



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 04/16/2026

Loargys® (pegzilarginase-nbln)

HCPCS: J1818

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved indication
 - b. FDA approved age
 - c. Confirmation of diagnosis by genetic testing showing biallelic mutations in the ARG1 gene
 - d. Must not be used in combination or with any other enzyme replacement therapy for arginase 1 deficiency (ARG1-D)
 - e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents.
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Authorization Period: One year at a time
 - c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Arginase 1 deficiency (ARG1-D) is an autosomal recessive urea cycle disorder caused by a mutation on the ARG1 gene. It is characterized by the buildup of plasma arginine and ammonia due to a dysfunctional arginase enzyme leading to progressive and debilitating neurologic manifestations. The hallmark feature of ARG1-D is prominent and progressive lower-limb spasticity leading to gait abnormalities, difficulty walking and climbing stairs, and the need for assistive devices. Most patients ultimately develop impairment of gross motor function and mobility, potentially becoming non-ambulatory or reliant on a wheelchair. Developmental delay and/or developmental regression, cognitive impairment, and seizures may also occur. Incidence has been estimated to occur in approximately 1 in 300,000-1,000,000 births.
- The 2019 guidelines for the diagnosis and management of urea cycle disorders recommend confirmation of ARG1-D diagnosis through genetic testing. Two pathogenic mutations in the ARG1 gene support an ARG1-D diagnosis.
- The standard of care for ARG1-D up until now has revolved around the treatment and prevention of hyperammonemia crisis. If a patient is experiencing hyperammonemia crisis, they should be rehydrated, nitrogen should be removed from the body using sodium benzoate or hemodialysis, and protein intake should be stopped. Once stabilization from hyperammonemia crisis occurs or prior to a crisis occurring, guidelines state the treatment goal is to reduce plasma arginine concentrations below 200 $\mu\text{mol/L}$ through extreme restriction of natural protein. The recommended daily protein intake varies with age, growth rate, and clinical course with up to 50% of a patient's required protein being supplied as an essential amino acid mixture. Patients should have regular monitoring of plasma ammonia and amino acid levels, neurodevelopmental milestones, growth monitoring, liver function, and renal status.
- Loargys provides an additional treatment option for ARG1-D. It is an enzyme replacement therapy indicated for the treatment of hyperargininemia in adult and pediatric patients 2 years of age and older with ARG1-D in conjunction with dietary protein restriction.
- Safety and efficacy of Loargys were evaluated in the PEACE trial, a phase III randomized, double-blind, placebo-controlled, parallel-group study of 32 patients with ARG1-D. Patients were randomized in a 2:1 ratio to Loargys or volume-matched placebo during the double-blind period. Randomization was stratified by severity of prior history of hyperammonemia to minimize potential bias from possible treatment group imbalance. Patients continued their current individualized disease management regimen for the duration of the trial. Patients were included in the study if they had documented ARG1-D diagnosis via elevated plasma arginine, pathogenic variants in the ARG1 gene, and/or diminished erythrocyte ARG1 activity; plasma arginine greater than or equal to 250 $\mu\text{mol/L}$; and impairment on any secondary functional mobility assessment. Key exclusion criteria included symptomatic hyperammonemia (ammonia ≥ 100 $\mu\text{mol/L}$ requiring acute care or hospitalization) within 6 weeks before first Loargys dose and extreme mobility impairment. The primary endpoint was change from baseline in plasma arginine at week 24. The key secondary endpoint was functional mobility as assessed through mean change from baseline in the Gross Motor Function Measure part E (GMFM-E) score or the 2-minute walk test (2MWT) distance at week 24. Loargys lowered geometric mean plasma arginine from 354.0 $\mu\text{mol/L}$ to 86.4 $\mu\text{mol/L}$ at week 24 vs. 464.7 $\mu\text{mol/L}$ to 426.6 $\mu\text{mol/L}$ for placebo (95% CI: -67.1%, -83.5%; p-value < 0.0001) and normalized levels in 90.5% of patients (vs. 0% with placebo). In addition, clinically relevant functional mobility improvements were demonstrated with Loargys treatment and were sustained long-term through an additional 24 weeks of subsequent exposure; however, these changes were not statistically significant.
- Loargys has not been studied and there is no data to support use in combination with other enzyme replacement therapies for the treatment of ARG1-D.

References:

1. Loargys [prescribing information]. Chicago, IL: Immedica Pharma US Inc.; February 2026.
2. Sanchez Russoa R, Gasperinib S, Bubba G, et al. Efficacy and safety of pegzilarginase in arginase 1 deficiency (PEACE): a phase 3, randomized, double-blind, placebo-controlled, multi-centre trial. Lancet. 2024 Feb; 68: 102405.
3. National Organization of Rare Disorders. Arginase-1 deficiency. 2023 April 11. Available at: <https://rarediseases.org/rare-diseases/arginase-deficiency/>. Accessed on February 26, 2026.
4. Häberle J, Burlina A, Chakrapani A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: first revision. JIMD. 2019 April 14; 42: 1192 – 1230.

Policy History												
#	Date	Change Description										
1.4	Effective Date: 04/16/2026	New policy - this criteria replaces previously approved preliminary criteria										
1.3	Effective Date: 04/01/2026	UM medical management system update for MAPPO and BCNA <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.2	Effective Date: 03/09/2026	UM medical management system update for BCBS and BCN <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
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BCBS	Yes											
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1.1	Effective Date: 02/12/2026	Annual review of policy - no changes were made to the criteria										
1.0	Effective Date: 02/13/2025	Preliminary Drug Review <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	No	MAPPO	No	BCNA	No
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* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

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Blue Cross Blue Shield/Blue Care Network of Michigan

Medication Authorization Request Form



This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

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PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. ☐ Male ☐ Female	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this request for: ☐ Initiation ☐ Continuation Date patient started therapy: _____
- Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
- Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
☐ Hospital outpatient facility (go to #4) Reason for Hospital Outpatient administration: _____
☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
- Please specify location of administration if hospital outpatient infusion: _____
- Please specify location of administration if hospital inpatient infusion: _____
- Please provide the NPI number for the place of administration: _____
- Initiation AND Continuation of therapy:**
 - What is the patient's diagnosis? _____
 - What other medication has the patient received for their condition? Please list _____
 - Please describe the response to previous therapies: _____
 - Will the patient be receiving any other treatment for the listed condition while on this medication? Please list: _____
 - Please list any labs values important for diagnosing or monitoring this patient's condition: _____
- Continuation of therapy:**
 - Has the patient progressed while on this medication? ☐ yes ☐ no
 - How has the patient's condition changed while on this medication?

☐ Improved: Please describe: _____
 ☐ Stable: please describe: _____
 ☐ Worsened; Please describe: _____
 ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review (required)

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021