

PESTICIDE TYPE	INSECTICIDE
Chemical Class	dsRNA Biopesticide
Common Trade Names	Ledprona Technical, Calantha™
Major Degradate	None
Application Rate (lb a.i./A/year)	Max Single: 0.0083 Max Annual: 0.0352 (four applications)
Registration Status	EPA: Dec. 2023 (three-year registration) Minnesota: 2024
Toxicity Profile for Applicators	Signal word: CAUTION Category IV: Inhalation, oral, dermal, and eye exposure
Basic Manufacturer	GreenLight Biosciences
MDA Laboratory Capabilities	Not applicable
HUMAN HEALTH	
Non-Cancer	No dietary endpoints identified due to the lack of human-relevant adverse effects, including toxicity
Cancer	No data – Mutagenicity testing requirement waived by EPA
ENVIRONMENTAL AQUATIC TOXICITY	
Fish	Testing requirements waived by EPA due to rapid degradation of dsRNA in aquatic environments
Invertebrate	Acute: > 0.75 ppb Chronic: No Data
Aquatic Plants	Testing requirements waived by EPA due to rapid degradation of dsRNA in aquatic environments
POLLINATOR TOXICITY	
Honey Bee (adult LD ₅₀)	Acute Contact: > 24.3 µg a.i./bee Chronic Oral: > 47.2 µg a.i./bee
<i>Level of Concern (LOC) has been applied to all aquatic toxicity and pollinator toxicity values.</i>	

INTRODUCTION

Ledprona is a new insecticide active ingredient recently registered by the United States Environmental Protection Agency (EPA) for use on potato plants to manage the Colorado potato beetle (CPB). Ledprona is the first sprayable RNAi-inducing insecticide in the world to be approved for commercialization and represents a new mode of action for CPB management (Group 35 Insecticide). Ledprona is a double-stranded ribonucleic acid (dsRNA) molecule that targets the CPB gene *proteasome subunit beta type-5 (PSMB5)*, which regulates proper protein folding within the cell. When CPB ingests ledprona, it leads to the silencing of the *PSMB5* gene within the insect and results in death. dsRNA-based pesticides interact with a target gene’s messenger RNA (mRNA) and do not interfere with DNA.

The Minnesota Department of Agriculture’s (MDA) extensive review of the EPA ledprona labels and risk assessments for issues relevant to Minnesota is summarized below.

PROJECTED USE IN MINNESOTA

As an insecticide with a novel mode of action, ledprona could be an important addition to Integrated Pest Management (IPM) programs in Minnesota and provide a new tool for managing increasing insecticide resistance in CPB populations. Ledprona may serve as an early season management tool of CPB larvae, reducing reliance on other modes of action. Field trials by University of Minnesota found that ledprona is as effective at limiting defoliation as well-established conventional insecticides.

As a biopesticide, the benefits of ledprona may include less harm to non-target species and a narrower spectrum of control than broad-spectrum conventional pesticides. As a dsRNA-based pesticide, ledprona is specific to CPB and a subset of other beetle (Coleoptera) species; therefore, it will not cause harm to non-coleopteran pollinators or other beneficial organisms. Reasons for limited to no off-target effects of ledprona include sequence specificity of the dsRNA molecule and the presence of physical barriers to dsRNA within the body, preventing cellular uptake.

Application methods for ledprona include foliar broadcast and aerial application. Single application rate is 0.0083 lb a.i./A and the maximum annual application rate is 0.0352 lb a.i./A. Up to four applications are allowed per year with a recommended 7-to-10-day interval between applications.

One end-use product is currently registered by the EPA and is registered for use in Minnesota.

- **Calantha™ Bioinsecticide** (EPA Reg. No. 94614-E) – Foliar applied dsRNA based bioinsecticide containing 0.8% Ledprona Technical for use on potatoes to manage defoliation from the Colorado potato beetle (*Leptinotarsa decemlineata*).

LABEL ENVIRONMENTAL HAZARDS

Water Quality

- Do not apply directly to water, or to areas where surface water is present, or to intertidal areas below the mean high-water mark. Do not contaminate water when disposing of equipment wash water or rinsate.

TOXICOLOGY AND EXPOSURE

EPA's screening models generate high-end, conservative exposure estimates for active ingredients and toxicologically significant degradates. Model inputs include annual usage at maximum use rates, maximum treated acres, maximum food residues, peak runoff, and drift scenarios, etc. Some proposed products, application rates, and use scenarios are not relevant to Minnesota. EPA's estimates, therefore, may not reflect future use and impacts in Minnesota.

Human Health

- **Carcinogenic Effects** – EPA waived mutagenicity testing requirements due to available acute toxicology data, bioinformatic analysis, low application rate and history of safe exposure to RNA in humans.
- **Drinking Water Guidance** – Exposure to ledprona through dietary and drinking water routes is expected to be minimal due to low application rates, high environmental degradation, and the presence of physiological barriers to dsRNA in humans. The EPA expects human risk through dietary exposure to be negligible.
- **Occupational Exposure** – Ledprona is of low acute oral, dermal, and inhalation toxicity. However, due to potential, yet unknown, non-sequence specific effects, the EPA requires the use of a respirator and protective eyewear along with baseline attire when mixing, loading, and applying ledprona, and adhering to the label restricted entry interval of 4 hours.

Non-target Species

- **Aquatic Life Exposure** – The likelihood of freshwater fish exposure to ledprona is negligible. Due to beetle (Coleoptera) specificity, adverse toxicity to aquatic beetles is possible, while potential adverse effects to non-coleopteran aquatic invertebrates is minimal. The overall likelihood of risk to aquatic systems from ledprona is considered negligible.
- **Terrestrial Life Exposure** – EPA expects ledprona's acute and chronic risks to birds, wild mammals, and terrestrial plants will be negligible. Ledprona's pesticidal activity is specific to a subset of beetles (Coleoptera), and while there is potential for adverse effects on nontarget coleopteran species, risk to non-coleopteran invertebrates is expected to be low. EPA concludes that the exposure potential of any non-target organisms to ledprona is limited to on-field exposure and off-site exposure is negligible.

- **Pollinators** - Discernible effects of ledprona to honey bees are not expected due to beetle specificity. However, negative impacts to potential coleopteran pollinators could occur within a sprayed field. Low application rates and high degradation of the active ingredient limit the impact of ledprona drift, reducing contact with nontarget organisms.
- **Endangered Species** – Potato growing regions in the U.S. overlap with the distribution of four listed coleopteran species. Because no discernible effects from ledprona exposure are expected, the EPA made a "No Effect" determination under the Endangered Species Act for all listed species and their designated critical habitats resulting from the use of ledprona. None of the four listed beetle species are found in Minnesota.

ENVIRONMENTAL FATE

Ledprona in the formulated product Calantha rapidly degrades under aerobic and aquatic conditions and is unlikely to persist in the environment, thus limiting the probability of exposure.

Soil

- **Soil aerobic half-life** – 0.571 to 2.92 days
- **Aquatic aerobic half-life** – 1.27 to 1.87 days

Degradates

Ledprona does not have degradates in the traditional sense. The dsRNA in ledprona is degraded and digested in a manner consistent with naked and unmodified RNA, thus residuals were deemed unimportant. Additionally, no observable differences between the dsRNA in ledprona and in the product Calantha were found, indicating the final formulation does not impact dsRNA persistence in the environment.