Clinical Policy: Edaravone (Radicava, Radivaca ORS)

Reference Number: LA.PHAR.343
Effective Date: 12.21.23
Last Review Date: 05.12.25
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Edaravone (Radicava®, Radicava ORS®) is a member of the substituted 2-pyrazolin-5-one class that acts as a free-radical scavenger of peroxyl radicals and peroxynitrite.

FDA Approved Indication(s)

Radicava and Radicava ORS are indicated for the treatment of amyotrophic lateral sclerosis (ALS).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that edaravone, Radicava, and Radicava ORS are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Amyotrophic Lateral Sclerosis (must meet all)**:**

1. Diagnosis of definite or probable ALS per the revised El Escorial/Airlie House diagnostic criteria (*see Appendix D)*;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Concomitant use of riluzole (at up to maximally indicated doses) unless contraindicated or clinically significant adverse effects are experienced;
5. Independent living status (defined as patients who can eat a meal, excrete, or move with oneself alone, and do not need assistance in everyday life);
6. Percent predicted forced vital capacity (% FVC) ≥ 80%;
7. Disease duration of ≤ 2 years;
8. Baseline revised ALS Functional Rating Scale (ALSFRS-R) score with ≥ 2 points in each of the 12 items;
9. For brand intravenous Radicava requests, member must use generic intravenous edaravone, unless contraindicated or clinically significant adverse effects are experienced;
10. Dose does not exceed any of the following (a, b, and c):
    a. One of the following (i or ii):
        i. For intravenous administration: 60 mg per day for each treatment cycle;

ii. For oral administration: 105 mg per day for each treatment cycle;

b. For initial treatment cycle: daily dosing for 14 days followed by a 14-day drug-free period;

c. For subsequent treatment cycles: daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

II. Continued Therapy

A. Amyotrophic Lateral Sclerosis (must meet all)**:**

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member continues to meet all of the following criteria (a, b, and c):
   a. Independent living status;
   b. Percent predicted forced vital capacity (% FVC) ≥ 80%;
   c. Revised ALSFRS-R score with ≥ 2 points in each of the 12 items;
4. For brand intravenous Radicava requests, member must use generic intravenous edaravone, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. Either of the following (i or ii):
      i. For intravenous administration: 60 mg per day for each treatment cycle;
      ii. For oral administration: 105 mg per day for each treatment cycle;
   b. Treatment cycle consisting of daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods.

Approval duration: 6 months

B. Other diagnoses/indications (1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALS: amyotrophic lateral sclerosis
ALSFRS-F: revised ALS Functional Rating Scale
FDA: Food and Drug Administration
FVC: forced vital capacity
LMN: lower motor neuron
UMN: upper motor neuron

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
riluzole (Rilutek®)	50 mg PO BID	100 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to edaravone or any of the inactive ingredients in Radicava and/or Radicava ORS
- Boxed warning(s): none reported

Appendix D: General Information

- Revised El Escorial/Airlie House diagnostic criteria for ALS requires the presence of:
  1. Signs of lower motor neuron (LMN) degeneration by clinical, electrophysiological or neuropathologic examination,
  2. Signs of upper motor neuron (UMN) degeneration by clinical examination, and
  3. Progressive spread of symptoms or signs within a region or to other regions, together with the absence of:
     a. Electrophysiological evidence of other disease processes that might explain the signs of LMN and/or UMN degenerations; and
     b. Neuroimaging evidence of other disease processes that might explain the observed clinical and electrophysiological signs.
- The definitions of ALS diagnoses provided by the revised El Escorial/Airlie House criteria are as follows:

	Revised El Escorial/Airlie House diagnostic criteria
Clinically definite ALS	Clinical evidence alone of UMN and LMN signs in ≥ 3 regions
Clinically probable ALS	Clinical evidence alone of UMN and LMN signs in ≥ 2 regions with some UMN signs rostral to (above) LMN signs

	Revised El Escorial/Airlie House diagnostic criteria
Clinically probable lab-supported ALS	Clinical signs of UMN and LMN dysfunction in 1 region OR UMN signs in 1 region, and LMN signs defined by EMG criteria in ≥ 2 regions
Clinically possible ALS	Clinical signs of UMN and LMN dysfunction in 1 region OR Isolated UMN signs in ≥ 2 regions OR LMN signs rostral to UMN signs

- Two pivotal phase III trials that were conducted in Japan were used for the approval of Radicava in the USA. One of the phase III trials of Radicava found no statistically significant difference in delay of ALS progression, but a post-hoc analysis found that a certain subset of patients may benefit. Based on the post-hoc analysis, the second phase III was performed with a much more strict eligibility criteria and found a statistically significant difference in ALS progression in favor of Radicava. Therefore, patients not meeting the strict eligibility criteria at any time (at the time of initial or continued approval) can be assumed that no benefit will be provided by the use of Radicava for the treatment of ALS until further studies support its use in a wider population with ALS.
- The revised ALS Functional Rating Scale (ALSFRS-R) score consists of a total of 12 items and 48 points. It is a physician-generated estimate of the patient's degree of functional impairment. Each item assesses the patient's functional ability on daily tasks, such as walking and hand-writing. Each item is scored from 0 to 4 points, with 0 indicating no ability and 4 indicating normal ability.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ALS	Oral: 105 mg PO in the morning per initial and subsequent treatment cycles below IV: 60 mg IV (60 mg dose as an intravenous infusion over a total of 60 minutes at an infusion rate approximately 1 mg per minute) per initial and subsequent treatment cycles below Treatment cycles for oral and IV administrations: • 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, followed by 14-day drug-free periods. Patients treated with 60 mg of Radicava IV infusion may be switched to 105 mg (5 mL) Radicava ORS using the same dosing frequency.	Oral: 105 mg/day IV: 60 mg/day

VI. Product Availability

Drug Name	Availability
edaravone (Radicava)	Single-dose polypropylene bags for injection: • Brand: 30 mg/100 mL • Generic: 30 mg/100 mL, 60 mg/100 mL
edaravone (Radicava ORS)	Multi-dose oral suspension: 105 mg/5 mL

VII. References

1. Radicava Prescribing Information. Jersey City, NJ: MT Pharma America, Inc.; November 2022. Available at: https://www.radicava.com. Accessed January 15, 2025.
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3. 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. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration. 2014;15(7-8), 610-617.
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6. Anderson PM, Borasio GD, Dengler R, et al. Good practice in the management of amyotrophic lateral sclerosis: Clinical guidelines. An evidence-based review with good practice points. EALSC Working Group. Amyotrophic Lateral Sclerosis. 2007; 8:195-231.
7. Hardiman O, van den Berg LH, and Kiernan MC. Clinical diagnosis and management of amyotrophic lateral sclerosis. Nature Reviews Neurology 2011; 7: 639-649. doi:10.1038/nrneurol.2011.153
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9. Shoesmith C, Abrahao A, Benstead T, et al. Canadian best practice recommendations for the management of amyotrophic lateral sclerosis. CMAJ. 2020 Nov;192(46):E1453-E1468.
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11. Van Damme P, Al-Chalabi A, Andersen PM, et al. European Academy of Neurology (EAN) guideline on the management of amyotrophic lateral sclerosis in collaboration with European Reference Network for Neuromuscular Diseases (ERN EURO-NMD). Eur J Neurol. 2024;31(6):e16264.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals (edaravone oral suspension)
J1301	Injection, edaravone, 1 mg
J8499	Prescription drug, oral, non chemotherapeutic, nos (edaravone oral suspension)

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	06.20.23	10.24.23
Annual review: no significant changes; updated Appendix D table of ALS diagnosis definitions per revised El Escorial criteria; references reviewed and updated.	05.07.24	07.29.24
Annual review: added edaravone to the Policy/Criteria applicability section; added generic redirection for IV Radicava request to initial and continued criteria; in initial criteria and Appendix D, clarified that "El Escorial" refers to revised El Escorial or Airlie House; references reviewed and updated.	05.12.25	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between

the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

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