Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Edaravone (Radicava®)	MP-RX-FP-75-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B DRUG

Service Description

This document addresses the use of edaravone (Radicava®) , a drug approved by the Food and Drug Administration (FDA) for the treatment of Amyotrophic Lateral Sclerosis (ALS).

Background Information

This document addresses the use of Radicava® (edaravone) for the 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 available intravenously (IV) and as an oral suspension (ORS). It is a free radical scavenger that is thought to reduce oxidative stress, which may contribute to ALS. Radicava® may be used alone or in combination with the oral ALS drug riluzole.

Early studies of Radicava® IV 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 ≥ 80%.

Of note, a 24-week, exploratory double-blind, parallel group, placebo-controlled study of Radicava IV (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.

Radicava® ORS FDA-approval was based on a bioavailability study comparing it to Radicava® IV. Radicava® ORS may be taken orally or via feeding tube.

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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.

El Escorial/revised Airlie House criteria (El 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

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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

Approved Indications

A. Amyotrophic Lateral Sclerosis (ALS)

Other Uses

i. N/A

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J1301	Injection, edaravone, 1 mg [Radicava®]

ICD-10	Description
G12.21	Amyotrophic lateral sclerosis

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Medical Necessity Guidelines

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.

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

edaravone (Radicava®)

A. Criteria For Initial Approval

Initial 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. 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 (ALSFRSR) 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.

B. Criteria For Continuation of Therapy

Continuation requests for Radicava® (edaravone) may be if approved if the following criteria is met:

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

C. Authorization Duration

i. Initial Approval Duration: 6 months
ii. Reauthorization Approval Duration: 12 months

D. Conditions Not Covered

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

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Radivaca® (edaravone) inj. 60 mg IV	• *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.
Radicava ORS® 105 mg (5ml) oral	
Exceptions	
None	

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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.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 4/28/2025	Information reviewed to ensure it is up to date. Minimal changes in word formatting.	6/9/2025	6/19/2025
Annual Review 6/13/2024	Added sections: Other Uses, Authorization Duration, Conditions Not Covered, Limits or Restrictions. Wording and formatting changes. Coding Reviewed: No Changes	3/14/2025	4/2/2025
Policy Inception 6/13/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Choose an item.