



# **Draft Assessment Report**

## **Evaluation of Active Substances**

Plant Protection Products

Prepared according to **Regulation (EC) 1107/2009**  
as it applies in Great Britain

**Pydiflumetofen**

**Volume 3 – B.3 (AS)**

**Data on application**

Great Britain

June 2023

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## Version History

When	What
October 2022	Initial DAR
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## **B.3. DATA ON APPLICATION**

### **B.3.1. USE OF THE ACTIVE SUBSTANCE**

Pydiflumetofen is intended to be used as a fungicide for the control of foliar diseases in winter and spring barley, winter and spring wheat, winter and spring oat, winter and spring rye, winter and spring triticale, durum wheat, spelt, and winter and spring oilseed rape.

### **B.3.2. FUNCTION**

Fungicide.

### **B.3.3. EFFECTS ON HARMFUL ORGANISMS**

Pydiflumetofen is a foliar fungicide in the carboxamide chemical group that acts by inhibition of respiration at complex II (succinate-dehydrogenase).

Pydiflumetofen is a lipophilic molecule with limited solubility and limited xylem translocation; it does not move in the phloem and has no vapour activity. Pydiflumetofen has low uptake into leaf tissues, and limited systemicity of absorbed compound resulting in a substance with predominantly protectant properties. However, although translaminar and xylem systemic properties of pydiflumetofen are limited, the molecule also reduces intercellular mycelial growth and thus may provide some curative activity.

Pydiflumetofen is most active at stages of the fungal life cycle which are particularly energy demanding. It shows strong effects in early growth stages; it inhibits spore germination and germ tube growth and consequently hinders establishment of the fungus in the host plant.

### **B.3.4. FIELD OF USE ENVISAGED**

Agriculture.

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

Pydiflumetofen is intended to be used for the control of the following fungal pathogens:

- *Septoria tritici*, *Septoria nodorum*, *Puccinia recondita*, *Pyrenophora tritici-repentis*, *Erysiphe graminis* and *Fusarium* spp. in winter and spring wheat, durum wheat, and spelt.
- *Pyrenophora teres*, *Rhynchosporium secalis*, *Ramularia collo-cygni*, *Puccinia hordei*, *Erysiphe graminis* and *Fusarium* spp. in winter and spring barley.
- *Fusarium* spp. in winter and spring oats, winter and spring rye, and winter and spring triticale.
- *Sclerotinia sclerotiorum* in winter and spring oilseed rape.

### **B.3.6. MODE OF ACTION**

Pydiflumetofen is a carboxamide fungicide belonging to the proposed chemical group of the phenyl-ethyl pyrazole carboxamides. It is a succinate dehydrogenase inhibitor (SDHI) acting at the respiration complex II target site and will therefore belong to FRAC (Fungicide Resistance Action Committee) Code 7.

Succinate dehydrogenase activity is a mandatory step of the mitochondrial TCA cycle which is the main route for energy production in the cells. Normally, the TCA cycle continuously feeds the respiratory chain with reducing equivalents. The binding of pydiflumetofen blocks this cycle which leads to a major cellular energy breakdown.

The succinate dehydrogenase enzyme catalyses succinate oxidation resulting in reduction of ubiquinone. The enzyme is built of four sub-units encoded by four different genes in the genome, designated as SDH A, B, C and D. SDH A (flavoprotein unit) is responsible for the oxidation of succinate to fumarate, whereas the subunits SDH B (iron-sulphur unit), C and D represent the ubiquinone reducing transmembrane part. Pydiflumetofen strongly binds to the ubiquinone binding site of the enzyme thus preventing ubiquinone reduction.

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

Pydiflumetofen is a member of the SDHI fungicide group, known as complex II respiration inhibitors (FRAC Code 7). SDHIs do not show cross resistance with other chemical classes such as strobilurins, benzimidazoles, anilinopyrimidines or demethylation inhibitors. Therefore, no cross resistance to fungicides from different mode of action groups is expected. However, within the SDHI group, cross-resistance is expected and has been shown using field isolates and lab mutants. Among the different members of the SDHI group, a relation is assumed for isolates differing in sensitivities, since they share the same binding properties. The similar overall chemical structures of SDHIs leads to similar intermolecular interaction at the target site. However, the effect of the various mutations in resistance isolates on the activity of the different SDHIs is specific regarding the respective pathogen - active substance combination. As shown by a heatmap provided in the BAD, some mutations have a higher cross resistance factor.

The results of tests comparing the intrinsic activity of different SDHIs (pydiflumetofen, isopyrazam, benzovindiflupyr, bixafen and fluopyram) against *Septoria tritici* and *Pyrenophora teres* have been provided in the BAD. In *S. tritici*, pydiflumetofen shows the highest intrinsic activity compared to the other SDHIs with all tested strains (field and lab-mutant strains) with EC50 values lower than 1 ppm. The EC50 values were >1 ppm for some strains with all other tested SDHIs, and >10 ppm for some strains for bixafen and fluopyram. Pydiflumetofen also shows the highest intrinsic activity against the tested *P. teres* strains compared to the other SDHIs with all EC50 values <10 ppm; however, the difference between pydiflumetofen and other SDHIs is less noticeable than in *S. tritici*. For *P. teres* bixafen and benzovindiflupyr have EC50 values just above 10 ppm for some strains, whereas isopyrazam and fluopyram have EC50s well above 10 ppm for some strains.

In cereals in GB, it is common for up to 4 foliar fungicides to be applied per crop. However, there is a FRAG-UK (Fungicide Resistance Action Committee) restriction in GB that prevents more than 2 foliar applications of any SDHI fungicide to the same cereal crop. Additionally, a solo SDHI product, such as Miravis Plus, must always be used in mixture with another product, recommended for control of the same target disease that contains a fungicide from a different cross resistance group and is applied at a dose that will give robust control. Where powdery mildew is present, an eradicant partner is required.

Pydiflumetofen is a single site inhibitor and resistance, which is due to target site mutations in the SDH subunit genes, has been selected by SDHI usage. SDHI fungicides are currently classified as having a medium to high resistance risk by FRAC and pydiflumetofen is expected to have the same risk. Cereal pathogens have a high potential for causing serious epidemics due to the production of large numbers of spores released to the air. The degree of sexual recombination is significant for *S. tritici* and *P. teres*, for which reduced sensitive strains are found. These 2 pathogens along with *Pyrenophora tritici-repentis* are classified as having a medium resistance risk, whereas the other target pathogens of Miravis Plus have a low resistance risk.

To manage the resistance risk, a resistance management strategy has been proposed on the Miravis Plus label as follows:

- The avoidance of repetitive and sole use of a particular fungicide or those with the same mode of action
- The mixing or alternating sequences of fungicides with different modes of action
- Do not reduce rates of fungicides in tank mixtures
- Integrate fungicide use with cultural control methods
- Limiting the number of treatments per season
- Avoid unnecessary prophylactic treatments, ensure preventative treatments are applied in accordance with recommendations for disease control
- The use of disease resistant crop varieties and appropriate agronomic and hygienic practices are also valuable anti-resistance measures. They help both to reduce disease incidence and to decrease selection of fungicide resistant forms.

The exact management strategy for Miravis Plus and other products containing pydiflumetofen can be considered at the product authorisation stage.

Baseline sensitivity data for a range of pathogens have been produced and will be examined at the product authorisation stage.

#### **B.3.8. CONSIDERATION OF RACEMIC MIXTURE**

Pydiflumetofen is a racemic mixture, consisting therefore of a 50:50 ratio of the plus-enantiomer and the minus-enantiomer.


The efficacy of the individual isomers was investigated in a 2016 greenhouse trial (see KCA\_3.3-01). In this trial, the racemate mixture, as well as the R (-) and S (+) enantiomers, were all tested against the following target pathogens:

- 1) *Botrytis cinerea* in tomato
- 2) *Uncinula necator* in grape
- 3) *Septoria tritici* in wheat
- 4) *Pyrenophora teres* in barley
- 5) *Venturia inaequalis* in apple
- 6) *Alternaria solani* in tomato
- 7) *Mycosphaerella arachidis* in peanuts

The concentrations tested in this trial were 2, 6, 20, 60 and 200 ppm. In this trial the S (+) enantiomer showed a similar activity as the racemate mixture, while the R (-) enantiomer was slightly less efficacious, particularly at lower concentrations. However, even at the lowest concentration, the R (-) enantiomer still provided  $\geq 70\%$  activity against all tested pathogens.

On the basis of these results, it is concluded that both enantiomers have good biological activity and will contribute to the efficacy of the racemate mixture of pydiflumetofen.

**B.3.9. REFERENCES RELIED ON**

<b>Data Point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Data protection claimed Y/N</b>	<b>Justification if data protection is claimed</b>	<b>Owner</b>	<b>Previous evaluation</b>
Volume 3CA point B.3	Unknown	2020	Section 3  Efficacy Data and Information  Biological Assessment Dossier  Product code: A21857B  Product name: MIRAVIS PLUS  Chemical active substance: ADEPIDYN™ technology, 62.5 g/L	N	Y	Biological Assessment Dossier for the representative product	Syngenta	N.A.
Volume 3CA point B.3.8		2016	KCA_3.3-01 Comparison of the fungicidal activity of SYN545974 and its 2 enantiomers	N	N	N.A.	Syngenta	N.A.