| WellMed<br>Doctors helping patients for more than 25 years | **Effective Date: 10/27/23** | **Revision Date(s):** |
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| **Department: PHARMACY** | **MMC Review/ Approval Date(s):**<br>10/25/23 | **Page(s): 12** |

**Policy Number: 063.000**
**Title: Coverage Determination Policy for Qalsody (Tofersen)**

**Regions:** ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

**Impacted Areas:**

| | |
|---|---|
| ☒ Network Management/Provider Services | ☒ Utilization Management |
| ☐ Member services | ☐ Case management |
| ☐ Quality Management | ☐ Disease management |
| ☐ Credentialing | ☒ Claims |
| ☐ IT | ☐ Human resources |
| ☐ Administration | ☐ Finance |
| ☐ Compliance/delegation | ☒ Pharmacy |
| | ☐ ALL |

**Available LCD/NCD/LCA: None**

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# Title: Coverage Determination Policy for Qalsody (Tofersen)

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**Coverage Policy Number: 063.000**

**Line of Business:** Medicare Part B

**Policy Type:** Prior Authorization

## Coverage Determination:

## Initial/New Requests

**Qalsody (tofersen)** is proven and medically necessary for the treatment of **Amyotrophic Lateral Sclerosis (ALS**) when **ALL** of the following criteria are met:

1. Submission of medical records (e.g., chart notes, previous medical history, diagnostic testing including: imaging, nerve conduction studies, laboratory values) to support the diagnosis of ALS
2. Submission of medical records confirming mutation in the superoxide dismutase 1 (SOD1) gene
3. Provider attestation that the patient's baseline functional ability has been documented prior to initiating treatment (e.g., speech, walking, climbing stairs, etc.)
4. Patient is not dependent on invasive ventilation or tracheostomy
5. Qalsody is prescribed by, or in consultation with a neurologist.
6. Qalsody dosing for ALS is in accordance with the United States Food and Drug Administration approved labeling
7. Initial authorization will be for no more than 6 months

## Renewal/Continuation of Therapy Requests

Continuation of therapy requests for Qalsody for the treatment of **ALS** will be approved if **ALL** of the following criteria are met:

1. Diagnosis of ALS
2. Patient is currently receiving Qalsody therapy
3. Provider attestation that the patient has slowed disease progression from baseline
4. Patient is **not** dependent on invasive ventilation or tracheostomy
5. Qalsody is prescribed by, or in consultation with a neurologist
6. Qalsody dosing for ALS is in accordance with the United States Food and Drug Administration approved labeling
7. Authorization will be for no more than 6 months

## FDA Approved Dose and Indication

| FDA Approved Indication | Approved Dosing |
|---|---|
| Amyotrophic lateral sclerosis (ALS) in adults with a mutation in the superoxide dismutase 1 (SOD1) gene | 100 mg (15 mL) intrathecally by lumbar puncture every 14 days for 3 doses and then every 28 days thereafter |

**NOTE: This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain observed in patients treated with Qalsody. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).**

## General Background

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a rapidly progressive, invariably fatal neurological disease that attacks neurons responsible for controlling voluntary muscles. The disease belongs to a group of disorders known as motor neuron diseases, which are characterized by the gradual degeneration and death of motor neurons. Eventually, all muscles under voluntary control are affected. Individuals lose their strength and the ability to move their arms, legs, and body. When muscles in the diaphragm and chest wall fail, individuals lose the ability to breathe without ventilatory support. Individuals with ALS usually survive for only 3 to 5 years from the onset of symptoms. However, about 10 percent of those with ALS survive for 10 or more years.

ALS can be categorized as familial or sporadic disease, depending on whether the patient has a family history of the disease or not. Familial ALS accounts for approximately 10% of cases, and among these, C9ORF72 and SOD1 are the two most common causative genes. SOD1 encodes for superoxide dismutase, a mutated protein which has been associated with the degeneration of motor neurons. SOD1-ALS is the second most common form of familial ALS. There are approximately 16,000 people living with ALS in the United States, with an estimated prevalence of 5 patients per 100,000 population, and with 5,000 new cases diagnosed each year. 5-10% of ALS cases are familial and associated with approximately 50 different genes and approximately 2% of ALS cases are associated with mutations in the SOD1 gene. Familial ALS generally has an earlier onset (by about 10 years) than sporadic ALS.

Qalsody (tofersen) is an antisense oligonucleotide that causes degradation of SOD1 mRNA through binding to SOD1 mRNA, which results in a reduction of SOD1 protein synthesis.

## Clinical Evidence

The efficacy of tofersen was assessed in a 28-week randomized, double-blind, placebo-controlled clinical study in patients 23 to 78 years of age with weakness attributable to ALS and a SOD1 mutation confirmed by a central laboratory (Study 1 Part C, NCT02623699). One hundred eight (108) patients were randomized 2:1 to receive treatment with either tofersen 100 mg (n = 72) or placebo (n = 36) for 24 weeks (3 loading doses followed by 5 maintenance doses). Concomitant riluzole and/or edaravone use was permitted for patients. The prespecified primary analysis population (n = 60, modified intent to treat [mITT]) had a slow vital capacity (SVC) ≥ 65% of predicted value and met prognostic enrichment criteria for rapid disease progression, defined based on their pre-randomization ALS Functional Rating Scale–Revised (ALSFRS-R) decline slope and SOD1 mutation type. The non-mITT population (n = 48) had a slow vital capacity (SVC) ≥ 50% of predicted value and did not meet the enrichment criteria for rapid disease progression. Baseline disease characteristics in the overall intent-to-treat (ITT) population (combined mITT and non-mITT population) were generally similar in patients treated with tofersen and patients who received placebo, with slightly shorter time from symptom onset and higher plasma neurofilament (NfL) at baseline in the tofersen group. At baseline, 62% of patients were taking riluzole, and 8% of patients were taking edaravone. Mean baseline ALSFRS-R score was 36.9 (5.9) in the tofersen treatment group and 37.3 (5.8) in the placebo group. Median time from symptom onset was 11.4 months in the tofersen treatment group and 14.6 months in the placebo group. The primary efficacy analysis was the change from baseline to Week 28 in the ALSFRS-R total score in the mITT population, analyzed using the joint rank test to account for mortality in conjunction with multiple imputation (MI) to account for missing data for withdrawals other than death. Patients treated with tofersen experienced less decline from baseline in the ALSFRS-R compared to placebo, but the results were not statistically significant (tofersen-placebo adjusted mean difference [95% CI]: 1.2 [-3.2, 5.5]). Specifically, in the faster-progression subgroup (primary analysis), the change to week 28 in the ALSFRS-R score was −6.98 with tofersen and −8.14 with placebo (difference, 1.2 points; 95% confidence interval [CI], −3.2 to 5.5; p = 0.97). Other clinical secondary outcomes also did not reach statistical significance. Secondary endpoints of change from baseline at Week 28 in plasma NfL and CSF SOD1 protein were nominally statistically significant. NfL reduction was consistently observed for all subgroups based on sex, disease duration since symptom onset, site of onset, and riluzole/edaravone use. After completion of Study 1, patients had the option to enroll in an open-label extension study. A total of 95 participants (88%) entered the open-label extension. At an interim analysis at 52 weeks, reductions in NfL were seen in patients previously receiving placebo who initiated tofersen in the open-label extension study, similar to the reductions seen in patients treated with tofersen in Study 1. Specifically, at 52 weeks, the change in the ALSFRS-R score was −6.0 in the early-start cohort and −9.5 in the delayed-start cohort (difference, 3.5 points; 95% CI, 0.4 to 6.7); non–multiplicity-adjusted differences favoring early-start tofersen were seen for other end points. Lumbar puncture– related adverse events were common. Neurologic serious adverse events occurred in 7% of tofersen recipients. Earlier initiation of tofersen compared to placebo/delayed initiation of tofersen was associated with trends for reduction in decline on ALSFRSR, SVC percent-predicted, and hand-held dynamometry (HHD) megascore that were not statistically significant. Through all open-label follow-up at the time of the interim analysis, earlier initiation

of tofersen was also associated with a trend towards reduction of the risk of death or permanent ventilation, although it was not statistically significant. These exploratory analyses should be interpreted with caution given the limitations of data collected outside of a controlled study, which may be subject to confounding.

## HCPCS Code

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|---|---|
| **HCPCS Code** | J3490 - Unclassified drugs<br>J3590 - Unclassified biologics<br>C9399 - Unclassified drugs or biologicals |
| **Available Dosage Form** | Intrathecal Solution: 6.7 MG/1 ML |
| **Route of Administration** | Intrathecal |

## Acronyms

Amyotrophic lateral sclerosis = ALS

Superoxide dismutase 1 = SOD1

Modified intent to treat = mITT

Slow vital capacity = SVC

ALS Functional Rating Scale–Revised = ALSFRS-R

Neurofilament = NfL

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