Clinical Policy: Edaravone (Radicava)

Reference Number: PA.CP.PHAR.343
Effective Date: 01/18
Last Review Date: 04/18 Revision Log

Description
Edaravone (Radicava™) 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
Radicava is indicated for the treatment of amyotrophic lateral sclerosis (ALS).

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with PA Health and Wellness® that Radicava is **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 El Escorial and revised Airlie House diagnostic criteria - **see appendix B*;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 20 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. Forced vital capacity ≥ 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 (total 48 points);
9. Dose does not exceed 60 mg/day for:
   a. Initial treatment cycle: daily dosing for 14 days followed by a 14-day drug-free period;
   b. 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:

1. Refer to CP.PMN.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via PA Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g.per prescriber's assessment);
3. Patient continues to meet the following criteria:
   a. Independent living status;
   b. Forced vital capacity ≥ 80%;
   c. Revised ALSFRS-R score with ≥ 2 points in each of the 12 items (total 48 points);
4. If request is for a dose increase, new dose does not exceed 60 mg/day for each 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. Currently receiving medication via PA Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to CP.PMN.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

Appendix B: General Information

- Revised El Escorial 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 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 El Escorial criteria and the revised Airlie House criteria (incorporating the Awaji–Shima criteria, which has been shown to have high specificity and sensitivity) are as follows:

	El Escorial criteria, 1994	Revised Airlie House criteria, 1998 (incorporating the Awaji–Shima criteria, 2008)

Definite ALS	Upper and lower motor neuron signs in three regions	Clinical or electrophysiological evidence, demonstrated by the presence of upper and lower motor neuron signs in the bulbar region and at least two spinal regions, or the presence of upper and lower motor neuron signs in three spinal regions
Probable ALS	Upper and lower motor neuron signs in at least two regions, with upper motor neuron signs rostral to lower motor neuron signs	Clinical or electrophysiological evidence, demonstrated by upper and lower motor neuron signs in at least two spinal regions, with some upper motor neuron signs necessarily rostral to the lower motor neuron signs
Possible ALS	Upper and lower motor neuron signs in one region, upper motor neuron signs alone in two or more regions, or lower motor neuron signs rostral to upper motor neuron signs	Clinical or electrophysiological signs of upper and lower motor neuron dysfunction in only one region, or upper motor neuron signs alone in two or more regions, or lower motor neuron signs rostral to upper motor neuron signs
Suspected ALS	Lower motor neuron signs only, in two or more regions	N/A

- 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.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

ALS	60 mg IV (2 consecutive 30 mg intravenous infusion bags) over 60 minutes at an infusion rate of approximately 1 mg/3.33mL per minute) as follows: • 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.	60 mg/day

V. Product Availability

Single-dose polypropylene bag for injection: 30 mg/100 mL

VI. References

1. Radicava Prescribing Information. Jersey City, NJ: MT Phrama America, Inc.; May 2016. Available at: www.radicava.com. Accessed January 2018.
2. The Writing Group. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomized, double-blind, placebo-controlled trial. Lancet Neurol. 2017; S1474-4422(17)30115-1.
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.
4. Yoshino H and Kimura A. Investigation of the therapeutic effects of edaravone, a free radical scavenger, on amyotrophic lateral sclerosis (Phase II study). Amyotrophic Lateral Sclerosis. 2006;7(4), 247-251.
5. 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.
6. 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

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: added continuity of care language; references reviewed and updated.	02.02.18	