Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 02/13/2025

Radicava® (edaravone)

HCPCS: J1301

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Prescribed by or in consultation with a neurologist
   d. Start of treatment is within 2 years of diagnosis with amyotrophic lateral sclerosis (ALS)
      OR
      After 2 years of diagnosis, with a percent predicted vital capacity value of ≥ 80 %.
   e. Submission of a baseline metrics from the ALSFRS-R (Revised ALS Functional Rating Scale)
   f. Currently receiving treatment and will continue to receive treatment with riluzole, if tolerated
   g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 6 months
   c. Renewal Criteria: Continuation of coverage requires submission of patient assessments using the ALSFRS-R or other clinical documentation to determine if Radicava is slowing the progression of ALS

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Radicava and Radicava ORS are indicated for the treatment of ALS

- ALS is a neurodegeneration disease characterized by rapid loss of upper and lower motor neurons, resulting in death by paralysis and respiratory failure usually within 24-48 months. It has been suggested that pathogenesis of neuronal degeneration in ALS may be unique in different individuals, which is one reason ALS research and development has had minimal advancements. One primary suggestion is that oxidative stress to motor neurons is largely responsible for the pathogenesis of ALS onset and progression.

- It is proposed that by reducing free radicals that cause oxidative stress on motor neurons, radical damage may be minimized, thus preventing progression of ALS. One primary tool to measure progression of ALS is called Revised ALS Functional Rating Scale (ALSFRS-R), which has been used in many clinical trials to determine treatment efficacy.

- The American Academy of Neurology updated guidelines from 2009 (reaffirmed on January 25, 2023) titled "Update: The care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies" recommend that riluzole should be offered to slow the disease progression in patients with ALS. These guidelines have not been updated to include the most recent ALS drug approvals, including Radicava® or Qalsody™. The European Academy of Neurology (EAN) guideline on the management of amyotrophic lateral sclerosis in collaboration with European Reference Network for Neuromuscular Diseases (ERN EURO-NMD), which is an update of the 2012 European Federation of Neurological Societies guidelines strongly recommends lifelong riluzole at diagnosis, and to offer Qalsody (tofersen) as first-line for progressive ALS caused by pathogenic SOD1 mutations.

- Both guidelines recommend initiating riluzole as soon as possible after diagnosis along with non-pharmacotherapy. Non-pharmacotherapy goals are to maintain autonomy as long as possible through supportive care. The AAN recommends a multidisciplinary care approach that includes a neurologist when treating/caring for patients with ALS.

- The first of two Phase III trials failed to show significant difference between the treatment group and placebo in relativity to the ALSFRS-R score. Researchers determined that inclusion criteria (duration of disease within 3 years and forced vital capacity (FVC) at least 70%) had to be more stringent to observe responders. [Please see **Table 1** below for additional information regarding the trials].

- The second Phase III trial was conducted over 24 weeks and met a power of 80%. Based on the modified inclusion criteria (duration of disease within 2 years and FVC at least 80%), the trial concluded a significant difference in ALSFRS-R score between treatment group and placebo group.

- It is the Northeast Amyotrophic Lateral Sclerosis Consortum (NEALS) clinical investigators' opinion that a therapy that results in a change of 20-25% or greater in the slope of the ALSFRS-R would be considered clinically meaningful.

References:

1. Hardiman O, Van Den Berg L. Edaravone: a new treatment for ALS on the horizon. The Lancet Neurology. 2017 May15.
2. 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. Amyotroph Lateral Scler Frontotemporal Degener. 2014 Dec;15(7-8):610-17.
3. Petrov D., Mansfield C., Moussy A., Hermine O. ALS clinical trials review: 20 years of failure. Are we any closer to registering a new treatment?. Front Aging Neurosci. 2017;9:63.

4. Yoshino H., Kimura A. Investigation of the therapeutic effects of edaravone, a free radical scavenger, on amyotrophic lateral sclerosis (phase II study). Amyotroph Lateral Scler. 2006 Dec;7(4):241-5.
5. Abe K, Aoki M, Tsuji S, et al. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. Lancet Neurology. 2017 May;[e-pub ahead of print].
6. Anon. Press Release: New Japan-originated ALS treatment option available to patients in the U.S. – U.S. FDA approves RADICAVA (edaravone) for the treatment of ALS. 2017 May 8.
7. Anon. Package insert: Radicava (edaravone). Mitsubishi Tanabe Pharma. Revised: 2017 May.
8. 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). American Academy of Neurology. 2009 Oct;73(15):1218-26.
9. Andersen PM, Abrahams S, Borasio GD, et al. EFNS guidelines on the management of amyotrophic lateral sclerosis (MALS) – revised report of an EFNS task force. Eur J Neurol. 2012;19(3)360-75.
10. Sawada H. Clinical efficacy of edaravone for the treatment of amyotrophic lateral sclerosis. Expert opin pharmacother. 2017 May;18(7)735-738.
11. Anon. Radicava (edaravone): for amyotrophic lateral sclerosis (ALS). IPD analytics; Drug Alert: Central Nervous System. 2017 May 10.
12. Cudkowicz M, Muhammad Q, Shefner J. Measures and markers in amyotrophic lateral sclerosis. NeuroRx. 2004 Apr;1(2):273-83.
13. Miller RG, Jackson 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 First published October 12, 2009, DOI https://doi.org/10.1212/WNL.0b013e3181bc01a4
14. Radicava/Radicava ORS (edaravone) [prescribing information]. Jersey City, NJ: Mitsubishi Tanabe Pharma Corp. May 2022

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.3</td><td>Effective Date: 02/13/2025</td><td>Annual review – no changes to the criteria were made.</td></tr>
<tr><td>2.2</td><td>Effective Date: 02/08/2024</td><td>Annual review – no changes to the criteria were made.</td></tr>
<tr><td>2.1</td><td>Effective Date: 02/02/2023</td><td>Updated FVC requirement to a vital capacity requirement</td></tr>
<tr><td>2.0</td><td>Effective Date: 12/01/2022</td><td>Updated renewal criteria to allow other clinical documentation outside of just patient assessments using the ALSFRS-R to determine if the medication is providing benefit</td></tr>
<tr><td>1.9</td><td>Effective Date: 08/04/2022</td><td>Update to include new oral suspension formulation Radicava ORS.</td></tr>
<tr><td>1.8</td><td>Effective Date: 08/12/2021</td><td>Annual Review</td></tr>
<tr><td>1.7</td><td>Effective Date: 08/13/2020</td><td>Updated to included FDA approved indication and age and the trial and failure of preferred products</td></tr>
<tr><td>1.6</td><td>Effective Date: 10/01/2019</td><td>UM medical management system update for BCNA and MAPPO
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>Yes</td></tr>
<tr><td>BCNA</td><td>Yes</td></tr>
</table></td></tr>
</table>

<table>
<tr><td>1.5</td><td>Effective Date:
08/15/2019</td><td>Annual Review of Medical Policy</td></tr>
<tr><td>1.4</td><td>Effective Date:
08/09/2018</td><td>Annual Review of Medical Policy</td></tr>
<tr><td>1.3</td><td>Effective Date:
10/01/2017</td><td>UM medical management system update for BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.2</td><td>Effective Date:
09/01/2017</td><td>UM medical management system update for BCBS
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.1</td><td>Effective Date:
08/10/2017</td><td>Changes to approved preliminary criteria</td></tr>
<tr><td>1.0</td><td>Effective Date:
06/08/2017</td><td>New policy
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
</table>

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Radicava® (edaravone) HCPCS CODE: J1301

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for Radicava. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female **Pt weight (in kg)** **Date recorded:**_____	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for initiation or continuation of therapy? ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #3) *Reason for Hospital Outpatient administration:* _____
3. Please specify location of administration if hospital outpatient infusion: _____
4. Please provide the NPI number for the place of administration: _____
5. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis?
      ☐ Amyotrophic Lateral Sclerosis (ALS) ☐ Other, list diagnosis: _____
   b. When was the diagnosis of ALS established? Date: _____
   c. Have baseline metrics from the ALSFRS-R (ALS functional rating scale) been submitted?
      ☐ Yes ☐ No
   d. Has a lung function test been performed on the patient? (*Please attach any tests results)* ☐ Yes ☐ No
   e. What is the patient's predicted vital capacity value? _____
   f. Is the patient currently receiving and continue to receive treatment with Rilutek (riluzole)? ☐ Yes ☐ No
6. **Continuation request: Radicava start date _____**
   a. Has a repeat assessment using the ALSFRS-R been done to determine whether the medication is having an effect? *(chart notes are required)*
      ☐ Yes ☐ No Comment: _____
   b. If the patient is continuing therapy, please give the patient's current disease status since beginning treatment:
      ☐ Improved: Please describe: _____
      ☐ Stable; Please describe: _____
      ☐ Worsened; Please describe: _____
      ☐ Other; Please describe: _____
7. Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached Chart Notes	☐ Weight (specify lb or kg), BSA
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

3/23/2017; 9/20/2017;10/11/2018;11/30/2018; 1/3/2019; 10/1/2020, 04/01/2023