Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
pegzilarginase-nbln (Loargys®)	**MP-RX-FP-191-26**	☒ **MMM MA** ☒ **MMM MultiHealth**	**7/22/2026**	**7/22/2026**
			Last Review Date: **7/22/2026**	**Frequently Revision:** **Annual**

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

This document addresses Loargys (pegzilarginase-nbln), an enzyme replacement therapy approved by the Food and Drug Administration (FDA) to treat hyperargininemia in adult and pediatric individuals 2 years of age and older with Arginase 1 Deficiency (ARG1-D), in conjunction with dietary protein restriction. This indication is approved under accelerated approval based on reduction of plasma arginine, and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Background Information:

Arginase 1 Deficiency (ARG1-D) is a rare, autosomal recessive urea cycle disorder caused by loss-of-function mutations in the *ARG1* gene, resulting in impaired conversion of arginine to ornithine and urea. The condition leads to chronic hyperargininemia, progressive spasticity, developmental regression, and neurological decline if left untreated. Historically, management has relied on dietary protein restriction and nitrogen-scavenging agents, which do not adequately normalize plasma arginine levels or halt disease progression.

Pegzilarginase-nbln (Loargys) is a recombinant human arginase 1 enzyme replacement therapy that directly addresses the underlying enzyme deficit by converting plasma arginine into ornithine and urea. The FDA granted accelerated approval to pegzilarginase on February 23, 2026, for the treatment of hyperargininemia in adult and pediatric patients 2 years of age and older with ARG1-D, as an adjunct to dietary protein restriction. Continued approval is contingent upon verification of clinical benefit in confirmatory postmarketing trials.

Efficacy was established in the PEACE trial (NCT03921541), a multicenter, randomized, double-blind, placebo-controlled phase 3 study (N=32) in which participants were randomized 2:1 to receive weekly pegzilarginase or placebo over 24 weeks. Treatment resulted in a significant reduction in plasma arginine levels compared to placebo (geometric mean reduction of 76.7%; $p<0.0001$), with 90.5% of treated patients achieving normalization of plasma arginine by Week 24, versus 0% in the placebo arm. Improvements in functional mobility, as measured by the Gross Motor Function Measure and the 2-Minute Walk Test, were also observed and sustained with long-term treatment. These findings, published by Russo et al. in eClinicalMedicine (2024), established pegzilarginase as the first disease-modifying therapy shown to normalize plasma arginine in patients with ARG1-D.

Loargys has a boxed warning for hypersensitivity reactions. Life-threatening reactions, including anaphylaxis, have been reported with enzyme replacement therapies. These reactions may occur early in treatment or after prolonged therapy. Loargys should be initiated in a healthcare setting with appropriate monitoring and support measures, including access to cardiopulmonary resuscitation equipment. If a severe hypersensitivity reaction occurs, Loargys should be discontinued and appropriate medical treatment should be provided. Individuals should be educated on symptoms of life-threatening hypersensitivity reactions and to seek immediate medical care should symptoms occur.

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Approved Indications

A. Treatment of hyperargininemia in adult and pediatric patients 2 years of age and older with Arginase 1 Deficiency (ARG1-D), in conjunction with dietary protein restriction.

Other Uses

A. None.

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

pegzilarginase-nbln (Loargys®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Initial requests for Loargys (pegzilarginase-nbln) may be approved if the following criteria are met:

i. Individual is 2 years of age or older; **AND**
ii. Individual has a diagnosis of hyperargininemia due to Arginase 1 Deficiency (ARG1-D); **AND**
iii. Documentation is provided that diagnosis has been verified by (Haberle 2019, Russo 2024):
    A. Genetic testing demonstrating a pathogenic mutation in the arginase 1 (ARG1) gene; **OR**
    B. Significantly decreased or absent arginase enzyme activity in erythrocytes; **OR**
    C. Plasma arginine level greater than 300 µmol/L; **AND**
iv. Individual is using Loargys in combination with dietary protein restriction.

B. Criteria For Continuation of Therapy

Continuation requests for Loargys (pegzilarginase-nbln) may be approved if the following criteria are met:

i. The member continues to meet the indication for hyperargininemia due to Arginase 1 Deficiency (ARG1-D); **AND**
ii. Documentation is provided that there has been a clinically significant reduction or maintenance of plasma arginine levels within the therapeutic target range plasma arginine levels while on Loargys (pegzilarginase-nbln) therapy; **AND**
iii. Documentation is provided that the individual has not experienced unacceptable toxicity from Loargys therapy, including severe hypersensitivity reactions, including anaphylaxis.

C. Authorization Duration

i. Initial Approval Duration: Up to 12 months
ii. Reauthorization Approval Duration: Up to 12 months

D. Conditions Not Covered

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Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Loargys (pegzilarginase-nbln) may not be approved when the above criteria are not met and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Approved Indication	Recommended Dosing/Limits
pegzilarginase-nbln (Loargys®) injection 2 mg/0.4mL and 5 mg/mL single-dose vial	• *Starting dose:* 0.1 mg/kg administered by intravenous infusion once weekly using actual body weight. • *Dose adjustment:* After 4 weeks of therapy, measure pre-dose plasma arginine, to determine whether dose adjustment is needed. • *Maximum dose:* 0.2 mg/kg once weekly.
Exceptions	
• After eight weeks of once weekly intravenous Loargys, patients may be switched to once weekly subcutaneous Loargys at the same dosage of intravenous therapy.	

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E72.21	Argininemia [Arginase 1 deficiency]

HCPCS Codes:

Codes	Description
C9399	Unclassified drugs or biologicals [when specified as Loargys (pegzilarginasenbln)]
J3590	Unclassified biologics [when specified as Loargys (pegzilarginase-nbln)]

Reference Information:

1. ClinicalTrials.gov. A Study of Pegzilarginase in Patients With Arginase 1 Deficiency (PEACE). Identifier: NCT03921541. Bethesda, MD: National Library of Medicine; updated 2024.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: March 4, 2026.
3. Diaz GA, Bechter M, Batshaw ML, et al. Pegzilarginase for the treatment of arginase 1 deficiency: results from the phase 3 PEACE trial. Genet Med. 2024;26(8):101122. doi:10.1016/j.gim.2024.101122
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Haberle J, Burlina A, Chakrapani A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: First revision. J Inherit Metab Dis. 2019;1–39. 4.
6. Immedica Pharma AB. LOARGYS® (pegzilarginase-nbln) injection, for intravenous or subcutaneous use: Prescribing Information. Immedica Pharma AB; 2026. Accessed July 1, 2026.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
8. Russo RS, Gasperini S, Bubb G, et al. Efficacy and safety of pegzilarginase in arginase 1 deficiency (PEACE): a phase 3, randomized, double-blind, placebo-controlled, multi-centre trial. EClinicalMedicine. 2024;68:102405.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	7/13/2026	7/22/2026