Renewal Assessment Report

under Regulation (EC) 1107/2009

Zoxamide

Volume 3

Active substance
B.3 Data on application

Rapporteur Member State: Latvia
Co-Rapporteur Member State: France

Version History

When	What
March 2016	Initial RAR

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B.3. DATA ON APPLICATION

B.3.1. USE OF THE ACTIVE SUBSTANCE

Fungicide in agriculture.

B.3.2. FUNCTION

Fungicide.

B.3.3. EFFECTS ON HARMFUL ORGANISMS

Zoxamide is a non-systemic fungicide claimed to have protectant properties. It is a residual fungicide for the control of Oomycete diseases such as *Phytophthora infestans* (late blight of potato), *Plasmopara viticola* (downy mildew of grapevines). It works protective and needs to be applied before the disease attack.

B.3.4. FIELD OF USE ENVISAGED

Agriculture and viticulture.

B.3.5. HARMFUL ORGANISMS CONTROLLED AND CROPS OR PRODUCTS PROTECTED OR TREATED

Uses supported for the renewal of authorisation of zoxamide are late blight (*Phytophthora infestans)* on potatoes and downy mildew *(Plasmopara viticola)* on grapevines.

An overview of the efficacy information for zoxamide, concerning representative and supported uses already authorised in Member States, is reported. This report is provided in accordance with the format provided in Appendix II of Commission Guidance SANCO/2012/11251 rev 1.2 of July 2012, concerning the renewal of active substances under Commission Implementing Regulation (EU) No. 844/2012. Efficacy information, Active substance: Zoxamide, Product code: Zoxium 240 SC (240 g/l), Applicant: Gowan Comercio Internacional e Servocos Limitada, Date: 08/09/2014.

The representative formulation supporting first inclusion and authorisations was RH-7281/mancozeb 75 WG and WP (containing mancozeb and zoxamide) supporting outdoor foliar treatment on grapes and potatoes.

Representative scenarios supporting the first inclusion:

Crop	Treatment	Dosage AI	Dosage formulation	Numbers of applications	Water volume range
potatoes	Foliar	150 g zoxamide/ha 1200 g mancozeb/ ha	1800 g/ha	6-10 app./season	200 to 500 l/ha (up to 600 l/ha in UK)
grape	Foliar	15 g Zoxamide/ hl 120 g mancozeb/hl	180 g/hl	up to 10 app./season	400-1600 l/ha

The representative formulation supporting the application for renewal approval is Zoxium 240 SC (containing 240 g/L zoxamide).

The representative uses includes grapes in Central and Southern EU and potatoes in Northern, Central and Southern EU.

Representative scenarios supporting the inclusion:

Crop	Treatment	Application rates	No of applications	Water volumes range
Potatoes	Foliar	0.15-0.18 kg as/ha	1-5 appl./season	1000 l/ha
Grapes	Foliar	0.15-0.18 kg as/ha	1-5 appl./season	1000 l/ha

The GAPs that have been evaluated in the dossier for the first inclusion are slightly more worst case than the GAPs evaluated for the renewal.

B.3.6. MODE OF ACTION

Zoxamide has been found to bind covalently only to the beta sub unit of the protein tubulin. This specific binding causes disruption of the microtubule cytoskeleton and arrests nuclear division. Zoxamide does not affect zoospore motility, encystment, or germination. However, germ tube elongation and mycelium growth is arrested concomitant with the first cycle of nuclear division, preventing fungal penetration of the host plant. Experiments have shown that the inhibition of nuclear division occurs rapidly and at very low concentrations of zoxamide.

Zoxamide is a racemic mixture of R and S isomers. In efficacy screening tests, only the S-isomer was found to have significant fungicidal activity.

The active substance presents a good absorption by the leaf waxy layer, no translaminar displacement and a not systemic behaviour.

B.3.7. INFORMATION ON THE OCCURRENCE OR POSSIBLE OF THE DEVELOPMENT OF RESISTANCE AND APPROPRIATE MANAGEMENT STRATEGIES

Zoxamide belongs to the chemical family of benzamides and works by disrupting mitosis and cell division (FRAC target site B3[1]) through inhibition of β-tubulin assembly (FRAC code 22[2]) and has specific biological activity on the oomycetes group of microorganisms, which include the proposed targets *Plasmopara viticola* and *Phytophtora infestans.* The Fungicide Resistance Action Committee (FRAC) considers that there is a low to medium risk of resistance developing and that resistance management is required for this group of chemistry. FRAC also consider that *Plasmopara viticola*

[1] http://www.frac.info/publication/anhang/FRAC%20Code%20List%202013-update%20April-2013.pdf

[2] http://www.frac.info/publication/anhang/FRAC%20Code%20List%202013-update%20April-2013.pdf

and *Phytophtora infestans* are of high and medium risk respectively of developing resistance to this chemistry[3]. The combined fungicide-pathogen risk is therefore considered to be medium.

For the first inclusion of zoxamide in Annex I to Directive 91/414/EEC, baseline responses of *Phytophtora infestans* to zoxamide were established which showed that the variation in sensitivity of naturally occurring and laboratory isolates was similar. **Note:** Although the potential for *Plasmopara viticola* to develop resistance to zoxamide was investigated, *Phytophtora infestans* was chosen to assess the possibility of fungicide resistance as it was considered to possess key attributes for the rapid development of resistance.

There was no indication of any cross-resistance between phenylamide resistance and sensitivity to zoxamide. In addition, no cross-resistance was found to other commonly used benzimidazoles which have a similar mode of action to zoxamide.

The *Phytophtora infestans* sensitivity study and lack of success at producing zoxamide cross-resistant strains in laboratory mutagenesis studies with *Phytophtora infestans*, suggest the risk of resistance development to zoxamide is low. However, it is considered that the disease has a high resistance risk because of its history, the life cycle of the disease and the large number of applications made to the crop.

As of January 2013, FRAC have stated that no resistance to zoxamide has been reported for any pathogen[4].

In light of the potential risk of resistance developing and to ensure the continued effectiveness of this active substance, the following risk management strategy is in place:

1. A limited number of repeated applications on the crop;
2. A program of disease management based on co-formulation with active substances with different modes of action and product alternation.
3. A respect of recommended product dose rate, timing and spray interval.
4. A rigorous program of stewardship

B.3.8. OTHER INFORMATION

For the first approval of zoxamide as an active substance, the Applicant was asked to clarify which isomer of zoxamide is the active one.
Data were presented from two trials carried out on potato in 1998 conducted in the UK. The performance against potato late blight of 'RH-7281/mancozeb 75WG' ('Electis 75WG') at 150 g zoxamides/ha and the S-isomer of 'RH-117281' (coded 'RH 16949') at 75 g a.s/ha in tank-mix with mancozeb was applied at a 7 day spray interval. Disease control was compared with the standard reference products 'Curzate M68' containing cymoxanil + mancozeb at a 10 day spray interval and 'Dithane DF' containing dithane using a 7 day spray interval. Trials were taken to yield. No trial details or methodology were submitted. However, it is assumed that the methodology was the same as

[3] http://www.frac.info/publication/anhang/FRAC_Pathogen_risk%20list.pdf

[4] http://www.frac.info/publication/anhang/List%20of%20resistant%20plant%20pathogenic%20organisms_February%202013%20updated.pdf

used for the efficacy trials included in the original dossier. Results of disease blight levels were presented in graphical representations and of yield in the form of bar charts.
One trial developed blight sufficiently early in the season to enable a calculation of 'days delay to 75% foliar blight' to be made. 'RH 16949 + mancozeb' gave 32 days delay in foliar blight and 'Electis 75WG' gave 36 days delay. Both standards gave 21 days delay. Yield results showed 'RH 16949 + mancozeb' gave 29.6 t/ha, 'Electis 75WG' gave 31.8 t/ha. The standard 'Dithane DF' gave 32.9 t/ha and 'Curzate M68' 27.8 t/ha.
At the other trial site where disease developed later, it was possible to make a calculation of 'days delay to 10% foliar blight'. 'RH 116949 + mancozeb' gave 41 days delay in foliar blight and 'Electis 75WG' gave 43 days delay. Both standards gave 37 days delay. Yield results were higher at this site. 'RH 16949 + mancozeb' gave 60.6 t/ha, 'Electis 75WG' gave 58.6 t/ha. The standard 'Dithane DF' gave 51.0 t/ha and 'Curzate M68' 47.8 t/ha.

Evidence from two trials showed there was little difference in terms of foliar blight control between 'RH 116949 + mancozeb' applied at 75 g a.s/ha of the active isomer and 'Electis 75WG' applied at 150 g a.s/ha of 'RH-117281'. Results were supported by data on yield in the presence of disease, which showed similar results between the test products.

The available data on the activity of the racemic zoxamide and S-zoxamide (RH-116949) against foliar blight, indicates that the s-enantiomer has double the potency of racemic zoxamide. Therefore, it can be concluded that the S-enantiomer is the active component within zoxamide.

B.3.9. REFERENCES RELIED ON

None.