Drug Monograph

Drug/Drug Class:	**Radicava® (edaravone) injection/ Amyotrophic Lateral Sclerosis (ALS)**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Radicava® is supplied for intravenous infusion in a single-dose polypropylene bag containing 30 mg of edaravone in 100 ml of clear, colorless aqueous solution. Manufacturer: Mitsubishi Tanabe Pharma Corporation, Jersey City, NJ 07310
Summary of Findings:	The efficacy of Radicava® was established in a randomized, double-blind, placebo-controlled, multicenter, phase 3 Japanese clinical trial. After 24 weeks, treatment with edaravone compared with placebo resulted in a lessened functional decline, a lower decline in total modified Norris Scale scores, and lower deterioration in quality of life.
Status Recommendation:	☒ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☐ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☒ Appropriate Indications ☐ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [4]

ALS, or amyotrophic lateral sclerosis, is a progressive neurodegenerative disease that affects nerve cells in the brand and the spinal cord. ALS usually strikes people between the ages of 40 and 70, and it is estimated there are more than 20,000 Americans who have the disease at any given time.

Motor Neurons reach from the brain to the spinal cord and from the spinal cord to the muscles throughout the body. The progressive degeneration of the motor neurons in ALS eventually leads to their demise. When the motor neurons die, the ability of the brain to initiate and control muscle movement is lost. With voluntary muscle action progressively affected, people may lose the ability to speak, eat, move and breathe.

Dosage Form(s) [1]

Radicava® is supplied for intravenous infusion in a single-dose polypropylene bag containing 30 mg of edaravone in 100 ml of clear, colorless aqueous solution.

Manufacturer [1]

Mitsubishi Tanabe Pharma Corporation, Jersey City, NJ 07310

Indication(s) [1]

Radicava® is indicated for the treatment of ALS.

Clinical Efficacy [1,2,3] (mechanism of action/pharmacology, comparative efficacy)

Radicava® is a substituted 2-pyrazolin-5-one. The mechanism for its therapeutic effects in ALS is unknown.

Pharmacokinetics:

	Radicava®
Protein binding	92%, primarily to albumin
Half Life	4.5 to 6 hours
Metabolism	Liver and kidney, via sulfotransferases, UGT1A6, UGT1A9, UGT2B7, and UGT2B17 to inactive metabolites.
Excretion	Urine, 70% to 90% (1%, unchanged)

Early Stage ALS

Radicava® lessened functional decline compared with placebo in specific patients with early stage ALS.

STUDY DESIGN	Randomized, double-blind, placebo-controlled, multicenter, phase 3 Japanese clinical trial (N=134).
INCLUSION CRITERIA	Patients 20 to 75 years of age with definite or probably ALS for up to 2 years, an independent living status, an ALSFRS-R score of at least 2 on all 12 items, a score change of -1 to -4 points during the 12 week pre-observation period, and a forced vital capacity of at least 80%.
EXCLUSION CRITERIA	Patients with a score of 3 or less for dyspnea, orthopnea, or respiratory insufficiency on the ALSFRS-R or a history of spinal surgery.
TREATMENT REGIMEN	Patients were randomized to receive Radicava® 60 mg IV infusion or placebo for 6 cycles.
RESULTS	After 24 weeks, treatment with Radicava® compared with placebo significantly lessened functional decline as measured by the ALSFRS-R score (-5.01 vs -7.5). Radicava® was also associated with a significantly lower decline in total modified Norris Scale scores (-15.91 vs -20.8) and lower deterioration in quality of life (ALS Assessment Questionnaire, 17.245 vs 26.04). There were no significant between-group differences in FVC, grip or pinch strength, classification of ALS severity at the end of cycle 6, or the incidence of death or disease progression.
SAFETY	The rates for treatment-emergent adverse events were similar between groups.

Contraindications (1)

- Hypersensitivity to edaravone or any components of the product

Warnings and Precautions (1)

- Hypersensitivity reactions and anaphylaxis have been reported; monitoring recommended and discontinuation if occurs.
- Product contains sodium bisulfite, which may cause allergic type reactions in susceptible patients, including anaphylactic symptoms and potentially life-threatening asthmatic episodes

Adverse Effects (1)

Most common, ≥ 2%	Radicava	Placebo

	(n=262)	(n=183)
Confusion	15%	9%
Gait disturbance	13%	9%
Headache	10%	6%
Dermatitis	8%	5%
Eczema	7%	4%
Respiratory disorder/hypoxia	6%	4%
Glycosuria	4%	2%
Tinea infection	4%	2%

Drug Interactions [(1)]

- No drug interactions have been reported

Dosage and Administration [(1)]

The FDA recommended initial cycle of Radicava® is 60 mg IV infusion over 60 minutes daily for 14 days, followed by a 14-day drug-free period. Subsequent cycles, 60 mg IV over 60 minutes daily for 10 days of a 14-day period, followed by 14 days drug-free.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	DOSE	COST/ MONTH*
Edaravone	Radicava	MT Pharma America	60 mg daily	$10,960
Riluzole	Rilutek	Covis	50 mg tablet twice daily	$150.60

* Maximum Allowable Cost

Conclusion

Radicava® is the first FDA approved agent for the treatment of ALS in over 20 years. The FDA granted Radicava® orphan drug designation for the treatment of rare diseases. Radicava® is given daily for 10 days out of 14 days via IV infusion followed by 14 days drug-free. It costs around $11,000 per month. A randomized, double-blind, placebo-controlled, phase 3 clinical trial found that patients with relatively well functions, definite or probably ALS experienced significantly less functional decline following 24 weeks of treatment with Radicava® compared with placebo.

Recommendation

The MO HealthNet Division recommends prior authorization status for this product.

References

1) Product Information: Radicava™, edaravone injection. MT Pharma America, Inc, Jersey City, NJ, 05/2017.
2) Writing Group & Edaravone (MCI-186) ALS 19 Study Group: Safety and efficacy of edaravone in well-defined patients with amyotrophic lateral sclerosis: a randomized, double-blind, placebo-controlled trial. Lancet Neurol 2017; 16(7): 505-512.
3) 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; 15(7-8): 610-617.
4) What is ALS? Retrieved 11/08/2017 from: www.alsa.org/about-als

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