WellMed Doctors helping patients for more than 25 years	**Effective Date: 12/21/22**	**Revision Date(s):** 10/16/18, 12/12/19, 03/11/2021, 10/20/2022
Department: PHARMACY	**MMC Review/ Approval Date(s):** 1/14/2020, 3/19/2021, 12/21/22	**Total Number of Pages: 8**

Policy Number: 033.003
Title: Coverage Determination Policy for Edaravone (Radicava)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

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Coverage Policy Number: 033.003

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

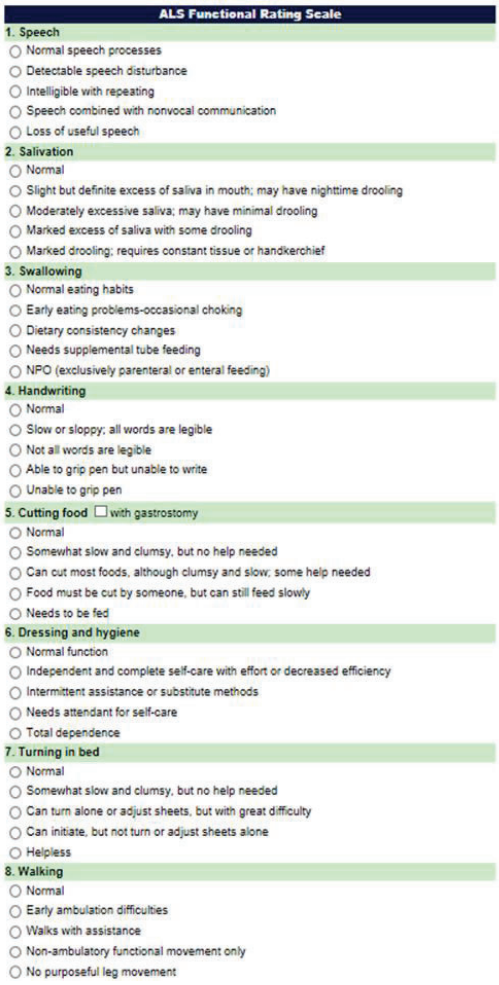
This policy refers to Radicava (edaravone) for administration by intravenous infusion by a healthcare professional. Radicava ORS (edaravone) oral suspension is obtained under the pharmacy benefit.

Coverage Determination (Initial/New Requests)

WellMed Medical Management will cover Radicava® (edaravone) for the treatment of: Amyotrophic Lateral Sclerosis (ALS) when ALL of the following criteria are met:

1) Medical records and documentation (e.g., chart notes, previous medical history, diagnostic testing including: imaging, nerve conduction studies, laboratory values) support the diagnosis of "definite" or "probable" ALS per the El Escorial/revised Airlie House diagnostic criteria:
    a. Definite ALS is defined on clinical grounds alone by the presence of UMN as well as LMN signs in the bulbar region and at least two of the other spinal regions or the presence of UMN and LMN signs in three spinal regions. The important determinants of diagnosis of definite ALS in the absence of electrophysiological, neuroimaging and laboratory examinations are the presence of UMN and LMN signs together in multiple regions.
    b. Probable ALS is defined on clinical grounds alone by UMN and LMN signs in at least two regions. While the regions may be different, some UMN signs must be rostral (above) the LMN signs. Multiple different combinations of UMN and LMN signs may be present in patients with probable ALS.
2) The patient's most recent ALS Function Rating Scale-Revised (ALSFRS-R) score* confirming that the patient has scores greater than or equal to 2 in all items at the start of treatment.
3) Patient has % forced vital capacity (%FVC) greater than or equal to 80% at the start of treatment
4) Dosing is in accordance with the United States Food and Drug Administration approved labeling
5) Provider attestation that the patient or caregiver is not competent or is physically unable to administer Radicava ORS oral suspension either orally or via feeding tube

*ALS Functional Rating Scale:



ALS Functional Rating Scale

1. Speech
- ○ Normal speech processes
- ○ Detectable speech disturbance
- ○ Intelligible with repeating
- ○ Speech combined with nonvocal communication
- ○ Loss of useful speech

2. Salivation
- ○ Normal
- ○ Slight but definite excess of saliva in mouth; may have nighttime drooling
- ○ Moderately excessive saliva; may have minimal drooling
- ○ Marked excess of saliva with some drooling
- ○ Marked drooling; requires constant tissue or handkerchief

3. Swallowing
- ○ Normal eating habits
- ○ Early eating problems-occasional choking
- ○ Dietary consistency changes
- ○ Needs supplemental tube feeding
- ○ NPO (exclusively parenteral or enteral feeding)

4. Handwriting
- ○ Normal
- ○ Slow or sloppy; all words are legible
- ○ Not all words are legible
- ○ Able to grip pen but unable to write
- ○ Unable to grip pen

5. Cutting food ☐ with gastrostomy
- ○ Normal
- ○ Somewhat slow and clumsy, but no help needed
- ○ Can cut most foods, although clumsy and slow; some help needed
- ○ Food must be cut by someone, but can still feed slowly
- ○ Needs to be fed

6. Dressing and hygiene
- ○ Normal function
- ○ Independent and complete self-care with effort or decreased efficiency
- ○ Intermittent assistance or substitute methods
- ○ Needs attendant for self-care
- ○ Total dependence

7. Turning in bed
- ○ Normal
- ○ Somewhat slow and clumsy, but no help needed
- ○ Can turn alone or adjust sheets, but with great difficulty
- ○ Can initiate, but not turn or adjust sheets alone
- ○ Helpless

8. Walking
- ○ Normal
- ○ Early ambulation difficulties
- ○ Walks with assistance
- ○ Non-ambulatory functional movement only
- ○ No purposeful leg movement

Coverage Determination (Renewal/Continuation of Therapy Requests)

For continuation of therapy, all of the following must be met:

1) Patient has been previously treated with Radicava®
2) Patient's medical records and documentation support the diagnosis of "definite" or "probable" ALS per the El Escorial/revised Airlie House diagnostic criteria
3) Patient is NOT dependent on invasive ventilation or tracheostomy
4) Dosing is consistent with FDA approved dosing
5) Provider attestation that the patient or caregiver is not competent or is physically unable to administer Radicava ORS oral suspension either orally or via feeding tube

FDA Approved Dose and Indication:

Amyotrophic lateral sclerosis	• Initial cycle, 60 mg IV administered over 60 minutes daily for 14 days, followed by 14 days drug free • Subsequent cycles, 60 mg IV administered over 60 minutes daily for 10 days of a 14-day period, followed by 14 days drug free

General Background:

Amyotrophic lateral sclerosis (ALS) is a group of rare neurological diseases that mainly involve the nerve cells (neurons) responsible for controlling voluntary muscle movement. Voluntary muscles produce movements like chewing, walking, and talking. The disease is progressive, meaning the symptoms get worse over time. Currently, there is no cure for ALS and no effective treatment to halt, or reverse, the progression of the disease. Early symptoms of ALS usually include muscle weakness or stiffness. Gradually all voluntary muscles are affected, and individuals lose their strength and the ability to speak, eat, move, and even breathe. Most people with ALS die from respiratory failure, usually within 3 to 5 years from when the symptoms first appear. However, about 10 percent of people with ALS survive for 10 or more years.

Treatment can help control symptoms, prevent unnecessary complications, and make living with the disease easier. Options include riluzole and stem cell therapy.

Radicava® is indicated for the treatment of amyotrophic lateral sclerosis (ALS). It's mechanism of action is unknown. It has been characterized as a free radical scavenger, which is thought to block radicals that mediate both neuronal and vascular damage. Radicava® was found to slow the decline in clinical assessment of daily functioning in persons with ALS.

Radicava® is contraindicated in patients with a history of hypersensitivity to edaravone or any of the inactive ingredients of the product. Radicava® contains sodium bisulfite which can cause allergic type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in susceptible people. Use caution in asthmatic patients.

Clinical Evidence:

BACKGROUND:

In a previous phase 3 study in patients with amyotrophic lateral sclerosis (ALS), edaravone did not show a significant difference in the Revised ALS Functional Rating Scale (ALSFRS-R) score compared with placebo. Post-hoc analysis of these data revealed that patients in an early stage with definite or probable diagnosis of ALS, defined by the revised El Escorial criteria, who met a select set of inclusion criteria showed a greater magnitude of effect than did the full study population. We aimed to substantiate this post-hoc result and assess safety and efficacy of edaravone in a phase 3 trial that focused on patients with early stage ALS who met the post-hoc analysis inclusion criteria.

METHODS:

In this phase 3, randomised, double-blind, parallel-group study, patients aged 20-75 years with ALS of grade 1 or 2 in the Japan ALS Severity Classification, scores of at least 2 points on all 12 items of ALSFRS-R, forced vital capacity of 80% or more, definite or probable ALS according to the revised El Escorial criteria, and disease duration of 2 years or less were recruited from 31 hospitals in Japan. Eligible patients also had a decrease of 1-4 points in the ALSFRS-R score during a 12-week observation period before randomisation. Patients meeting all criteria were then randomly assigned 1:1 to receive 60 mg intravenous edaravone or intravenous saline placebo for 6 cycles (4 weeks per cycle with 2 weeks on, 2 weeks off) for a total treatment duration of 24 weeks. In cycle 1, the study drug or placebo was administered once per day for 14 days within a 14 day period, followed by the drug-free period. In cycle 2 and thereafter, the study drug or placebo was administered for 10 days within a 14 day period, followed by a 2 week drug-free period. Participants and investigators, including those assessing outcomes, were masked to treatment allocation. The primary efficacy outcome was the change in ALSFRS-R score from the baseline to 24 weeks (or at discontinuation if this was after the third cycle) after randomisation. The primary outcome was assessed in all patients who had received at least one treatment infusion, had at least one assessment post-baseline, and reached the end of cycle 3. For patients with missing values at the end of cycle 6, data were imputed by the last observation carried forward (LOCF) method, provided the patients had completed at least cycle 3. Safety was assessed in all patients who had received at least one treatment infusion and had at least one assessment post-baseline. This trial is registered with ClinicalTrials.gov, NCT01492686.

FINDINGS:

Between Nov 28, 2011, and Sept 3, 2014, we screened 213 patients, and enrolled 192 as potential participants. Of these, 137 patients completed the observation period: 69 were randomly assigned to receive edaravone, and 68 were randomly assigned to receive placebo. 68 patients taking edaravone and 66 taking placebo were included in the primary efficacy analysis. For the primary outcome, the change in ALSFRS-R score was -5·01 (SE 0·64) in the edavarone group and -7·50 (0·66) in the placebo group. The least-squares mean difference between groups was 2·49 (SE 0·76, 95% CI 0·99-3·98; p=0·0013) in favour of edaravone. Treatment-emergent adverse

events were reported in 58 (84%) patients receiving edaravone and 57 (84%) patients receiving placebo. 11 (16%) patients taking edaravone and 16 (24%) taking placebo had serious adverse events, and one (1%) patient receiving edaravone and four (6%) patients receiving placebo had adverse events (one dysphagia in edaravone group and one dyspnoea, two respiratory disorder, and one rash in the placebo group) that led to withdrawal.

INTERPRETATION:

Edaravone showed efficacy in a small subset of people with ALS who met criteria identified in post-hoc analysis of a previous phase 3 study, showing a significantly smaller decline of ALSFRS-R score compared with placebo. There is no indication that edaravone might be effective in a wider population of patients with ALS who do not meet the criteria.

HCPCS Code:

Radicava (edaravone), Injection, 1 mg – J1301

Acronyms:

NCD = National Coverage Determination; LCD = Local Coverage Determinations; FDA = Food & Drug Administration; ALS = Amyotrophic Lateral Sclerosis; PBO = placebo; AE = adverse events; SAE = serious adverse events; ALSFRS-R = Amyotrophic Lateral Sclerosis Functional Rating Scale Revised; UMN = upper motor neuron; LMN = Lower motor neuron; %FVC = percent forced vital capacity

References:

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6. National Institute of Neurological Disorders and Stroke. Amyotrophic Lateral Sclerosis (ALS) Fact Sheet. Retrieved from: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet. Accessed on: October 4, 2022.