Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Tofersen (Qalsody®)	MP-RX-FP-146-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Tofersen (Qalsody®),* an antisense oligonucleotide approved by the Food and Drug Administration (FDA) for the treatment of amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (*SOD1*) gene.

Background Information

Amyotrophic lateral sclerosis 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.

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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
- 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

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
- 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

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
- 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 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

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Approved Indications

A. Treatment of amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (*SOD1*) gene.

Approval for this indication has been granted under accelerated approval, which is based on the observed reduction in plasma neurofilament light chain levels in patients treated with Qalsody. However, continued approval for this indication may depend on confirming the clinical benefit in subsequent confirmatory trial(s).

Other Uses

i. None

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document 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 Guidelines may apply.

HCPCS	Description
J1304	Injection, tofersen, 1 mg [Qalsody]

ICD-10	Description
G12.21	Amyotrophic lateral sclerosis

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Medical Necessity Guidelines

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.

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

Tofersen (Qalsody®)

A. Criteria For Initial Approval *(Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Tofersen (Qalsody®)therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when the following criteria are met:
    A. Individual does not require mechanical ventilation by intubation or tracheostomy.

C. Authorization Duration

i. Initial Approval Duration: 12 months
ii. Reauthorization Approval Duration: 12 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Qalsody may not be approved when the criteria above (section A: Criteria for Initial Approval) are not met and for all other indications.

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Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosage	Limit
Qalsody 100 mg/15 mL (6.7mg/mL) SDV	*Loading Dose:* Three (3) 100 mg (15 mL) doses administered at 14-day intervals.	May approve a total of three (3) 100 mg/15 mL doses (3 vials) in the first six weeks of treatment.
	Maintenance Dose: 100 mg (15 mL) every 28 days, starting 28 days after the third loading dose.	1 vial every 4 weeks.
Exceptions		
None.		

Reference Information

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 3, 2023.
2. Cedarbaum JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci. 1999; 169(1-2):13-21.
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.
4. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice Parameter update: The care of the patient with amyotrophic lateral sclerosis: Multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology Oct 2009, 73 (15) 1227- 1233; DOI: 10.1212/WNL.0b013e3181bc01a4. Reaffirmed Feb 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.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 12/20/2024	Updated service description to remove duplicative text. Updated quantity limits table to add dosage form and strength, and quantity limits. Minor wording and formatting changes. Coding reviewed: no changes.	3/20/2025	4/2/2025
Policy Inception 01/27/2024	Elevance Health's Medical Policy adoption	N/A	6/28/2024