Arylex™ active

Technical Bulletin

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Overview

Arylex™ active

A new herbicide for the control of broadleaf weeds with utility in multiple crops. Arylex is an innovative low-dose growth regulator herbicide for use in mixtures with other Dow AgroSciences proprietary herbicides creating a wide spectrum of products customized for specific geographies.

Discovered by and proprietary to Dow AgroSciences, Arylex is the first member of a new structural class of synthetic auxin herbicides. Postemergence use rates in cereals will typically range from 5 – 10 grams ae/hectare depending upon target weed species and geography. The auxinic mode of action of Arylex will be effective in managing weed biotypes resistant to other modes of action such as ALS inhibitor herbicides, glyphosate and triazine herbicides.

Product concepts containing Arylex are being evaluated across the globe in all major cereal markets. Arylex will provide growers with a powerful, low-dose herbicide with a desirable environmental profile.

Noteworthy Features

- Effective postemergence control of many common and economically damaging broadleaf weeds in cereals and other crops.
- Consistent weed control across variable climatic conditions (cold and dry conditions) allows for flexibility of application.
- Low use rates resulting in low environmental load of the herbicide.
- Alternative mode of action to help manage resistant weed biotypes.
- Rapid degradation in soil and plant tissues allowing for crop rotation flexibility.
- Favorable environmental and toxicological profile.

Formulations

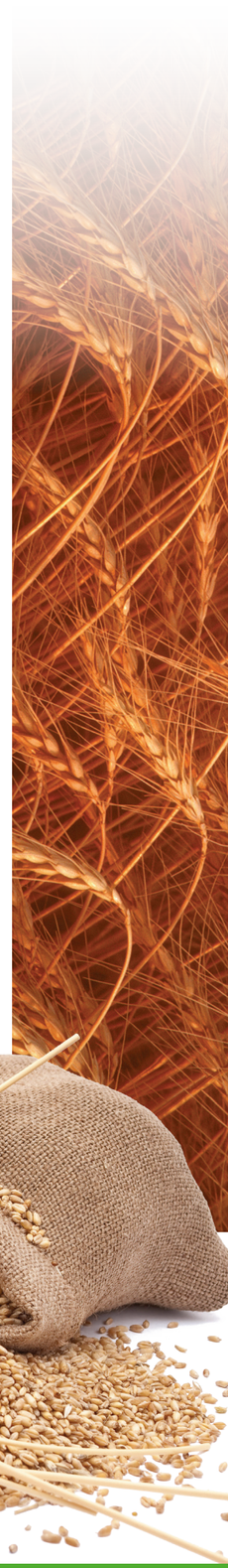
Arylex will be combined with other herbicides from Dow AgroSciences in a range of formulation concepts to meet the various needs of cereals and other crops grown around the world. Depending on the geography or premix combination, it will be offered in dry or liquid formulations. Some of the herbicide combinations being developed for Arylex include premix formulations with other Dow AgroSciences' active ingredients such as florasulam, fluroxypyr, pyroxsulam, or aminopyralid.

Registrations

Dow AgroSciences is seeking to widely register Arylex for use in all major cereal producing countries plus registrations in other countries where utility in additional crops is anticipated. Initial Arylex registrations are anticipated beginning 2014 in some geographies.

Arylex is currently not registered and is not available for sale. The registration dossier for Arylex was submitted for review in the United States, Canada, Australia and the European Union in September 2012.

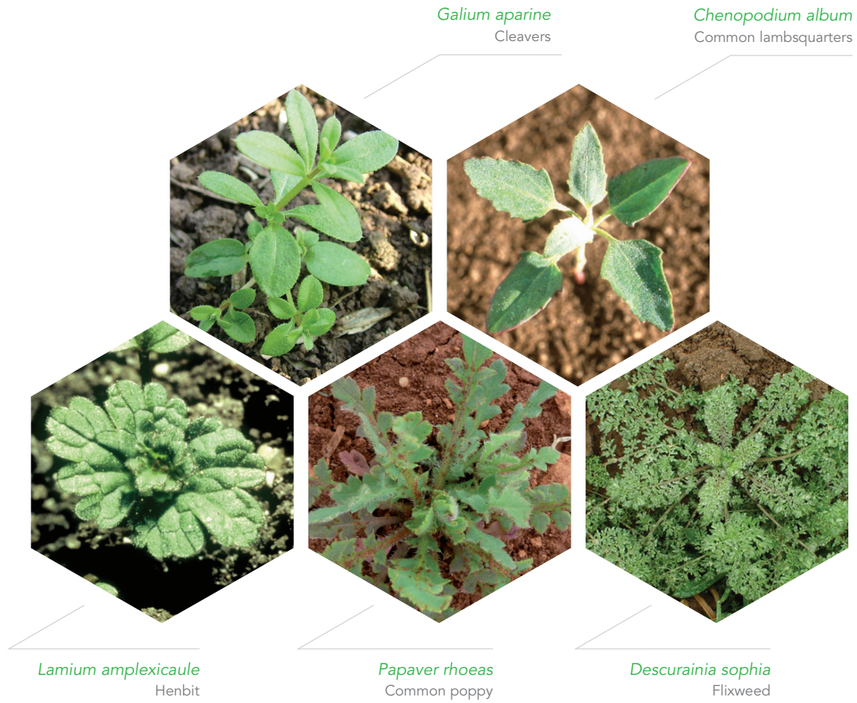
This educational material is provided for informational purposes only and is not intended to promote the sale of product. Any sale of this product after registration is obtained shall be solely on the basis of approved product labels, and any claims regarding product safety and efficacy shall be addressed solely by the label.



Weed Control

Arylex™ active provides a unique spectrum of selective, postemergence control of annual broadleaf weeds in cereals and other crops, and additionally some activity on certain perennial weed species. Control is influenced by weed size with smaller stages of weeds more easily controlled. However, unlike most growth regulator herbicides the activity of Arylex on target weeds is not significantly influenced by temperature so control can be achieved under cold (inactive periods of weed growth) and warm conditions with active growth.

Arylex efficacy is optimized when sprayed with an adjuvant, either included in the formulation or added in the tank-mix.



Galium aparine
Cleavers

Chenopodium album
Common lambsquarters

Lamium amplexicaule
Henbit

Papaver rhoeas
Common poppy

Descurainia sophia
Flixweed

Stellaria media
Common chickweed

Galeopsis tetrahit
Common hempnettle

Fumaria officinalis
Fumitory

The following table provides a listing of weeds that, based upon field trials, have been found to be susceptible to Arylex at anticipated label use rates. This table should be used as a guide and is not an endorsement of weed control.

Scientific Name	Common Name
Amaranthus retroflexus	Pigweed, redroot
Centaurea cyanus	Cornflower
Chenopodium album	Lambsquarters, common
Consolida orientalis	Larkspur, oriental
Conyza canadensis	Horseweed / Marestail
Conyza bonariensis	Fleabane
Descurainia sophia	Flixweed
Erodium cicutarium	Storksbill / Redstem filaree
Fumaria officinalis	Fumitory
Galeopsis tetrahit	Hempnettle, common
Galium aparine	Bedstraw, catchweed / cleavers
Geranium carolinianum	Geranium, carolina
Geranium dissectum	Geranium, cutleaf
Geranium pusillum	Geranium, smallflower
Glycine max	Volunteer soybean
Lamium amplexicaule	Henbit
Lamium purpuruem	Deadnettle, purple
Linum usitatissimum	Flax, volunteer
Papaver rhoeas	Poppy, corn
Stellaria media	Chickweed, common
Veronica persica	Persian speedwell
Vicia villosa	Vetch, hairy

Mode of Action

Arylex™ active is a synthetic auxin herbicide active ingredient that acts through a synthetic auxin mechanism (HRAC group O, WSSA group 4).

Absorption/Translocation

Arylex is a systemic, phloem and xylem mobile herbicide that is readily absorbed through leaves, shoots and roots. When foliar applied it will be symplastically translocated throughout the plant and will accumulate in meristematic tissue.

Herbicide Activity and Symptomology

Arylex is a member of the synthetic auxin class of herbicides. Treatment with Arylex mimics the effect of a persistent high-dose of the natural plant hormone auxin causing over-stimulation of specific auxin-regulated genes. This leads to profound long-lasting physiological and morphological effects on susceptible weeds that stop plant growth and result in cell death. Tissues that are undergoing active cell division and growth are particularly susceptible to injury.

Symptoms of Arylex herbicide damage to sensitive species normally occur within a few hours. Injury symptoms of herbicide damage on susceptible species include: cessation of growth, stem and petiole twisting (epinasty), leaf malformations (parallel venation, leaf strapping, and cupping), chlorosis, swelling, thickening and splitting of stems, callus tissue formation, and stunted root growth. Plant death may not occur for several weeks, but symptoms appear in new growth soon after application.

Crop Tolerance and Plant Metabolism

Spring and winter wheat, durum wheat, spelt, barley, rye and triticale show excellent tolerance to Arylex at projected label rates. Specific formulations have been designed to optimize selectivity by utilizing cloquintocet as a safener. Good selectivity over a wide window of cereal stages allows for autumn and spring application.

Arylex is de-esterified in all plants to the active and mobile form, halauxifen-acid (halauxifen). In tolerant cereal crops the rate of de-esterification is slower compared to susceptible weeds. The safener enhances the cereal crop's ability to metabolize Arylex through conjugation before halauxifen-acid is formed. Arylex degradation in wheat is rapid, preventing the accumulation of active herbicide residues in straw.

Crop Rotation

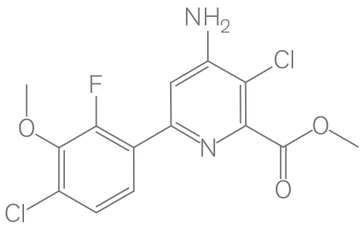
Arylex rapidly degrades in soil and plant residues, and generally does not persist long enough to impact crops the following season. Like many compounds that are microbially degraded, adequate moisture and temperature are required for breakdown to occur.

Triticum aestivum
Winter wheat

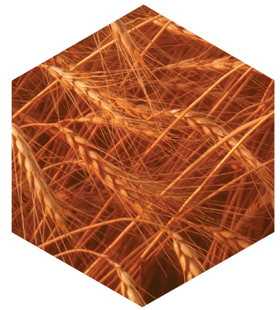
Hordeum vulgare
Barley

Triticosecale
Triticale

Physical and Chemical Properties

Description of Chemistry	
Common Name:	Halauxifen-methyl *(ISO provisionally approved)*
Code Names Tested:	*DE-729, XDE-729 methyl, XDE-729 ME, XD-729, XR-729*
Chemical Name (CAS):	*2-pyridinecarboxylic acid, 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl), methyl ester*
Chemical Name *(IUPAC)*:	*methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate*
CAS Number:	*943831-98-9*
Chemical Structure:	
Chemical Family:	Arylpicolinate
Empirical Formula:	$C_{14}H_{11}Cl_2FN_2O_3$
Molecular Weight:	345.17 *amu*
Odor:	Mild
Relative Density *(20°C)*:	1.5057 *g/cm³*
Melting Point:	145.5°C
Boiling Point:	Decomposes before boiling
Flammability:	Not highly flammable
Explosive Properties:	Not explosive
Dissociation Constant *(pKa)*:	2.84 at 20°C
Vapor Pressure:	5.9 x 10^{-9} *Pa* at 20°C
Octanol/Water Partition Co-Efficient *(log P_{ow})*:	pH 7 = 3.76

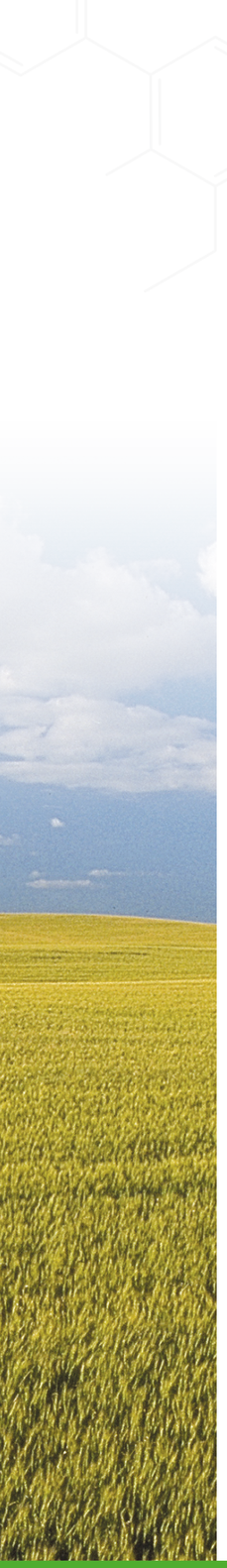




Hydrolytic Stability *(DT_{50})*:	pH 4 = 81 days;
	pH 7 = 155 days;
	pH 9 = 3 days

Aqueous Photostability *(DT_{50})*:	0.129 hours at pH 7 *(corrected for summer sunlight conditions at 40° N latitude)*
Soil Photolysis *(DT_{50})*:	Insignificant
Soil Adsorption *(Kd)*:	13 – 340 *mL/g* (average = 73 *mL/g*)
Soil Adsorption Constant *(K_{OC})*:	473 – 2659 *mL/g* (average = 1418 *mL/g*)

Solubility (g/L) at 20°C	Solvent	Solubility
	Water:	pH 5: *1.66 mg/L* pH 7: *1.67 mg/L* pH 9: *1.69 mg/L*
	Acetone:	*>250 g/L*
	Ethyl Acetate:	*114 g/L*
	1,2-Dichloroethane:	*54.3 g/L*
	Methanol:	*31.7 g/L*
	Octanol:	*8.90 g/L*
	Xylene:	*8.24 g/L*
	Heptane:	*0.0375 g/L*

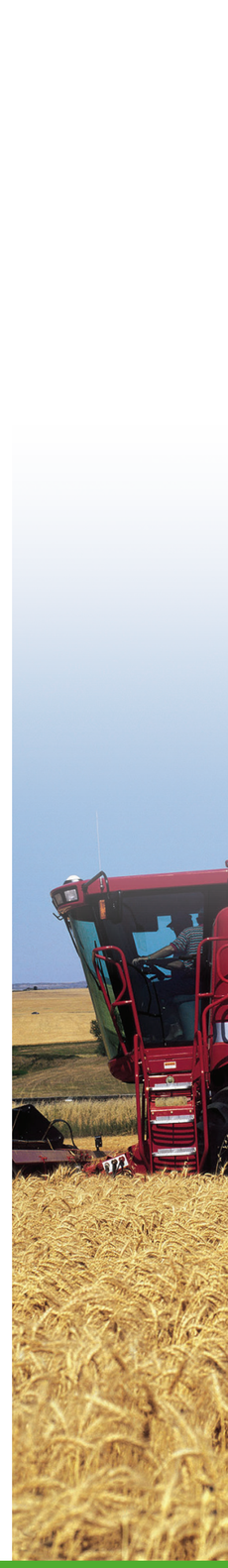


Toxicology

Mammalian Toxicology

A complete set of mammalian toxicology studies was conducted with halauxifen-acid (halauxifen) and an extensive set of additional toxicity studies was conducted with Arylex™ active in order to provide comparative information. The acute mammalian toxicity of halauxifen-acid and Arylex are low by the oral and dermal routes of exposure. The compounds are minimally irritating to the eyes and skin and are not dermal sensitizers. Long-term toxicity and carcinogenicity studies with halauxifen-acid in rats and mice did not demonstrate any potential for carcinogenicity. The results of these studies are summarized in the following table.

Study	Results
Acute oral, rat	LD50 >5000 mg/kg bw – Arylex LD50 >5000 mg/kg bw – Halauxifen-acid
Acute dermal, rat	LD50 >5000 mg/kg bw – Arylex LD50>5000 mg/kg bw – Halauxifen-acid
Acute inhalation, rat	Waiver for studies based on physical-chemical properties that precluded generation of an aerosol exposure.
Eye irritation, rabbit	Mild irritation, resolved in 24 hours – Arylex Mild irritation, resolved in 72 hours – Halauxifen-acid
Skin irritation, rabbit	Mild irritation, resolved in 24 hours – Arylex Mild irritation, resolved in 48 hours – Halauxifen-acid
Skin sensitization (LLNA), mouse	Negative: Arylex Negative: Halauxifen-acid
Genotoxicity, in vitro and in vivo	Negative: Arylex Negative: Halauxifen-acid Not genotoxic
Immunotoxicity, rat	NOAEL = 500 mg/kg bw/day – Arylex Not immunotoxic
Acute Neurotoxicity, rat	NOAEL = 250 mg/kg bw (single-dose average) – Halauxifen-acid Not neurotoxic
Subchronic Neurotoxicity, rat	NOAEL = 250 mg/kg bw/day – Halauxifen-acid Not neurotoxic
Chronic Toxicity/ Carcinogenicity, rat	NOAEL = 100 mg/kg bw/day – Halauxifen-acid Not carcinogenic
Carcinogenicity, mice	NOAEL = 50 mg/kg bw/day – Halauxifen-acid Not carcinogenic
Developmental Toxicity, rat	Developmental NOAEL>323 mg/kg bw/day – Arylex Maternal NOAEL = 41 mg/kg bw/day – Arylex Developmental NOAEL >526 mg/kg bw/day – Halauxifen-acid Maternal NOAEL = 140 mg/kg bw/day – Halauxifen-acid Neither is a developmental toxicant
Developmental Toxicity, rabbit	Developmental NOAEL = 18 mg/kg bw/day – Arylex Maternal NOAEL = 6 mg/kg bw/day – Arylex Developmental NOAEL > 1000 mg/kg bw/day – Halauxifen-acid Maternal NOAEL = 434 mg/kg bw/day – Halauxifen-acid Neither is a developmental toxicant
2-Generation Reproduction, rat	Reproductive NOAEL > 450 mg/kg bw/day – Halauxifen-acid Parental NOAEL = 100 mg/kg bw/day – Halauxifen-acid Not a reproductive toxicant



Toxicology Continued

Environmental Toxicology

Testing of Arylex™ active indicates that the active ingredient exhibits very low acute toxicity to terrestrial species: birds, honeybees and earthworms. Arylex exhibits moderate acute toxicity to fish and aquatic invertebrates, and moderate to high toxicity to freshwater and marine algae depending upon species.

Test	Species	Results
	Avian Organisms	
Avian oral	Bobwhite Quail *Colinus viginianus*	LD_{50} > 2250 *mg/kg bw*
Avian oral	Zebra finch *Poephila guttata*	LD_{50} > 2250 *mg/kg bw*
Avian dietary	Bobwhite Quail *Colinus viginianus*	LC_{50} > 5620 *mg/kg diet*
Avian dietary	Mallard duck *Anas platyrhynchos*	LC_{50} > 5620 *mg/kg diet*
	Aquatic Organisms	
Fish acute	Rainbow trout *Oncorhynchus mykiss*	LC_{50} = 2.01 *mg/L*
Invertebrate acute	Water flea *Daphnia magna*	EC_{50} = 2.12 *mg/L*
Freshwater Algae	Green alga *Pseudokirchneriella subcapitata*	EC_{50} > 0.245 *mg/L*
Freshwater Algae	Diatom *Navicula pelliculosa*	EC_{50} = 0.663 *mg/L*
Freshwater Algae	Bluegreen alga *Anabaena flos-aquae*	EC_{50} > 0.775 *mg/L*
Marine Algae	Diatom *Skelotonema costatum*	EC_{50} = 1.07 *mg/L*
	Terrestrial Organisms	
Honeybee, contact	Honeybee *Apis mellifera*	LD_{50} > 98.1 *ug/bee*
Honeybee, oral	Honeybee *Apis mellifera*	LD_{50} > 108 *ug/bee*
Earthworm, acute	Compost worm *Eisenia fetida*	LC_{50} > 1000 *mg/kg soil*

Environmental Fate

Laboratory and field studies have been conducted to determine the fate of Arylex in the environment. Arylex was found to degrade rapidly in the environment to halauxifen-acid (halauxifen). Halauxifen-acid was also observed to degrade rapidly to non-active compounds.

Soil

Arylex degrades in soil to halauxifen-acid which is then metabolized to non-active compounds. Arylex undergoes rapid degradation with an average DT_{50} of 1.5 days under aerobic soil conditions in the laboratory. Halauxifen-acid had an average DT_{50} of 14 days. Terminal soil metabolism products were CO_2 and non-extractable residues.

Photodegradation in soil of Arylex is insignificant compared to the rate of aerobic soil degradation.

Field dissipation studies following spring applications at 6 sites in North America resulted in an average half-life of 15 days for Arylex.

Field dissipation studies following spring or autumn (fall) applications at 4 sites in Europe resulted in an average half-life of 17 days for Arylex.

Laboratory experiments yielded an average K_{OC} of 1418 mL/g (range 473-2659 mL/g) indicating that Arylex is strongly adsorbed. The average K_{OC} of halauxifen-acid is 179 mL/g (range 34-539 mL/g) indicating that the halauxifen-acid is potentially mobile.

Water

However, field dissipation studies show limited movement in the soil profile of either the Arylex or halauxifen-acid with residues mainly detected in the top 15 cm of the soil profile.

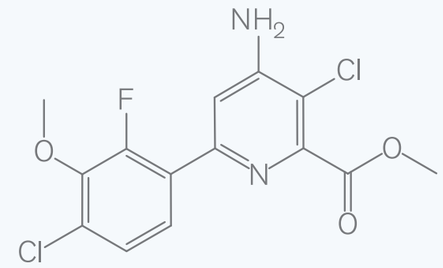
In water, photodegradation is rapid and is anticipated to be the important route of degradation for Arylex. Degradation by purely chemical pathways in sterile buffered conditions has been demonstrated by the rapid hydrolysis of Arylex to halauxifen-acid under mild alkaline conditions.

The Arylex degradation rate is ≤ 4 days in water/sediment systems under laboratory conditions; the halauxifen-acid degradation rate is 2-11 days in water/sediment systems.

Air

The potential for transport of Arylex via volatilization of residues is extremely low due to its low vapor pressure and small Henry's Law constant (1.22×10^{-6} Pa m^3/mol at pH 7).

As with any herbicide, susceptible non-target plants may be injured via physical spray drift. Spray applications should be made such that spray drift cannot injure desirable, susceptible plant species.



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