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Edaravone

(Radicava®) J1301 (1mg)

Covered with prior authorization

Requests for Radicava® (Edaravone) may be approved if the following criteria are met:

- Amyotrophic Lateral Sclerosis (ALS). Individual meets **ALL** of the following criteria:
    - Documented diagnosis of "definite" or "probable" amyotrophic lateral sclerosis (ALS) based on El Escorial – Revised (Airlie House) criteria.
    - Individual has retained most activities of daily living (defined as a score of 2 points or better on each item of the ALS Functional Rating Scale – Revised [ALSFRS-R] [for example, a minimum score of 24]).
    - Individual has normal respiratory function (defined as percent-predicted forced vital capacity values [% FVC] of at least 80%).
    - Individual has a disease duration of 2 years or less.
    - Medication is prescribed by or in consultation with a neurologist, a neuromuscular disease specialist, or a physician specializing in the treatment of ALS.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Initial authorization is up to 6 months and reauthorization is up to 12 months.

Annual reauthorizations will require medical chart documentation that the patient has been seen within the past 12 months and that markers of disease are improved by therapy.

Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Exclusion criteria:

- Aneurysmal Subarachnoid Hemorrhage
    - Radicava® is not indicated for the treatment of aneurysmal subarachnoid hemorrhage (SAH). One randomized controlled study (published) [n = 91] evaluated the efficacy of Radicava® (formulation/dose not specified) in patients with aneurysmal SAH. 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.

- Myocardial Infarction
  - Radicava® is not indicated for the treatment of myocardial infarction; there are no U.S. or North American studies of Radicava® for this indication. 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. 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). Additional data from well-designed clinical studies are needed to establish if Radicava® has a role in therapy for this indication.
- Radiation-Induced Brain Injury
  - Radicava® is not indicated for the treatment of radiation-induced brain injury; there are no U.S. or North American studies of Radicava® for this indication. 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. 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.
- 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 U.S. or North American studies of Radicava® for this indication. 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. 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.

- Sensorineural Hearing Loss
  - Radicava® is not indicated for the treatment of sensorineural hearing loss; there are no U.S.-based studies of Radicava® for this indication. One small, Japanese study evaluated 14 patients with idiopathic sudden sensorineural hearing loss were treated with Radicava® (foreign formulation; dose not specified). 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.
- Stroke
  - Radicava® is not FDA-approved for the treatment of patients who have experienced stroke. Radicava® has been approved in other countries for this indication and there are some foreign data supporting its use.There are no U.S.-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. 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. Additional data from large randomized controlled trials are needed evaluating the use of edaravone in acute ischemic stroke.
- Requests for edaravone (Radicava®)may **not** be approved if the above criteria are not met and for all other indications not included above.
- Doses, durations, or dosing intervals that exceed FDA maximum limits for any FDA-approved indication or are not supported by industry-accepted practice guidelines or peer-reviewed literature for the relevant off-label use.
- Individuals with significant known risk factors unless the record provides an assessment of clinical benefit that outweighs the risk.

U.S. Food and Drug Administration:
This section is to be used for informational purposes. FDA approval alone is not a basis for coverage. Radicava® 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.

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Key References Accessed 8/2022:

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7. Tsujita K, Shimomura H, Kaikita K, et al. Long-term efficacy of edaravone in patients with acute myocardial infarction. Circ J. 2006; 70(7):832-837.
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10. Sano H, Kamijo T, Ino T, et al. Edaravone, a free radical scavenger, in the treatment of idiopathic sudden sensorineural hearing loss with profound hearing loss. Auris Nasus Larynx. 2010; 37(1):42-46.
11. Feng S, Yang Q, Liu M, et al. Edaravone for acute ischaemic stroke. Cochrane Database Syst Rev. 2011; 12:CD007230.

Date	Summary of Changes
August 2022	Criteria for use summary developed by the Ascension Medical Specialty Prior Authorization Team.
September 2022	Criteria for use summary approved by the Ascension Ambulatory Care Expert Review Panel.
October 2022	Criteria for use summary approved by the Ascension Therapeutic Affinity Group.

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If you have questions, call 833-980-2352 to speak to a member of the Ascension Rx prior authorization team, or email your questions to smarthealthspecialty@ascension.org.