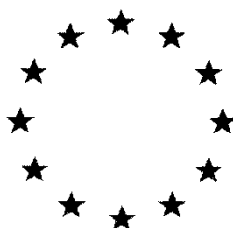


# ***European Commission***



**Draft Assessment Report prepared according to the Commission  
Regulation (EU) N° 1107/2009**

## **ISOFLUCYPRAM**

### **Volume 3 – B.3 (PPP) – Isoflucypram EC 50**

**Rapporteur Member State : United Kingdom  
Co-Rapporteur Member State :France**

## Version History

When	What
March 2019	Initial DAR

## Table of contents

<b>B.3. DATA ON APPLICATION AND EFFICACY .....</b>	<b>4</b>
<b>B.3.1. FIELD OF USE ENVISAGED .....</b>	<b>4</b>
<b>B.3.2. EFFECTS ON HARMFUL ORGANISMS .....</b>	<b>4</b>
<b>B.3.3. DETAILS OF INTENDED USE .....</b>	<b>5</b>
<b>B.3.4. APPLICATION RATE AND CONCENTRATION OF THE ACTIVE SUBSTANCE .....</b>	<b>7</b>
<b>B.3.5. METHOD OF APPLICATION.....</b>	<b>7</b>
<b>B.3.6. NUMBER AND TIMING OF APPLICATIONS AND DURATION OF PROTECTION.....</b>	<b>7</b>
<b>B.3.7. NECESSARY WAITING PERIODS OR OTHER PRECAUTIONS TO AVOID PHYTOTOXIC EFFECTS ON SUCCEEDING CROPS.....</b>	<b>7</b>
<b>B.3.8. PROPOSED INSTRUCTIONS FOR USE .....</b>	<b>7</b>
<b>B.3.9. APPLICATION RATE AND CONCENTRATION OF THE ACTIVE SUBSTANCE .....</b>	<b>8</b>
<b>B.3.10. METHOD OF APPLICATION.....</b>	<b>8</b>
<b>B.3.11. NUMBER AND TIMING OF APPLICATIONS AND DURATION OF PROTECTION.....</b>	<b>8</b>
<b>B.3.12. NECESSARY WAITING PERIODS OR OTHER PRECAUTIONS TO AVOID PHYTOTOXIC EFFECTS ON SUCCEEDING CROPS.....</b>	<b>8</b>
<b>B.3.13. EFFECTIVENESS .....</b>	<b>8</b>
<b>B.3.14. INFORMATION ON THE DEVELOPMENT OF RESISTANCE .....</b>	<b>9</b>
<b>B.3.15. ADVERSE EFFECTS ON TREATED CROPS .....</b>	<b>10</b>
<b>B.3.16. OBSERVATIONS ON OTHER UNDESIRABLE OR UNINTENDED SIDE-EFFECTS .....</b>	<b>11</b>
<b>B.3.17. REFERENCES RELIED ON.....</b>	<b>11</b>

### **B.3. DATA ON APPLICATION AND EFFICACY**

BAYF31262 is a novel fungicide containing 50g/L Isoflucypram as an emulsifiable concentrate (EC). This document summarises information related to the efficacy of Isoflucypram with the representative formulation BAYF31262.

As this is the first submission for approval of the active substance Isoflucypram, a concise summary of efficacy will be included. Detailed efficacy data will be provided in the subsequent product authorisation process when full biological assessment dossiers will be submitted for each regulatory zone.

#### **B.3.1. FIELD OF USE ENVISAGED**

SY EC 50, containing 50 g isoflucypram/L, is used as a broad spectrum foliar fungicide in cereal crops. The intended uses of ISY EC 50 comprise winter- and summer-wheat (including Durum wheat and spelt), winter- and summer-barley, rye, triticale, and oats. The representative crops for the approval of isoflucypram referred to in this dossier are wheat and barley.

#### **B.3.2. EFFECTS ON HARMFUL ORGANISMS**

The biochemical mode of action of isoflucypram has been shown to rely on the inhibition of the fungal enzyme succinate dehydrogenase, which is part of the mitochondrial respiration chain. The inhibition of this enzyme is affecting both, the generation of energy as well as the formation of precursors needed for the synthesis of essential cellular compounds such as amino acids within the target fungus.

At the biological level, this corresponds to an inhibition of spore germination and/or a reduction in germ tube elongation at the surface of the plant. Moreover, the appressorium formation is affected and the fungus is unable to penetrate through the host tissue. In case isoflucypram is applied after the fungus has already penetrated the plant tissue, isoflucypram is able to inhibit further fungal growth due to its intrinsic curativity.

### B.3.3. DETAILS OF INTENDED USE

Crop and/or situation (a)	Member State	Product Name	F G I (b)	Pests or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Rate L/ha	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	Kg a.i./hl min max (g/ha)	Water l/ha min max	Lk a.i./ha min max (*) (g/ha)		
Wheat	EU	BAYF31262	F	Mycosphaerella graminicola, Puccinia recondita, Puccinia striiformis, Pyrenophora tritici-repentis	EC50	1.5	Foliar spray	BBCH 30-69	1	-	-	100-400	0.075	*	* A Pre-Harvest Interval for use in wheat (including durum wheat and spelt), rye and triticale is not applicable: the timing is defined by the growth stage at application.
Rye	EU	BAYF31262	F	Puccinia recondita, Rhynchosporium secalis	EC50	1.5	Foliar spray	BBCH 30-69	1	-	-	100-400	0.075	*	
Triticale	EU	BAYF31262	F	Mycosphaerella graminicola, Puccinia recondita, Puccinia striiformis, Pyrenophora tritici-repentis	EC50	1.5	Foliar spray	BBCH 30-69	1	-	-	100-400	0.075	*	
Barley	EU	BAYF31262	F	Rhynchosporium secalis, Pyrenophora teres, Puccinia hordei, Ramularia collo-cygni	EC50	1.5	Foliar spray	BBCH 30-61	1	-	-	100-400	0.075	*	
Oats	EU	BAYF31262	F	Puccinia coronata, Pyrenophora avenae	EC50	1.5	Foliar spray	BBCH 30-61	1	-	-	100-400	0.075	*	

- 
- \*- For uses where the column „Remarks“ in marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
- (a) For crops, the EU and Codex classification (both) should be taken into account ; where relevant, the use situation should be described (e.g. fumigation of a structure)
- (i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant synthesised, it is more appropriate to give the rate for the variant (e.g. benthialdicarb-isopropyl).**

- (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
- (c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
- (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
- (e) GCPF Codes – GIFAP Technical Monograph N° 2, 1989
- (f) All abbreviations used must be explained
- (g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant – type of equipment used must be indicated
- (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
- (k) Indicate the minimum and maximum number of application possible under practical conditions of use
- (l) The values should be given in g or kg whatever gives the more manageable number (*e.g.* 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)
- (m) PHI - minimum pre-harvest interval

**B.3.4. APPLICATION RATE AND CONCENTRATION OF THE ACTIVE SUBSTANCE**

ISY EC 50 is used only once per cereal crop and season at a maximum rate of 1.5 L/ha, corresponding to 75 g isoflucypram/ha. Please see the table presented above within the section titled “**B.3.3 Details of intended use**” according to Regulation (EC) 1107/2009, Article 4 (3).

**B.3.5. METHOD OF APPLICATION**

Isoflucypram containing products are applied as foliar treatment to cereals using hydraulic vehicle mounted spray equipment. The standard water rate for use in cereals is between 100 and 400 L/ha providing the equipment is in good working order and have been calibrated to manufacturer instructions.

The proposed application timings are at growth stages from BBCH 30 to BBCH 69.

**B.3.6. NUMBER AND TIMING OF APPLICATIONS AND DURATION OF PROTECTION**

No conclusion drawn on the duration of protection so it is concluded that the duration of protection is in line with the assessment timings tested as part of efficacy trials. Evidence presented suggest mid term protection between 20-36 days after application and long term protection 35-56 days after protection.

	BAYF 31262 (50 g/L Isoflucypram)
Crop/situation	Wheat and barley
Outdoor/protected/ ground/aerial use	Outdoor
Maximum individual dose/concentration	1.5 L/ha
Maximum total dose	1.5 L/ha
Rate of isoflucypram from individual dose	75 g as/ha
Latest time of application	Wheat: BBCH 69 (end of flowering). Barley: up to BBCH 61 (beginning of flowering)
Interval between applications	n/a
Water volumes	100-400
Method(s) of application	Ground sprayer

**B.3.7. NECESSARY WAITING PERIODS OR OTHER PRECAUTIONS TO AVOID PHYTOTOXIC EFFECTS ON SUCCEEDING CROPS**

BAYF31262 is a highly selective fungicide. No restriction is proposed on the draft label. This will need to be considered further at product authorisation.

**B.3.8. PROPOSED INSTRUCTIONS FOR USE**

BAYF31262 is a fungicide with protectant and curative properties for disease control in cereal crops.

### Time of application

For cereal disease control, apply BAYF31262 prior to disease infection as a preventative treatment. Where disease pressure remains high a second application may be required with an equally effective product. Applications made to established infections are likely to be less effective.

Application (BBCH 30) until end of flowering (latest application at BBCH 69). The described application window can be more limited in specific countries or for specific uses.

Please refer to Document D1 for full use instructions.

### **B.3.9. APPLICATION RATE AND CONCENTRATION OF THE ACTIVE SUBSTANCE**

Please see the table presented above within the section titled “**B.3.3 Details of intended use**” according to Regulation (EC) 1107/2009, Article 4 (3).

### **B.3.10. METHOD OF APPLICATION**

BAYF31262 containing products are used as foliar sprays, and can be applied through all conventional sprayers providing they are in good working order and have been calibrated to manufacturer instructions. The proposed application timings are at growth stages from BBCH 30 to BBCH 69.

### **B.3.11. NUMBER AND TIMING OF APPLICATIONS AND DURATION OF PROTECTION**

The application timing of isoflucypram in wheat, rye and triticale lies between growth stages BBCH 30 and 69 and in barley and oats between BBCH 30 and 61. Due to the outstanding and long-lasting efficacy of isoflucypram one application in BBCH 39 can give season-long control of leaf diseases under a wide range of environmental conditions. However, local conditions and disease pressure may require a follow up application of another effective product in a programme of applications and this is normal practice in some countries.

### **B.3.12. NECESSARY WAITING PERIODS OR OTHER PRECAUTIONS TO AVOID PHYTOTOXIC EFFECTS ON SUCCEEDING CROPS**

BAYF31262 is a highly selective fungicide. No restriction is proposed on the draft label. This will need to be considered further at product authorisation.

### **B.3.13. EFFECTIVENESS**

The representative formulation Isoflucypram EC 50 (in the following abbreviated as ISY EC 50) has been tested in field development trials between 2015 and 2017, which demonstrate high efficacy against the targeted diseases and appropriate crop safety. Efficacy data towards the key representative targets in wheat and barley are used to demonstrate the activity of ISY EC 50. In wheat, ISY EC 50 was applied for the control of *Mycosphaerella graminicola* and *Puccinia recondita/Puccinia triticina* and in barley for the control of *Pyrenophora teres* and *Rhynchosporium secalis*. These are major target diseases and are considered to support the proposed GAP.

To evaluate the efficacy of ISY EC 50 in the Maritime EPPO climatic zone, 17 field trials on winter wheat (TRZAW) and 19 field trials on spring/winter barley (HORVS and HORVW) were conducted in the period of 2016-2017. These trials were undertaken by Bayer Crop Science Division country organisations and contract research organisations with 10 trials located in northern France (FRA), 14 trials in Germany (DEU), 2 trials in Ireland (IRL) and 10 trials in the United Kingdom (GBR).

The trials to generate representative efficacy data in spring/winter barley in the North East EPPO climatic zone were undertaken by Bayer Crop Science Division country organisations in Latvia (LVA; 2 trials) and in Poland (POL; 1 trial) in 2017.

All trials have been conducted according to EPPO standards by GEP accredited organisations, either by field development staff of Bayer country subsidiaries or by contract research organisations.

Trials were designed, conducted and reported in accordance with general EPPO standards PP1/225(2), PP1/135(4), PP1/152(4), PP1/026(3), and PP1/181(44) regarding design, analyses and reporting.

ISY EC 50 was applied once either at 1.5 L/ha (corresponding to 75 g isoflucypram/ha), 1.25 L/ha (corresponding to 62.5 g isoflucypram/ha) or 1.0 L/ha (corresponding to 50 g isoflucypram/ha) on spring and winter barley and winter wheat for the control of the main target diseases selected as targets for the representative uses. ISY EC 50 gave 86% reduction of *Mycosphaerella graminicola* in wheat over ten trials. Efficacy was tested under a range of environmental conditions to fully challenge the potential of the product.

The performance of ISY EC 50 applied at the 1 N dose (1.5 L/ha / 75 g a.s./ha) and at lower dose rates matched or exceeded the performance of the commercial standard Aviator Xpro EC 225 (applied at 1.25 L/ha or 1.0 L/ha). Although a minor dose response was observed as part of the applicant's product Biological assessment dossier further consideration of minimum effective dose is required as part of the detailed product assessment. Thus, the active substance isoflucypram can be considered as effective against foliar diseases. However this will be confirmed at product authorisation.

### **B.3.14. INFORMATION ON THE DEVELOPMENT OF RESISTANCE**

The applicant has provided the following case for resistance;

“As an SDH isoflucypram is assigned to FRAC Group 7. Therefore, to fulfil the requirements of an effective anti-resistance management strategy, isoflucypram will be offered in mixtures with non cross-resistant fungicides from different chemical classes with alternate biochemical modes of action delivering highly active solutions. These tailor-made and broad spectrum combinations of isoflucypram show – beside the long-lasting efficacy – highly beneficial properties in terms of plant physiology enabling treated crops to exhibit good disease control to maximize their full yield potential.”

However the zRMS has re-summarised this information in line with the steps outlined in EPPO standard PP1/213 (4).

#### Mode of action

Isoflucypram belongs to the chemical class of Succinate DeHydrogenase Inhibitor (SDHI) fungicides. It's mode of action has been shown to rely on the inhibition of the fungal enzyme succinate dehydrogenase resulting in the inhibition of spore germination and/or a reduction in germ tube elongation at the leaf surface.

#### Mechanisms of resistance

Although isoflucypram is a new active it shares the resistance risk typical for all SDHI fungicides. Resistance is known in various fungal species in field populations and lab mutants. Target site mutations in *sdh* gene, e.g. H/Y (or H/L) at 257, 267, 272 or P225L, dependent on fungal species. FRAC classifies SDHI fungicides as “medium to high risk”. The number and frequency of isolates with reduced sensitivity to SDHI fungicides is increasing hence the resistance type characteristic for SDHI is best described as "continuous selection" or "shifting". Resistance management is therefore required.

#### Evidence of resistance

As isoflucypram is a new active there are no specific reported cases of resistance. However, isoflucypram is a SDHI fungicide so will likely share the resistance risk typical for all other SDHI fungicides. No further evidence has been provided but this will be considered further as part of the product authorisation. The applicant is a member of the FRAC SDHI Working group and is known to actively monitor key diseases to assess sensitivity shifts.

The current FRAC SDHI Working group recommendations provide the following guidance for the use of foliar application on cereals

**Resistance management for SDHI fungicides in general**

- ☐ Apply SDHI fungicides always in mixtures
- ☐ The mixture partner should provide satisfactory disease control when used alone on the target disease and must have a different mode of action.
- ☐ Apply a maximum of 2 SDHI fungicide containing sprays per cereal crop.
- ☐ Apply the SDHI fungicide preventively or as early as possible in the disease cycle. Do not rely only on the curative potential of SDHI fungicides.
- ☐ Strongly reduced rate programs including multiple applications must not be used. Refer to manufacturers' recommendations for rates.

**Resistance risk conclusion**

The zRMS considers that isoflucypram represents an acceptable resistance risk when the appropriate resistance risk modifiers for SDHI fungicides are in use. However, the risk of resistance will require further consideration by the applicant at the National level during the product evaluation process.

**B.3.15. ADVERSE EFFECTS ON TREATED CROPS**

Data from efficacy trials with low to no disease pressure (<5% severity infection) has been summarized separately to demonstrate crop safety. This data has been used to highlight the absence of any potential unintentional adverse effects that might have been produced by the application of ISY EC 50 in absence of disease or under low disease pressure. To further evaluate the crop safety of ISY EC 50, 5 specific field trials on winter wheat (TRZAW) and 5 specific field trials on spring/winter barley (HORVS and HORVW) were conducted in 2015. These trials were also undertaken by Bayer Crop Science Division country organisations and contract research organisations with 3 trials located in northern France (FRA), 4 trials in Germany (DEU) and 3 trials in the United Kingdom (GBR).

The trials were designed and conducted according to approved EPPO standards. ISY EC 50 was applied at 1 N dose rate (1.5 L/ha) in all trials, in some cases including also treatments at lower dose rates.

Crop safety trials and efficacy trials were carried out on winter wheat (TRZAW) as well as on spring and winter barley (HORVS/HORVW) in three following years from 2015 to 2017. ISY EC 50 has been tested at rates up to 1.5 L/ha without producing significant adverse effects.

**Winter wheat (TRZAW)**

In winter wheat (TRZAW) a total of 17 efficacy trials, comprising 13 different varieties, and 5 crop safety trials with 3 additional varieties were performed across the Maritime EPPO climatic zone. Consequently ISY EC 50 has been tested on 16 different varieties of winter wheat (TRZAW).

No phytotoxicity damage has been observed in any of the 22 field trials up to the highest dose rate of ISY EC 50 of 1.5 L/ha (corresponding to 75 g isoflucypram/ha).

**Spring and winter barley (HORVS/HORVW)**

In spring and winter barley (HORVS/HORVW) a total of 19 efficacy trials, comprising 14 different varieties, and 5 crop safety trials with one additional variety were conducted across the Maritime EPPO climatic zone. Consequently ISY EC 50 has been tested on 15 different varieties of spring and winter barley (HORVS/HORVW).

No phytotoxicity damage was observed in any of the 24 field trials up to the highest dose rate of ISY EC 50 of 1.5 L/ha (corresponding to 75 g isoflucypram/ha).

These data have been complemented by 3 supportive trial results from the North East EPPO climatic zone representing 3 additional barley varieties. No phytotoxicity damage has been observed in any of these trials. While no adverse effects can be seen based on the initial conclusions, this must be considered in further detail at the national level as part of product authorisation.

[illegible]