Riluzole (Rilutek/Tiglutik)
Policy Number: C9697-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DUE BY OR BEFORE
9/1/2016	2/17/2021	4/2022
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
NA	RxPA	Q2 2021 20210428C9697-A

PRODUCTS AFFECTED:
Rilutek (riluzole), riluzole, Tiglutik (riluzole)

DRUG CLASS:
ALS Agents

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Retail Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered

AVAILABLE DOSAGE FORMS:
Riluzole TABS 50MG (60ct bottle) Tiglutik SUSP 50MG/10ML (300ml bottle)

FDA-APPROVED USES:
Indicated for the treatment of patients with amyotrophic lateral sclerosis (ALS). Rilutek (riluzole) extends survival and/or time to tracheostomy

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
amyotrophic lateral sclerosis

REQUIRED MEDICAL INFORMATION:
A. AMYOTROPHIC LATERAL SCLEROSIS (ALS):

1. Documented diagnosis of amyotrophic lateral sclerosis (ALS)
   AND
2. Documentation of aminotransferases prior to therapy and plan documenting liver enzyme monitoring for the first 3 months and periodically thereafter
   AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any

FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to riluzole include: Patients with a history of severe hypersensitivity reactions to riluzole or to any of its components
AND

4. FOR TIGLUTIK SUSPENSION REQUESTS: Documentation patient is unable to ingest a solid dosage form (i.e. tablet or capsule) due to ONE of the following: age, oral/motor difficulties, dysphagia, or patient utilizes a feeding tube for medical administration

DURATION OF APPROVAL:
Initial authorization: 12 months, Continuation of therapy: 12 months

QUANTITY:
Maximum dose: 50 mg twice daily.

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified neurologist experienced in the management/treatment of amyotrophic lateral sclerosis (ALS). Submit consultation notes if applicable.

AGE RESTRICTIONS:
18 years of age or older

CONTINUATION OF THERAPY:
A. AMYOTROPHIC LATERAL SCLEROSIS (ALS):

1. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)
   AND
2. Disease stability or mild progression indicating a slowing of decline and patient has not had a tracheostomy since initial authorization
   AND
3. Documentation of the patient having follow-up monitoring of a complete blood count (CBC) with differential and liver function tests (LFTs) every month for the first 3 months of therapy and every 3 months thereafter

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of riluzole are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. RILUTEK is of uncertain benefit in patients with: tracheostomy required for ventilation, other incurable life-threatening disorders, and other forms of anterior horn cell disease. The safety and efficacy of RILUTEK have not been studied in motor neuron diseases other than ALS. Therefore, RILUTEK should not be used in any other form of motor neuron disease.

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:
Amyotrophic Lateral Sclerosis (ALS)

- Also known as Charcot's disease and Lou Gehrig's disease, is a disease of unknown cause characterized by slowly progressive degeneration of upper motor neurons (UMNs) and lower motor neurons (LMNs).

- An adult-onset, neurodegenerative disease characterized by loss of motor neurons in the spinal cord, brainstem, and motor cortex. ALS primarily affects the upper and lower motor neurons and is characterized by muscle weakness, disability, and eventual death, usually from respiratory failure.
- Cause of the disease is unknown, and there is no cure.
- One of the most common neuromuscular disease worldwide and affects individuals of all races and ethnic backgrounds (NIND 2017). In 2016 the Centers for Disease Control and Prevention estimated that between 14,000 - 15,000 Americans have ALS.
- Most common in individuals 40-60 years old, but younger and older people can develop the disease. Men are more likely to develop ALS than women. Studies suggest an overall ratio of about 1.5 men to every woman who develops ALS in Western countries (ALS Association Epidemiology of ALS and Suspected Clusters)

A diagnosis of ALS is based upon evidence of upper and lower motor neuron signs, relentless disease progression, and the absence of an alternative etiology (Kiernan MC; Brooks BR; AAN 2009). ALS, as with other motor neuron diseases, does not have a diagnostic test that can confirm or entirely exclude its diagnosis.

ALS management is primarily managed with symptomatic treatment and palliative care. There is no known cure for ALS at the present time. There are currently two FDA approved therapies for management of ALS as of May 2017 with the approval of Radicava (edaravone):

3) Riluzole (Rilutek) was the first drug to receive FDA approval for ALS (December 1995). Riluzole is an oral formulation that acts to slow the progression of ALS symptoms and prolong survival. The exact mechanism in treating ALS is unknown; however, it is believed to block the release of glutamate from nerve cells thereby reducing the rate of glutamate-induced deterioration in nerve cells resulting in the slowing of initial progression of symptoms.
    - **Riluzole has demonstrated a slight increase overall survival (by 2-3 months), however it has not been shown to have an effect on physical functioning (has not been shown to modulate motor or respiratory function).** Clinical studies concluded that Rilutek may increase early survival by two to three months, but it does not improve muscle strength and neurological function and has no effect in later stages of ALS.
    - Compared with placebo, riluzole may prolong median tracheostomy-free survival by 2-3 months in patients younger than 75 years with definite or probable ALS who have had the disease for less than 5 years and who have a forced vital capacity (FVC) of greater than 60%.

APPENDIX:

Diagnostic criteria

The El Escorial revised Airlie House diagnostic criteria grades the certainty of the diagnosis based upon 4 clinical grades:

- Clinically “Definite ALS” is defined on clinical evidence alone by the presence of upper motor neuron (UMN), as well as lower motor neuron (LMN) signs, in the bulbar region and at least 2 spinal regions or the presence of UMN and LMN signs in 3 spinal regions.

- Clinically “Probable ALS” is defined on clinical evidence alone by UMN and LMN signs in at least 2 regions with some UMN signs necessarily rostral to (above) the LMN signs.
- Clinically “Probable ALS Laboratory supported” is defined when clinical signs of UMN and LMN dysfunction are in only 1 region, or when UMN signs alone are present in 1 region, and LMN signs defined by electromyography criteria are present in at least 2 regions, with properapplication of neuroimaging and clinical laboratory protocols to exclude other causes.
- Clinically “Possible ALS” is defined when clinical signs of UMN and LMN dysfunction are found together in only 1 region or UMN signs are found alone in 2 or more regions; or LMN signs are found rostral to UMN signs and the diagnosis of Clinically Probable ALS Laboratory supported cannot be proven by evidence on clinical grounds in conjunction with electrodiagnostic, neurophysiologic, neuroimaging, or clinical laboratory studies. Other diagnoses must have been excluded to accept a diagnosis of Clinically Possible ALS.

Note: “Suspected ALS” is deleted from the revised El Escorial Criteria

By the revised El Escorial criteria, diagnosis of ALS requires:

----Presence of evidence of lower motor neuron (LMN) degeneration by clinical, electrophysiologic, or neuropathologic exam evidence of upper motor neuron (UMN) degeneration by clinical exam progressive spread of symptoms or signs within a region or to other regions, determined by history or exam

----Absence of: electrophysiologic or pathologic evidence of other disease processes that might explain signs of LMN and/or UMN degeneration neuroimaging evidence of other disease processes that might explain observed clinical and electrophysiologic signs

ALS FUNCTIONAL RATING SCALE-REVISED (ALSFRS-R)

ALSFRS-R has been the most widely used composite measure of function in ALS over the last 15 years (Cedarbaum 1999) 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 to 4, with higher scores representing greater functional ability.

The ALSFRS-R includes 12 items measuring multiple aspects of daily functioning.

Bulbar	Fine Motor	Gross Motor	Breathing

1. Speech
4. Normal speech processes
3. Detectable speech disturbance
2. Intelligible with repeating
1. Speech combined with nonvocal communication
0. Loss of useful speech

2. Salivation
4. Normal
3. Slight but definite excess of saliva in mouth; may have nighttime drooling
2. Moderately excessive saliva; may have minimal drooling
1. Marked excess of saliva with some drooling
0. Marked drooling; requires constant tissue or handkerchief

3. Swallowing
4. Normal eating habits
3. Early eating problems-occasional choking
2. Dietary consistency changes
1. Needs supplemental tube feeding
0. NPO (exclusively parenteral or enteral feeding)

4. Handwriting
4. Normal
3. Slow or sloppy; all words are legible
2. Not all words are legible
1. Able to grip pen but unable to write
0. Unable to grip pen

5a. Cutting Food / Handling Utensils
4. Normal
3. Somewhat slow and clumsy, but no help needed
2. Can cut most foods, although clumsy and slow; some help needed
1. Food must be cut by someone, but can still feed slowly
0. Needs to be fed

5b. Cutting Food / Handling Utensils (Alt. for patients with Gastrostomy)
4. Normal
3. Clumsy but able to perform all manipulations independently
2. Some help needed with closures and fasteners
1. Provides minimal assistance to caregiver
0. Unable to perform any aspect of task

6. Dressing and hygiene
4. Normal function
3. Independent and complete self-care with effort or decreased efficiency
2. Intermittent assistance or substitute methods
1. Needs attendant for self-care
0. Total dependence

7. Turning in bed
4. Normal
3. Somewhat slow and clumsy, but no help needed
2. Can turn alone or adjust sheets, but with great difficulty
1. Can initiate, but not turn or adjust sheets alone
0. Helpless

8. Walking
4. Normal
3. Early ambulation difficulties
2. Walks with assistance
1. Non-ambulatory functional movement only
0. No purposeful leg movement

9. Climbing stairs
4. Normal
3. Slow
2. Mild unsteadiness or fatigue
1. Needs assistance
0. Cannot do

10. Dyspnea
4. None
3. Occurs when walking
2. Occurs with one or more of the following: eating, bathing, dressing (ADL)
1. Occurs at rest, difficulty breathing when either sitting or lying
0. Significant difficulty, considering using mechanical respiratory support

11. Orthopnea
4. None
3. Some difficulty sleeping at night due to shortness of breath. Does not routinely use more than two pillows
2. Needs extra pillow in order to sleep (more than two)
1. Can only sleep sitting up
0. Unable to sleep

12. Respiratory insufficiency
4. None
3. Intermittent use of BiPAP
2. Continuous use of BiPAP
1. Continuous use of BiPAP during the night and day
0. Invasive mechanical ventilation by intubation or tracheostomy

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