Pharmacy Management Drug Policy

SUBJECT: Amyotrophic Lateral Sclerosis (ALS)
POLICY NUMBER: PHARMACY-111
EFFECTIVE DATE: 05/11/2023
LAST REVIEW DATE: 11/19/2025

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Amyotrophic Lateral Sclerosis (ALS) is a rare neurodegenerative condition characterized by progressive muscle weakness and wasting (atrophy). Over time, patients lose the control of voluntary muscles used for walking, talking, eating, and breathing. ALS is ultimately fatal, typically due to respiratory failure, usually within five years from time of symptom onset.[1]

It is estimated that 30,000 people in the United States are affected by ALS and around 5,000 patients are newly diagnosed each year. In majority of cases there is no family history of the disease (sporadic) but approximately 10% of cases are hereditary (familial). A variety of genes have been linked to the disease. The two most common mutations involving the C9ORF72 gene or superoxide dismutase 1 (SOD1) gene, make up almost 50% of familial ALS cases.[2]

Diagnosis of ALS involves a thorough patient history, neurological examination, and a comprehensive series of tests to rule out other conditions. Common classification criteria used for clinical diagnosis of ALS includes the El Escorial and Awaji criteria. Genetic testing may also be useful, particularly in patients with suspected familial ALS.[3]

ALS treatment involves a multidisciplinary approach to manage symptoms, provide supportive care, and slow the progression of the disease. Symptom management may involve antispastic agents such as muscle relaxants, treatments for muscle cramping, and drugs that target excessive salivation. Physical and occupational therapy are important methods to maintain physical mobility while difficulties swallowing, or speaking, may involve speech-language therapy. As patients develop respiratory muscle weakness, non-invasive and invasive respiratory techniques and devices may be employed.[1-4]

FDA-approved treatments for ALS include riluzole (brand: Rilutek tablets,Tiglutik oral suspension), edaravone (brand: Radicava intravenous and Radicava ORS), and sodium phenylbutyrate/taurursodiol (brand Relyvrio). On April 25, 2023, tofersen (brand Qalsody) was FDA approved for the treatment of ALS in adults with the SOD1 gene mutation. Mutations in the SOD1 gene lead to the production of a toxic form of the SOD1 protein, which results in deterioration of motor nerve cells causing progressive muscle weakness. This indication for Qalsody is approved under

accelerated approval based on reduction in plasma neurofilament light chain and continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

According to the American Academy of Neurology (AAN), riluzole should be offered to slow disease progression in patients with ALS (level A recommendation). The guidelines do net yet address any other FDA-approved agents for the treatment of ALS.[4]

This policy contains coverage requirements for the following drugs: Tiglutik (riluzole oral suspension), Radicava and Radicava ORS (edaravone), and Relyvrio (sodium phenylbutyrate and taurursodiol). Qalsody is addressed in a separate policy (see Qalsody (tofersen) Pharmacy-116).

Tiglutik (riluzole oral suspension) is indicated for the treatment of ALS. The efficacy for Tiglutik was based upon bioavailability studies compared to oral riluzole tablets.[5]

Radicava and Radicava ORS (edaravone) is indicated for the treatment of ALS. The approval of Radicava ORS was based on bioavailability data comparing intravenous Radicava and Radicava ORS.[6]

Efficacy of intravenous Radicava was studied in a randomized, placebo-controlled, double-blind study in ALS patients over 6 months. Patients included in the study were required to have functionality retained in most activities of daily living, a percent-predicted forced vital capacity value (% FVC) of $\geq$ 80%, definite or probably ALS based on the El Escorial revised criteria, and a diseases duration of 2 years or less. Patients were randomized to either Radicava (n=69) or placebo (n=68).[6]

The primary efficacy endpoint was change from baseline in the revised ALS functional rating scale (ALSFRS-R) scores during the 24-week treatment period compared to placebo. When compared to placebo, patients in the Radicava group had statistically significant less decline in the ALSFRS-R score from baseline.

Radicava did not demonstrate clinical benefit in a separate 36-week confirmatory study, in patients with “definite”, “probable” or “probable laboratory-supported” ALS and a longer disease duration of 3 years or less.[7]

Relyvrio (sodium phenylbutyrate/taurursodiol) is indicated for the treatment of ALS in adults. The efficacy of Relyvrio was demonstrated in a 24-week, multi-center, randomized, double-blind, placebo-controlled, parallel group study (CENTAUR) trial. Patients had to have a definite diagnosis of sporadic or familial ALS as defined by the revised El Escorial criteria, with symptom onset within the past 18 months, and a slow vital capacity (SVC) $\geq$ 60% of predicted at screening. Patients were randomized 2:1 to receive either Relyvrio (n=89) or placebo (n=48) for 24 weeks intent-to-treat [ITT] population). The primary analysis involved the modified intent-to-treat (mITT) population, which excluded two early patient deaths, both in the Relyvrio arm (n=135 total mITT population).[8] The primary efficacy endpoint was the rate of reduction in ALSFRS-R score from baseline to week 24 compared to placebo. There was a statistically significant difference in the rate of reduction in the ALSFRS-R score from baseline to Week 24 favoring the Relyvrio treated group.

On April 4th,2024, Amylyx announced that it has started a process with the FDA to voluntarily discontinue the marketing authorization for Relyvrio and remove the product from the market in the U.S. This was based on the results from the phase 3 PHEONIX trial. [See below policy for further details].

POLICY:

Tiglutik-riluzole oral suspension (Rx) **Teglutik-riluzole oral suspension (Rx)**
1. Must be ≥ 18 years of age **AND** 2. Must be prescribed by or in consultation with a neurologist, or provider that specializes in Amyotrophic Lateral Sclerosis (ALS) **AND** 3. Must have a diagnosis of ALS **AND** 4. Provider must attest that patient is unable to swallow generic riluzole tablets 5. Quantity Limit: 600 mL/30 days 6. NOTE: Effective January 2024, the FDA granted temporary importation of Teglutik to mitigate the ongoing shortage of FDA-approved Tiglutik.
Radicava injection, generic edaravone injection (medical) **Radicava ORS kit (Rx)**
1. Must be greater than 18 years of age **AND** 2. Must be prescribed by or in consultation with a neurologist, or provider that specializes in Amyotrophic lateral sclerosis (ALS) **AND** 3. According to the prescriber, the patient must have a diagnosis of ALS that meets one of the following: a. "Definite" or "Probable" ALS as determined by revised El Escorial criteria or Awaji criteria (See appendix for criteria) **OR** b. Diagnosis of ALS in accordance with the Gold Coast Criteria (See appendix for criteria) **AND** 4. Must not have tracheostomy (trach) **OR** 5. For patients who have a trach, the provider must attest that the trach is for prevention of aspiration only 6. Radicava and generic edaravone will not be covered for any other non-FDA approved indication 7. Initial and recertification requests will be for 6 months at a time. Recertification requires provider attestation that: a. The patient continues to benefit from therapy **AND** b. The patient is not dependent on invasive ventilation or tracheostomy (unless the trach is for prevention of aspiration only). 8. Recommended Dosing: a. IV: 60mg administered as an IV infusion over 60 minutes. b. Oral Suspension: 105 mg (5 mL) taken orally or via feeding tube in the morning after overnight fasting. Food should not be consumed for 1 hour after administration except water. • Initial treatment cycle: daily dosing for 14 days followed by a 14-day drug-free period • Subsequent treatment cycles: daily dosing for 10 days out of 14-day periods 9. Quantity limits for oral suspension: a. 50 mL bottle: 1 per 28 days b. 70 mL bottle: 1 per 365 days

Relyvrio- sodium phenylbutyrate and taurursodiol (Rx)

On April 4th,2024, Amylyx announced that it has started a process with the FDA to voluntarily discontinue the marketing authorization for Relyvrio and remove the product from the market in the U.S. This was based on the results from the phase 3 PHEONIX trial.

Relyvrio will no longer be available for new patients as, April 4, 2024.

Patients currently on therapy who, in consultation with their physician, wish to continue can be transitioned to a free drug program. Further information may be found at: https://www.amylyx.com/news/amylyx-pharmaceuticals-announces-formal-intention-to-remove-relyvrior/albriozatm-from-the-market-provides-updates-on-access-to-therapy-pipeline-corporate-restructuring-and-strategy and https://www.amylyx.com/patient-support

Based on the above announcement from Amylyx, The Health Plan will not authorize coverage for Relvyrio for new patients or existing users.

APPENDIX:

Revised El Escorial and Awaji diagnostic criteria for amyotrophic lateral sclerosis (ALS)[9]

1. Progressive Symptoms
2. Lower motor neuron (LMN) signs by region (bulbar, cervical, thoracic, lumbosacral)
   a. Clinical: weakness, atrophy, fasciculations
   b. Electromyography (EMG) (limbs: 2 or more muscles innervated by different roots/nerves. Bulbar and thoracic: 1 or more muscles):
      i. Lower motor neuron loss: fibrillation potentials, positive sharp waves, fasciculation potentials (Awaji only)
      ii. Reinnervation: large motor units and reduced recruitment
3. Upper motor neuron (UMN) signs by region (bulbar, cervical, thoracic, lumbosacral)
   a. Clinical: hyperreflexia, spasticity, pathologic reflexes

Clinically Possible ALS

- Clinical/EMG evidence of UMN and LMN signs in 1 region **OR**
- Isolated UMN signs in 2 or more regions **OR**
- LMN signs rostral to UMN signs

Clinically Probable Laboratory-supported ALS (El Escorial only)

- Clinical UMN and LMN signs in 1 region and LMN signs in 2 regions.

Clinically Probable ALS

- Clinical/EMG evidence of LMN and UMN signs in 2 or more regions
- Some UMN signs necessarily rostral to LMN signs

Clinically Definite ALS

- Clinical/EMG evidence of LMN and UMN signs in 3 or more regions.

Reference: Quinn C, Elman L. Amyotrophic lateral sclerosis, and other motor neuron diseases. Continuum 2020; 26:1323.

Gold Coast criteria[10]

1. Progressive motor impairment documented by history or repeated clinical assessment, preceded by normal motor function, **AND**
2. Presence of upper and lower motor neuron dysfunction in at least 1 body region, (with upp and lower motor neuron dysfunction noted in the same body region if only one body regio involved) or lower motor neuron dysfunction in at least 2 body regions, **AND**
3. Investigations excluding other disease processes

See reference for criteria details: Shefner JM, Al-Chalabi A, Baker MR, et al. A proposal for new diagnostic criteria for ALS. *Clin Neurophysiol*. 2020;131(8):1975-1978.

APPROVAL TIME PERIODS – INITIAL AND RECERTIFICATION REVIEWS:

1. Unless otherwise stated within the individual drug criteria, approval time periods are listed in the table below
2. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary [Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics or other guideline-supported treatment options)] and the requested dose must continue to meet FDA approved or off-label/guideline supported dosing

Line of Business	Rx Initial approval	Rx Continued approval	Medical Initial approva	Medical Recert
Commercial, Exchange SafetyNet (Medicaid, HARP, CHP, Essential Plan)	6 months (or as stated within individual drug policy)	6 months (or as stated within individual drug policy)	All sites of service – 6 months	All sites of service – 6 months
Medicare	Defined in Medicare Drug Policy	Defined in Medicare Drug Policy	All sites of service – 6 months	All sites of service – 6 months

POLICY GUIDELINES:

1. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
2. This policy is applicable to drugs that are included on a specific drug formulary (Rx benefit only). If a drug referenced in this policy is non-formulary, please reference the Non-Formulary Medication Exception Review Policy for review guidelines.
3. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
4. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.

5. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
6. Supportive documentation of previous drug use must be submitted for any criterion that requires the trial of a preferred agent if the preferred drug is not found in claims history.
7. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, and imaging.
8. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
9. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required. The provider must make their intent to override a trial of the preferred drugs clear and must provide rationale and supporting documentation for one of the following:
    - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    - The required prescription drug(s) is (are) not in the patient’s best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
    - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
    - The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.
10. Some drugs will require prior authorization prior to criteria being added to the policy.
11. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
12. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.

13. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).

HCPCS:

Drug Name	J-code (if assigned)
Radicava and edaravone injection	J1301

UPDATES:

Date	Revision
11/19/2025	Revised
05/08/2025	Reviewed / P&T Committee Approval
03/06/2025	Revised
12/19/2024	Revised
08/20/2024	Revised
06/24/2024	Revised
05/09/2024	P&T Committee Approval
04/12/2024	Revised
03/27/2024	Revised
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02/09/2024	Revised
12/06/2023	Revised
05/30/2023	Revised
05/11/2023	Created
05/11/2023	P&T Committee Approval

REFERENCES:

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3. Quinn C, Elman L. Amyotrophic lateral sclerosis, and other motor neuron diseases. *Continuum*. 2020; 26:1323
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5. Tiglutik [package insert]. Berwyn, PA: Itf Pharma, Inc.; April 2021.
6. Radicava and Radicava ORS [package insert]. Jersey City, NJ: Mitsubishi Tanabe Pharma America, Inc.; December 2022.
7. Abe K, Itoyama Y, Sobue G, et al. Confirmatory double-blind, parallel-group, placebo-controlled study of efficacy and safety of edaravone (MCI-186) in amyotrophic lateral sclerosis patients. *Amyotroph Lateral Scler Frontotemporal Degener*. 2014;15(7-8):610-617.
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