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Edaravone

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Edaravone (Radicava®) **may be considered medically necessary** for the treatment of individuals with amyotrophic lateral sclerosis (ALS) who meet the following criteria on initiation:

- Individuals 18 years of age and older; AND
- Individuals diagnosed with definite or probable ALS based on El Escorial revised criteria (see **NOTE 1**); AND
- Individuals have retained most activities of daily living (defined as scores of 2 points or better on each individual item of the ALS Functional Rating Scale-Revised (ALSFRS-R; see **NOTE 1)**; AND
- Normal respiratory function (defined as percent-predicted forced vital capacity values of [% FVC] greater than or equal to 80%) **(see Policy Guidelines)**; AND
- Disease duration of 2 years or less.

Edaravone (Radicava®) **is considered experimental, investigational, and/or unproven** when the criteria above are not met and for all other non-Food and Drug Administration approved indications.

NOTE 1: Refer to the Description section for definitions of the El Escorial revised criteria and the ALSFRS-R.

NOTE 2: Radicava ORS® is self-administered. For self-administered medications, please refer to applicable pharmacy benefit plan.

Policy Guidelines

Spirometry results (particularly % predicted values) should not be adjusted for race or, if race was included in the calculations, results should be recalculated without the race-based adjustment. (2)

Description

Edaravone (Radicava®) is a drug for the treatment of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. ALS is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. The onset of ALS often involves muscle weakness or stiffness as early symptoms. Progression of weakness, wasting and paralysis of the muscles of the limbs and trunk as well as those that control vital functions such as speech, swallowing and

later breathing generally follows. Currently, there is no cure for ALS and no effective treatment to halt, or reverse, the progression of the disease. As of 2024, the Centers for Disease Control and Prevention reported that every year around 5,000 people are newly diagnosed with ALS in the United States. Most people find out they have it when they are between 55 and 75 years of age and live from 2 to 5 years after symptoms develop. (3, 4)

The clinical standard for the diagnosis of ALS is the revised El Escorial World Federation of Neurology criteria, also known as the Airlie House criteria. These criteria allow assignment of diagnostic certainty and were designed for research purposes to ensure appropriate inclusion of patients into clinical trials. (5)

Revised El Escorial Schema for the Clinical Diagnosis of ALS
(The body is divided into four regions: cranial, cervical, thoracic, and lumbosacral)

- Clinically Definite ALS: Defined on clinical evidence alone by the presence of upper motor neuron (UMN) signs, as well as lower motor neuron (LMN) signs, in three regions.
- Clinically Probable ALS: Defined on clinical evidence alone by UMN and LMN signs in at least two regions with some UMN signs necessarily rostral to the LMN signs.
- Clinically Probable-Laboratory-Supported ALS: Defined when clinical signs of UMN and LMN dysfunction are in only one region, or when UMN signs alone are present in one region, and LMN signs defined by electromyography (EMG) criteria are present in at least 2 limbs, with proper application of neuroimaging and clinical laboratory protocols to exclude other causes.
- Clinically Possible ALS: Defined when clinical signs of UMN and LMN dysfunction are found together in only one region or UMN signs are found alone in two or more regions; or LMN signs are found rostral to UMN signs and the diagnosis of Clinically Probable-Laboratory-Supported ALS cannot be proven by evidence on clinical grounds in conjunction with electrodiagnostic, neurophysiologic, neuroimaging or clinical laboratory studies. Other diagnoses must have been excluded to accept a diagnosis of Clinically Possible ALS.
- Clinically Suspected ALS: Defined as a pure LMN syndrome, wherein the diagnosis of ALS could not be regarded as sufficiently certain to include the patient in a research study.

ALS Functional Rating Scale-Revised (ALSFRS-R)
The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (speech, salivation, swallowing, handwriting, cutting food, dressing/hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency). (1) Each item is scored from 0 to 4, with higher scores representing greater functional ability.

Regulatory Status
On May 5, 2017, the U.S. Food and Drug Administration (FDA) approved edaravone (Radicava®) (Mitsubishi Tanabe Pharma America, Inc.) for treatment of patients with amyotrophic lateral sclerosis. (1) Edaravone is for intravenous infusion and oral suspension. Radicava ORS® is an oral suspension and self-administered. For self-administered medications, please refer to applicable

pharmacy benefit plan. Safety and effectiveness in pediatric patients have not been established.

Rationale

This policy is based on the U.S. Food and Drug Administration (FDA) labeled indications for edaravone (Radicava®).

The efficacy of edaravone (Radicava®) for the treatment of amyotrophic lateral sclerosis (ALS) was based on a 6-month, phase III, randomized, placebo-controlled, double-blind study. (1) The study was conducted in Japanese patients who lived independently and met the following criteria at screening:

1. Functionality retained most activities of daily living (defined as scores of 2 points or better on each individual item of the ALS Functional Rating Scale – Revised (ALSFRS-R);
2. Normal respiratory function (defined as percent-predicted forced vital capacity values of [%FVC] ≥ 80%);
3. Definite or probable ALS based on El Escorial revised criteria;
4. Disease duration of 2 years or less.

The study enrolled 69 patients in the Radicava® arm and 68 in the placebo arm. Baseline characteristics were similar between these groups, with over 90% of patients in each group being treated with riluzole. Radicava® was administered as an intravenous infusion of 60 mg given over a 60-minute period according to the following schedule:

- An initial treatment cycle with daily dosing for 14 days, followed by a 14-day drug-free period (Cycle 1);
- Subsequent treatment cycles with daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods (Cycles 2-6).

The primary efficacy endpoint was a comparison of the change between treatment arms in the ALSFRS-R total scores from baseline to Week 24. The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (speech, salivation, swallowing, handwriting, cutting food, dressing/hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency). Each item is scored from 0-4, with higher scores representing greater functional ability. The decline in ALSFRS-R scores from baseline was significantly less in the Radicava®-treated patients as compared to placebo. The most common adverse reactions that occurred in ≥ 10% of Radicava® treated patients were contusion, gait disturbance, and headache. Radicava® is also associated with serious risks that require immediate medical care, such as hives, swelling, or shortness of breath, and allergic reactions to sodium bisulfite, an ingredient in the drug. Sodium bisulfite may cause anaphylactic symptoms that can be life-threatening in people with sulfite sensitivity.

Summary of Evidence

The evidence is sufficient to support the use of edaravone (Radicava®) for the U.S. Food and

Drug Administration (FDA) approved indications, which is based on the clinical trial outcomes documented in the published FDA labeling.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J1301

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. FDA - Radicava® (edaravone injection) – Product Label (May 2017, revised November 2022). U.S. Food and Drug Administration. Available at <https://www.accessdata.fda.gov> (accessed May 5, 2025).

Other:

2. Bhakta NR, Bime C, Kaminsky DA, et al. Race and Ethnicity in Pulmonary Function Test Interpretation: An Official American Thoracic Society Statement. Am J Respir Crit Care Med. Apr 15 2023; 207(8):978-995. PMID: 36973004
3. ALS Association. What is ALS? (Updated April 2024). Available at <https://www.als.org> (accessed May 5, 2025).
4. CDC – Center for Disease Control and Prevention. National Amyotrophic Lateral Sclerosis (ALS) Registry. FAQ (November 12, 2024). Available at <https://www.cdc.gov> (accessed May 5, 2025).
5. Elman LB, McCluskey L. Diagnosis of amyotrophic lateral sclerosis and other forms of motor neuron disease. In: UpToDate, Shefner JM (Ed), UpToDate, Waltham, MA. Available at <https://www.uptodate.com> (accessed May 5, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
08/15/2025	Document updated with literature review. The following change was made to coverage: Added “non-Food and Drug Administration approved” to the existing experimental, investigational and/or unproven statement. Coverage reorganized with movement of some criteria to Policy Guidelines; no change to policy intent. Added reference 2; others removed/updated.
05/15/2024	Document updated with literature review. The following changes were made to Coverage: 1) Removed 6-month limitation on initial approval; and 2) Removed continuation criteria. No new references added.
03/15/2023	Document updated with literature review. Coverage unchanged. Reference 2 added; some updated and others removed.
08/15/2022	Reviewed. Coverage unchanged, except NOTE 3 added for Radicava ORS.
05/01/2021	Document updated with literature review. Coverage unchanged. One reference removed and others updated.
08/15/2020	Reviewed. No changes.
09/15/2019	Document updated with literature review. Coverage unchanged. References 8-11 added.
07/15/2018	Reviewed. No changes.
10/01/2017	New medical document. Edaravone (Radicava™) may be considered medically necessary for the treatment of individuals with amyotrophic lateral sclerosis (ALS) who meet the following criteria: For initial 6-month therapy, ALL of the following: Individuals 18 years of age and older; and Individual is diagnosed with definite or probable ALS based on El Escorial revised criteria; and Individuals have retained most activities of daily living (defined as scores of 2 points or better on each individual item of the ALS Functional Rating Scale-Revised; and Normal respiratory function (defined as percent-predicted forced vital capacity values of [%FVC] greater than or equal to 80%); and Disease duration of 2 years or less. For continuation therapy, ALL of the following: There is documentation indicating that edaravone (Radicava™) use has slowed the progression of ALS; and Overall function should be improved/superior relative to that projected for the natural course of ALS. Edaravone (Radicava™) is considered experimental, investigational, and/or unproven when the criteria above are not met and for all other indications.