

# Clinical Criteria

<b>Subject:</b>	Radicava (edaravone)		
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## Overview

This document addresses the use of Radicava (edaravone) for treatment of Amyotrophic Lateral Sclerosis (ALS). ALS (commonly known as Lou Gehrig's disease) is a refractory and progressive neuromuscular disease that attacks nerve cells in the spine and brain that are responsible for controlling voluntary movement; the cause of the disease is not known. Median survival from onset to death in ALS is reported to vary from 20 to 48 months. Radicava is an intravenously administered free radical scavenger that is thought to reduce oxidative stress, which may contribute to ALS. It may be used alone or in combination with the oral ALS drug riluzole.

Early studies of Radicava included patients with a wide range of disease severity. These studies suggested that Radicava may be effective in a subgroup of patients who were in an earlier stage of the disease. This prompted a phase 3 study (Writing Group 2017) which included patients with definite or probable ALS with a disease duration of 2 years or less, Japan ALS severity classification grade <3, preserved functionality in most activities of daily living (defined as a score of 2 or higher on all items of the ALS Functional Rating Scale-revised; ALSFRS-R), and normal respiratory function with FVC  $\geq$  80%.

Of note, a 24-week, exploratory double-blind, parallel group, placebo-controlled study of Radicava (n=25) was also conducted in patients with later stages or more advanced disease, specifically, those with Japan ALS severity classification of Grade 3. This exploratory analysis did not show a statistically significant difference in the ALSFRS-R score compared to placebo. Due to various limitations of the study, the authors concluded that the effect of Radicava in those with Japan ALS Grade 3 disease remains a topic to be explored.

## Diagnostic Criteria

**Awaji-Shima criteria** (Douglass, 2010; Hardiman, 2011): Diagnostic criteria used for ALS consisting of the following categories:

**Clinically definite ALS** is defined on 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.

**Clinically probable ALS** is defined on 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.

**Clinically possible ALS** is defined on 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.

**EI Escorial/revised Airlie House criteria** (EI Escorial is also known as Airlie House; Brooks 2000; Douglass 2010): Diagnostic criteria for ALS. Designed for research purposes to ensure appropriate inclusion of subjects into clinical trials. Consists of the following categories:

**Clinically Definite ALS** is defined on clinical evidence alone by the presence of upper motor neuron (UMN), as well as lower motor neuron (LMN) signs, in the bulbar region and at least two spinal regions or the presence of UMN and LMN signs in three spinal regions.

**Clinically Probable ALS** is defined on clinical evidence alone by UMN and LMN signs in at least two regions with some UMN signs necessarily rostral to (above) the LMN signs.

**Clinically Probable - Laboratory-Supported ALS** is 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 EMG criteria are present in at least two regions, with proper application of neuroimaging and clinical laboratory protocols to exclude other causes.

**Clinically Possible ALS** is 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.

### Japan ALS Severity Classification; (Abe 2014)

Classification grade based on the severity of the disease; ranges from 1 to 5 as follows:

1. Able to work or perform housework;\*
2. Independent living but unable to work;\*
3. Requiring assistance for eating, excretion, or ambulation;
4. Presence of respiratory insufficiency, difficulty in coughing out sputum, or dysphagia; and
5. Using a tracheostomy tube, tube feeding, or tracheostomy positive pressure ventilation.

\*\*Individuals who can eat a meal, excrete, or move with oneself alone, and do not need assistance in everyday life

### ALS Functional Rating Scale-revised (ALSFRS-R); (Cedarbaum 1999)

A commonly used functional rating system for persons with ALS, scored as follows:

#### Speech

- 4 Normal speech processes
- 3 Detectable speech disturbance
- 2 Intelligible with repeating
- 1 Speech combined with nonvocal communication
- 0 Loss of useful speech

**Salivation**

- 4 Normal
- 3 Slight but definite excess of saliva in mouth; may have nighttime drooling
- 2 Moderately excessive saliva; may have minimal drooling
- 1 Marked excess of saliva with some drooling
- 0 Marked drooling; requires constant tissue or handkerchief

#### Swallowing

- 4 Normal eating habits
- 3 Early eating problems — occasional choking
- 2 Dietary consistency changes
- 1 Needs supplemental tube feeding
- 0 NPO (exclusively parenteral or enteral feeding)

#### Handwriting

- 4 Normal
- 3 Slow or sloppy; all words are legible
- 2 Not all words are legible
- 1 Able to grip pen but unable to write
- 0 Unable to grip pen

#### Cutting food and handling utensils (patients without gastrostomy)

- 4 Normal
- 3 Somewhat slow and clumsy, but no help needed
- 2 Can cut most foods, although clumsy and slow; some help needed
- 1 Food must be cut by someone, but can still feed slowly
- 0 Needs to be fed

#### Cutting food and handling utensils (alternate scale for patients with gastrostomy)

- 4 Normal
- 3 Clumsy but able to perform all manipulations independently
- 2 Some help needed with closures and fasteners
- 1 Provides minimal assistance to caregiver
- 0 Unable to perform any aspect of task

#### Dressing and hygiene

- 4 Normal function
- 3 Independent and complete self-care with effort or decreased efficiency
- 2 Intermittent assistance or substitute methods
- 1 Needs attendant for self-care
- 0 Total dependence

#### Turning in bed and adjusting bed clothes

- 4 Normal
- 3 Somewhat slow and clumsy, but no help needed
- 2 Can turn alone or adjust sheets, but with great difficulty
- 1 Can initiate, but not turn or adjust sheets alone
- 0 Helpless

#### Walking

- 4 Normal
- 3 Early ambulation difficulties
- 2 Walks with assistance
- 1 Nonambulatory functional movement
- 0 No purposeful leg movement

#### Climbing stairs

- 4 Normal
- 3 Slow
- 2 Mild unsteadiness or fatigue
- 1 Needs assistance
- 0 Cannot do

#### Dyspnea (new)

- 4 None
- 3 Occurs when walking
- 2 Occurs with one or more of the following: eating, bathing, dressing (ADL)
- 1 Occurs at rest, difficulty breathing when either sitting or lying
- 0 Significant difficulty, considering using mechanical respiratory support

#### Orthopnea (new)

- 4 None
- 3 Some difficulty sleeping at night due to shortness of breath, does not routinely use more than two pillows
- 2 Needs extra pillows in order to sleep (more than two)
- 1 Can only sleep sitting up
- 0 Unable to sleep

#### Respiratory insufficiency (new)

- 4 None
- 3 Intermittent use of BiPAP
- 2 Continuous use of BiPAP during the night
- 1 Continuous use of BiPAP during the night and day
- 0 Invasive mechanical ventilation by intubation or tracheostomy

## Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

### Radicava (edaravone)

Requests for Radicava (edaravone) may be approved if the following criteria are met (Writing Group 2017):

- I. Individual is diagnosed with definite or probable amyotrophic lateral sclerosis (based on El Escorial/revised Airlie House criteria or Awaji-Shima criteria); **AND**

II. Onset of amyotrophic lateral sclerosis (ALS) has been less than 2 years at time of therapy initiation; **AND**  
III. Japan ALS severity classification grade is less than 3 at time of therapy initiation; **AND**  
IV. Score of 2 or more points on each single revised ALS Functional Rating Scale (ALSFRS-R) item at time of therapy initiation; **AND**  
IV-V. Individual has normal respiratory function defined as forced vital capacity (FVC) of greater than or equal to 80%.

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Requests for Radicava (edaravone) may not be approved when the above criteria are not met and for all other indications.

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

### HCPCS

J1301 Injection, edaravone, 1 mg [Radicava]

### ICD-10 Diagnosis

G12.21 Amyotrophic lateral sclerosis

## Document History

Revised: 02/21/2020

Document History:

- 02/21/2020 – Select Review: Update criteria to include requirement of normal respiratory function per clinical trials. Coding Review: No changes.
- 11/15/2019 – Annual Review: Wording and formatting changes.
- 11/16/2018 – Annual Review: Initial P&T review of Radicava (edaravone); Minor wording and formatting changes; add references. HCPCS, ICD-10 coding update. Deleted C9399, J3490. Added J1301 effective 1/1/2019.

## References

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