Radicava (edaravone)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Initial requests: 6 months Continuation requests: 1 year

Medications	Quantity Limit
Radicava IV (edaravone)	N/A
Radicava ORS (edaravone oral suspension)	May be subject to quantity limit

APPROVAL CRITERIA

Initial requests for Radicava (edaravone) IV or ORS 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. Documentation is provided that Japan ALS severity classification grade* is less than 3 at time of therapy initiation; **AND**
IV. Documentation is provided that there is a score of 2 or more points on each single revised ALS functional Rating Scale (ALSFRS-R)* item at time of therapy initiation; **AND**
V. Documentation is provided that individual has normal respiratory function defined as forced vital capacity (FVC) of greater than or equal to 80% at the time of initiation.

Continuation requests for Radicava (edaravone) IV or ORS may be approved if the following criteria are met:

I. Individual does not require mechanical ventilation by intubation or tracheostomy.

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

*See definition section below for description

***DEFINITIONS**:
ALS functional rating scale (revised) (ALSFRS-R): A commonly used functional rating system for persons with ALS (Cedarbaum, 1999):

1. Speech
   4 Normal speech processes
   3 Detectable speech disturbance
   2 Intelligible with repeating

1 Speech combined with nonvocal communication
0 Loss of useful speech

2. 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

3. 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)

4. 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

5. 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

6. 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

7. 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

8. 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

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

10. Climbing stairs
    4 Normal
    3 Slow
    2 Mild unsteadiness or fatigue
    1 Needs assistance
    0 Cannot do

11. 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

12. 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

13. 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

Awaji-Shima criteria: Diagnostic criteria used for ALS (Douglass, 2010; Hardiman, 2011) 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.

El Escorial/revised Airlie House criteria (El Escorial is also known as Airlie House): Diagnostic criteria for ALS (Brooks, 2000; Douglass, 2010). 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 grade: A Japanese ALS classification grade based on the severity of the disease. The grade ranges from 1 to 5 as follows (Abe, 2014):

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.

Key References:

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2. Brooks BR, Miller RG, Swash M, Munsat TL. World Federation of Neurology Research Group on Motor Neuron Diseases. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2000; 1(5):293-299.
3. Cedarbaum JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci. 1999; 169(1-2):13-21.
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5. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: May 25, 2022.
6. Douglass CP, Kandler RH, Shaw PJ, McDermott CJ. An evaluation of neurophysiological criteria used in the diagnosis of motor neuron disease. J Neurol Neurosurg Psychiatry. 2010; 81(6):646-649.
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9. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2021; Updated periodically.
10. Miller RG, Jackson CE, Kasarskis EJ,et al. Practice Parameter update: The care of the patient with amyotrophic lateral sclerosis: Drug, nutritional, and respiratory therapies (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology Oct 2009, 73 (15) 1218-1226; DOI: 10.1212/WNL.0b013e3181bc0141. Reaffirmed Jan 2020. Accessed October 11, 2021.
11. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice Parameter update: The care of the patient with amyotrophic lateral sclerosis: Multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology Oct 2009, 73 (15) 1227-1233; DOI: 10.1212/WNL.0b013e3181bc01a4. Reaffirmed Jan 2020. Accessed October 11, 2021.
12. Writing Group; Edaravone (MCI-186) ALS 19 Study Group. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. *Lancet Neurol*. 2017;16:505-512.
13. The Writing Group on behalf of the edaravone (MCI-186) ALS 18 study group (2017) Exploratory double-blind, parallel-group, placebo-controlled study of edaravone (MCI-186) in amyotrophic lateral sclerosis (Japan ALS severity classification: Grade 3, requiring assistance for eating, excretion or ambulation), Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 18:sup1, 40-48.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.