**FUNGICIDE**

### Isofetamid

**New chemical class of SDHI**

Isofetamid is a novel SDHI (Succinate Dehydrogenase Inhibitor, FRAC code 7) fungicide discovered and under development by ISK.

Isofetamid is a new chemical group (phenyl-oxo-ethyl thiophene amide) based on its thiophene carboxamide moiety. Due to this unique chemical structure, Isofetamid remains highly effective against the majority of fungal isolates that have developed resistance to other SDHI fungicides.

As a broad-spectrum fungicide, Isofetamid exhibits excellent activity against a broad range of fungi, but is especially effective on the Ascomycota (such as Botrytis spp., Sclerotinia spp., Monilinia spp., Venturia spp.) at low dose rates.

In addition to its outstanding efficacy, Isofetamid has no negative impacts on beneficial insects and mites, making it an excellent choice for integrated pest management programs.

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**Physico-Chemical Properties**

- **Class:** Phenyl-oxo-ethyl thiophene amide
- **IUPAC name:** N-[1,1-dimethyl-2-(4-isopropoxy-o-tolyl)-2-oxoethyl]-3-methylthiophene-2-carboxamide
- **Molecular weight:** 359.48
- **Molecular formula:** C_{20}H_{25}NO_{3}S
- **Vapour pressure:** 4.2 x 10^{-7} Pa (25°C)
- **Water solubility:** 5.33 mg/L (20°C)
- **Form:** White Solid (powder)
- **Development code:** IKF-5411

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**Toxicology & Ecotoxicology**

- **Rat LD_{50} (oral):** > 2,000 mg/kg (f)
- **Rat LD_{50} (dermal):** > 2,000 mg/kg (m/f)
- **Rat LC_{50} (inhalation):** > 4.82 mg/L (m/f)
- **Skin irritation:** non irritant (rabbit)
- **Eye irritation:** slightly irritating to eyes (rabbit)
- **Skin sensitization:** not a sensitizer (mouse, guinea pig)
- **Avian LD_{50} (acute oral):** > 2,000 mg/kg (quail, m/f)
- **Avian LD_{50} (subacute oral):** > 5,000 ppm in feed (quail)
- **Fish LC_{50}:** > 7.12 mg/L (carp, 96 h)
- **Bees LD_{50} (acute oral):** > 30 μg a.i./bee (48 h)
- **Bees LD_{50} (acute contact):** > 100 μg a.i./bee (48 h)
- **Daphnia magna EC_{50}:** 4.7 mg/L (48 h)

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**Product**

- **Trade Names:** KENJA, ZENBY, KRYOR, HAREGI, KABUTO, ASTUN, etc.
- **Formulations:** 40%SC
- **Registered Countries**
  - Asia: China, Japan, Korea
  - Europe: Belgium, Bulgaria, Czech Republic, France, Germany, Greece, Hungary, Italy, Luxembourg, Poland, Portugal, Romania, Spain, Slovenia, UK, etc.
  - Oceania: Australia
  - Americas: Brazil, Canada, Chile, Colombia, Ecuador, Mexico, Peru, USA, etc.

**Characteristics**

- **SDHI class (FRAC code 7) with broad-spectrum fungicidal activity**
- **Flexible molecular structure makes it effective on major SDHI resistant isolates**
- **Inhibits all growth stages of fungal life cycle**
- **Good persistence and rainfastness**
- **Extension of shelf life by pre-harvest application**
- **High safety for crop and beneficial organisms**

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Always read and follow the product label instructions in your country.
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**Mode of Action**

Isofetamid acts specifically on the succinate dehydrogenase (SDH) of Complex II, a key enzyme of the mitochondrial respiratory chain at the crossroads of two metabolic pathways essential to fungal cell life. By inhibiting SDH, Isofetamid impairs energy (ATP) production by the respiratory chain and the synthesis of amino acids, lipids, and fatty acids (metabolites essential to cell function) at the Krebs cycle stage.

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**Advantages of Isofetamid for resistance management**

Isofetamid can control numerous isolates with confirmed resistance to other SDHI fungicides, including SdhB H272R and H272Y, which are the two most common field-collected isolates. Research has confirmed that Isofetamid fits the mutated binding pocket of SDHI-resistant fungal isolates (SdhB H272R and H272Y). It is hypothesized that the unique molecular structure of Isofetamid gives the molecule flexibility at the binding site, allowing Isofetamid to retain efficacy on these mutants. Other SDHI fungicides have a rigid structure, are unable to bind at sites where mutations have occurred, and are therefore ineffective as control options.

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**Fungicidal spectrum**

<table>
<thead>
<tr>
<th>Disease name</th>
<th>Commercial standard</th>
<th>Disease Incidence or Severity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerotinia rot</td>
<td>Dicarboximides</td>
<td>Isofetamid Standard 266 ppm</td>
</tr>
<tr>
<td>Botrytis cinerea</td>
<td>Anilino-pyrimidines</td>
<td>Isofetamid Standard 750 g a.i./ha</td>
</tr>
<tr>
<td>Gummy stem blight</td>
<td>Dicarboximides</td>
<td></td>
</tr>
<tr>
<td>Didymella broniae</td>
<td>500 ppm</td>
<td>2011: 5.0 2012: 1.0 2013: 5.0 2014: 1.0 2016: 8.0 2017: 4.0 2020: 4.0</td>
</tr>
<tr>
<td>Wilsonomyces spp.</td>
<td>TPN 400 ppm</td>
<td></td>
</tr>
<tr>
<td>Corynespora leaf spot</td>
<td>Quinoxaline</td>
<td></td>
</tr>
<tr>
<td>Powdery mildew</td>
<td>Podosphaera xanthii</td>
<td></td>
</tr>
</tbody>
</table>

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**Control of fruit rots on strawberries during storage**

After Isofetamid applications in the field, fruit were collected the next day and stored on trays at room temperature. Postharvest disease incidence was evaluated 7 days after harvest.

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**Multiple disease control (Cucumber field trials in Japan)**

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<thead>
<tr>
<th>Disease name</th>
<th>Commercial standard</th>
<th>Disease Incidence or Severity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerotinia sclerotiorum</td>
<td>Dicarboximides 250 ppm</td>
<td>Isofetamid Standard 266 ppm</td>
</tr>
<tr>
<td>Botrytis cinerea</td>
<td>200 ppm</td>
<td></td>
</tr>
<tr>
<td>Didymella broniae</td>
<td>500 ppm</td>
<td></td>
</tr>
<tr>
<td>Corynespora cassicola</td>
<td>TPN 400 ppm</td>
<td></td>
</tr>
<tr>
<td>Powdery mildew</td>
<td>Quinoxaline 83 ppm</td>
<td></td>
</tr>
</tbody>
</table>

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**Stable control against Gray mold (Grape field trials in EU)**

![Simulation modeling of enzyme 3D structure](image)