MEDICAL MUTUAL®

Drug Policy

Policy:	Radicava ORS (edavarone)	Annual Review Date: 06/20/2024 Last Revised Date: 06/20/2024

OVERVIEW

Radicava ORS is indicated for the treatment of **amyotrophic lateral sclerosis** (ALS).

Radicava is an anti-oxidative, free radical scavenger which eliminates lipid peroxide and hydroxyl radicals; however, it is unknown exactly how Radicava exerts its therapeutic effect in ALS.

POLICY STATEMENT

This policy involves the use of Radicava ORS. Prior authorization is recommended for pharmacy benefit coverage of Radicava ORS. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Radicava ORS as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Radicava ORS be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Radicava ORS is recommended in those who meet the following criteria:

1. **Amytrophic Lateral Sclerosis**
   Criteria. *Patient must meet the following criteria*
   - **A.** Patient has diagnosis of clinically definite or probable ALS based on El Escorial revised criteria or Awaji criteria; AND
   - **B.** Patient has a disease duration of 2 years or less; AND
   - **C.** Patient has a percent-predicted forced vital capacity (%FVC) ≥ 80%; AND
   - **D.** Baseline documentation of retained functionality for most activities of daily living [i.e., score of 2 or better on each individual item of the ALS Functional Rating Scale- Revised (ALSFRS-R)] [documentation required];
   - **E.** Patient meets one of the following (i, ii, or iii)

i. Patient has previously received a riluzole product; OR
ii. Patient is currently receiving a riluzole product; OR
iii. Patient will take Radicava ORS concomitantly with a riluzole product;

F. Patient will not use Radicava ORS concomitantly with any other medications containing Edvaraone; AND
G. The medication is prescribed by or in consultation with a neurologist, a neuromuscular disease specialist, or a physician specializing in the treatment of ALS.

2. <u>Amytrophic Lateral Sclerosis – Continuation of therapy</u>
Criteria. *Patient must meet the following criteria*

A. Patient does not require invasive ventilation; AND
B. According to the prescriber, the patient continues to benefit from therapy; AND
C. The medication is prescribed by or in consultation with a neurologist, a neuromuscular disease specialist, or a physician specializing in the treatment of ALS; AND

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months (180 days)
B) *Extended Approval:* 6 months (180 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Radicava ORS has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Aneurysmal Subarachnoid Hemorrhage.** Radicava is not indicated for the treatment of aneurysmal subarachnoid hemorrhage (SAH).[1] One randomized controlled study (published) [n = 91] evaluated the efficacy of Radicava (formulation/dose not specified) in patients with aneurysmal SAH.[11] At 3 months post-SAH, the incidence of delayed ischemic neurologic deficits (DINDs) in patients treated with Radicava was 10% vs. 21% in patients in a control group; the between-group treatment difference was not significant (P = 0.118). In patients who had DINDs, 66% of patients in the control group had a cerebral infarction caused by vasospasm compared with 0% of Radicava-treated patients (P = 0.028). Additional, well-designed clinical studies are needed to establish if Radicava has a role in therapy post-SAH.

2. **Myocardial Infarction.** Radicava is not indicated for the treatment of myocardial infarction; there are no US or North American studies of Radicava for this indication.[1] One randomized, placebo-controlled, open-label, Japanese study (published) [n = 101] evaluated the effect of Radicava on the long term prognosis in patients experiencing an acute myocardial infarction.[12] Patients were randomized to receive either Radicava (foreign formulation) 30 mg intravenous (IV) or placebo immediately prior to reperfusion. In all patients, successful reperfusion was obtained within 6 hours post-symptom onset. Radicava significantly attenuated

the infarct size and incidence of reperfusion arrhythmia compared with placebo (P = 0.035 and P = 0.031, respectively).

3. **Radiation-Induced Brain Injury.** Radicava is not indicated for the treatment of radiation-induced brain injury; there are no US or North American studies of Radicava for this indication.[1] One randomized, open-label, 3-month, Chinese study (published) [n = 137] evaluated the protective effect of Radicava on radiation-induced brain necrosis in patients with nasopharyngeal carcinoma.[13] Patients were randomized to receive Radicava (foreign formulation) 30 mg IV twice daily for 2 weeks (not FDA-approved dosing) + IV corticosteroid therapy or placebo + IV corticosteroid therapy. Following 3 months of therapy, radiologic improvement (reduction in edema of ≥ 25%) was observed in 55.6% of patients who received Radicava (n = 40/72) compared with 35.4% of patients treated with placebo (n = 23/65) [P = 0.025]. The area of T1-weighted contrast enhancement was reduced from baseline with both Radicava and placebo (-1.67 cm and -1.20 cm, respectively); however, the difference between the treatment arms was not statistically significant. Improvement in neurologic signs and symptoms evaluated by the Late Effects of Normal Tissues – Subjective, Objective, Management, Analytic (LENT/SOMA) scale was also observed in 61.1% of Radicava-treated patients vs. 38.5% of placebo-treated patients (P = 0.006). Further research is warranted to determine if Radicava has a place in therapy in the treatment of radiation-induced brain injury.

4. **Retinal Vein Occlusion.** Radicava is not indicated for the prevention of macular edema and improvement of visual acuity after arteriovenous sheathotomy in patients with branch retinal vein occlusion; there are no US or North American studies of Radicava for this indication.[1] A single, small, prospective, Japanese study [published] (n = 47) evaluated the efficacy of Radicava (foreign formulation) in patients with branch retinal vein occlusion undergoing vitrectomy.[14] Patients either received Radicava 30 mg IV at the time of the procedure or no additional therapy. Visual acuity was measured before and 12 months after the procedure. At 12 months following the operation, the logarithm of the minimum angle of resolution (logMAR) units improved from 0.22 to 0.56 logMAR units in patients who had received Radicava and from 0.20 to 0.27 logMAR units in patients who did not receive active treatment (P = 0.016). Additional data are needed to support the use of Radicava for this indication.
5. **Sensorineural Hearing Loss.** Radicava is not indicated for the treatment of sensorineural hearing loss; there are no US-based studies of Radicava for this indication.[1] One small, Japanese study evaluated 14 patients with idiopathic sudden sensorineural hearing loss were treated with Radicava (foreign formulation; dose not specified).[15] These patients were compared with a control group of 14 patients with similar prognostic factors who had been treated with hyperbaric oxygenation therapy. No significant differences were observed between the Radicava group and the control group.

6. **Stroke.** Radicava is not FDA-approved for the treatment of patients who have experienced stroke.[1] Radicava has been approved in other countries for this indication and there are some foreign data supporting its use.[16] There are no US-based studies of Radicava for stroke at this time. A systematic review assessed available efficacy data from three clinical trials (n = 496) of Radicava for acute ischemic stroke.[17] These trials

compared Radicava 30 mg twice daily IV infusion for 14 days + another treatment vs. the other treatment alone within 72 hours of stroke symptom onset. One trial did not find significantly reduced mortality with Radicava vs. the control group; the other two studies did not report this endpoint. Overall, there was a significantly higher proportion of patients who had neurologic improvement in the Radicava group vs. control.

7. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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