RADICAVA™ (EDARAVONE)

Policy Number: CS2017D0062A **Effective Date**: September 1, 2017

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INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

Radicava (edaravone) is proven and medically necessary for:[1]

1. **The treatment of amyotrophic lateral sclerosis (ALS) in patients who meet ALL of the following criteria**:
   a. For **initial therapy**, ALL of the following:
      (1) Submission of medical records (e.g., chart notes, previous medical history, diagnostic testing including: imaging, nerve conduction studies, laboratory values) to support ONE of the following:[14]
         (a) Diagnosis of "definite" or "probable" ALS per the revised EL Escorial and Airlie House diagnostic criteria, and prescribed by a neurologist with expertise in the diagnosis of ALS
         (b) Diagnosis of "definite" or "probable" ALS per the revised EL Escorial and Airlie House diagnostic criteria, and prescribed by a physician in consultation with a neurologist with expertise in the diagnosis of ALS;
      AND
      (2) Submission of the most recent ALS Functional Rating Scale-Revised (ALSFRS-R) score confirming that the patient has scores ≥ 2 in ALL items of the ALSFRS-R criteria at the start of treatment;[13]
      AND
      (3) Submission of medical records (e.g., chart notes, laboratory values) confirming that the patient has a % forced vital capacity (%FVC) ≥ 80% at the start of treatment;[13]
      AND

(4) Radicava dosing for ALS is in accordance with the United States Food and Drug Administration approved labeling;
AND
(5) Initial authorization will be for no more than 6 cycles (64 doses over 168 days).

b. For **continuation therapy**, ALL of the following:
(1) ONE of the following:[14]
(a) Diagnosis of "definite" or "probable" ALS per the revised EL Escorial and Airlie House diagnostic criteria, and prescribed by a neurologist with expertise in the diagnosis of ALS
(b) Diagnosis of "definite" or "probable" ALS per the revised EL Escorial and Airlie House diagnostic criteria, and prescribed by a physician in consultation with a neurologist with expertise in the diagnosis of ALS;
AND
(2) Patient is currently receiving Radicava therapy;
AND
(3) Patient is NOT dependent on invasive ventilation or tracheostomy;
AND
(4) Radicava dosing for ALS is in accordance with the United States Food and Drug Administration approved labeling;
AND
(5) Authorization will be for no more than 6 cycles (60 doses over 168 days).

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Radicava is indicated for the treatment of amyotrophic lateral sclerosis (ALS).[1]

BACKGROUND

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a rapidly progressive, invariably fatal neurological disease that attacks neurons responsible for controlling voluntary muscles. The disease belongs to a group of disorders known as motor neuron diseases, which are characterized by the gradual degeneration and death of motor neurons. Eventually, all muscles under voluntary control are affected. Individuals lose their strength and the ability to move their arms, legs, and body. When muscles in the diaphragm and chest wall fail, individuals lose the ability to breathe without ventilatory support. Individuals with ALS usually survive for only 3 to 5 years from the onset of symptoms. However, about 10 percent of those with ALS survive for 10 or more years.[8]

The mechanism by which Radicava (edaravone) exerts its therapeutic effect in patients with ALS is unknown.[1] It has been characterized as a free radical scavenger, which is thought to block radicals that mediate both neuronal and vascular damage.[9-10]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J3490	Unclassified drugs

ICD-10 Diagnosis Code	Description
G12.21	Amyotrophic lateral sclerosis

CLINICAL EVIDENCE

The efficacy and safety of edaravone for amyotrophic lateral sclerosis (ALS) was examined in a double-blind, parallel-group, placebo-controlled, phase III trial.[10] The 36-week confirmatory trial consisted of a 12-week pre-observation period followed by a 24-week treatment period. The eligible patient population included those who were diagnosed with ALS as defined as "definite ALS," "probable ALS" or "probable-laboratory-supported ALS," met diagnostic criteria revised EL Escorial for Airlie House. With their baseline disease state, patients also must be able to eat a meal, excrete, or move with oneself alone, and do not need assistance in everyday life. Patients must begin the trial within 3 years after onset of ALS and have a FVC of at least 70%. Patients who complain of dyspnea and have deterioration

of respiratory function, among other criteria were excluded from the study. Patients age 20 to 75 were randomized to receive either placebo (saline, n=104), or edaravone (n=102) 60mg intravenously per day. A single treatment cycle consisted of 14 days of study drug administration period followed by a 14-day observation period. Study drugs were administered every day for 14 days in the administration period of the first cycle, and for 10 out of 14 days in the administration periods of cycles 2 to 6. The end of the administration period in each cycle was followed by a 14-day observation period. Primary efficacy endpoint was the change in ALSFRS-R score. Secondary endpoints were: changes of FVC, grip strength (left/right mean), pinch strength (left/right mean), Modified Norris Scale score, ALSAQ-40 (ALS Assessment Questionnaire), and time to death or a specified state of disease progression (incapable of independent ambulation, loss of function in upper limbs, tracheotomy, artificial respirator with intubation, or tube feeding). Changes in ALSFRS-R during the 24-week treatment were -6.35±0.84 in the placebo group (n=99) and -5.70±0.85 in the edaravone group (n=100), with a difference of 0.65±0.78 (p=0.411). The results with primary outcome, the inter-group difference in the change of the ALSFRS-R at the end of treatment, was not statistically significant. Of all of the secondary outcomes, edaravone only showed statistically significant benefit over placebo in pinch strength (-1.03±0.15 placebo vs. -0.83±0.15 edaravone; difference of 0.20±0.14; p=0.165). There were no significant differences in the safety profile reported between the two experimental groups. The authors admit that this study failed to demonstrate efficacy of edaravone to delay the progression of ALS.

There are additional completed studies that have unpublished results on edaravone's efficacy and safety as a treatment for ALS. These studies include, after a 12 week observation period, patients who meet the diagnostic criteria of the revised EL Escorial for Airlie House, have had onset of ALS symptoms less than 2 years, and can still function to the requirements stated in the inclusion criteria. Patients with certain organ and neurological dysfunction, have dyspnea or deteriorating respiratory function were excluded from these studies. The primary outcome measure of each of these trials is the score of the ALSFRS-R. Additional secondary outcome measures include, but not limited to: Period until death or a certain state (i.e., inability to walk alone, failure of arm function, tracheostomy, respirator installation, tubal feeding replenishment), %FVC, and others. The studies also examine adverse events, drug reactions, laboratory tests and sensory examinations.[11-13]

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for Radicava (edaravone). Local Coverage Determinations (LCDs) do not exist at this time.

Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf. (Accessed March 6, 2017)

STATE EXCEPTIONS

State	Note
Iowa	Drug policy not approved for use in this market
Kansas	Drug policy not approved for use in this market
Maryland	Drug is not a covered benefit at this time
Michigan	Drug is not a covered benefit at this time

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
09/01/2017	• New policy