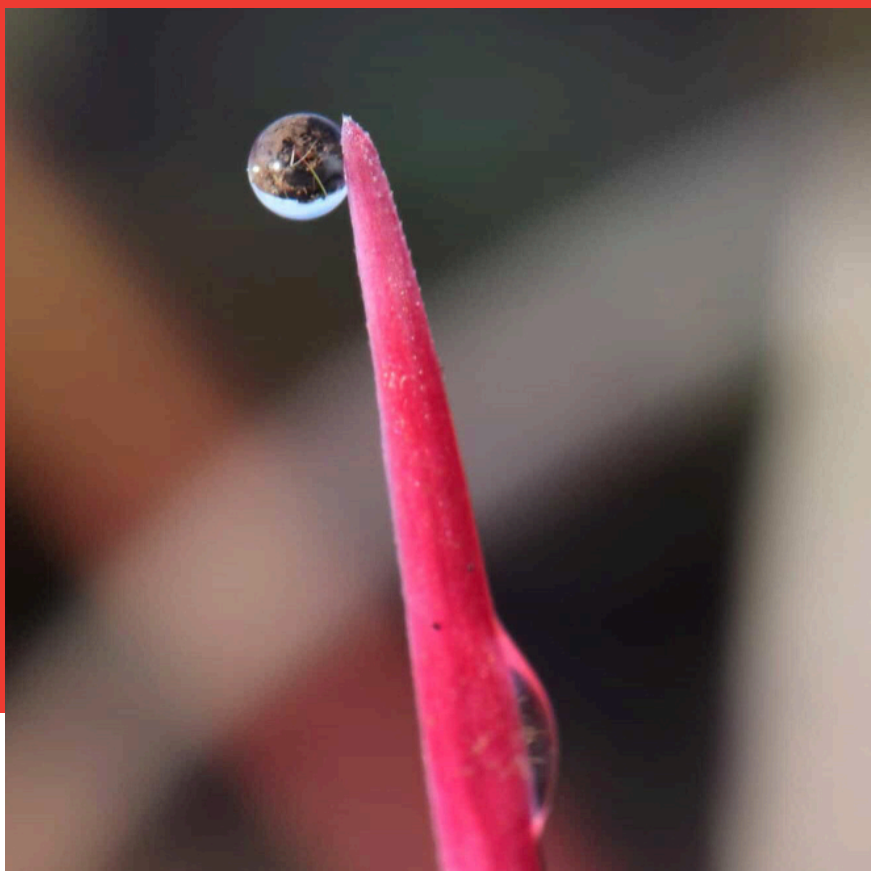


GLOBAL STEWARDSHIP BULLETIN



Introduction

FMC's bixlozone herbicide, trademarked Isoflex™ active, is a unique selective herbicide for use in crops, such as cereals, canola, oilseed rape, corn and sugarcane. Isoflex™ active provides residual and early post-emergence control of small-seeded broadleaves and is especially active on annual grass weeds. Products containing Isoflex™ active provide good crop tolerance and serves as an excellent mixing partner in several cropping systems. Isoflex™ active is only the second herbicide representing the isoxazolidinone family, preventing carotenoid biosynthesis in susceptible plants via inhibiting DXP synthase.



Features & Benefits

Key Features

Isoflex™ active belongs to the isoxazolidinone family, the same chemical family as the FMC active clomazone (various trade names), with a history of success and recognition for its adaptability and preventive weed control.

When used in cereal crops, products containing Isoflex™ active are considered a new novel herbicide mode of action.

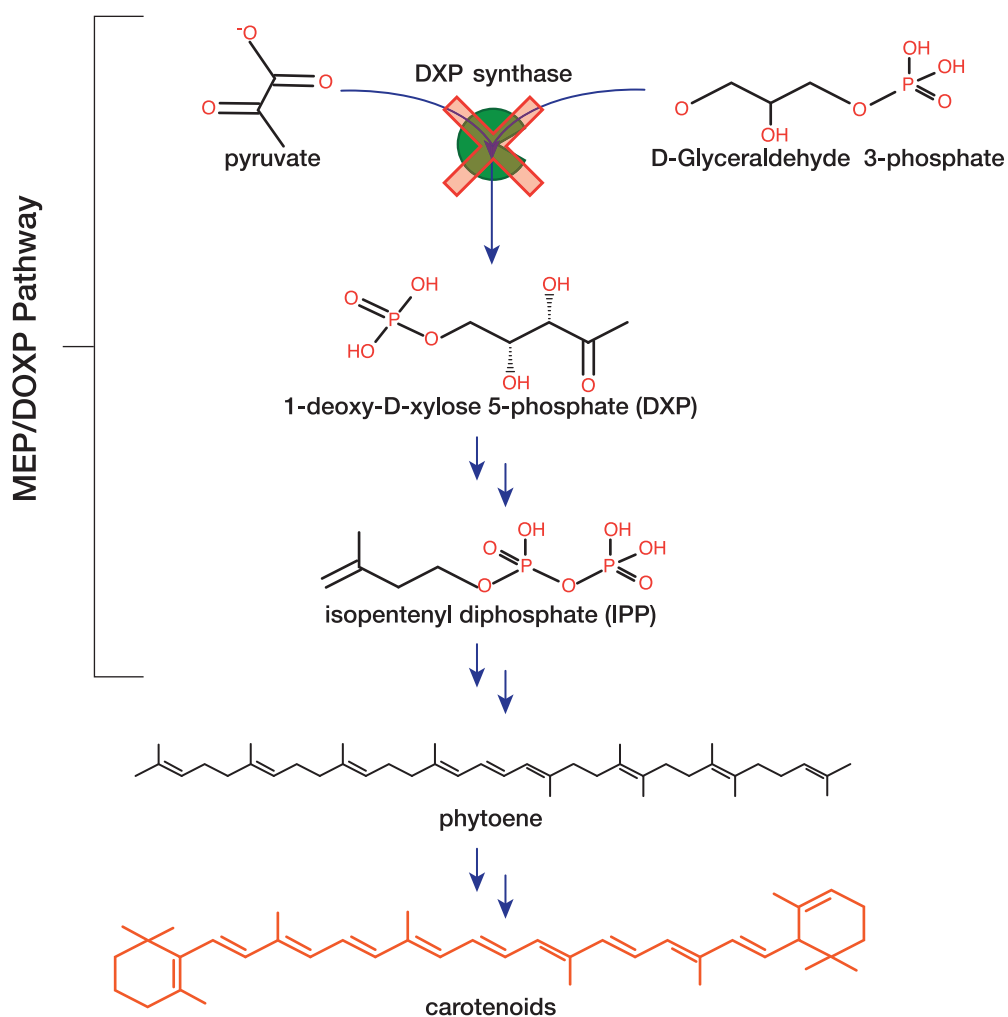
Products containing Isoflex™ active can be used to control weeds prior to planting through the early crop growth stage in many of the registered crops (please refer to the product label for proper usage), providing a flexible application window for targeting problematic weeds.

Mode of Action

Biochemical Mode of Action

Isoflex™ active belongs to the isoxazolidinone class of herbicides and is classified by Global HRAC as a Group 13 herbicide due to its inhibition of the Deoxy-D-Xylulose Phosphate Synthase (DXP synthase) which is a component of the carotenoid biosynthetic pathway (Figure 1).

Figure 1.
Diagram of the MEP/DOXP biological pathway for building the terpenoid backbone required in carotenoid biosynthesis.

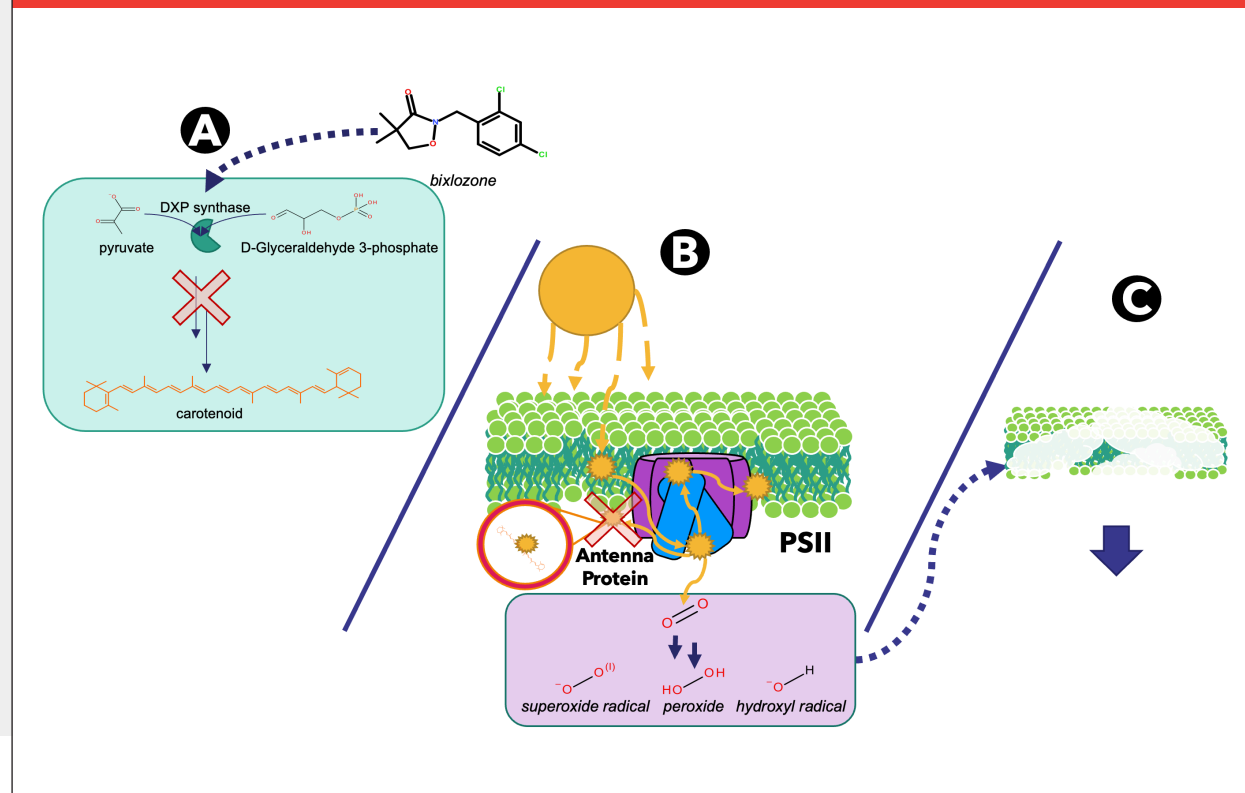


Mode of Action (continued)

DXP synthase is the known target site for Isoflex™ active; however, the plant is ultimately injured and/or killed from the disruption in carotenoid biosynthesis and photodamage due to the extensive role of the DOXP pathway and the use of the terpenoid backbone in other processes (Figure 2).

Figure 2.

In plants, carotenoid pigments serve as accessory chemicals in protection against excess energy generated during photosynthesis. The figure demonstrates the biochemical mode of action for Isoflex™ active whereby the active keto-bixlozone molecule inhibits the DXP synthase enzyme, preventing carotenoid biosynthesis, leading to a buildup of free radicals and lipid peroxidation.



The above describes only the primary mode of action resulting in the visible symptoms (bleaching); additional pleiotropic effects due to a lack of terpenoids affecting secondary metabolite formation and hormones are also impacted.

Mode of Action (continued)

Selectivity

Crop selectivity in labeled crops is primarily through plant metabolism and herbicide placement when using products containing Isoflex™ active as a pre-emergence application.

To avoid significant injury, it is best to avoid direct contact of the herbicide with the seed; always follow the seeding depth recommendation on the label for the specific crop. If seeding is too shallow, typical symptomology will occur (Figure 3).

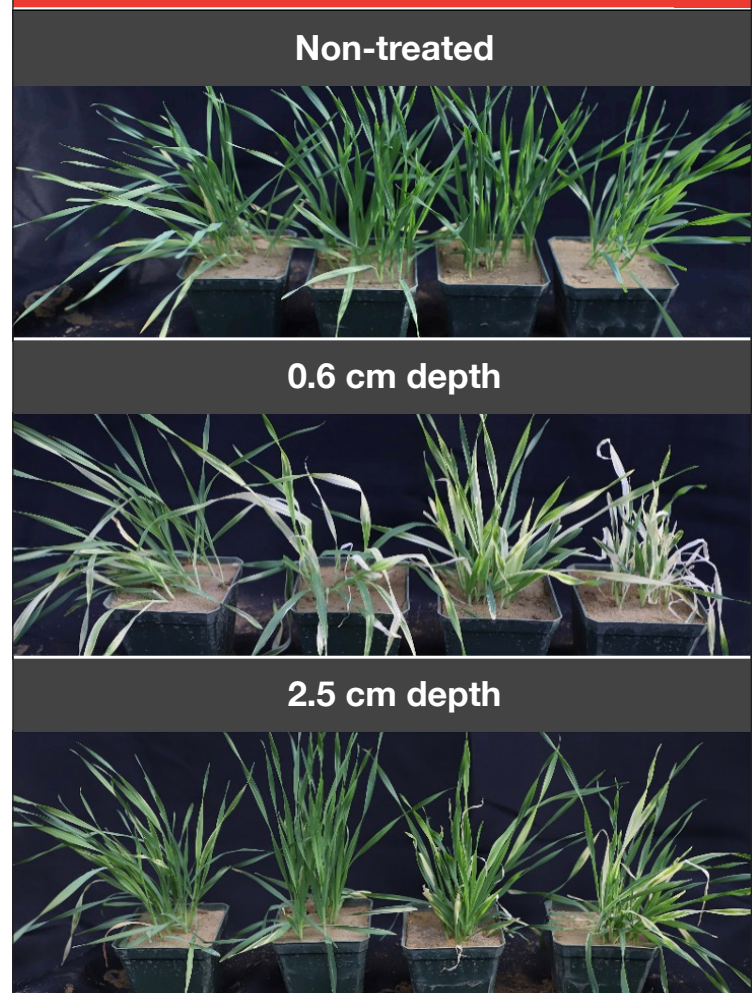
If injury does occur when following label recommendations, resulting in crop bleaching, the symptoms should be considered transient with no long-term impact on yield.

Environmental factors that reduce the physiological activity of the plant (including low temperatures and high soil moisture) may result in higher than anticipated visible injury to labeled crops.



Figure 3.

Comparison of the response for barley (HORSS) treated with Isoflex™ active applied at 500 g/ha across four varieties at common seeding depths.



Directions for Use

Water Quality

Water quality attributes, such as hardness (PPM of CaCO₃) and solution pH have been assessed with Isoflex™ active in a suspension concentrate (SC) formulation. Neither component has been demonstrated to affect the suspensibility of the product under the controlled conditions evaluated.

If water quality is a concern within the targeted market, it is highly recommended that, at minimum, a jar test with local water is done to assess for potential incompatibility concerns.

Compatibility

In general, glyphosate-based formulations have exhibited some sedimentation or poor suspensibility. Given the large number of products containing this active ingredient, it is highly recommended that mixtures with these products be tested using standard jar tests prior to recommending them for use.

Application Conditions and Methods

The best results will be obtained if the soil is humid at the time of application and/or a rainfall event occurs within 7 to 15 days of application.

The seedbed should be established with a firm and fine tilth free of clods, thereby confirming optimal soil conditions for pre-emergence residual activity; ensure seeding depths using appropriate local agronomic recommendations is necessary to help minimize crop injury.

Products containing Isoflex™ active can be used in no- to minimum tillage production systems. However, to achieve adequate soil contact, regionally specific application rates and irrigation/rainfall are recommended to prevent a reduced effect on weed control.

Clean-Out Instructions

Standard tank clean-out procedure should be followed to adequately remove product residues from the tank and spray equipment. Always follow recommendations on the product label and any other product in the tank mix.



Stewardship & Application Recommendations

Stewardship of products containing Isoflex™ active must be considered for managing the application, use and long-term utility of the herbicide in the market. The novel mode of action of Isoflex™ active in cereal-cropping systems provides a new tool for herbicide resistance management in a segment with few remaining options. At the same time, off-target movement due to improper application can be a concern. Using the outlined mitigation approaches below can significantly reduce or eliminate this risk. Lastly, a key feature of Isoflex™ active is its residual activity, which can be beneficial to users for season-long management. However, a lack of understanding of the factors impacting soil activity may cause unexpected and unnecessary problems in succeeding crops. The following guidance will support the sustainability of this product offering.

DRIFT

Particle droplet drift with products containing Isoflex™ active occurs from misapplication originating at the spray boom/nozzle. Factors that increase the risk of particle drift are high tractor speed, spray pressure, high windspeed, elevated boom height, low relative humidity, high temperatures and/or temperature inversion events present at the time of application.

Particulate drift includes the movement of product carried by dust from strong winds or machinery. This can be aggravated by surface temperature inversion, high relative humidity conditions that prolong the survival of airborne droplets, and high traffic conditions in the field following treatment, including tillage, cultivation or planting when used pre-plant.

The following recommendations should be followed when using products containing Isoflex™ active to minimize off-target risk:

- Spray applications should be made when the temperatures are appropriate and no inversions are present.
- Select a nozzle with a droplet size rated as coarse or greater.
- Avoid spraying under still or high wind conditions of >10 mph (16 km/h); spray when there is a consistent low crosswind.
- **DO NOT** spray if the wind direction is moving toward sensitive areas.
- **DO NOT** operate with a boom height greater than the recommended nozzle equipment's specifications. Typically, 50 cm above the soil surface is recommended.
- **DO NOT** make applications at speeds greater than those recommended by the nozzle manufacturer.

Stewardship & Application Recommendations (continued)

Application conditions which result in off-target movement to sensitive crops will likely cause visible symptoms (Figure 4).

Figure 4.

Visible symptoms of Isoflex™ active (500 g/ha) applied post-emergence to sunflower.



- Most off-target symptoms are similar to pre-applications, including green discoloration, chlorosis and ultimately bleaching.
- In more mature and less susceptible species, bleaching symptoms may be present, but this will be transient and not observable approximately three to four weeks after the treatment.
- For more susceptible species, such as sunflowers, the foliage that receives a higher dose of the herbicide will have highly visible bleaching symptoms. If the growing point is also treated, the symptoms may be visible for longer.
- Visible necrosis is rare; however, general leaf senescence can occur in susceptible species following bleaching.
- If the application results in high concentrations of soil deposition, which results in root uptake, symptoms may be present longer and/or exhibited in non-contacted foliage.

Stewardship & Application Recommendations (continued)

VOLATILITY

Four significant physical properties demonstrate that the volatility of Isoflex™ active from the soil, if any, is low and confined to a relatively short distance from the application site.

- Isoflex™ active has a low vapor pressure (2.3 mPa, 25°C), meaning the bixlozone molecule will preferentially stay in solution with less conversion and transfer to the atmosphere.
- Isoflex™ active has a low water solubility (42 mg/L), indicating greater preferential soil adsorption, reducing the release to the atmosphere in water droplets.
- Isoflex™ active has a logP of 3.3 and a KOC of 382 mL/g, indicating a potential for organic matter interactions that would also bind the molecule and reduce subsequent release in most soil types.
- Isoflex™ active is expected to degrade rapidly in air due to photolysis, (under ideal conditions) with a half-life of 0.25 days, further reducing the volume that could be transported from volatility.

TEMPERATURE INVERSION

Surface temperature inversions usually occur on clear, calm mornings and evenings. Windy or turbulent conditions may prevent inversion formation.

Inversions can transport pesticides long distances, not only into adjacent paddocks or fields.

Inversions must be monitored and avoided during and/or immediately following application to prevent negative effects on nearby susceptible areas.

CROP REPLACEMENT AND ROTATION

The half-life (DT50) of Isoflex™ active in soil derived from field trials (aerobic conditions) is within the range of 17.9 to 200 days. Geometric mean DT50 values in soil are 88 days (field) and 133.5 days (lab).

Tillage application will affect the duration of degradation following treatment. Inversion ploughing will significantly reduce the time Isoflex™ active remains active in the soil.

Across the different geographies and a wide variety of agronomic and climatic conditions, field trials evaluating possible effects on rotational crops (following normal harvest) and replacement crops (premature replanting within the season) have been established to assess recommendations for planting of common crops following application of products containing Isoflex™ active (see Annex Table 1). Always consult local Isoflex™ active product labels.

Additional warnings are recommended for specific situations, such as dry conditions for which a deep soil cultivation will be advised and when significant rainfall occurs immediately post-planting.

RESISTANCE INFORMATION

Since 2017, research to assess the baseline sensitivity of key target weed species, such as ryegrass (LOLSS) and blackgrass (ALOMY) to Isoflex™ active is ongoing.

Most populations, regardless of biotype, species and/or country of origin, have been controlled at or below 250 g/ha under greenhouse conditions. Some populations required rates closer to or greater than 500 g/ha, but this was location/population-specific.

To effectively steward the Isoflex™ active products and minimize the risk of resistance developing, the following must be considered;

1. Labeled application rates must be used.
2. Tank mixtures including more than one effective mode of action for the target species must be used.
3. A full-season program using selective post-emergent herbicides must be used.
4. Crop rotations should be implemented.

Human & Environmental Safety

Personal Protection

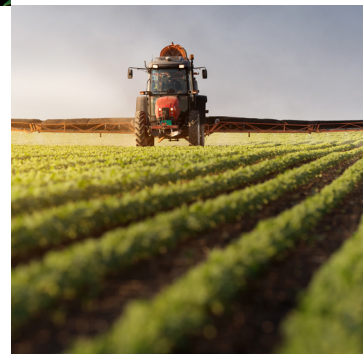
Studies of Isoflex™ active have shown low toxicity levels and that it is not irritating to eyes or skin. However, users should always consult the label of the specific formulation, as co-formulants could alter the risk. As with all herbicides, when handling a product containing Isoflex™ active, protective clothing and equipment should be worn as per label instructions. At a minimum, product users and handlers should wear full-length clothing (pants and shirt), covered shoes or boots and chemical-resistant gloves.

Environmental Protection

The directions listed in the **Stewardship & Application Recommendations** section should be followed to prevent drift outside the field of application, including to non-crop environments. Any spills of products containing Isoflex™ active should be managed to prevent entry into waterways and cleanup material should be disposed of in accordance with local regulations.

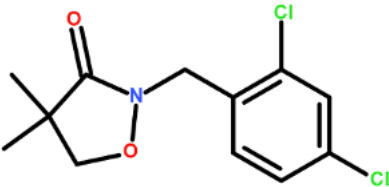
First Aid

If exposed to products containing Isoflex™ active, the instructions listed on the label or the Safety Data Sheet for the specific product should be followed.



Technical Information

Physical and Chemical Properties

Physical Properties - Technical Active Ingredient	
Global Brand Name	Isoflex™ active
Code/Experimental Name	F9600
ISO Name	Bixlozone
CAS Number	81777-95-9
Chemical Formula	C ₁₂ H ₁₃ Cl ₂ NO ₂
IUPAC Name	2-[[2,4-dichlorophenyl)methyl]-4,4-dimethyl-1,2-oxazolidin-3-one
Chemical Class	Isoxazolidinone
Structure	
Molecular Weight (g/mol)	274.14
Appearance	White crystalline solid (PAI) Pale yellow/brown crystalline solid (TGAI)
Water Solubility (mg/L)	42.0 mg/L (purified water) (PAI)
Vapor Pressure (Pa)	2.3×10^{-3} (PAI, 25°C)
Henry's Law Constant (20°C, Pa m ³ /mol)	7.2×10^{-3}
Boiling Point (°C)	ND; starts to decompose at 188°C (PAI)
Melting Point (°C)	81.5-83.5 (PAI)
Flammability	Not highly flammable (TGAI)
Explosive Properties	Not explosive (TGAI)
Auto Ignition Temperature	382°C (TGAI)
Oxidizing Properties	Not oxidizing (TGAI)
Specific Gravity (Relative Density @20°C)	1.37 (PAI)
Surface Tension (20°C)	66.5 mN/m (PAI)
Decomposition Temperature (°C)	Onset of decomposition 188°C
Stability pH	Hydrolytically stable in water
KowLogP (20°C)	3.3 (PAI)

Technical Information (continued)

Environmental Fate	
Soil Degradation, DT ₅₀ (days) @20°C, pF2.0	133.5 (lab)
Mobility, Koc (mL/g)	381.5

Toxicological & Eco-Toxicological Properties	
Acute - Oral LD ₅₀ (mg/kg)	>2000
Acute - Dermal LD ₅₀ (mg/kg)	>2000
Inhalation LC ₅₀ (mg/L)	>2.11
Eye Irritation	Not irritating
Skin Irritation	Not irritating
Birds - Acute Oral LD ₅₀ (mg/kg)	Unclassified
WHO Classification	>2000
<i>Daphnia</i> - Acute 48 hour EC ₅₀ (mg/L)	0.14
Aquatic Invertebrates - Acute 48 hour EC ₅₀ (mg/L)	13
Honeybees - Contact & Oral Acute 48 hour LD ₅₀ (µg as/bee)	>100

Annex

Annex Table 1: Recommended regional timing and recommendations for rotational crops (following normal harvest) following application of Isoflex™ active.

Crop	Regions/Countries and Recommendation ¹
Barley (spring)	Australia, Europe: no restriction
Barley (winter)	Australia, Europe: no restriction
Canola	Australia: no restriction
Carrot	Brazil: after 90 days
Chickpea	Australia: after 9 months and minimum 250mm rain
Chili	China: no restriction
Corn/Maize	Australia: after 3-6 months Brazil: after 30-120 days China, Europe: no restriction
Cotton	Australia, Brazil: no restriction
Field bean (Vicia fabae)	Australia, Brazil, Europe: no restriction
Garlic	Brazil: after 180 days
Green bean (Phaseolus)	Europe: no restriction
Lentil	Australia: after 9 months and 350mm rain
Lucerne	Australia: after 9 months and 250mm rain Europe: no restriction
Lupin	Australia: after 9 months and 350mm rain
Millet	Brazil: after 120 days
Mung bean	Australia, China: no restriction
Mustard	Europe: no restriction
Oats	Australia: after 9 months and 250mm rain Europe: no restriction
Oilseed rape	Europe: no restriction

Crop	Regions/Countries and Recommendation ¹
Onion	Europe: no restriction
Pea	Australia, Europe: no restriction
Peanut	China: no restriction
Potato	Brazil: after 90 days Europe: no restriction
Radish (oil)	Europe: no restriction
Rye (winter cereal)	Europe: no restriction
Ryegrass	Europe: no restriction
Sorghum	Australia: no restriction Brazil: after 120 days
Soybean	Australia, China, Europe: no restriction
Subclover	Australia: after 9 months and 250mm rain
Sugar beet	Europe: no restriction
Sunflower	Australia: after 9 months Brazil: after 150 days Europe: no restriction
Sweet potato	China: no restriction
Tomato (industry)	Brazil: after 120 days
Tomato (transplanted)	Europe: no restriction
Triticale (winter)	Europe: no restriction
Vetch	Australia: after 9 months and 250mm rain Europe: no restriction
Watermelon	China: no restriction
Wheat (winter)	Australia, Brazil, Europe: no restriction

¹ These trials were established in targeted assessments for plant-back and rotation; some were located on sites used for efficacy trial work. Data is generated with local targeted rates and often include overlapping rates. ² Data for replanting or premature break has been generated for these crops.

This technical bulletin is intended for use only as a guide in providing general information about Isoflex™ active. It must be emphasized that products containing Isoflex™ active must be used in accordance with local regulations and registrations. We strongly recommend that users read, understand, and follow all label directions, warnings and precautions prior to using products containing Isoflex™ active.

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