Clinical Policy: Edaravone (Radicava)
Reference Number: CP.PHAR.343
Effective Date: 07.01.17
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Edaravone (Radicava™) is a member of the substituted 2-pyrazolin-5-one class that acts as a free-radical scavenger of peroxyl radicals and peroxynitrite.

FDA Approved Indication(s)
Radicava is indicated for the treatment of amyotrophic lateral sclerosis (ALS).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Radicava is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Amyotrophic Lateral Sclerosis (must meet all):
      1. Diagnosis of definite or probable ALS per El Escorial diagnostic criteria (see Appendix C);
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 20 years;
      4. Concomitant use of riluzole (at up to maximally indicated doses) unless contraindicated or clinically significant adverse effects are experienced;
      5. Independent living status (defined as patients who can eat a meal, excrete, or move with oneself alone, and do not need assistance in everyday life);
      6. Forced vital capacity ≥ 80%;
      7. Disease duration of ≤ 2 years;
      8. Baseline revised ALS Functional Rating Scale (ALSFRS-R) score with ≥ 2 points in each of the 12 items;
      9. Dose does not exceed 60 mg per day for:
         a. Initial treatment cycle: daily dosing for 14 days followed by a 14-day drug-free period;
         b. Subsequent treatment cycles: daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods.

   Approval duration: 6 months

   B. Other diagnoses/indications:
      1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is
II. Continued Therapy
A. Amyotrophic Lateral Sclerosis (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met
      initial approval criteria;
   2. Member is responding positively to therapy;
   3. Patient continues to meet the following criteria:
      a. Independent living status;
      b. Forced vital capacity ≥ 80%;
      c. Revised ALSFRS-R score with ≥ 2 points in each of the 12 items;
   4. If request is for a dose increase, new dose does not exceed 60 mg/day for each cycle
      consisting of daily dosing for 10 days out of 14-day periods, followed by 14-day
      drug-free periods.
   **Approval duration: 6 months**

B. Other diagnoses/indications (1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports
      positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less); or**
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT
      specifically listed under section III (Diagnoses/Indications for which coverage is
      NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance
      marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is
      sufficient documentation of efficacy and safety according to the off label use policies –
      CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and
      CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information
   **Appendix A: Abbreviation/Acronym Key**
   ALS: amyotrophic lateral sclerosis
   ALSFRS-F: revised ALS Functional Rating Scale
   FDA: Food and Drug Administration
   LMN: lower motor neuron
   UMN: upper motor neuron

   **Appendix B: Therapeutic Alternatives**
   This table provides a listing of preferred alternative therapy recommended in the approval
   criteria. The drugs listed here may not be a formulary agent for all relevant lines of business
   and may require prior authorization.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>riluzole (Rilutek®)</td>
<td>50 mg PO BID</td>
<td>100 mg/day</td>
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</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- Revised El Escorial diagnostic criteria for ALS requires the presence of:
  1. Signs of lower motor neuron (LMN) degeneration by clinical, electrophysiological or neuropathologic examination,
  2. Signs of upper motor neuron (UMN) degeneration by clinical examination, and
  3. Progressive spread of signs within a region or to other regions, together with the absence of:
     a. Electrophysiological evidence of other disease processes that might explain the signs of LMN and/or UMN degenerations; and
     b. Neuroimaging evidence of other disease processes that might explain the observed clinical and electrophysiological signs.

- The definitions of ALS diagnoses provided by the El Escorial criteria are as follows:

<table>
<thead>
<tr>
<th></th>
<th>El Escorial criteria, 1994</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definite ALS</strong></td>
<td>Upper and lower motor neuron signs in three regions</td>
</tr>
<tr>
<td><strong>Probable ALS</strong></td>
<td>Upper and lower motor neuron signs in at least two regions, with upper motor neuron signs rostral to lower motor neuron signs</td>
</tr>
<tr>
<td><strong>Possible ALS</strong></td>
<td>Upper and lower motor neuron signs in one region, upper motor neuron signs alone in two or more regions, or lower motor neuron signs rostral to upper motor neuron signs</td>
</tr>
<tr>
<td><strong>Suspected ALS</strong></td>
<td>Lower motor neuron signs only, in two or more regions</td>
</tr>
</tbody>
</table>

- Two pivotal phase III trials that were conducted in Japan were used for the approval of Radicava in the USA. One of the phase III trials of Radicava found no statistically significant difference in delay of ALS progression, but a post-hoc analysis found that a certain subset of patients may benefit. Based on the post-hoc analysis, the second phase III was performed with a much more strict eligibility criteria and found a statistically significant difference in ALS progression in favor of Radicava. Therefore, patients not meeting the strict eligibility criteria at any time (at the time of initial or continued approval) can be assumed that no benefit will be provided by the use of Radicava for the treatment of ALS until further studies support its use in a wider population with ALS.

- The revised ALS Functional Rating Scale (ALSFRS-R) score consists of a total of 12 items and 48 points. It is a physician-generated estimate of the patient’s degree of functional impairment. Each item assesses the patient’s functional ability on daily tasks, such as walking and hand-writing. Each item is scored from 0 to 4 points, with 0 indicating no ability and 4 indicating normal ability.
V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALS</td>
<td>60 mg IV (2 consecutive 30 mg intravenous infusion bags) over 60 minutes at an infusion rate of approximately 1 mg/3.33mL per minute) as follows:</td>
<td>60 mg/day</td>
</tr>
<tr>
<td></td>
<td>• Initial treatment cycle: daily dosing for 14 days followed by a 14-day drug-free period</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Subsequent treatment cycles: daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods.</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability

Single-dose polypropylene bag for injection: 30 mg/100 mL

VII. References


Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.
<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J1301</td>
<td>Injection, edaravone, 1 mg</td>
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**Reviews, Revisions, and Approvals**

<table>
<thead>
<tr>
<th>Date</th>
<th>P &amp; T Approval Date</th>
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<tbody>
<tr>
<td>06.17</td>
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<td>02.02.18</td>
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<td>02.05.19</td>
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<td>02.25.20</td>
<td>05.20</td>
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**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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