Drug Use Research & Management Program
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Orphan Drug Evaluation: Loargys (pegzilarginase-nbln), intravenous or subcutaneous

Date of Review: June 2026
Generic Name: pegzilarginase-nbln

End Date of Literature Search: 03/19/2026
Brand Name (Manufacturer): Loargys (Immedica Pharma AB)

Dossier Received: No

Purpose for Review:

- Review the evidence for the safety and efficacy for pegzilarginase, recently Food and Drug Administration (FDA)-approved as therapy for hyperargininemia in people aged 2 years and older with Arginase 1 Deficiency (ARG1-D), to establish medically appropriate prior authorization (PA) criteria.
- Wholesale acquisition cost (WAC) per 2 mg vial is $11,469. Dosing is weight based, starting at 0.1 mg/kg/week and dosed based upon plasma arginine levels to a maximum dose of 0.2 mg/kg/week. Price ranges from $357,000 per year for a 2-year-old to over $4 million per year for a 70 kg adult at the maximum dose.

Plain Language Summary:

- Deficiency of the arginase enzyme is a rare condition passed down from the parents that causes the amino acid arginine (a building block of proteins) and ammonia to build up gradually in the blood. Arginine is toxic to the nervous system if levels in the blood become too high.
- Arginase deficiency usually becomes evident by about 3 years of age. It most often appears as stiffness, especially in the legs, caused by abnormal tensing of the muscles (spasticity). Other symptoms may include slower than normal growth, developmental delays and eventual loss of developmental milestones, intellectual disabilities, seizures, tremors, and difficulty with balance and coordination (ataxia).
- People with arginase deficiency are treated by monitoring food (protein) intake, taking certain amino acids supplements, and sometimes taking medicines called nitrogen-scavengers. Nitrogen-scavengers help the body get rid of nitrogen to decrease levels of ammonia in the blood.
- Pegzilarginase is a new medicine that the Food and Drug Administration (FDA) approved to treat people with arginase deficiency. It is given once a week into the veins (intravenously). This medicine must be given by a health care provider in medical setting because this medicine may cause a severe allergic reaction. After 8 weeks of treatment, people can switch to getting this medicine at home, with an injection under the skin (subcutaneously), given by a health care provider.
- In a clinical study that compared intravenous administration of pegzilarginase to placebo (or no active treatment), pegzilarginase reduced blood arginine levels more than people that received placebo. There were no significant changes in the ability to walk a short distance over 2 minutes or the ability to walk, run or jump.
- Side effects with pegzilarginase include vomiting, fever, cough, nausea, and stomach pain.
- The Drug Use Research and Management group recommends that the Oregon Health Authority pay for pegzilarginase in patients with arginase deficiency that is indicated by the FDA after their provider documents medical appropriateness through a process called prior authorization.

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Research Questions:

1. What is the efficacy of pegzilarginase in treating arginine deficiency?
2. What are the harms of pegzilarginase in management of arginine deficiency?
3. Are there subgroups of patients based on demographics (e.g., age, racial or ethnic groups, gender), other medications, or co-morbidities for which pegzilarginase is more effective or associated with fewer adverse events?

Conclusions:

- Low-quality evidence shows that pegzilarginase administration resulted in a statistically significant reduction in plasma arginine levels by 71% compared to placebo (95% confidence interval [CI], 89% to -55%; P<0.0001) over 24 weeks.[1] This reduction in plasma arginine did not result in statistically significant improvements in the 2 minute walk test (2MWT) or motor function evaluated by the Gross Motor Function Measure part E (GMFM-E).
- In the clinical trial evaluating the safety of pegzilarginase (n=32), the most frequently reported adverse events with pegzilarginase included vomiting, pyrexia, infusion-associated reactions, constipation, dizziness, and elevated liver function tests.[2]
- The label for pegzilarginase has a black boxed warning regarding the risk of anaphylaxis in patients treated with this drug.[2] Hypersensitivity reactions that were mild to moderate in severity occurred in 13% (6/48) of pegzilarginase-treated patients in clinical trials.[2] The reactions generally occurred with the first few doses but may also occur later in treatment.[2] Pre-medication with antihistamine should be considered when administering pegzilarginase.[2] In patients who have previously developed hypersensitivity reactions to pegzilarginase, corticosteroids can be considered.[2]
- No subgroups of patients based on demographics were identified to show that pegzilarginase is more effective or associated with fewer adverse events in patients 2 years of age and older. Pegzilarginase is currently being evaluated in another Phase 3 clinical trial in pediatric patients less than 2 years of age diagnosed with ARG1-D.

Recommendations:

- Implement clinical PA criteria to ensure pegzilarginase use in appropriate populations that are FDA-approved (**Appendix 2**).

Background:

The urea cycle consists of six consecutive enzymatic reactions that convert waste nitrogen into urea.[3] Arginase is the enzyme involved in the last step of the urea cycle.[3] Hyperargininemia or ARG1-D is a rare inherited metabolic disorder of the urea cycle with an autosomal recessive transmission.[4] It occurs due to a deficiency of the enzyme arginase 1 and causes progressive neurological damage.[4] Unlike other urea cycle disorders, this condition is not generally associated with a hyperammonemic encephalopathy in the neonatal period.[3] The pathophysiologic profile of ARG1-D strongly suggests that elevated arginine, rather than hyperammonemia, plays the key role in development and progression of clinical manifestations.[5] ARG1-D typically presents later in childhood between 2 and 4 years of age with predominantly neurological features.[3] Although increased plasma arginine is the disease hallmark, arginine may not always be exceedingly high.[5] The diagnosis can be confirmed by enzymatic assays (in erythrocytes) or by genetic analysis.[5]

The hallmark feature of ARG1-D is prominent and progressive lower-limb spasticity leading to gait abnormalities, difficulty walking and climbing stairs, and need for assistive devices.[1] The burden of illness is substantial and increases over time as neurologic manifestations progress.[1] Most patients ultimately develop impairment of gross motor function and mobility, potentially becoming non-ambulatory or reliant on a wheelchair.[1] Based on this clinical profile, ARG1-D is uniquely recognized among urea cycle disorders as a clinical mimic of cerebral palsy and hereditary spastic paraplegia.[5] The overall prevalence of ARG1-D is estimated to be of 1:726,000.[6] In the United States, there are an estimated 250 persons diagnosed with ARG1-D.[7] Patients require lifelong treatment and

monitoring, with strict multimodal management regimens.[1] Continued decline into adulthood is associated with significant morbidity and potential early mortality.[1] The age at death for most published ARG1-D cases is less than 50 years.[8]

Treatment of hyperargininemia focuses on dietary protein restriction, supplementation of essential amino acids, symptomatic treatments, and the use of alternative pathways to remove the nitrogen waste.[3] Preventing symptomatic hyperammonemia does not prevent progression or improve long-term outcomes in these patients.[5] Treatment aims at reducing plasma arginine concentrations below 200 µmol/L, to reduce the neurotoxic effects including intellectual disability, developmental delay, and seizures.[5] Lowering plasma arginine levels has the potential to slow disease progression in patients with ARG1-D.[1] Initiation of treatment in younger patients has been described to yield more meaningful neurological benefits.[5] It may take months to years to improve motor function when reductions in plasma arginine are achieved.[5] Significant improvements in spasticity, muscle strength, and mobility—such as the ability to run, climb stairs, and ride a bicycle—have been documented in one patient after 2.5 years of sustained arginine reduction via strict dietary restriction.[5] Due to rare nature of this disease, most clinical evidence to date is largely anecdotal and based on individual cases, familial series, or retrospective case analyses.[5] In the past year (April 2024 to March 2025), 589 patients enrolled in CCOs and Fee-for-Service FFS had a diagnosis of an unspecified type of urea cycle disorder. No patients were identified in the Oregon Medicaid population with the specific diagnosis of ARG1-D (ICD10 code E72.21) during the same time frame.

The National Institute for Health and Care Excellence (NICE) published guidance for the use of pegzilarginase in patients with ARG1-D in March 2026.[9] Usual treatment for arginase-1 deficiency includes dietary protein restrictions, essential amino acid supplementation and ammonia-lowering drugs.[9] Pegzilarginase is the first treatment that specifically treats ARG1-D.[9] Clinical trial evidence shows that pegzilarginase plus usual treatment reduces levels of arginine in the blood compared with placebo plus usual treatment.[9] However, plasma arginine levels do not have a consistent relationship with disease severity.[9] Evidence also suggests improvements in mobility and mental processing, but this is uncertain because the studies were small and short.[9] So, it is unclear how large these benefits are or how long these improvements will last.[9] Long-term outcomes were uncertain because of the lack of a comparator arm in the long-term extension trial and a small number of enrolled participants resulting in underpowered outcomes.[9] The committee also noted the absence of survival data in the company's submission.[9] The clinical experts explained it is plausible that pegzilarginase would extend survival, but this is uncertain.[9] Despite the uncertainties in the clinical and economic evidence, NICE recommended that pegzilarginase can be used, within its marketing authorization, as an option to treat ARG1-D in people 2 years and over.[9]

Drug Information

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies, indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations.

Pegzilarginase is a recombinant, cobalt-substituted and pegylated human ARG1 enzyme therapy with increased catalytic activity due to the cobalt-substitution and prolonged half-life.[1] Pegzilarginase provides an exogenous source of the ARG1 enzyme and reduces plasma arginine by converting it to urea and ornithine.[2] Before starting pegzilarginase therapy, baseline plasma arginine concentrations should be obtained and consideration given to pre-medication with antihistamines.[2] It must be administered under the supervision of a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis.[2] After 4 weeks of treatment, plasma arginine levels should be obtained to determine the need for pegzilarginase dose adjustment to maintain plasma arginine levels in normal range (40 to 115 µmol/L).[2] After 8 weeks of once weekly intravenous (IV) pegzilarginase, patients may be switched to once weekly subcutaneous (SC) therapy at the same IV dose.[2]

The FDA initially denied approval of pegzilarginase because there were questions as to whether the drug improved the motor function of enrolled patients. The reduction in plasma arginine was statistically significant, but the mobility scores should not show statistically significant improvements. The manufacturer submitted additional long-term use data to support clinical stabilization of patients with ARG1-D, which led to the FDA-approval. The FDA approved pegzilarginase in February 2026 under the accelerated approval requirements with ongoing approval contingent on confirmatory postmarketing outcomes to verify the benefit of pegzilarginase in patients with ARG1-D.[7]

Clinical Efficacy and Safety:

The clinical trial used to support FDA approval is described and evaluated below in **Table 1.** Noteworthy trial design and patient characteristics include:

- The PEACE (Pegzilarginase Effect on Arginase 1 Clinical Endpoints) trial was designed to investigate efficacy and safety of pegzilarginase in lowering arginine levels and improving clinical outcomes, as compared with placebo, when added to standard-of-care in children and adults with ARG1-D.[1] Standard of care included dietary protein restriction and individualized disease management regimens to manage spasticity, epilepsy, and hyperammonenmia.[1]
- Trial duration: screening period (n=44), 24-week RCT (n=32), followed by open-label long-term extension (LTE) over 150 weeks (n=31).[1]
- Intervention: In the 24-week phase, patients were randomized 2:1 to pegzilarginase or volume-matched placebo administered via 30-minute IV infusion. Patients could be switched to SC injection at any point after the first 8 weeks of the LTE, using the same pegzilarginase formulation and dose level as their last IV dose.[1]
- Key inclusion criteria:
    - Aged 2 years and older
    - Documented ARG1-D diagnosis (as detected through elevated plasma arginine, pathogenic variants in ARG1, and/or diminished erythrocyte ARG1 activity)
    - Plasma arginine ≥250 µmol/L
    - Impairment on any secondary functional mobility assessment
    - On stable medication regimen including ammonia scavengers, anti-epileptic drugs, and/or spasticity medications at least 4 weeks prior to randomization. The investigators did not provide details about concurrent medication regimens for the patients enrolled in this trial.
    - All patients were managed with dietary protein restriction.
- Key exclusion criteria:
    - Symptomatic hyperammonemia (ammonia ≥100 µmol/L) requiring acute care or hospitalization within 6 weeks of first study dose
    - Extreme mobility impairment which did not allow for assessment of improvements in mobility
    - Treatment with botulinum toxin for spasticity-related complications
- Primary outcome: Change from baseline in plasma arginine at week 24 (normal range 40-115 µmol/L).
- Secondary outcomes
    - 2MWT: evaluates distance travelled on a flat surface in 2 minutes (with bracing or assistive devices). In the PEACE trial, a 9% change from baseline in distance travelled was considered clinically significant.[1]
    - GMFM-E: includes 24 tasks involving walking, running, and jumping with a score range of 0-72.[1] Individual tasks are scored as: 0 = does not initiate, 1 = initiates, 2 = partially completes, 3 = completes, or NT = not tested; the total score reflects the sum of all scored tasks.[1] Lower scores indicate greater functional mobility impairment.[1] In the PEACE trial, a score change from level 1 to level 3 was considered clinically significant.[1]
    - Clinically important response thresholds were defined using criteria established for cerebral palsy.[1]
- Baseline disease severity and population characteristics (see **Table 1**):

- Mean age: 10.7 years
  - Pegzilarginase group: 9.6 years
  - Placebo treated group: 12.9 years
- Mean baseline plasma arginine: 402 μmol/L
  - Pegzilarginase group: 365 μmol/L
  - Placebo treated group: 472 μmol/L
- Mean baseline GMFM-E Score: 47.7 points. Anyone scoring < 68 points is considered impaired. More than half of enrolled patients had gross motor functional impairment of GMFCS level ≥ 2 (range 1 to 3).
- Mean baseline 2MWT distance: 105.8 meters

- Magnitude of benefit and clinical relevance of results:
  - In patients treated with pegzilarginase, mean baseline plasma arginine was statistically significantly reduced by 77.9% compared to placebo at week 24 (95% CI, −67.1% to −83.5%; p<0.0001).[2] Arginine plasma levels are a surrogate endpoint that are not consistently correlated with clinical outcomes or functional improvement.
  - Key secondary outcomes showed numeric improvements from baseline to 24 weeks but were not statistically significant per hierarchical testing.[2]
- Safety signals:
  - Adverse events reported with pegzilarginase during the 24-week double blind phase of the PEACE trial included vomiting (29%), pyrexia (19%), cough (19%), increased ammonia (14%), nausea (5%), and abdominal pain (5%).[1] Serious adverse events were reported for 19% on pegzilarginase and 36% on placebo, and consisted of hyperammonemia (pegzilarginase, 10% vs. placebo, 27%), hyperammonemic encephalopathy (pegzilarginase 5% vs. placebo 9%) and vomiting (5%, pegzilarginase only).[2]
  - Transient, generally low-titer anti-drug antibodies (ADAs) were detected in both treatment arms during the double-blind period (pegzilarginase, 19% [n = 4/21]; placebo, 27% [n = 3/11]), including 1 patient in each arm with pre-existing ADAs at baseline.[1]
  - The label for pegzilarginase has a black boxed warning regarding the risk of anaphylaxis in patients treated with this drug.[2] Life-threatening hypersensitivity reactions, including anaphylaxis, have occurred in patients treated with enzyme replacement therapies (ERTs) including pegzilarginase.[2] Hypersensitivity reactions that were mild to moderate in severity occurred in 13% (6/48) of pegzilarginase-treated patients in clinical trials.[2] Hypersensitivity reactions have included facial swelling, rash, flushing and dyspnea.[2] The reactions generally occurred with the first few doses but may also occur later in treatment.[2] Pre-medication with antihistamine should be considered when administering pegzilarginase. In patients who have previously developed hypersensitivity reactions to pegzilarginase, corticosteroids can be considered.[2]

See **Table 1** for major evidence limitations including:
- Short duration of comparative treatment with placebo (24 weeks) for a chronic, progressive, life-long condition.
- Small population enrolled due to rare nature of ARG1-D.
- Differences in baseline demographics (mean plasma arginine level and age) increase the risk of selection bias. It is unclear what impact these differences had on trial results.
- Although primary outcome showed a significant improvement from baseline, secondary outcomes that assessed mobility did not show statistically significant improvements.

Table 1. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. Russo, RS, et al[1,2] NCT03921541 PEACE trial Phase 3, DB, PC, RCT	1. Pegzilarginase IV once a week via weight-based dosing started at 0.1 mg/kg/week and titrated within a range of 0.05 mg to 0.2 mg/kg as clinically indicated to maintain plasma arginine levels 50 to 150 µmol/L 2. Volume-matched placebo IV once a week Duration of this phase of the trial: 24 weeks	Demographics: -Mean age: 10.7 yo -Male: n=19 (59%) -Race White: 44% Asian: 19% Black: 65 Other: 19% -Age at diagnosis: 3.3 yo -Mean baseline plasma arginine: 402 µmol/L -Baseline GMFM-E score: 47.7 points -Baseline 2MWT distance: 105 meters Key Inclusion Criteria: -Diagnosis of arginase 1 deficiency -Aged ≥2 yo -Plasma arginine ≥250 µmol/L -Impaired mobility -Stabilized on scavenger therapy, anti-epileptic drugs, and/or spasticity medications for at least 4 weeks prior to randomization Key Exclusion Criteria: -Hyperammonemic episode within 6 weeks of study entry -Extreme mobility impairment (unable to complete assessments) --Current treatment with botulinum toxin	ITT: 1. 21 2. 11 PP: 1. 20 2. 11 Attrition: 1. 1 2. 0	Primary Endpoint: Mean percent change in the arginine plasma level from baseline to week 24 1. -74% 2. -3% Treatment difference: -71% 95% CI -89% to -55% P<0.0001 Secondary Endpoints: -Mean change from baseline in 2MWT 1. 7.3 meters 2. 2.7 meters LSMD: 5.5 meters 95% CI -15.6 to 26.7 NS -Mean change from baseline in GMFM-E 1. 4.2 points 2. -0.4 points LSMD: 4.6 points 95% CI -1.1 to 10.2 NS	NA	Any TEAE: 1. 18 (85.7%) 2. 11 (100%) Serious AE: 1. 4 (19%) 2. 4 (36.4%) AE leading to discontinuation: 1. 0 2. 0 Hypersensitivity: 1. 2 (9.5%) 2. 0 (0%) Hyperammonemia episode 1. 3 (14.3%) 2. 4 (36.4%)	NA	**Risk of Bias (low/high/unclear)**: Selection Bias: High. Randomized 2:1 via a central, computer-generated randomization protocol. Stratified by prior history of hyperammonemia. Mean baseline plasma arginine levels were higher in placebo group vs. treatment group (472 vs. 365 µmol/L) and mean age of treatment group was younger than placebo (9.6 yo vs 12.9 yo) which may bias results in favor of treatment. Other baseline demographics were similar. Performance Bias: Low. Patients, caregivers, and investigators blinded with matching placebo. Detection Bias: Unclear. Outcome assessors blinded to treatment arm. Lab results for arginine may have resulted in unblinding. Investigators were blinded to lab results. Each site had one unblinded physician to manage to protocol-defined dosage adjustments. Attrition Bias: Low. One person in the active treatment arm withdrew from the study for personal reasons. For the primary outcome missing data imputed as change from baseline = 0. No imputation for missing values for secondary outcomes. Reporting Bias: Low. Study protocol available on-line. All prespecified outcomes reported per protocol. Other Bias: High. Funded by the manufacturer. Manufacturer involved in study design, data collection, data analysis, data interpretation and writing of the report. Several authors reported financial support from manufacturer. **Applicability**: Patient: Recruitment limited by the rare prevalence of this condition. The number of people who were on concomitant therapy for hyperammonemia with a nitrogen scavenger was not reported. The average time between diagnosis and treatment was 7 years, and it is unclear if earlier treatment would have more benefit. Intervention: Pegzilarginase dosing assessed in a Phase 2 trial and 90% of people in the treatment group achieved target plasma arginine levels (below 200 µmol/L) and improvements in functional mobility (total n=16). Comparator: Placebo is an appropriate comparator as there are no other approved treatments for arginine deficiency. Outcomes: Plasma arginine levels are a surrogate outcome for treatment efficacy. Improvements in motor function would have been better primary outcomes. 24 weeks may have not been sufficient duration to assess changes in motor function.

Author: Moretz

Date: June 2026

								Setting: Conducted at 19 sites in 7 countries: United States, United Kingdom, Canada, Austria, France, Germany, and Italy. 44% of participants were in the US.

Abbreviations: 2MWT = 2 minute walk test; AE = adverse event; ARR = absolute risk reduction; CI = confidence interval; DB = double-blind; GMFM-E = Gross Motor Function Measure Part E; ITT = intention to treat; IV = intravenous; L = liters; LSMD = least square mean difference; mITT = modified intention to treat; µmol = micromolar; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NS = non-significant; PC = placebo-controlled; PG = parallel group; PP = per protocol; PEG = polyethylene glycol; RCT = randomized controlled trial; TEAE = treatment emergent adverse events; yo = years old

References:

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9. National Institute for Health and Care Excellence. Pegzilarginase for Treating Arginase-1 Deficiency in People 2 years and Over. March 2026. https://www.nice.org.uk/guidance/hst35.

Appendix 1: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LOARGYS safely and effectively. See full prescribing information for LOARGYS.

LOARGYS (pegzilarginase-nbln) injection, for intravenous or subcutaneous use
Initial U.S. Approval: 2026

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS
See full prescribing information for complete boxed warning

Initiate LOARGYS in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. (5.1)

If a severe hypersensitivity reaction (e.g. anaphylaxis) occurs, discontinue LOARGYS, and immediately initiate appropriate medical treatment, including use of epinephrine. (5.1)

----------INDICATIONS AND USAGE----------
LOARGYS 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. (1)

This indication is approved under accelerated approval based on reduction of plasma arginine. (14) Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. (1)

----------DOSAGE AND ADMINISTRATION----------
- Administer LOARGYS under the supervision of a health care provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis. (2.1)
- Initiate LOARGYS in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. (2.1)
- Consider pre-medication with antihistamines. (2.1)
- Obtain a baseline plasma arginine concentration prior to initiating treatment. (2.1)
- Recommended starting dosage of LOARGYS is 0.1 mg/kg administered by intravenous infusion once weekly. (2.2)
- Maximum recommended dosage is 0.2 mg/kg once weekly. (2.2)
- See the Full Prescribing Information for recommended titration and maintenance dosage and recommended plasma arginine level testing during treatment. (2.2)
- After eight weeks of once weekly intravenous LOARGYS, patients may be switched to once weekly subcutaneous LOARGYS at the same dosage of intravenous therapy. (2.4)
- See Full Prescribing Information for dosage and administration modifications due to hypersensitivity reactions. (2.5)
- See Full Prescribing Information for instructions on preparation, storage, and administration. (2.7, 2.8, 2.9, 2.10)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 2 mg/0.4 mL and 5 mg/mL in a single-dose vial. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
Hypersensitivity: If a severe hypersensitivity reaction occurs, discontinue LOARGYS and immediately initiate appropriate medical treatment, including epinephrine. (5.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions (>10%) are vomiting, pyrexia, infusion associated reactions and constipation. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Immedica at toll-free phone 1-844-627-4687 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 2/2026

Appendix 2: Proposed Prior Authorization Criteria

Pegzilarginase-nbln (Loargys®) Injection

Goal(s):

- Ensure appropriate utilization of pegzilarginase-nbln in FDA-approved indications.

Length of Authorization: Up to 12 months

Requires PA:

- LOARGYS (pegzilarginase-nbln) for IV or SC administration (pharmacy and provider administered claims)

Covered Populations: FFS and CCO patients beginning 5/1/26

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for a patient with a prior FFS approval for the requested drug?	**Yes**: Go to **Renewal Criteria**	**No:** Go to #3
3. Is this an FDA approved age and indication?	**Yes**: Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Is the drug prescribed by or in consultation with a provider with expertise in managing metabolic disorders (i.e., urea cycle disorders)?	**Yes**: Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Is the request for therapy to treat hyperargininemia in a patient with arginase 1 deficiency?	**Yes**: Go to #6	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
6. Has the diagnosis been confirmed by genetic testing or documentation of reduced arginase enzyme activity in red blood cells?	**Yes**: Go to #7 Document date and results____ _____	**No:** Pass to RPh. Deny; medical appropriateness
7. Is the patient prescribed a protein restricted diet (below 1.5 g/kg/day at 2 years of age to 0.83 g/kg/day at 18 years of age per World Health Organization guidance)?	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness
8. Is there documentation of elevated plasma arginine levels (>200 µmol/L) within the past 3 months?	**Yes:** Go to #9 Document date and results_____	**No:** Pass to RPh. Deny; medical appropriateness
9. Does the patient have symptomatic hyperammonemia (ammonia ≥100 µmol/L)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #10
10. Is the patient on a stable medication regimen including ammonia scavengers, anti-epileptic drugs, and/or spasticity medications?	**Yes:** Go to #11	**No:** Pass to RPh. Deny; medical appropriateness
11. Is there a documented plan to evaluate arginine levels within the next 4 weeks to determine need for dose adjustments?	**Yes:** Pass to RPh. Pend; Refer to DMAP for secondary review. Duration: Approve for 6 months	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
1. Is the request to renew therapy for treatment of arginase 1 deficiency?	**Yes**: Go to #2	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
2. Have arginine levels decreased by at least 25% from baseline assessment?	**Yes**: Pass to RPh. Pend; Refer to DMAP for secondary review. Duration: Approvals cover up to 12 months. Document results: _____	**No:** Go to #3.
3. Has the provider assessed adherence to treatment and protein restricted diet with a plan to address any identified barriers to care?	**Yes:** Document treatment plan. Pass to RPh. Pend; Refer to DMAP for secondary review. Duration: Approvals cover up to 12 months.	**No:** Pass to RPh. Deny; medical appropriateness. Refer to DMAP for secondary review.

P&T/DUR Review: 6/26 (DM)
Implementation: TBD