VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Enzyme Replacement Therapy – Loargys Utilization Management Medical Policy

- Loargys™ (pegzilarginase-nbln intravenous infusion or subcutaneous injection – Immedica)

REVIEW DATE: 03/11/2026; selected revision 03/25/2026

OVERVIEW

Loargys, an arginine specific enzyme, is indicated for the treatment of **hyperargininemia in adult and pediatric patients ≥ 2 years of age with Arginase 1 Deficiency (ARG1-D)**, in conjunction with dietary protein restriction.[1]

The prescribing information notes that this indication is approved under accelerated approval based on the reduction of plasma arginine.[1] Continued approval for this indication may be contingent on verification and description of clinical benefit in a confirmatory trial.

Disease Overview

ARG1-D is an ultra-rare, inherited, metabolic disorder caused by autosomal recessive variants in the *ARG1* gene.[2-4] It results in partial or complete loss of arginase 1 function, which is the final enzyme in the urea cycle pathway that converts arginine to ornithine and urea. Lack of arginase activity leads to elevated arginine levels and its metabolites, the guanidino compounds. ARG1-D is a distinct type of urea cycle disorder (UCD); hyperargininemia is the characteristic biochemical and pathological abnormality, typically manifesting around 2 years to 4 years of age as a distinct and progressively neurological phenotype. Manifestations associated with the disease include spastic paraparesis, progressive neurological and motor deterioration affecting mobility, growth and developmental delays, cognitive delays, seizures, the potential for early mortality; progressive lower-limb spasticity is the hallmark feature of ARG1-D. ARG1-D is the least common of all UCDs, with an estimated incidence of approximately 1 in 726,000 to 1 in 950,000; estimates suggest it affects fewer than 300 patients in the US. It is diagnosed by assessment of plasma arginine levels, genetic testing, or arginase enzyme activity in red blood cells.

Clinical Efficacy

The efficacy of Loargys was evaluated in a multicenter, double-blind, placebo-controlled trial followed by a long-term open-label extension of up to 150 weeks.[1] A total of 32 patients were randomized in a 2:1 ratio to receive once-weekly intravenous (IV) infusions of Loargys or placebo for 24 weeks. Patients assigned to Loargys initiated treatment at a dose of 0.1 mg/kg, with dose titration permitted within a range of 0.05 mg/kg to 0.2 mg/kg based on clinical need.

Patients receiving ARG1-D–related dietary management or ammonia scavenger therapy at baseline were allowed to continue these treatments throughout the double-blind period.[1] The primary endpoint was the change from baseline in plasma arginine levels at Week 24. Loargys-treated patients demonstrated a significant mean reduction in plasma arginine levels from baseline to Week 24, with 90% achieving target plasma arginine concentrations (< 200 micromolar) and normalization of levels, compared with 0% of patients receiving placebo.

During the open-label extension, the median duration of Loargys exposure was 94 weeks, with a range of 62 to 152 weeks.[1]

Dosing Information

The recommended starting dose of Loargys is 0.1 mg/kg via IV infusion once weekly.[1] For the recommended dose, actual body weight should be used.

Prior to use of Loargys, a baseline plasma arginine concentration should be obtained.[1] 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, measure pre-dose plasma arginine (168 hours after prior dose) to determine the need for dose adjustment.

If two consecutive weekly pre-dose plasma arginine measurements are not in the desired therapeutic range, increase or decrease the weekly Loargys dose as follows:[1]

- Plasma arginine level < 50 micromolar: reduce the weekly Loargys dose by 0.05 mg/kg.
- Plasma arginine level > 150 micromolar: increase the weekly Loargys dose by 0.05 mg/kg.

The maximum recommended Loargys dose is 0.2 mg/kg once weekly.[1] Monitor plasma arginine levels (prior to Loargys dosing) weekly for 2 weeks, after any Loargys dose adjustment, and as clinically indicated. Patients may be switched from IV administration to subcutaneous (SC) administration after eight weeks of once-weekly IV administration; patients are switched to the same dosage of IV therapy.

Guidelines

In 2019, expert consensus guidelines for the diagnosis and management of UCDs were published.[5] The primary goal of long-term management in patients with ARG1-D is reduction of plasma arginine levels to < 200 micromolar. Current standard-of-care management centers on dietary therapy, with restriction of natural protein intake to limit arginine exposure, typically through a low-protein diet supplemented with arginine-free essential amino acid formulas. Nitrogen-scavenging agents may also be used to reduce the risk of hyperammonemia by facilitating alternative nitrogen excretion pathways; however, these agents do not directly reduce plasma arginine concentrations. The National Institute for Health and Care Excellence published a recommendation endorsing the use of Loargys for the treatment of ARG1-D.[6]

Safety

Loargys has a Boxed Warning for hypersensitivity reactions including anaphylaxis.[1] Loargys should be initiated in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue Loargys, and immediately initiate appropriate medical treatment, including use of epinephrine.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Loargys. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Loargys as well as the monitoring required for adverse events and long-term efficacy, approval requires Loargys to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Loargys is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Arginase-1 Deficiency.** Approve for the duration noted if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 2 years of age; AND
   - **B)** According to the prescriber, the diagnosis was confirmed by ONE of the following (i, ii or iii):
     - **i.** Approve for 1 year if genetic testing confirms pathogenic variants in the *ARG*-1 gene; OR
     - **ii.** Approve for 1 year if enzymatic testing confirms partial or complete loss of arginase 1 activity in red blood cells; OR
     - **iii.** Approve for 3 months if the patient has elevated plasma arginine levels diagnosed with a level above the upper limit of the normal reference range for the reporting laboratory; AND
   - **C)** Loargys is prescribed in conjunction with a protein-restricted diet; AND
   - **D)** Loargys is prescribed by or in consultation with a geneticist, neurologist or metabolic disease specialist (or specialist who focuses in the treatment of metabolic diseases).

   Dosing. Approve the following dosing regimens (A or B):
   - **A)** For the first eight doses, approve up to 2 mg/kg given intravenously no more than once weekly; OR
     Note: Actual body weight should be used for weight-based dosing.
   - **B)** For any doses thereafter, approve up to 2 mg/kg given intravenously or subcutaneously no more than once weekly.
     Note: Actual body weight should be used for weight-based dosing.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Loargys is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Loargys™ intravenous infusion, subcutaneous injection [prescribing information]. Chicago, IL: Immedica; February 2026.
2. Rudebeck M, Braverman N, Chang R, et al. Clinical characteristics of arginase 1 deficiency: natural history insights from international clinical trials. *J Inherit Metab Dis*. 2026;49(2):e70156.
3. Bin Sawad A, Jackimiec J, Bechter M, et al. Epidemiology, method of diagnosis, and clinical management of patients with arginase 1 deficiency (ARG1-D): a systematic review. *Mol Genet Metab*. 2022;137(1-2):153-163.
4. Bin Sawad A, Pothukuchy A, Badeaux M, et al. Natural history of arginase 1 deficiency and the unmet needs of patients: a systemic review of case reports. *JIMD Rep*. 2022;63(4):330-340.
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;42(6): 1192-1230.
6. National Institute for Health and Care Excellence (NICE). Pegzilarginase for treating arginase-1 deficiency in people 2 years and over. Published March 4, 2026. Available at: 1 Recommendation | Pegzilarginase for treating arginase-1 deficiency in people 2 years and over | Guidance | NICE. Accessed on March 5, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	03/11/2026
Selected Revision	**Arginase 1 Deficiency.** A geneticist was added to the specialist requirement.	03/25/2026