Medical Drug Clinical Criteria

Subject:	Loargys (pegzilarginase-nbln)		
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Overview

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.

Arginase 1 Deficiency is a rare inherited metabolic disorder characterized by a deficiency in arginase, an enzyme in the urea cycle that transforms nitrogen for excretion from the body. Individuals with Arginase 1 Deficiency experience persistently high levels of plasma arginine, leading to progressive and severe neurological symptoms. Accurate diagnosis is important to provide disease-specific enzyme replacement therapy. Diagnosis is confirmed through elevated plasma arginine levels, enzymatic activity measurement or genetic testing.

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.

Clinical Criteria

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.

Loargys (pegzilarginase-nbln)

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 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 in combination with dietary protein restriction.

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

I. Individual has a diagnosis of Arginase 1 Deficiency (ARG1-D); **AND**
II. 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**

III. Individual is using in combination with dietary protein restriction; **AND**
IV. Documentation is provided that there has been a clinically significant reduction in plasma arginine levels while on Loargys (pegzilarginase-nbln) therapy.

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

Quantity Limits

Loargys (pegzilarginase-nbln) Quantity Limit

Drug	Limit
Loargys (pegzilarginase-nbln) 2 mg/0.4 mL, 5 mg/mL vial	0.2 mg/kg once weekly

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J1818	Injection, pegzilarginase-nbln, 0.05 mg [Loargys]

ICD-10 Diagnosis

E72.21	Argininemia [Arginase 1 deficiency]

Document History

New: 3/9/2026
Document History:

- 09/08/2026 – Coding Update: Removed HCPCS NOC C9399, J3590 effective 9/30/26 and added J1818 effective 10/1/26.
- 3/9/2026 – Annual Review: New clinical criteria and quantity limit for Loargys. Administrative update to add documentation. Coding Reviewed: Added HCPCS NOC C9399, J3590, and ICD-10-CM E72.21 for Loargys.

References

1. 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.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. 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. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
5. 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 policies may take precedence over the application of this clinical criteria.

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