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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.

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 $\geq 80\%$.
 - 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 (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 Consortium (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 May 15.
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.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

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

Policy History												
#	Date	Change Description										
2.2	Effective Date: 02/08/2024	Annual review – no changes to the criteria were made.										
2.1	Effective Date: 02/02/2023	Updated FVC requirement to a vital capacity requirement										
2.0	Effective Date: 12/01/2022	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										
1.9	Effective Date: 08/04/2022	Update to include new oral suspension formulation Radicava ORS.										
1.8	Effective Date: 08/12/2021	Annual Review										
1.7	Effective Date: 08/13/2020	Updated to included FDA approved indication and age and the trial and failure of preferred products										
1.6	Effective Date: 10/01/2019	UM medical management system update for BCNA and MAPPO <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
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1.5	Effective Date: 08/15/2019	Annual Review of Medical Policy										
1.4	Effective Date: 08/09/2018	Annual Review of Medical Policy										

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1.3	Effective Date: 10/01/2017	UM medical management system update for BCN <table border="1"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
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1.1	Effective Date: 08/10/2017	Changes to approved preliminary criteria										
1.0	Effective Date: 06/08/2017	New policy <table border="1"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	No	MAPPO	No	BCNA	No
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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>.

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



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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. <input type="checkbox"/> Male <input type="checkbox"/> Female	Address
Pt weight (in kg) Date recorded: _____	
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

- Is this request for initiation or continuation of therapy? Initiation Continuation *Date patient started therapy:* _____
- Site of administration? Provider office/Home infusion Other: _____
 Hospital outpatient facility (go to #3) *Reason for Hospital Outpatient administration:* _____
- Please specify location of administration if hospital outpatient infusion: _____
- Please provide the NPI number for the place of administration: _____
- Initiation AND Continuation of therapy:**
 - What is the patient's diagnosis?
 Amyotrophic Lateral Sclerosis (ALS) Other, list diagnosis: _____
 - When was the diagnosis of ALS established? Date: _____
 - Have baseline metrics from the ALSFRS-R (ALS functional rating scale) been submitted?
 Yes No
 - Has a lung function test been performed on the patient? (Please attach any tests results) Yes No
 - What is the patient's predicted vital capacity value? _____
 - Is the patient currently receiving and continue to receive treatment with Rilutek (riluzole)? Yes No
- Continuation request: Radicava start date** _____
 - 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:* _____
 - 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: _____
- 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
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Step 2: Checklist	<input type="checkbox"/> Form Completely Filled Out <input type="checkbox"/> Attached Chart Notes	<input type="checkbox"/> 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

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