Introduction

Amyotrophic lateral sclerosis (ALS)—often called Lou Gehrig disease—is a rare condition. It affects nerve cells that control movements like walking, chewing, and breathing. Because the nerve cells can no longer stimulate muscles, they get weak and paralysis sets in. ALS usually affects people between 40 and 70 years old, although some people develop the condition in their twenties and thirties. Symptoms can start in the arms or legs or in the muscles that control swallowing and speech. Regardless of where the symptoms start, the symptoms advance to other areas of the body. ALS usually is a progressive condition. This means it gets worse over time. The rate of progression—how fast is gets worse—varies from person to person. Radicava® (edaravone) is a drug that studies have shown helps slow the rate of decline in function. This policy discusses when Radicava may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
**Drug** | **Medical Necessity**
---|---
Radicava® (edaravone) | Radicava® (edaravone) may be considered medically necessary when the patient meets the following criteria:
- Patient has been diagnosed with Amyotrophic Lateral Sclerosis (ALS)
- Functionality retained for most activities of daily living
- Normal respiratory function retained (FVC \( \geq 80\% \) of predicted)
- Disease duration of 2 years or less

**Initial authorization can be granted for 6 months.**

**Re-authorization criteria:**
- Criteria for re-authorization after 6 months of initial therapy will be contingent upon:
  - Patient’s continued ability to perform most activities of daily living
  - Patient’s respiratory function remains unchanged

**Investigational**
Radicava® (edaravone) | All other uses of Radicava® (edaravone) for conditions not outlined in this policy are considered investigational.

<p>| <strong>Dosage and Quantity Limits</strong> |</p>
<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosage and Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amyotrophic Lateral Sclerosis (ALS)</td>
<td>30mg/100mL in a single-dose polypropylene bag</td>
</tr>
</tbody>
</table>

**Documentation Requirements**
The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:
- Office visit notes that contain the relevant history and physical evaluation information
- Results of the respiratory function tests


**Documentation Requirements**

- Other relevant information that could support medical necessity consideration

**Coding**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J1301</td>
<td>Injection, edaravone (Radicava®), 1 mg (new code effective 1/1/19)</td>
</tr>
</tbody>
</table>

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**Related Information**

**Benefit Application**

Radicava® (edaravone) is covered under medical benefit.

**Evidence Review**

**Clinical Trials**

The efficacy of RADICAVA for the treatment of ALS was established in a 6-month, randomized, placebo controlled, double-blind study conducted in Japanese patients with ALS who were living independently and met the following criteria at screening:

1. Functionality retained most activities of daily living (defined as scores of 2 points or better on each individual item of the ALS Functional Rating Scale – Revised [ALSFRS-R; described below])

2. Normal respiratory function (defined as percent-predicted forced vital capacity values of [%FVC] ≥80%)
3. Definite or Probable ALS based on El Escorial revised criteria

4. Disease duration of 2 years or less

The study enrolled 69 patients in the RADICAVA arm and 68 in the placebo arm. Baseline characteristics were similar between these groups, with over 90% of patients in each group being treated with riluzole.

RADICAVA was administered as an intravenous infusion of 60 mg given over a 60 minute period according to the following schedule:

- An initial treatment cycle with daily dosing for 14 days, followed by a 14-day drug-free period (Cycle 1)
- Subsequent treatment cycles with daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods (Cycles 2-6)

The primary efficacy endpoint was a comparison of the change between treatment arms in the ALSFRS-R total scores from baseline to Week 24. The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (speech, salivation, swallowing, handwriting, cutting food, dressing/hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency). Each item is scored from 0-4, with higher scores representing greater functional ability. The decline in ALSFRS-R scores from baseline was significantly less in the RADICAVA-treated patients as compared to placebo.

**Safety**

In randomized, placebo-controlled trials, 184 ALS patients were administered RADICAVA 60 mg in treatment cycles for 6 months. The population consisted of Japanese patients who had a median age of 60 years (range 29-75) and were 59% male. Most (93%) of these patients were living independently at the time of screening.

Table below lists the adverse reactions that occurred in ≥ 2% of patients in the RADICAVA-treated group and that occurred at least 2% more frequently than in the placebo-treated group in randomized placebo-controlled ALS trials. The most common adverse reactions that occurred in ≥10% of RADICAVA-treated patients were contusion, gait disturbance, and headache.

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Radicava (N=184)</th>
<th>Placebo (N=184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contusion</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Adverse Reaction</td>
<td>Radicava (N=184)</td>
<td>Placebo (N=184)</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Gait disturbance</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Headache</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Eczema</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory failure, respiratory disorder, hypoxia</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Glycosuria</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Tinea infection</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

**Regulatory Status**

FDA approved.

**References**


**History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/01/17</td>
<td>New policy, approved June 13, 2017. Added newly approved agent for ALS.</td>
</tr>
<tr>
<td>01/30/18</td>
<td>Minor formatting edits were made to the policy.</td>
</tr>
<tr>
<td>07/01/18</td>
<td>Annual Review, approved June 22, 2018. Literature review was conducted from 06/13/2017 to 06/13/2018. Benefit application information was added to reflect medical benefit and no changes to criteria made.</td>
</tr>
<tr>
<td>01/01/19</td>
<td>Coding update, added new HCPCS code J1301 (new code effective 1/1/19). Removed HCPCS code J3490.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and
local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2019 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
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Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  • Qualified sign language interpreters
  • Written information in other formats (large print, audio, accessible electronic formats, other formats)
• Provides free language services to people whose primary language is not English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5952. TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at
https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.
Call 800-722-1471 (TTY: 800-842-5357).

Oromo (Cushite):
Kaffatii irraa bilisa haala ta’en afaan keessanin odoozannah argachuu fi deeggarsa argachuu miga ni qabaattu.
Lakkoofoisa bibiliaa 800-722-1471 (TTY: 800-842-5357) ti bibilaa.

Français (French):
Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):

Deutsche (German):

Kreyòl nanmo (Hmong):

Italiano (Italian):
Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.
Chiama 800-722-1471 (TTY: 800-842-5357).

中文 (Chinese):
本通知有重要的訊息。本通知可能有關於您通過 Premera Blue Cross 提交的申請或保障的重要訊息。本通知可能有重要日期。您可能需要在特定日期之前採取行動，以保留您的健康保險或費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357).

Arabic (عربية):
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所有信息均以英文呈现。
Premera Blue Cross (TTY: 800-842-5357).