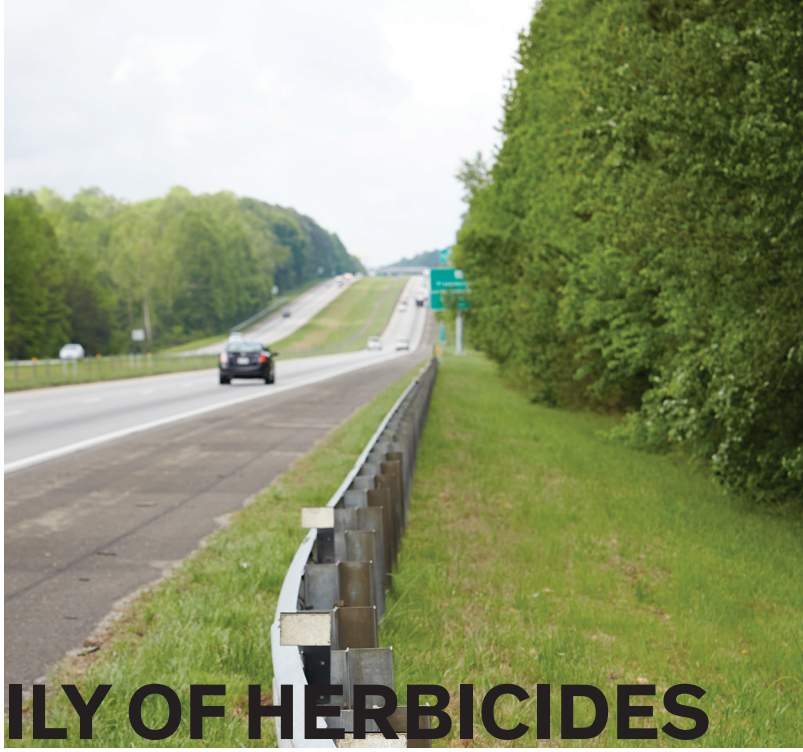


AMINOPYRALID FAMILY OF HERBICIDES

Veg Management

Milestone® SPECIALTY HERBICIDE

Opensight® SPECIALTY HERBICIDE

Capstone® SPECIALTY HERBICIDE

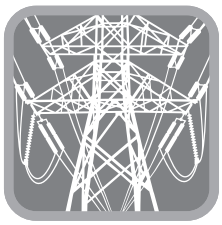
DOW® Dow AgroSciences

Solutions for the Growing World

General Information

The family of aminopyralid herbicides is a strong part of the Dow AgroSciences portfolio. Aminopyralid is a pyridine carboxylic acid active ingredient that provides systemic control of target species with good tolerance of cool- and warm-season grasses. Aminopyralid products are postemergence herbicides that control the entire plant, including the roots, and offer soil residual activity to extend control. Aminopyralid also provides preemergence weed control on many susceptible weeds, including some that are not susceptible to foliar applications. In addition, aminopyralid has very low toxicity to birds, fish, mammals and aquatic invertebrates. Because of this and other factors, Milestone® specialty herbicide was accepted for review and registration under the Reduced Risk Pesticide Initiative of the U.S. Environmental Protection Agency — a program designed for compounds that demonstrate less risk to humans and the environment than market standards. The family of aminopyralid herbicides is an important part of any vegetation manager's program that includes weed, vine and brush control.

UTILITY

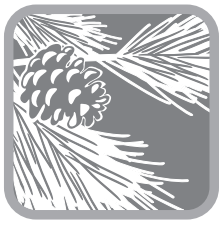


ROADSIDE

INVASIVE

RAILROAD

FORESTRY



PRODUCTS AND FEATURES

The aminopyralid family of herbicides includes Milestone®, Capstone® and Opensight® specialty herbicides. Each of these products is registered for use on rights-of-way (including roadsides, electric utility lines, railroads, pipelines and more), industrial sites, nonirrigation ditch banks, natural areas (including wildlife management areas, wildlife openings, recreation areas and campgrounds), and grazed areas in and around these sites. The herbicides are labeled for use on pastures around industrial sites with no grazing restrictions.[1]

Milestone is labeled to control a number of tough annual, biennial and perennial broadleaf weeds, including noxious and invasive species, and certain woody plants. It delivers effective control at multiple stages of growth, including pre- and postemergence control of susceptible species following applications. As part of a tank mix of herbicides, Milestone improves control of many tough-to-control species, such as Virginia pine, cedar and elm. It features low use rates of 3 to 7 fluid ounces per acre for broadcast applications and 0.25 percent to 0.5 percent spray solutions for spot treatments. Milestone also is labeled for use in forest management areas.[2]

Capstone combines aminopyralid with the amine formulation of triclopyr contained in Garlon® 3A specialty herbicide to provide control of herbaceous broadleaf weeds, vines and woody plants. This combination allows for a broader spectrum of control while remaining selective to most cool- and warm-season perennial grasses. It is essentially nonvolatile and carries a "Caution" signal word. Capstone is labeled for foliar and cut-surface treatments, and can be used on forest management and utility sites, and as a chemical side trimming application.

Opensight is a combination of aminopyralid and metsulfuron methyl formulated as a water-dispersible granule formulation. Opensight controls invasive species and broadleaf weeds at use rates of 1 to 3.3 ounces per acre in roadsides, rights-of-way, utilities and many other noncrop sites listed on the label. It also provides selective vine and woody species control at low use rates of 3.3 ounces per acre for broadcast applications, making it a good tank-mix partner where a broader spectrum of control is desired. Opensight is selective to many established grass species, and where mowing is used to provide safety, an application of Opensight can extend treatment and mowing cycles by providing seedhead suppression of bahiagrass and fescue grass along with broad-spectrum broadleaf weed control.

MODE OF ENTRY

Because it's a systemic herbicide, aminopyralid must be absorbed by the plant and moved into the site(s) of action. It is absorbed by the foliage and roots of actively growing plants and translocated to the meristematic (high-growth-rate) areas of the plants, including the roots. Prior to use as foliar treatments, the herbicides

are usually diluted with water to facilitate better coverage. In most cases, the label rate of spray solution is approximately 91 percent to 99 percent water.

All products in the aminopyralid family of herbicides can be applied as a foliar treatment to control labeled species.

MODE OF ACTION

Plant growth is a complex process that is controlled, in part, by a variety of plant growth regulators, including auxin compounds. To ensure proper growth, plants produce very controlled amounts of these materials. Auxins bind to specific cell surface receptor proteins, turning on and off vital plant processes. Aminopyralid is a systemic auxin herbicide possessing auxinlike (plant growth regulator) qualities. Aminopyralid moves systemically throughout the plant and deregulates plant growth metabolic pathways affecting the growth process of the plant. This disruption of plant growth processes, by binding of aminopyralid at receptor sites normally used by the plant's natural growth hormones, results in death of susceptible plant species.

Within hours or days of application, depending on the weed species, aminopyralid causes symptoms such as thickened, curved and twisted stems and leaves, cupping and crinkling of leaves, stem cracking, narrow leaves with callus tissue, hardened growth on stems, enlarged roots and proliferated growth. Most annual susceptible weeds are controlled within four to eight weeks after application. Complete control of the main stems and the root systems of woody and semi-woody plants may require two or more months after application. Plant growth will stop within 24 to 48 hours after treatment.

GRASS TOLERANCE

Aminopyralid offers a high level of tolerance on a wide range of warm- and cool-season grasses. More than 20 different grasses evaluated in field trials from 1999 to 2004, with aminopyralid applied at rates up to two times the maximum use rate, demonstrated tolerance to aminopyralid. The grasses evaluated include *Agropyron* sp., *Andropogon gerardii*, *A. saccharoides*, *A. scoparius*, *Bouteloua curtipendula*, *B. gracilis*, *Brachiaria brizantha*, *B. decumbens*, *Bromus inermis*, *Buchloe dactyloides*, *Cynodon dactylon*, *C. nlemfuensis*, *C. plectostachyus*, *Dactylis glomerata*, *Digitaria decumbens*, *Eragrostis ciliaris*, *Festuca* sp., *Lolium* sp., *Panicum maximum*, *P. virgatum*, *Paspalum notatum*, *Phleum pratense*, *Poa* sp. and *Sorghastrum nutans*.

RESISTANCE MANAGEMENT

Aminopyralid has an auxinic growth regulator mode of action. Other growth regulator herbicides used on rights-of-way, natural areas and other noncropland areas include 2,4-D, clopyralid, dicamba, picloram and triclopyr. Despite extensive use, herbicides with this mode of action have demonstrated a low risk of resistance development compared with other herbicide mode-of-action classifications, such as ALS-inhibitor herbicides, photosystem II inhibitor herbicides and ACCase-inhibitor herbicides.

The International Survey of Resistant Weeds lists only eight weed species in the United States and 28 species worldwide with resistance to the growth regulator mode of action. The risk of resistance development is less on rights-of-way, natural areas and other noncropland sites because herbicide applications are not typically made every year, thus slowing the increase of resistant genotypes in weed populations. Because of the low resistance risk, aminopyralid will be a useful herbicide tool in tank mixes with or in rotation with ALS-inhibitor herbicides and urea herbicides in targeted control areas.

Worldwide, there currently are 107 weed species with confirmed ALS-inhibitor resistance and 21 with urea herbicide resistance. Many of these weed biotypes are encountered on rights-of-way and natural areas, including *Kochia scoparia*, *Conyza canadensis*, *Ambrosia artemisiifolia*, *Bromus tectorum*, *Setaria faberi*, *Hydrilla verticillata*, *Sorghum halepense*, *Salsola iberica* and *Daucus carota*. Chlorsulfuron and sulfometuron are ALS-inhibiting herbicides that have been used repeatedly and extensively on rights-of-way. Metsulfuron, another ALS-inhibiting herbicide, has been used repeatedly and extensively on rights-of-way and other noncropland sites.

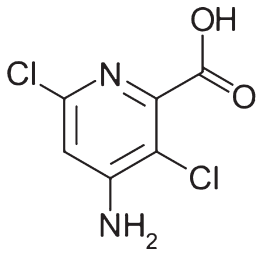
There are only a limited number of herbicide modes of action available for rights-of-way, and natural and noncropland areas. The existence of multiple known examples of ALS-inhibitor-resistant weeds in these sites confirms the need for a sound weed resistance management strategy. Aminopyralid has a growth regulator mode of action and will control biotypes resistant to ALS-inhibitor and urea herbicides for species within the aminopyralid weed spectrum.

REGISTRATION AND TESTING

Before pesticides can be sold or distributed in the United States, they must be registered by the U.S. Environmental Protection Agency (EPA). They must undergo laboratory testing for short-term (acute) and long-term (chronic) health effects. These tests help scientists determine how chemicals might affect humans, domestic animals or wildlife in cases of overexposure. However, it is important to recognize that most of these tests use exposure rates that are significantly higher than those expected under normal use conditions at labeled application rates.

Initial pesticide registrations require a minimum of 120 tests which can take companies more than a decade to complete. This is done at a cost to the company sometimes in excess of $120 million. The EPA requires these studies be conducted with each active ingredient to show the pesticide can be used properly without posing unreasonable adverse effects to humans, animals or the environment.

Table 1: Description of Chemistry

Product	Oral LD_{50} (Rat)
Chemical Name (IUPAC)	4-amino,-3, 6-dichloropyridine-2-carboxylic acid
Chemical Name (CAS)	2-pyridinecarboxylic acid, 4-amino-3, 6-dichloropyridine
Common Name	Aminopyralid (ISO proposed)
Code Names	DE-750, XDE-750, XR-750
Chemical Class	Pyridine carboxylic acid
CAS Registry No.	150114-71-9
Empirical Formula	$C_6H_4Cl_2N_2O_2$
Structural Formula	
Molecular Weight	207.026 g/mole
Relative Density	1.72 at 20° C
Appearance	Off-white, odorless powder
Melting Point	163.5° C

Product	Oral LD_{50} (Rat)
Boiling Point	Decomposes upon melting
Vapor Pressure	At 20° C, 7.14e-11 mmHg
Octanol/Water Partition Coefficient (log K_{ow}) at 19° C	Unbuffered water = 0.201 pH 5 = 1.76 pH 7 = 2.87 pH 9 = 2.96
Dissociation Constant (pK_a)	2.56
Hydrolytic Stability (DT_{50})	Stable
Aqueous Photostability (DT_{50})	0.6 day
Soil Photolysis (DT_{50})	61 days
Solubility in Water (g/L @ 18° C)	2.48
Buffered Water pH= 5	212 g/L
Buffered Water pH = 7	205 g/L
Buffered Water pH = 9	203 g/L
Methanol	52 g/L
Acetone	29 g/L
Heptane	Insoluble (< 10 µg/L)

GENERAL TOXICOLOGY INFORMATION

Any substance can be toxic, but the dose level, or amount, of that substance along with conditions of exposure is what makes its effect toxic or harmful to a living organism.

Acute toxicity is commonly measured by the single-exposure lethal dose or lethal concentration that causes death in 50 percent of treated laboratory animals. LD_{50} indicates the lethal dose of a chemical per unit body weight of an animal and is expressed as milligrams per kilogram (mg/kg). LC_{50} is the lethal concentration of a chemical per volume of air or water and is expressed as milligrams per liter (mg/L). More toxic compounds carry a low value of LD50 or LC50, while practically nontoxic compounds have a high value.

ACTIVE INGREDIENT STUDIES

The EPA classifies acute toxicity of pesticides by placing results of different laboratory tests into categories, with Toxicity Category I being the most toxic and Toxicity Category IV being the least toxic. Categories are based on dosage at which the toxic effect was observed. Aminopyralid is rated a Category IV compound for acute oral and dermal toxicity. All tests were done by using technical active ingredient. (See Tables 2 and 3).

Table 2: Mammalian acute toxicity studies with aminopyralid

Test	Species	Toxicity Parameters
Acute Oral	Rat	LD_{50} > 5,000 mg/kg
Acute Dermal	Rat	LD_{50} > 5,000 mg/kg
Acute Inhalation	Rat	LD_{50} male > 5.50 mg/L
Dermal Irritation	Rabbit	Negative
Eye Irritation	Rabbit	Irritating
Skin Sensitization	Guinea pig	No sensitization

Table 3: Mammalian chronic toxicity studies with aminopyralid

Test	Species	Toxicity Parameters
2-year chronic feeding	Rat	No carcinogenic NOAEL (mg/kg/day): Male = 50, Female = 500
Teratogenicity	Rat	Not teratogenic NOAEL (mg/kg/day): Maternal = 1,000 Development = 1,000
Teratogenicity	Rabbit	Not teratogenic NOAEL = (mg/kg/day) Maternal = 250 Development = 500
Reproductive toxicity	Rat	No adverse reproductive effects NOAEL (mg/kg/day) Parental = 1,000 Reproductive = 1,000
Acute and chronic neurotoxicity	Rat	No adverse neurological effects NOAEL (mg/kg/day) = 1,000
Mutagenicity Assay (*in vitro*)	Ames test	Negative
Mutagenicity Assay (*in vitro*)	CHO/HGPRT	Negative
Mutagenicity Assay (*in vivo*)	Mouse micronucleus	Negative

Carcinogenicity

Aminopyralid is classified by the EPA as "not likely to be carcinogenic to humans." There were no increases in any tumors in case studies with rats or mice.

Mutagenicity

Tests were conducted to evaluate the potential for cell damage from exposure to aminopyralid; these include chromosome aberrations, gene mutations, and DNA repair and damage. The potential of mutagenicity for aminopyralid has been conducted in vivo (in living organisms) and in vitro (in laboratory environments). Genetic toxicity studies demonstrate that aminopyralid is nonmutagenic.

Reproductive Tests

Research shows no evidence that aminopyralid causes birth defects or reproductive problems in laboratory animals exposed to concentrated levels. Fertility, delivery and number of offspring of second generations after exposure to aminopyralid at the highest doses tested demonstrates aminopyralid did not interfere with reproduction.

NEUROTOXICITY

Based on available data, repeated exposure is to anticipated to cause significant adverse effects. In a metabolism study in rats, aminopyralid was excreted unchanged, indicating an absence of uptake or metabolism; in cattle feeding studies, aminopyralid was cleared from the system within three days. Repeated administration of aminopyralid was not associated with bioaccumulation buildup in tissues.

ENVIRONMENTAL TOXICOLOGY

In Dow AgroSciences laboratory testing, aminopyralid has been shown to be "practically nontoxic" to birds, fish, honeybees, earthworms and aquatic invertebrates. "Practically nontoxic" is the EPA's least toxic category. While aminopyralid is slightly toxic to the eastern oyster, algae and aquatic vascular plants, the expected environmental concentration resulting from the use of this material for weed control is orders of magnitude below any level of concern established for these organisms by the EPA. (See Table 4).

ENVIRONMENTAL FATE STUDIES

Additional tests were conducted with aminopyralid to determine how it acts and breaks down in the environment.

DEGRADATION AND DISSIPATION

Aerobic microbial degradation is the primary route of breakdown of aminopyralid in soil. The rate of degradation in the field resulted in an average half-life of 34.5 days for eight North American sites and 25 days for four European sites. Laboratory experiments yielded an average K_{OC} of 10.8/L/kg, indicating some potential for mobility. However, field experiments showed limited movement in the soil profile. No degradation metabolites of concern were produced in any studies.

When treating areas in and around roadside or utility rights-of-way that are or will be grazed or planted to forage, important label precautions apply regarding harvesting hay from treated sites, using manure from animals grazing on treated areas or rotating the treated area to sensitive crops. See the product label for details.

WATER QUALITY

In water, the primary route of degradation of aminopyralid is photolysis. The photolysis half-life under standard conditions is 0.6 day, indicating rapid degradation in surface water. Aminopyralid was stable to direct hydrolysis and in anaerobic

sediment-water systems, degradation had total system half-lives of 462 to 990 days; however, partitioning into sediment was minor and aminopyralid in the water column was available for photodegradation. The degradation resulted in the formation of nonextractable residues and no other major products.

Groundwater contamination potential for aminopyralid is considered to be low because of it slow use rates, its moderate field degradation rates and limited motility observed in field studies. Using this information as inputs to the EPA and European Union simulation models, Dow AgroSciences research shows aminopyralid demonstrated for groundwater contamination.

VOLATILITY

The potential for transport of aminopyralid via volatilization of residues is extremely low, due to its low vapor pressure and small Henry's law constant. As with any herbicide, susceptible nontarget plants may be injured via physical spray drift. Spray applications should be made to minimize drift to desirable, susceptible plant species.

Table 4: Environmental toxicology tests with aminopyralid

Study	Species	Value
Birds		
Avian oral	Bobwhite quail	LD_{50} > 2,250 mg ae/kg bw
Avian dietary	Bobwhite quail	LD_{50} > 5,620 mg ae/kg diet
Avian dietary	Mallard duck	LD_{50} > 5,620 mg ae/kg diet
Fish		
Acute toxicity	Rainbow trout	96 hr LC_{50} > 100 mg ae/L
Acute toxicity	Bluegill	96 hr LC_{50} > 100 mg ae/L
Acute toxicity	Sheepshead minnow	96 hr LC_{50} > 120 mg ae/L
Aquatic Invertebrates		
Acute toxicity	Water flea (*Daphnia magna*)	48 hr EC_{50} > 100 mg ae/L
Acute toxicity	Mysid shrimp	96 hr LC_{50} > 100 mg ae/L
Acute toxicity	Eastern oyster	Slightly toxic 48 hr EC50 > 89 mg ae/L
Growth and reproduction	Water flea (*Daphnia magna*)	NOEC = 100 mg ae/L
Chronic toxicity	Midge	NOEC - 130 mg ae/L
Honeybees		
Acute contact	Honeybee	48 hr LD_{50} > 100 ug ae/bee
Acute oral	Honeybee	48 hr LD_{50} > 120 ug ae/bee
Earthworm		
Acute toxicity	Earthworm	14 d LC_{50} > 1,000 mg ae/kg soil
Algae and Aquatic Plants		
Acute toxicity	Freshwater green algae	Slightly toxic 72 hr E_rC_{50} = 30 mg ae/L
Acute toxicity	Freshwater blue-green algae	Slightly toxic
		120 E_bC_{50} = 27 mg ae/L
Acute toxicity	Freshwater diatom	Slightly toxic 96 hr EC_{50} = 14 mg ae/L
Acute toxicity	Duckweed (*Lemna gibba*)	Slightly toxic 14 d EC_{50} > mg ae/L

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[1]When treating areas in and around roadside or utility rights-of-way that are or will be grazed or planted to forage, important label precautions apply regarding harvesting hay from treated sites, using manure from animals grazing on treated areas or rotating the treated area to sensitive crops. See the product label for details.
[2]Milestone specialty herbicide is labeled for use in forestry site preparation treatments in AL, AR, GA, MS, NC, SC and VA. For additional details and updated state and/or federal registration information, visit www.vegetationmgmt.com to check current labeling.

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