Original Effective Date: 06/06/2026
Current Effective Date: 06/06/2026
Last P&T Approval/Version: 04/29/2026
Next Review Due By: 07/2026
Policy Number: C30652-A

Loargys (pegzilarginase-nbln)

PRODUCTS AFFECTED

Loargys (pegzilarginase-nbln)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hyperargininemia

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. This clinical policy will be reviewed along with state and federal requirements, the benefit being administered and formulary preferencing. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available. The Pharmacy and Therapeutics Committee has determined that biosimilars may be preferred.

A. HYPERARGININEMIA:
   1. Documented diagnosis of hyperargininemia due to arginase 1 deficiency (ARG1-D)
      AND

2. Documentation diagnosis was confirmed by genetic testing that shows mutations in the ARG1 gene [DOCUMENTATION REQUIRED]
   AND
3. Documentation of baseline plasma arginine level at diagnosis to be used to evaluate efficacy of therapy at renewal
   AND
4. Member's condition has failed to be managed by dietary protein restriction and/or ammonia-targeting agents (e.g. sodium phenylbutyrate, sodium benzoate and sodium phenylacetate) alone
   AND
5. Loargys (pegzilarginase-nbln) therapy will be used concomitantly with dietary protein restrictions

CONTINUATION OF THERAPY:

A. HYPERARGININEMIA:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by decreased plasma arginine levels

DURATION OF APPROVAL:

Initial authorization: 3 months, Continuation of Therapy: 12 months
MOLINA REVIEWER NOTE: For Illinois Marketplace, please see Appendix.

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified geneticist, metabolic specialist or physician experienced in the management of urea cycle disorder. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

2 years of age and older

QUANTITY:

0.1 mg/kg once weekly (see Appendix 1)

Maximum Quantity Limits – 0.2 mg/kg once weekly

PLACE OF ADMINISTRATION:

The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location.

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Subcutaneous, Intravenous

DRUG CLASS:

FDA-APPROVED USES:
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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Illinois (Source: Illinois General Assembly)
"(215 ILCS 200/65) Sec. 65. Length of prior authorization approval for *treatment for chronic or long-term conditions*. If a health insurance issuer requires a prior authorization for a recurring health care service or maintenance medication for the treatment of a chronic or long-term condition, *the approval shall remain valid for the lesser of 12 months from the date the health care professional or health care provider receives the prior authorization approval or the length of the treatment as determined by the patient's health care professional*. This Section shall not apply to the prescription of benzodiazepines or Schedule II narcotic drugs, such as opioids. Except to the extent required by medical exceptions processes for prescription drugs set forth in Section 45.1 of the Managed Care Reform and Patient Rights Act, nothing in this Section shall require a policy to cover any care, treatment, or services for any health condition that the terms of coverage otherwise completely exclude from the policy's covered benefits without regard for whether the care, treatment, or services are medically necessary. (Source: P.A. 102-409, eff. 1-1-22.)"
Illinois (Source: Illinois General Assembly)
"(215 ILCS 134/45.1) Sec. 45.1. Medical exceptions procedures required. … (c) An off-formulary exception request shall not be denied if: (1) the formulary prescription drug is contraindicated; (2) the patient has tried the formulary prescription drug while under the patient's current or previous health insurance or health benefit plan and the prescribing provider submits evidence of failure or intolerance; or (3) the patient is stable on a prescription drug selected by his or her health care provider for the medical condition under consideration while on a current or previous health insurance or health benefit plan. (d) Upon the granting of an exception request, the insurer, health plan, utilization review organization, or other entity shall authorize the coverage for the drug prescribed by the enrollee's treating health care provider, to the extent the prescribed drug is a covered drug under the policy or contract up to the quantity covered. *(e) Any approval of a medical exception request made pursuant to this Section shall be honored for 12 months following the date of the approval or until renewal of the plan*."

Appendix 1:
The recommended starting dosage of Loargys (pegzilarginase-nbln) is 0.1 mg/kg administered via intravenous infusion once weekly. For the recommended dosage use actual body weight.

After eight weeks of once weekly intravenous Loargys, patients may be switched to once weekly subcutaneous Loargys at the same dosage of intravenous therapy.

To maximize the time within the normal range of 40 µmol/L to115 µmol/L, 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 µmol/L, reduce the weekly Loargys dosage by 0.05 mg/kg.
- Above 150 µmol/L, increase the weekly Loargys dosage by 0.05 mg/kg.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Arginase 1 Deficiency (ARG1-D) is a rare urea cycle disorder (UCD) caused by pathogenic variants in the ARG1 gene, resulting in elevated plasma arginine levels (hyperargininemia). This condition is associated with progressive neurological manifestations, including spasticity, seizures, developmental delay, and intellectual disability.

The gold standard for diagnosing a UCD is through genetic testing, and a detailed family history serves as an important first step. If genetic test results are not adequate to properly characterize the disease, additional enzyme testing is available for select UCDs. In some U.S. states, newborn screening (NBS) panels can include specific enzyme deficiencies of the UC, but not all of them. Even so, NBS is not a reliable means of diagnosis due to low sensitivity and specificity.

Although several medications (e.g., phenylacetate, sodium benzoate, phenylbutyrate, glycerol phenylbutyrate [Ravicti], sodium phenylbutyrate [Pheburane], and Olpruva) are approved as adjunctive therapies for urea cycle enzyme deficiencies, none are specifically indicated for the treatment of ARG1-D.

Loargys (pegzilarginase-nbln), a novel, recombinant, human arginase-1 enzyme was approved by the FDA in February 2026. Loargys is indicated for the treatment of hyperargininemia in adult and pediatric patients ≥2 years of age with ARG1-D, in conjunction with dietary protein restriction.

The effectiveness of Loargys for the treatment of hyperargininemia in adult and pediatric patients with ARG1-D was evaluated in the PEACE study (NCT03921541). The study consisted of a screening period; a 24-week randomized, double-blind (DB) treatment period; an open-label long-term extension (LTE) period of up to 150 weeks; and a follow-up visit for final safety assessments.

The primary endpoint in the PEACE study was the change from baseline in plasma arginine at Week 24. Loargys-treated patients had a significant mean reduction in plasma arginine levels from baseline to Week 24. Additionally, 90% of Loargys-treated patients achieved target plasma arginine levels (below 200 µmol/L) and normalized levels (40 µmol/L to115 µmol/L), compared to 0% of placebo-treated patients.

Loargys was well tolerated, with adverse events (AEs) being mostly transient, mild/moderate in severity, and either self-limiting or manageable with standard medical care. No AEs led to discontinuation or dose reduction, and there were no notable adverse trends in liver function tests or other laboratory assessments.

During the first 8 weeks of the DB period, 2 patients on Loargys experienced nonserious hypersensitivity reactions that were managed successfully with antihistamines. Loargys-treated patients who developed antidrug antibodies (ADA) generally had a greater incidence of hypersensitivity reactions compared to those who did not develop ADA.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Loargys (pegzilarginase-nbln) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Loargys (pegzilarginase-nbln) include: no labeled contraindications.

Exclusions/Discontinuation:

If a severe hypersensitivity reaction occurs (e.g. anaphylaxis), discontinue Loargys (pegzilarginase-nbln) and immediately initiate appropriate medical treatment, including use of epinephrine.

OTHER SPECIAL CONSIDERATIONS:

Loargys (pegzilarginase-nbln) has a Black Box Warning for risk of life-threatening hypersensitivity reactions,

including anaphylaxis.

Initiate Loargys (pegzilarginase-nbln) 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.

Loargys is administered once weekly, either by intravenous infusion or subcutaneous injection. If a dose is missed, administer Loargys as soon as possible. Do not administer two doses on the same day or within four days of another dose to make up for a missed dose. A minimum interval of four days must be maintained between doses.

Subcutaneous doses may be administered at home under the supervision of a healthcare provider.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
J3590	Loargys (pegzilarginase-nbln) injection, IV or SC

AVAILABLE DOSAGE FORMS:
Loargys SOLN 2MG/0.4ML single-dose vial

REFERENCES

1. Loargys (pegzilarginase-nbln) injection, for intravenous or subcutaneous use [prescribing information]. Chicago, IL: Immedica Pharma US Inc.; February 2026.
2. Aeglea Biotherapeutics. (2024). Efficacy and safety of pegzilarginase in patients with arginase 1 deficiency (ClinicalTrials.gov Identifier: NCT03921541). ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT03921541
3. National Organization for Rare Disorders. (2023). Arginase deficiency. https://rarediseases.org/rare-diseases/arginase-deficiency/
4. Immedica Pharma AB. (2025). Pegzilarginase in subjects <24 months old with arginase 1 deficiency (ClinicalTrials.gov Identifier: NCT06582524). ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06582524
5. Russo, R. S., Gasperini, S., Bubb, G., Neuman, L., Sloan, L. S., Diaz, G. A., & Enns, G. M., on behalf of the PEACE Investigators. (2024). Efficacy and safety of pegzilarginase in arginase 1 deficiency (PEACE): A phase 3, randomized, double-blind, placebo-controlled, multi-centre trial. eClinicalMedicine, 68, 102405. https://doi.org/10.1016/j.eclinm.2023.102405
6. National Organization for Rare Disorders. (2023, April 11). Arginase-1 deficiency. Available at https://rarediseases.org/rare-diseases/arginase-deficiency/ Accessed April 2026.
7. Rare Diseases Clinical Research Network. Urea Cycle Disorders Consortium. Urea Cycle Disorders Treatment Guidelines. National Institutes of Health, Rare Diseases Clinical Research Network. Available at https://rarediseases.org/organizations/urea-cycle-disorders- consortium/ Accessed April 2026.

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q2 2026