Loargys® (pegzilarginase-nbln)
(Intravenous/Subcutaneous)

Effective Date: 11/01/2026
Review Date: 8/17/2026
Pharmacy Scope: Medicaid
Medical Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Coverage is provided for six months and is eligible for renewal for 6 months.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- **Hyperargininemia**
  - 320 units once weekly

III. Summary of Evidence

Loargys (pegzilarginase-nbln) is an arginine specific enzyme indicated for the 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. Loargys was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial (NCT03921541) with a 24-week treatment period followed by a long-term open-label extension of up to 150 weeks in patients with ARG1-D-associated hyperargininemia. In the controlled phase, 32 pediatric and adult patients were randomized 2 to 1 to receive weekly intravenous Loargys or placebo. Patient ages ranged from 2 to 29 years old, 90% of which were between the ages of 2 to 17 years of age. Patients were initiated at a dose of 0.1 mg/kg and titrated, ranging from 0.05 mg to 0.2 mg/kg. The primary endpoint was change from baseline plasma arginine at week 24. Loargys treatment resulted in a statistically significant reduction in plasma arginine levels at week 24, with a mean decrease of 74% from baseline vs. 3% in the placebo group ($p < 0.0001$). Ninety percent of Loargys-treated patients achieved target levels of (<200 μM) as well as normalized levels (40–115 μM), compared with 0% in the placebo group. During the extension period, sustained reductions in plasma arginine were observed, and patients who switched from placebo to Loargys achieved similar improvements to those treated from study initiation. Loargys has a black box warning for hypersensitivity reactions including anaphylaxis, and the most common adverse reactions (>10%) include vomiting, pyrexia, infusion associated reactions and constipation.

IV. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

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Arginase-1 Deficiency (ARG1-D) – Hyperargininemia † Φ [1-4]

- Member is at least 2 years of age; AND
- This medication must be prescribed by or in consultation with a physician who specializes in the treatment of enzyme or metabolic disorders; AND
- Documentation that member has a confirmed diagnosis of Arginase-1 Deficiency (ARG1-D), as evidenced by at least one (1) of the following features of disease:
    - Identification of biallelic pathogenic (or likely pathogenic) variants in ARG1 on molecular genetic testing; OR
    - Reduced RBC arginase enzyme activity (i.e., <1% of normal in red blood cell extracts); AND
- Documentation that member has a history of elevated plasma arginine levels (i.e., greater than or equal to 250 micromol/L), with baseline level provided; AND
- Member will maintain a protein-restricted diet; AND
- Physician has assessed objective signs of disease manifestations, such as baseline motor function/mobility (e.g., including, but not limited to, the Two-Minute Walk Test (2MWT), Gross Motor Function Measure (GMFM)-D (Standing), GMFM-E (Walking, Running, and Jumping), etc.); AND
- The member has not received previous liver or hematopoietic transplant procedure; AND
- Documentation of member's current weight; AND
- Initial and subsequent doses of the requested medication will not exceed 0.2 mg/kg once weekly, and current prescribed dose is provided; AND
- Subsequent pre-dose plasma arginine levels will be obtained and monitored as outlined in the manufacturer's prescribing information, with the dose of the requested medication adjusted if the member's pre-dose plasma arginine levels fall outside of the therapeutic range (i.e., 50 micromol/L to 150 micromol/L) [*Note: Monitor plasma arginine levels (prior to Loargys dosing) weekly for 2 weeks after any dosage adjustments and as clinically indicated*]

† FDA-approved indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1-4]

- If member has not been approved for this drug by Neighborhood in the past, clinician must submit documentation that initial criteria is met; AND
- This medication continues to be prescribed by or in consultation with a physician who specializes in the treatment of enzyme or metabolic disorders; AND
- Documentation of lab results with pre-dose plasma arginine levels; AND
- Documentation that member has demonstrated a beneficial response to therapy compared to pretreatment baseline as evidenced by stabilization or improvement in plasma arginine levels and/or complications of disease manifestations (i.e., improvement in motor function/mobility); AND

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- The member has achieved a pre-dose plasma arginine level between 50 micromol/L and 150 micromol/L; OR
- The member has not achieved a pre-dose plasma arginine level between 50 micromol/L and 150 micromol/L, and the dose of the requested medication will be adjusted as outlined in the manufacturer's prescribing information *(Note: Dose adjustments are permitted only if two consecutive weekly pre-dose plasma arginine levels are outside the therapeutic target and at least 2 weeks have elapsed since the previous dose adjustment)*; AND

- Documentation of member's current weight and prescribed dose; AND
- The requested dose does not exceed 0.2 mg/kg once weekly.

VI. Dosage/Administration [1]

Indication	Dose
Arginase 1 Deficiency (ARG1-D)	The recommended starting dosage of Loargys is 0.1 mg/kg administered via intravenous infusion once weekly. ***NOTE:*** *For the recommended dosage, use actual body weight.*
Recommendations Prior to Loargys Treatment • Administer Loargys under the supervision of a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis. • Initiate Loargys in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. • Obtain a baseline plasma arginine concentration. • Consider pre-medication with antihistamines. Note: After eight weeks of once weekly intravenous therapy, members may be switched to once weekly subcutaneous therapy at the same dosage of the intravenous dose. If members tolerate maintenance subcutaneous administration of Loargys, they may receive subcutaneous administration at home under the supervision of a healthcare provider. When switching members from subcutaneous administration in a supervised clinical setting to the home, initially use the same dose. Do not change the dose without supervision of a healthcare provider.	
Recommended Adjustment, Maximum Dosage, and Monitoring To maximize the time within the normal range of 40 to 115 micromolar, dose adjustments should be aimed at achieving a pre-dose level of plasma arginine near the upper limit of normal (ULN). After four weeks of Loargys administration, measure pre-dose plasma arginine (168 hours after prior dose) to determine the need for dosage adjustment. If two consecutive weekly pre-dose plasma arginine measurements are not in the desired therapeutic range, increase or decrease the weekly Loargys dosage as follows: • Below 50 micromolar, reduce the weekly Loargys dosage by 0.05 mg/kg. • Above 150 micromolar, increase the weekly Loargys dosage by 0.05 mg/kg.	

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The maximum recommended Loargys dosage is 0.2 mg/kg once weekly.
Collect Plasma Arginine Using Specific Collection Tubes and Measure Arginine Concentration Using a Specific Assay Collect samples into Immedica Pharma's Nor-NOHA Blood Collection Tubes, which contain Nω-hydroxy-nor-Arginine (nor-NOHA), an enzyme inhibitor used to inhibit post-sampling degradation of arginine by Loargys, and measure arginine concentration using Immedica Pharma's LOARGYS Arginine Assay. Loargys is only available to a member if the member is enrolled in Study IMM-PEG-005 to obtain Immedica Pharma's Nor-NOHA Blood Collection Tubes and LOARGYS Arginine Assay. Further information is available by contacting Immedica Pharma at 1-844-627-4687.

VII. Billing Code/Availability Information

HCPCS Code:

- J1818, Injection, pegzilarginase-nbln, 0.05 mg, *effective 10/1/26*

NDC:

- Loargys 2 mg/0.4 mL single-dose vial: 81583-0102-xx

VIII. References

1. Loargys [package insert]. Stockholm, Sweden; Immedica Pharma AB; February 2026. Accessed June 2026.
2. Sun A, Combez EA, Wong D. Arginase Deficiency. GeneReviews. Arginase Deficiency - GeneReviews® - NCBI Bookshelf. Initial Posting: October 21, 2004; Last Update: May 28, 2020. Accessed March 2026.
3. ClinicalTrials.gov. NCT03921541. PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints): A Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Efficacy and Safety of Pegzilarginase in Children and Adults With Arginase 1 Deficiency. | ClinicalTrials.gov.
4. 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, Volume 68, 102405.
5. Catsburg C, et al. Arginase 1 deficiency: using genetic databases as a tool to establish global prevalence. Orphanet J Rare Dis. 2022;17(1):94.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E72.21	Argininemia/ARG

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

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The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY,	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Loargys was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Loargys according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

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