Medical Drug Clinical Criteria

Subject:	Qalsody (tofersen)		
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Overview

This document addresses the use of Qalsody (tofersen), an antisense oligonucleotide agent, for the treatment of Amyotrophic Lateral Sclerosis (ALS) in those with superoxide dismutase 1 (SOD1) gene mutation. ALS (commonly known as Lou Gehrig's disease) is a refractory and progressive neuromuscular disease that attacks nerve cells in the spine and brain that are responsible for controlling voluntary movement; the cause of the disease is not known. Median survival from onset to death in ALS is reported to vary from 20 to 48 months.

Estimates are 2% of ALS patients have mutations in the gene encoding superoxide dismutase 1 (SOD1). Neuronal degeneration in ALS is caused by toxic gain in function of the mutant SOD1 protein. Qalsody (tofersen), an anti-sense oligonucleotide, reduces the synthesis of SOD1 protein. Approximately 330 people in the US have SOD1 associated ALS (Miller 2022).

Qalsody was studied in a phase 3 randomized, double-blind trial against placebo for 24 weeks with a follow-up period of 4 to 8 weeks, and then followed by an open label extension period (VALOR, VALOR OLE, Miller 2022). Trial participants were enrolled if they had weakness attributable to ALS and a confirmed SOD1 mutation. Concomitant use of riluzole and/or edaravone was permitted. The primary efficacy outcome was rate of decline in the total score on the ALS Functional Rating Scale–Revised (ALSFRS-R) from baseline to week 28. Primary efficacy measure did not reach statistical significance.

Qalsody, an intrathecal injection, was approved under the FDA's accelerated program based on the surrogate endpoint of reduction of plasma neurofilament light chain in individuals enrolled in the trial. Continued approval is contingent upon verification of clinical benefits in confirmatory trials.

ALS Functional Rating Scale-revised (ALSFRS-R); (Cedarbaum 1999)

A commonly used functional rating system for persons with ALS, scored as follows:

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

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

Swallowing
- 4 Normal eating habits

Cutting food and handling utensils (patients without gastrostomy)
- 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

Cutting food and handling utensils (alternate scale for patients with gastrostomy)
- 4 Normal
- 3 Clumsy but able to perform all manipulations independently
- 2 Some help needed with closures and fasteners

Walking
- 4 Normal
- 3 Early ambulation difficulties
- 2 Walks with assistance
- 1 Nonambulatory functional movement
- 0 No purposeful leg movement

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

Dyspnea (new)
- 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

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

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

- 1 Provides minimal assistance to caregiver
- 0 Unable to perform any aspect of task

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

Turning in bed and adjusting bed clothes
- 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

- 0 Significant difficulty, considering using mechanical respiratory support

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

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

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Qalsody (tofersen)

Initial requests for Qalsody (tofersen) may be approved if the following criteria are met:

I. Individual has a diagnosis of amyotrophic lateral sclerosis (ALS); **AND**
II. Individual meets both of the following:
   A. Weakness associated with ALS; **AND**
   B. Documentation is provided that genetic test is positive for SOD1 mutation.

Continuation requests for Qalsody (tofersen) may be approved if the following criteria are met:

I. Individual does not require mechanical ventilation by intubation or tracheostomy.

Qalsody (tofersen) may not be approved when the above criteria are not met and for all other indications.

Approval Duration:
Initiation: 6 months
Continuation: 12 months

Quantity Limits

Qalsody (tofersen) Quantity Limits

Drug	Limit
Qalsody (tofersen) 100 mg/15 mL vial intrathecal solution	15 mL (1 vial) every 4 weeks
Override Criteria	
Initiation of therapy for Qalsody (tofersen): May approve a total of three (3) 100 mg/15 mL doses (3 vials) in the first six weeks of treatment.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
J1304	Injection, tofersen, 1 mg [Qalsody]
ICD-10 Diagnosis	
G12.21	Amyotrophic lateral sclerosis

Document History

Reviewed: 11/17/2023
Document History:

- 11/17/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 04/26/2023 – New Review: Add new clinical criteria document for Qalsody (tofersen). Coding Reviewed: Added HCPCS J3490, J3590. All diagnoses pend. Effective 10/1/2023 Added HCPCS C9157. Effective 1/1/2024 Added HCPCS J1304. Removed HCPCS J3490, J3590, C9157. Added ICD-10-CM G12.21.

References

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3. Miller RG, Jackson CE, Kasarskis EJ,et al. Practice Parameter update: The care of the patient with amyotrophic lateral sclerosis: Drug, nutritional, and respiratory therapies (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology Oct 2009, 73 (15) 1218-1226; DOI: 10.1212/WNL.0b013e3181bc0141. Reaffirmed Jan 2023. Accessed October 3, 2023.
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5. Miller TM, Cudkowicz ME, Genge A, et al. VALOR and OLE Working Group. Trial of Antisense Oligonucleotide Tofersen for *SOD1* ALS. *N Engl J Med*. 2022;387(12):1099-1110. doi:10.1056/NEJMoa2204705. Available at https://www.nejm.org/doi/suppl/10.1056/NEJMoa2204705/suppl_file/nejmoa2204705_appendix.pdf.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.