Blue Cross Blue Shield Blue Care Network of Michigan

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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.

Effective Date: 02/08/2024

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.

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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 (AAN) and the European Federation of Neurological Sciences (EFNS) have provided guidelines for the management of ALS. 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 guidelines were reaffirmed in January of 2020 and have not yet been updated to include Radicava.

- 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.

- 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.

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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>2.2</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>
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<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>
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<tr><td>1.3</td><td>Effective Date:
10/01/2017</td><td>UM medical management system update for BCN
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09/01/2017</td><td>UM medical management system update for BCBS
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<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
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** 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.*

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