up to 4 rates of product Zorvec Encantia Fungicide ranging from 500 to 1400mL pr/ha (0.7-to-2-x label rate), along with commercial standards. All of the fungicide treatments were applied 7–10 days apart, as recommended on the label.

Each of the efficacy and crop safety trials were replicated and randomised, with measure of the level of disease incidence and severity over time up to 27 days after application (DAA) to quantify fungicide efficacy and crop safety/phytotoxicity. The individual sets of plot observations were transformed as required and statistically analysed for significant treatment effects using analysis of variance and least significant difference ($P = 0.05$).

Efficacy

Out of the 18 efficacy and crop safety trials provided with this application, 12 tested the product for efficacy against downy mildew caused by *Peronospora spp.* The efficacy results depended on the geographical

region and the statistical method employed; however, overall the product demonstrated acceptable level of control of downy mildew caused by *Peronospora spp* in the tested crops:

Spinach

Out of the 12 efficacy trials provided, 4 tested efficacy against downy mildew caused by *Peronospora spp* in spinach. These trials demonstrated control of downy mildew in spinach after the recommended 3 applications of Zorvec 7–10 apart.

Rocket

Out of the 12 efficacy trials provided, 8 tested efficacy against downy mildew caused by *Peronospora spp* in rocket. These trials demonstrated control of downy mildew in spinach after the recommended 3 applications of Zorvec 7–10 apart.

The other trials mainly suffered from low disease pressure or assessments being conducted after the fourth application which are outside of label use. These were unsupportive of efficacy but were used to support crop safety.

The efficacy data provided with this application was supportive of a label claim for the control of Downy mildew caused by *Peronospora spp* in spinach and rocket.

Crop safety

A total of 18 Australian trials assessed crop safety of the Zorvec Encantia Fungicide, all conducted between 2015 and 2020. Four trials were conducted in spinach (*Spinacea oleracea*) in 5 varieties (Bloomsdale, Black grove, Acadia, Guitar F1 and SV3580VC). These trials included one trial conducted in Queensland, 2 in Victoria and one in Western Australia. Eight trials were conducted in rocket (*Eruca sativa*) in 5 varieties (Adagio, Ramjet, Nature, Dentallata, Gemini and Speedy). These trials included 3 in Victoria, 2 in South Australia, 2 in Tasmania and one in Queensland. Finally, 6 trials were conducted in lettuce (*Lactuca sativa*) in 4 varieties (Esky, Expertise, Marksman and Balboa) and included 3 trials from South Australia and 3 from Victoria.

Crop safety was estimated as a percent of the plant affected by phytotoxic symptoms at each post-spray assessment. The trials tested high product pressure with up to double label rate and up to 4 applications 7–10 days apart. No phytotoxicity was observed in any trial. In addition to these 18 crop safety trials, further evidence of safety of Zorvec Encantia Fungicide to leafy vegetable can be derived from one residues trials submitted with this application, where no symptoms of phytotoxicity were observed when the product was applied at up to x2 the maximum proposed label rate to Chinese cabbage.

The crop safety data provided with this application was supportive for safe use on leafy vegetables at the proposed label rate.

Recommendations

Trial data demonstrated that Zorvec Encantia Fungicide will be effective in controlling downy mildew caused by *Peronospora spp.* in spinach and rocket when applied at the proposed label rates of 700 mL/ha, 700mL/ha as up to 3 applications, 7 to 10 days apart. The product was safe to use at the proposed label rates in all varieties of leafy vegetables tested.

There are no objections on efficacy or target-crop safety grounds to the registration of the product that Zorvec Encantia Fungicide, containing 300 g/L famoxadone and 30 g/L oxathiapiprolin, when used as directed.

Spray drift assessment

Regulatory Acceptable Levels (RALs) for each risk area were used in the APVMA Spray Drift Risk Assessment Tool (SDRAT) in order to calculate the appropriate spray drift buffer zones for Zorvec Encantia Fungicide.

Human health

As a worst-case screening test, the APVMA used the famoxadone ADI of 1.3 mg/kg bw/d to generate a RAL of 36.5. No buffer zones are required for ground boom application at product application rates up to 700 mL/ha, using MEDIUM or larger spray droplet size category.

Residues and trade

A Regulatory Acceptable Level (RAL) for famoxadone of 0.075 ppm was determined and the following spray drift buffer zones are recommended for livestock areas and the protection of international trade:

For a boom height above the target canopy of 0.5 m or lower a minimum downwind buffer zone of 220 m would be required. For a boom height above the target canopy of 1.0 m or lower a minimum downwind buffer zone of 350 m would be required.

Environment

Spray drift risks to aquatic species are driven by the high toxicity of famoxadone. Based on an aquatic RAL of 0.14 µg a.c./L (from EC₅₀ 0.0014 mg a.c./L, *Crassostrea virginica* and an assessment factor of 10), a buffer zone of 300 metres is advised for a MEDIUM spray quality and low boom height.

Famoxadone and Zorvec Encantia Fungicide had low toxicity to adult bees (*Apis mellifera*) by contact exposure with a LD₅₀ >100 µg a.c./bee and >61 µg a.c./bee, respectively. Based on the pollinator RAL of 10167 g a.c./ha for Zorvec Encantia Fungicide (contact LD₅₀ >61 µg a.c./bee and a conversion factor of LOC 0.4/ExpE2.4 * 1000), spray drift risks to bees are considered to be acceptable and no buffer zones for pollinators are required.

Famoxadone has low toxicity to non-target terrestrial plants (pre-emergent and post-emergent exposure tests), with ER₂₅ and ER₅₀ values >210 g a.c./ha for 10 tested species; spray drift risks are considered to be acceptable and no buffer zones for protection of non-target terrestrial plants are required.

Table 6: Summary of RALs for Zorvec Encantia Fungicide (300 g/L famoxadone + 30 g/L oxathiapiprolin)

Sensitive area	Regulatory Acceptable Level	
	Level of active	Units
Bystander	36.5	g/ha

Sensitive area	Regulatory Acceptable Level	
	Level of active	Units
Livestock	0.075	ppm
Aquatic	0.14	µg/L
Pollinator	10167	g/ha
Vegetation	21	g/ha

Buffer zones calculated by the SDRAT, using the above RALs, were incorporated into the Zorvec Encantia Fungicide label spray drift instructions (see *Labelling requirements* below).

Labelling requirements

Label Name:

Zorvec Encantia Fungicide

Signal Headings:

POISON
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Constituent Statements:

ACTIVE CONSTITUENT: 300 g/L FAMOXADONE
30 g/L OXATHIPIPROLIN

Mode of Action:

GROUP 11 and 49 Fungicide

Statement of Claims:

For the control of downy mildew caused by *Peronospora spp* in spinach and rocket

Net Contents:

1 L - 20 L

Restrictions:

DO NOT apply by aircraft.
DO NOT apply if heavy rains or storms are forecast within 3 days.
DO NOT irrigate to the point of field runoff for at least 3 days after application.
DO NOT apply in Victoria and South Australia from December to February.
DO NOT apply in Burdekin region in October.
DO NOT apply in Mackay/Whitsunday region from May to December.
DO NOT use on hydroponic crops.
DO NOT apply in nursery production of transplanted crops.
DO NOT apply by equipment carried on the back of the user or by other manual application methods (e.g., hand wand/handgun)

Spray Drift Restrictions:

Specific definitions for terms used in this section of the label can be found at apvma.gov.au/spraydrift.
DO NOT allow bystanders to come into contact with the spray cloud.
DO NOT apply in a manner that may cause an unacceptable impact to native vegetation, agricultural crops, landscaped gardens and aquaculture production, or cause contamination of plant or livestock commodities, outside the application site from spray drift. The buffer zones in the relevant buffer zone tables below provide guidance but may not be sufficient in all situations. Wherever possible, correctly use application equipment designed to reduce spray drift and apply when the wind direction is away from these sensitive areas.
DO NOT apply unless the wind speed is between three (3) and twenty (20) kilometres per hour at the application site during the time of application.
DO NOT apply if there are hazardous surface temperature inversion conditions present at the application site during the time of application. Surface temperature inversion conditions exist most evenings one to two hours before sunset and persist until one to two hours after sunrise.

Boom sprayers

DO NOT apply by a boom sprayer unless the following requirements are met:

- Spray droplets are not smaller than a MEDIUM spray droplet size category.
- Only to be applied with boom height above the target canopy 0.5 m or lower
- Minimum distances between the application site and downwind sensitive areas are observed (see 'Mandatory buffer zones' section of the following table titled 'Buffer zones for boom sprayers').

Buffer zones for boom sprayers

Application rate	Boom height above the target canopy	Mandatory downwind buffer zones (metres)				
		Bystander areas	Natural aquatic areas	Pollinator areas	Vegetation areas	Livestock areas
Up to 700 mL/ha	0.5 m or lower	0	300	0	0	220

Directions for Use:

Apply Zorvec Encantia as a preventative treatment, or at earliest sign of disease. Maintain a regular protectant spray program. Use the shorter spray interval where a range is listed, when conditions favour rapid disease development. Always apply Zorvec Encantia with an adjuvant – see Adjuvant – General Instructions.

CROP GROUP	DISEASE	RATE	CRITICAL COMMENTS
Spinach and rocket	Downy mildew (<i>Peronospora</i> spp.)	0.7 L/ha	Apply two consecutive sprays of Zorvec Encantia™, 7 to 10 days apart. DO NOT apply more than 3 sprays of Zorvec Encantia™ to each crop. See Resistance Management – General Instructions.

NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION.

Withholding period:

Spinach and rocket:

Harvest (H): DO NOT harvest for 3 days after application.

Grazing (G): DO NOT graze or cut for stock food.

General Instructions:

Zorvec® Encantia® is a suspension emulsion (SC) formulation and is broadly active against diseases listed on this label. Zorvec® Encantia® has preventive, residual and antispore activity. Zorvec® Encantia® is locally systemic, translaminar and moves systemically in the plant xylem. Uptake into the leaf tissue allows good translaminar movement and protection of new plant growth. Zorvec® Encantia® must be applied in a regularly scheduled protective spray program in rotation with other fungicides. See the Directions for use table for specific crop/disease recommendations.

MIXING

Fill spray tank to ¼ to ½ full of water. Measure the amount of Zorvec® Encantia® required for the area to be sprayed. Add Zorvec® Encantia® directly to the spray tank with the agitation engaged. Mix thoroughly to disperse the fungicide. Once dispersed, the material must be kept in suspension at all times by continuous agitation. Use mechanical or hydraulic means, DO NOT use air agitation, premix or slurry. The mixing sequence recommended is: water soluble bags, water soluble granules, dry flowable or water dispersible granules, wettable powders, water-based suspension concentrates, capsule suspension, suspo emulsion (e.g. Zorvec® Encantia®), oil-based suspension concentrates, emulsion in water, emulsifiable concentrates, water-soluble concentrates, adjuvants, surfactants, oils, soluble fertilisers, and drift retardants. If spray solution is left standing, ensure thorough re agitation of the spray mix until fully resuspended. DO NOT allow spray mix to sit overnight, as resuspension may be difficult.

ADJUVANTS

Zorvec® Encantia® may be used with a non-ionic surfactant such as Agral 60 at recommended rates. Zorvec Encantia is compatible with Maxx spray adjuvant, DuWett, or Agral 60.

COMPATIBILITY

Zorvec® Encantia® is physically compatible with many commonly used fungicides, insecticides, biological control products, liquid fertilizers, adjuvants, crop oils, methylated seed oils and drift control additives. However, since the formulations of products change, it is important to test the physical compatibility of desired tank mixes and check for undesirable physical effects, including settling out or flocculation. To determine physical compatibility, add the proportions of the tank mix products and water to a small container, mix thoroughly and allow to stand for 20 minutes. If the combination remains mixed, or can be re-mixed readily, it may be considered physically compatible. Zorvec® Encantia® is compatible with Avatar®1, Benevia®1, Coragen®1, Fontelis®, imidacloprid, Movento®1, Octave®1, Rovral®1, Success® Neo, and Sumagic®1. The crop safety of all tank-mixes, including additives and other pesticides, which may include physically compatible pesticides, fertilisers, adjuvants, and/or additives, has not been tested. Before applying any tank mix not specifically recommended on this label or other Corteva Agriscience product use instructions, it is important to understand crop safety. To test for crop safety, prepare a small volume of the intended tank mixture, apply it to an area of the target crop as directed by both this label and the tank mix partner product labels, and observe the treated crop to ensure that a phytotoxic response does not occur. Corteva agriscience will not be responsible for any crop injury arising from the use of a tank mixture that is not specifically described on Zorvec® Encantia® product labelling or in other Corteva Agriscience product use instruction.

APPLICATION

A spray drift minimisation strategy should be employed at all times when applying this product. The interaction of many equipment and weather-related factors determines the potential for spray drift.

Ground application

Use a sprayer fitted with high flow rate nozzles to apply the highest practical spray volume. Use sufficient water 250 - 500 L/ha to obtain thorough coverage of plants. Increase the water volume as plants mature to ensure thorough coverage of the foliage. Droplet size should be of MEDIUM spray quality. Nozzles with higher rated flows produce larger droplets. Use the lower spray pressures recommended for the nozzle. Higher pressure reduces droplet size, and DOES NOT improve canopy penetration and may increase drift potential. WHEN HIGHER FLOW RATES ARE NEEDED, USE A HIGHER-CAPACITY NOZZLE INSTEAD OF INCREASING PRESSURE. Use a nozzle type that is designed for the intended application. With most nozzle types, narrower spray angles produce larger droplets. Consider using low-drift nozzles.

SPRAY EQUIPMENT CLEANOUT

Prior to application, start with clean, well-maintained application equipment. Immediately following application, thoroughly clean all spray equipment to reduce the risk of forming hardened deposits which might become difficult to remove. Drain application equipment.

Thoroughly rinse sprayer and flush hoses, boom, and nozzles with clean water. Clean all other associated application equipment. Take all necessary safety precautions when cleaning equipment. DO NOT clean near wells, water sources or desirable vegetation. Dispose of waste rinse water in accordance with local regulations.

Resistance Management

Zorvec® Encantia® use is subject to a CropLife Australia resistance management strategy. Please refer to this strategy at <http://www.croplife.org.au/industry-stewardship/resistancemanagement/> before use.

The following restrictions also apply to the use of Zorvec® Encantia®:

- When conditions favour disease development, DO NOT wait for the disease to appear, but apply two consecutive sprays of Zorvec® Encantia® at the recommended interval, where recommended in the Directions for Use table. Then resume the spray program with treatments that have a different mode-of-action to Group 11 and 49. Exposure to Zorvec® Encantia® (or any other Group 49 containing product) should not exceed thirty three percent (33%) of the total period of protection needed per crop.

- For crops when three (3) or more fungicide applications are made, use Zorvec® Encantia® (or any other Group 49-containing product) in no more than 33% of the total number of fungicide applications, with a maximum number of sprays as specified in the Critical Comments section of the Directions for Use table. Where less than three (3) fungicide applications are made per crop, make no more than one (1) application of Zorvec® Encantia® (or any other Group 49-containing product).
- Zorvec® Encantia® applications are to be made preventatively and no more than two (2) times in sequence before applying a fungicide with a different mode of action.
- Where a fungicide with a different mode of action follows Zorvec® Encantia® (or any other Group 49-containing product) application(s), this fungicide preferably should have curative activity.
- Continue alternation of fungicides between successive crops. There will be no more than six (6) applications of Zorvec® Encantia® (or any other Group 49 containing product) per year on the same area, targeting the same pathogen. Do not use a Group 49 product such as Zorvec® Encantia® if it will be the last fungicide applied to the crop. A disease management program that includes rotation and/or tank mixing with fungicides with a different mode of action is essential to reduce the risk of fungicide resistance development. For guidance on a particular crop and disease control situation, contact your farm chemical supplier, consultant, local Department of Agriculture or Primary Industries, local Corteva Agriscience representative or CropLife Australia.

INTEGRATED DISEASE MANAGEMENT

Corteva Agriscience recommends the use of Integrated Disease Management (IDM) programs to control diseases. Zorvec® Encantia® may be used as part of an IDM program which can include biological, cultural, and genetic practices aimed at preventing economic disease damage. Application of this product should be based on IDM principles and practices including field scouting or other detection methods, correct target disease identification, population monitoring, and treating when disease forecasting models reach locally determined action levels. Consult your farm chemical supplier, consultant, local Department of Agriculture or Primary Industries, local Corteva Agriscience representative or other qualified authorities to determine the appropriate management, cultural practice and treatment threshold levels for the specific crop, geography and diseases.

Resistance Warning:

RESISTANT WEEDS WARNING

GROUP 11 and 49 Fungicide

Zorvec® Encantia® is a combination of a Quinone outside inhibitor and an oxysterol binding protein homologue inhibition (OSBPI) fungicide. For fungicide resistance management Zorvec® Encantia® is both a Group 11 and Group 49 fungicide. Some naturally occurring individual fungi resistant to Zorvec® Encantia® and other Group 11 and or Group 49 fungicides may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungal population if Zorvec® Encantia® and other Group 11 and/or Group 49 fungicides are used repeatedly. These resistant fungi will not be controlled by Zorvec® Encantia® and other Group 11 and/ or Group 49 fungicides, thus resulting in a reduction in efficacy and possible yield loss.

Since the occurrence of resistant fungi is difficult to detect prior to use, Corteva Agriscience accepts no liability for any losses that may result from the failure of Zorvec® Encantia® to control resistant fungi.

Precautions:

DO NOT enter treated areas until spray has dried. If prior entry is necessary, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

Protections:

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS

IMPORTANT: Not all crops within a crop group, and not all varieties, cultivars or hybrids of crops, have been individually tested for crop safety. It is not possible to evaluate for crop safety all applications of Zorvec® Encantia® on all crops within a crop group, on all varieties, cultivars, or hybrids of those crops, or under all environmental conditions and growing circumstances. To test for crop safety, apply the product in accordance with the label instructions to a small area of the target crop to ensure that a phytotoxic response

will not occur, especially where the application is a new use of the product by the applicator. Some materials including oils, surfactants, adjuvants, and pesticide formulations when applied individually, sequentially, or in tank mixtures may solubilise the plant cuticle, facilitate penetration into plant tissue and increase potential for crop injury.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with this product or used containers.

PROTECTION OF HONEY BEES AND OTHER INSECT POLLINATORS

Bee brood development may be harmed by exposure to residues transported into the hive by foraging bees or overspray. DO NOT apply where bees from managed hives are known to be foraging. DO NOT allow spray drift to flowering weeds or flowering crops in the vicinity of the treatment area. Before spraying, notify beekeepers to move hives to a safe location with an untreated source of nectar and pollen, if there is potential for managed hives to be affected by the spray or spray drift.

Storage and Disposal:

Store in the closed, original container in a cool well-ventilated area. Do not store for prolonged periods in direct sunlight. Triple rinse containers before disposal. Add rinsings to spray tank. DO NOT dispose of undiluted chemicals on site. This container can be recycled if it is clean, dry, free of visible residues and has the drumMUSTER logo visible. Triple rinse containers before disposal. Add rinsings to spray tank. DO NOT dispose of undiluted chemicals on site. Wash outside of the container and the cap. Store cleaned container in a sheltered place with cap removed. It will then be acceptable for recycling at any drumMUSTER collection or similar container management site. The cap should not be replaced but may be taken separately. If not recycling, break, crush, or puncture and deliver empty packaging for appropriate disposal to an approved waste management facility. If an approved waste management facility is not available bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots, in compliance with relevant Local, State or Territory government regulations. DO NOT burn empty containers or product.

Safety Directions:

May irritate the eyes, nose and throat and skin. Repeated exposure may cause allergic disorders. Avoid contact with eyes and skin. Avoid inhaling vapour. When using together with other products, consult their safety directions. When opening the container and preparing spray wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and washable hat and elbow length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

First Aid Instructions:

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26, New Zealand 0800 764 766.

Acronyms and abbreviations

Shortened term	Full term
a.c.	Active constituent
acs	Active constituents
ADI	Acceptable daily intake (for humans)
ai	Active ingredient
ARfD	Acute reference dose
bw	Bodyweight
d	Day
DAF	Dermal absorption factor
DAT	Days after treatment
DFU	Directions for use
DT ₅₀	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
EC ₅₀	Concentration at which 50% of the test population are immobilised
E _r C ₅₀	Concentration at which the rate of growth of 50% of the test population is impacted
EI	Export interval
EGI	Export grazing interval
ESI	Export slaughter interval
F ₀	Original parent generation
g	Gram
GAP	Good Agricultural Practice
GLP	Good Laboratory Practice
h	Hour
ha	Hectare
HPLC	High pressure liquid chromatography or high performance liquid chromatography
id	Intradermal
<i>in vitro</i>	Outside the living body and in an artificial environment

Shortened term	Full term
<i>in vivo</i>	Inside the living body of a plant or animal
kg	Kilogram
K _{OC}	Organic carbon partitioning coefficient
L	Litre
LC ₅₀	Concentration that kills 50% of the test population of organisms
LD ₅₀	Dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of detection – level at which residues can be detected
Log K _{OW}	Log to base 10 of octanol water partitioning co-efficient, synonym P _{OW}
LOQ	Limit of quantitation – level at which residues can be quantified
mg	Milligram
MOE	Margin of Exposure
mL	Millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short-Term Intake
ng	Nanogram
NOEC/NOEL	No observable effect concentration level
NOAEL	No observed adverse effect level
OPHEC	US EPA Occupational Pesticide Re-entry Calculator
OPREC	US EPA Occupational Pesticide Re-entry Calculator
OC	Organic carbon
OM	Organic matter
po	Oral
ppb	Parts per billion
PPE	Personal protective equipment
ppm	Parts per million

Shortened term	Full term
RAL	Regulatory Acceptable Level
RBC	Red blood cell count
REI	Re-entry interval
s	Second
SC	Suspension concentrate
SDMT	Spray Drift Management Tool
SDRAT	Spray Drift Risk Assessment Tool
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
µg	Microgram
vmd	Volume median diameter
WG	Water dispersible granule
WHP	Withholding period

Glossary

Term	Description
Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration
CAS registry number	Unique numerical identifier assigned by the Chemical Abstracts Service (CAS) to every chemical substance
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Henry's law constant	A gas law that states that the amount of dissolved gas in a liquid is proportional to its partial pressure above the liquid
Leaching	Removal of a compound by use of a solvent
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Toxicology	The study of the nature and effects of poisons

References

APVMA, 2023, Spray Drift Risk Assessment Tool (SDRAT), accessed July 2024 at <https://www.apvma.gov.au/resources/using-chemicals/spray-drift/sdrat>

EFSA, 2014, Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 12(10):3874. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2014.3874>

EFSA, 2017, EFSA Guidance on Dermal Absorption. EFSA Journal 15(6):4873. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.4873>

EFSA, 2015, Conclusion on the peer review of the pesticide risk assessment of the active substance famoxadone. European Food Safety Authority, Parma, Italy. EFSA Journal 2015:13(7):4194. <https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2015.4194>

EU, 2014, Famoxadone – European Commission Renewal Assessment Report (RAR). Annex B (volume 3). B6a Toxicology & Metabolism.

JMPR, 2003, Joint Meeting on Pesticide Residues. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment. Geneva, Switzerland, 15–24 September 2003. <https://www.fao.org/4/y5221e/y5221e00.htm>

OECD, 2021, Test No.509: Crop Field Trial, OECD website, accessed July 2024 at: https://www.oecd.org/en/publications/test-no-509-crop-field-trial_9789264076457-en.html US EPA, 2020, Famoxadone: Human Health Draft Risk Assessment in Support of Registration Review. Report No. D449290. 14 December 2020.

US EPA, 2021, Occupational Pesticide Handler Exposure Calculator (OPHEC) (version date: May 2021). [Occupational Pesticide Handler Exposure Data | Pesticide Science and Assessing Pesticide Risks | US EPA](https://www.epa.gov/sites/production/files/2021-05/opp-hed-occupational-handler-exposure-may-2021.xlsx) <https://www.epa.gov/sites/production/files/2021-05/opp-hed-occupational-handler-exposure-may-2021.xlsx>