Radicava (edaravone) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	12-01-2022

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Radicava® (edaravone) Intravenous infusion	Treatment of amyotrophic lateral sclerosis (ALS)		1
Radicava ORS® (edaravone) Oral suspension Oral suspension starter kit	Treatment of amyotrophic lateral sclerosis (ALS)		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Amyotrophic Lateral Sclerosis (ALS)	Amyotrophic lateral sclerosis (ALS) is an idiopathic, fatal neurodegenerative disease.(2) It is characterized by loss of motor neurons in the spinal cord, brainstem, and motor cortex.(3) Age of onset is between 58-63 years for sporadic disease and 47-52 years for familial disease, with rapidly decreased incidence after 80 years. The clinical hallmark of ALS is the presence of upper and lower motor neuron (UMN and LMN) features involving the brainstem and multiple spinal cord regions of innervation.(2) ALS is a rapidly progressive disease with 50% of patients dying within 30 months of symptom onset, and about 20% of patients survive between 5 years and 10 years after symptom onset. Older age at symptom onset, early respiratory muscle dysfunction, and bulbar-onset disease are associated with reduced survival, whereas limb-onset disease, younger age at presentation, and longer diagnostic delay are independent predictors of prolonged survival. Dysphagia develops in most patients, with consequent weight loss and malnutrition. Respiratory compromise eventually develops in most cases, leading to exertional dyspnea, orthopnea, hypoventilation with

	resultant hypercapnia, and early morning headaches. Progressive weakening of the respiratory muscles leads to respiratory failure, often precipitated by pneumonia.(2) Respiratory function is a critical predictor of survival in ALS. International guidelines recommend the assessment of respiratory function in ALS patients at first visit and every 3 months thereafter.(7) Forced (FVC) and slow (SVC) vital capacities are non-invasive conventional tests used to estimate respiratory function in ALS. Their results depend on age, gender, height, and ethnicity, in addition to the functional integrity of the inspiratory and expiratory muscles. FVC is sensitive to detect hypoventilation in ALS and can be more sensitive in detecting diaphragmatic weakness when performed in the supine position.(8) However, the patient must expel air quickly and forcefully, which may cause fatigue and induce bronchospasm and result in an underestimation of actual lung capacity. SVC is easier for the patient with ALS to perform even in the presence of orofacial paresis because it involves exhalation of air in a slow, gentle manner after a maximal inspiration. FVC and SVC have been shown to be tightly correlated, can be used interchangeably, and decline similarly in ALS (about 2%/month).(8,9) Symptomatic treatments remain the cornerstone for management of patients with ALS. Disease modifying treatment options for ALS are limited. Riluzole is the only agent shown to have any impact on survival in ALS. The American Academy of Neurology (AAN) has recommended that riluzole be offered to slow disease progression in patients with ALS.(2) While edaravone has been shown to slow the decline of functional and quality of life ratings in patients with ALS, the short duration of trials did not allow for the assessment of an effect on survival.(6) According to CADTH Common Drug Review (CDR) of Radicava, Radicava should be considered for the majority of newly diagnosed ALS patients with preserved respiratory function and with functional independence. Patients with advanced ALS with severe disability, such as ventilator-dependence with very little limb function, are unlikely to benefit from therapy and should not be offered Radicava.(5)
Efficacy	The efficacy of edaravone was evaluated in a post-hoc analysis of a 6-month, phase III randomized, placebo-controlled, double-blind study, in patients aged 20 to 75 years with ALS. All study patients had to meet all of the following criteria at screening: 1. Functionality retained most activities of daily living (defined as scores of 2 points or better on each individual item of the ALS Functional Rating Scale – Revised [ALSFRS-R]) 2. Normal respiratory function (defined as percent-predicted forced vital capacity [%FVC] values of greater than or equal to 80%) 3. Definite or probable ALS based on the El Escorial revised criteria 4. Disease duration of 2 years or less Patients who met the criteria above (n= 137) were randomized to receive either edaravone 60 mg intravenously (IV) or placebo for 6 cycles (4 weeks per cycle with 2 weeks on, 2 weeks off). 91% of patients in both the edaravone and placebo group were also receiving treatment with riluzole. The primary efficacy endpoint was change in the Revised ALS Functional Rating Scale (ALSFRS-R) score from baseline to 24 weeks or therapy discontinuation (if discontinuation occurred after the third cycle) after randomization. The change in ALSFRS-R score was -5.01 (SE 0.64) and -7.50 (0.66) in the edaravone and placebo group respectively. The trial authors concluded edaravone showed efficacy in a small subset of patients (i.e., those meeting the criteria noted above) and that "there is no indication that edaravone might be effective in a wider population of patients with ALS who do not meet the criteria".(1,4)
Safety	Edaravone is contraindicated in patients with history of hypersensitivity to edaravone or any of its inactive ingredients.(1)

REFERENCES

Number	Reference
1	Radicava prescribing information. Mitsubishi Tanabe Pharma Corporation. November 2022.

Number	Reference
2	Kiernan M. C., Vucic S., Cheah B. C., Turner M. R., Eisen A., Hardiman O., et al. (2011). Amyotrophic lateral sclerosis. Lancet 377 942–955. 10.1016/S0140-6736(10)61156-7.
3	Miller R.G., Jackson C.E., Kasarskis E.J., England J.D., Forshew D., Johnston W., Kalra S., Katz J.S., Mitsumoto H., Rosenfeld J., 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 of Neurology. Neurology. 2009;73:1227–1233.
4	Koji Abe, Mashashi Aoki, Shoji Tsuji, et al. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomized double-blind, placebo-controlled trial. Lancet Neurology. 2017 May 15, S1474-4422(17)30115-1.
5	Clinical Review Report: Edaravone (Radicava): (Mitsubishi Tanabe Pharma Corporation): Indication: For the treatment of amyotrophic lateral sclerosis. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Apr. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542359/.
6	Oskarsson B., Gendron T., Staff N. Amyotrophic Lateral Sclerosis: An Update for 2018. Mayo Clin Proc. 2018;93(11):1617-1628.
7	EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis. Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, et al.. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)–revised report of an EFNS task force. Eur J Neurol. (2012) 19:360–75.
8	Pinto S, de Carvalho M. SVC Is a Marker of Respiratory Decline Function, Similar to FVC, in Patients With ALS. Front Neurol. 2019 Feb 28;10:109. doi: 10.3389/fneur.2019.00109.
9	Andrews JA, Meng L, Kulke SF, et al. Association Between Decline in Slow Vital Capacity and Respiratory Insufficiency, Use of Assisted Ventilation, Tracheostomy, or Death in Patients With Amyotrophic Lateral Sclerosis. JAMA Neurol. 2018;75(1):58–64. doi:10.1001/jamaneurol.2017.3339.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Radicava ors ; Radicava ors starter kit	edaravone oral susp	105 MG/5ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Radicava ors ; Radicava ors starter kit	Edaravone Oral Susp	105 MG/5ML	50	mLs	28	DAYS	Starter Kits QL set up at NDC		
Radicava ors starter kit	edaravone oral susp	105 MG/5ML	70	mLs	180	DAYS	Starter Kits QL set up at NDC		70510232101 ; 70510232102

ADDITIONAL QUANTITY LIMIT INFORMATION

Wildcard	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Additional QL Information	Targeted NDCs When Exclusions Exist	Effective Date	Term Date
74509030001820	Radicava ors ; Radicava ors starter kit	Edaravone Oral Susp	105 MG/5ML	Starter Kits QL set up at NDC			
74509030001820	Radicava ors starter kit	edaravone oral susp	105 MG/5ML	Starter Kits QL set up at NDC	70510232101 ; 70510232102		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Radicava ors ; Radicava ors starter kit	edaravone oral susp	105 MG/5ML	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Radicava ors ; Radicava ors starter kit	Edaravone Oral Susp	105 MG/5ML	Medicaid
Radicava ors starter kit	edaravone oral susp	105 MG/5ML	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
All target agents are eligible for continuation of therapy

      1. The patient has been treated with the requested agent within the past 90 days **OR**
      2. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed **OR**
   B. ALL of the following:
      1. The patient has a diagnosis of amyotrophic lateral sclerosis (ALS) **AND**
      2. The patient has had the diagnosis of ALS for a duration of 2 years or less **AND**
      3. The patient has a baseline percent forced vital capacity (FVC%) or slow vital capacity (SVC) of 80% or greater **AND**
      4. The patient is able to perform most activities of daily living, defined as scores of 2 points or better on each individual item of the ALS Functional Rating Scale – Revised [ALSFRS-R] **AND**
      5. ONE of the following:
         A. BOTH of the following:
            1. The patient is currently being treated with riluzole **AND**

Module	Clinical Criteria for Approval
	2. The patient will continue riluzole in combination with the requested agent **OR** B. The patient's medication history includes riluzole AND ONE of the following: 1. The patient has had an inadequate response to riluzole **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over riluzole **OR** C. The patient has an intolerance, hypersensitivity, or FDA labeled contraindication to riluzole **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that riluzole cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months **NOTE:** For patients initiating therapy, approval will include 28 bags per 28 days (initial dose) for the first month and 20 bags per 28 days for the remainder of the 6 months. For patients initiating therapy with oral suspension, approval will include 70 mL starter kit per 180 days (initial dose) and 50 mL per 28 days for the remainder of the 6 months. NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient is NOT dependent on invasive ventilation or tracheostomy **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval:** Initial: up to 6 months; Renewal: up to 12 months