

Initium®: a new fungicidal active ingredient for the control of Oomycetes

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SUMMARY

Initium is an innovative fungicidal active ingredient developed by BASF. Initium is a mitochondrial respiration inhibitor and belongs to a new class of chemistry, the triazolo-pyrimidylamines. In numerous field trials performed in several climatic zones around the world, Initium has proven its high efficacy and its excellent crop safety. Initium is highly active against Oomycete pathogens, inhibiting zoospores in their formation and release, mobility and germination. In addition Initium inhibits the direct germination of zoosporangia. Initium has a high affinity for the epicuticular wax layers of plant surfaces. Initium redistributes under the influence of dew and due to this effect an increasing area can be protected. Because of this effect, Initium has also good protection on new growth. Taken together these characteristics lead to a premium preventive activity with long residual activity in the field. Initium containing products will be positioned in preventive spray applications against late blight in potatoes and against downy mildews in a wide range of speciality crops. Due to its excellent toxicological and ecotoxicological profile, Initium will be an important active ingredient for sustainable spray programs. Initium will only be sold in combination with other active ingredients. First registrations have been achieved in Romania, The Netherlands and The United Kingdom. The worldwide registration initiatives will continue from 2010 onwards and will ensure a coordinated setting of maximum residue limits and import tolerances.

INTRODUCTION

Late blight and downy mildews are devastating diseases of speciality crops world wide and play an important economic role in commercial food production. Economic losses by *Phytophthora infestans* in potatoes were estimated alone in developing countries by more than 2,7 Mrd. \$ (CIP, Centro Internacional de la Papa, Lima [Peru]). Initium is a fungicide developed by BASF with high activity against these Oomycete pathogens. Since its discovery in 2004, Initium has undergone detailed evaluation in laboratory tests and in extensive global field testing programmes. The aim of this paper is to give an overview of Initium's chemical and physical properties, mode of action and biological profile, field performance in potatoes, resistance management and safety profile.

CHEMICAL AND PHYSICAL PROPERTIES

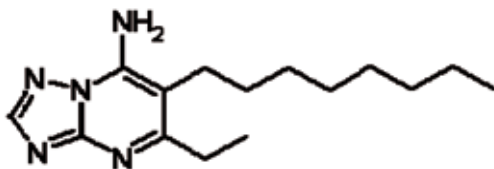


Figure 1: Structural formula of Initium

The following table shows the most important physical and chemical properties of the new active ingredient Initium:

Table 1: Physical and chemical properties of Initium

Common name:	Ametoctradin
CAS no:	865318-97-4
Chemical name (IUPAC):	[1,2,4] triazolo [1,5- <i>a</i>] pyrimidin-7 amine, 5-ethyl-6-octyl
Molecular formula:	C ₁₅ H ₂₅ N ₅
Molecular weight:	275.4 g/mol
Vapour pressure:	2.1 × 10 ⁻¹⁰ PA at 20° C
Solubility (Water at 20° C Ph7):	0.15 mg/l
Partition coefficient	log P _{ow} = 4.4
Hydrolytical stability	Stable at pH 4-9
Photolytical stability	Slowly degraded by direct photolysis in neutral aqueous solution

MODE OF ACTION

Initium is a potent inhibitor of the mitochondrial respiratory chain in target pathogens. More specifically, Initium interferes with complex III, which is a membrane protein complex. By inhibiting complex III, Initium impairs the electron transport in the respiratory chain of the pathogen, thus making it unable to generate the energy required for keeping the organism alive. Research has demonstrated that Initium is not cross-resistant to phenylamides (e.g. metalaxyl), Qo inhibitors (e.g. strobilurins) and carboxylic acid amides (e.g. dimethomorph).

Initium is a highly effective inhibitor of zoospore formation, release, mobility and germination. In addition Initium inhibits the direct germination of zoosporangia. Microscopic observations show that Initium immediately stops the movement of zoospores and makes them burst within a few seconds at very low concentrations (ED₅₀ = 0.021 ppm) (Figs. 2). Sporangia were examined as well under the microscope. They failed to germinate after treatments with Initium (ED₅₀ = 0.08 ppm).

The efficacy of Initium against *Phytophthora infestans* during different stages of its life cycle was proven for very sensitive strains as well as for the more aggressive A2-mating-type populations, including Blue 13 strains from the UK. Initium's high activity against the different *Phytophthora* strains is important to ensure reliable control under different situations in the field with changing *Phytophthora* populations.

Due to the long acyl side chain of the Initium molecule, the AI exhibits a high log P_{ow} value of 4,4 and has a high affinity for the epicuticular wax layers of the plant epidermis.

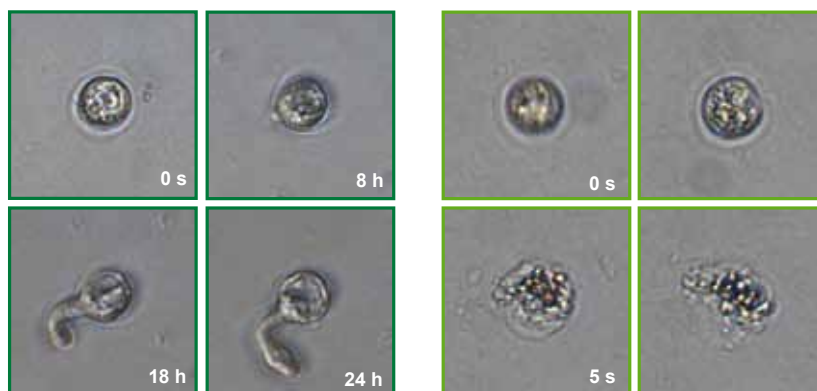


Figure 2: Light microscope images of *Phytophthora infestans* zoospores. The untreated zoospore (left) remained intact and forms a germ tube. The Initium-treated zoospore (right) ruptured within 5 seconds and cytoplasm leaked from the spore.

Through the adsorption of Initium to the wax layers and through the formation of AI depots on the plant surfaces, Initium forms a stable protective film on plants with a long-lasting efficacy against Oomycete pathogens (Fig. 3). Initium exhibits very good rainfastness, however, under the influence of moisture such as dew, a small but effective portion of the active ingredient is gradually redistributed from the protective film leading to a significant increase in protection. This effect ensures that growing leaves can be protected during the phase of active growth.

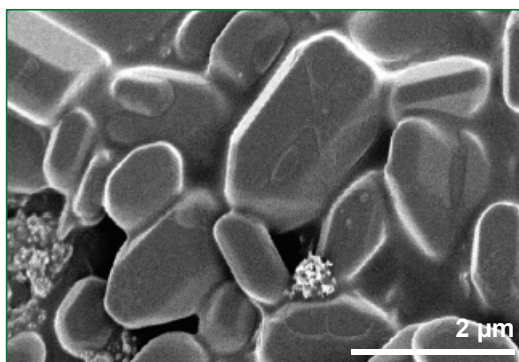


Figure 3. Scanning electron microscopy image of Initium spray deposit on a tomato leaf. The particles of the active ingredient are bound to the surface like a film.

Less than 10% of the applied active ingredient is taken up by the leaves after 1-7 days. The majority of the active ingredient remains on the leaf surface where it is adsorbed to the epicuticular wax layer. The vapour phase activity is minimal. These characteristics indicate that Initium is a non-systemic fungicide.

BIOLOGICAL PROFILE

Crop safety

Initium is characterised by excellent crop safety. At the recommended rates, no crop injury has been observed over several years of testing in a broad variety of crops.

Spectrum of activity

Initium controls all major Oomycete diseases, e.g. downy mildew caused by *Plasmopara viticola* in grapes, late blight caused by *Phytophthora infestans* in potatoes and tomatoes, and a broad range of downy mildews and late blights in vegetables (e.g. cucurbits, brassicas, onions, and lettuce).

The performance of Initium in potatoes was proven in several field trials on research stations in different countries. Summarized results are shown in the Table 2.

Table 2: Control of *Phytophthora infestans* in potatoes in Spain, Germany, Brazil and Taiwan in 2004 – 2005 (orthogonal summary)

Treatment ¹	Dose g a.i./ha	Mean % index of attack Leaves	Statistics ²
Initium	300	11	C
Fluazinam	200	16	B
Untreated	-	78	A
Number of trials		8	

¹ 3-7 applications at BBCH 19-85 following a 5-11 day spray interval. Ave. of 8 trials.

² Statistical analysis: SNK-Test

In the registered combinations products, Initium will be used at 200 to 300 g active ingredient per hectare.

RESISTANCE MANAGEMENT

Initium is not cross-resistant to Oomycete fungicide classes with confirmed field resistance (e.g. phenylamides, Qo inhibitors or carboxylic acid amides). Very important in potatoes and other crops attacked by *Phytophthora infestans* is that Initium is fully effective against metalaxyl-resistant *Phytophthora infestans* strains.

To ensure the long-term efficacy of Initium in all target crops, Initium will only be available in ready formulations combined with other fungicidal active ingredients of a different mode of action. To use the full activity of Initium, all applications should be done in a preventive manner following the recommendations on the product label.

TOXICOLOGICAL AND ECOTOXICOLOGICAL PROPERTIES

Initium displays an excellent toxicological profile. Acute mammalian toxicology studies indicate that Initium is not harmful after ingestion, dermal exposure or inhalation. It is also not irritating to eyes or skin and is not a sensitizer.

Furthermore Initium shows an excellent ecotoxicological profile. It is practically non toxic to birds, mammals, honeybees, earthworms and other soil macro-organisms, or to non-target soil micro-organisms and their ecosystem function. The use of Initium in accordance with good agricultural practice does not pose any risk to aquatic ecosystems. It is ideal for use in integrated crop management programmes.

CONCLUSIONS

Initium is a highly active preventive fungicide from a new chemical class for the use against Oomycete diseases. It has an excellent toxicological and ecotoxicological profile and is suitable for use in a range of speciality crops in integrated crop management programmes. BASF plans worldwide registrations for Initium. Initium will be marketed in ready-mixtures with other Oomycete active compounds to complement the spectrum of activity and to reduce selection pressure for resistance.

ACKNOWLEDGEMENTS

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Anonymus, CIP, Centro Internacional de la Papa, Lima [Peru],
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