tofersen (Qalsody™)

Policy # 00854
Original Effective Date: 11/13/2023
Current Effective Date: 11/11/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of tofersen (Qalsody™)‡ for the treatment of amyotrophic lateral sclerosis (ALS) in adults with a mutation in the superoxide dismutase 1 (*SOD1*) gene to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of tofersen (Qalsody) for NON-FDA approved indications to be **investigational.***

Background/Overview

Qalsody is indicated for the treatment of ALS in adults who have a mutation in the *SOD1* gene. It is proposed to work by reducing the synthesis of SOD1 protein through degradation of the SOD1 mRNA which then decreases plasma and cerebrospinal fluid neurofilament light chain concentrations. Neurofilament light chains (NfL) are a nonspecific marker of damage and degeneration of neurons and are positively correlated with disease progression in ALS. It should be noted that NfL levels have not been used before as a surrogate biomarker for approval for other ALS medications. Additionally, in clinical practice, NfL levels are not routinely monitored. Qalsody must be administered intrathecally every month by a trained healthcare professional.

ALS is a rapidly progressing, degenerative disease in which the patient's upper and lower motor neurons degenerate leading to loss of motor function. Patients with ALS present with painless, progressive muscle atrophy and weakness, which eventually leads to paralysis. Death due to respiratory failure typically occurs within 3-5 years of diagnosis. Approximately 13,000-15,000 people in the U.S. have ALS with 95% of these cases being sporadic. Approximately 5-10% of ALS

cases is due to a family history of ALS with around 2% of these cases being caused by mutations in the *SOD1* gene. *SOD1* mutations usually follow an autosomal-dominant inheritance pattern and cause the production and accumulation of a toxic form of SOD1 protein leading to axonal injury, neurodegeneration, and death of motor neurons. For all forms of ALS, disease progression is monitored using the ALS Functional Rating Scale- Revised (ALSFRS-R), a 13-question scale that assesses the patient's ability to perform normal daily activities such as speech, handwriting, cutting food, and climbing stairs. Each question is scored on a scale of 0-4 with higher scores representing greater functional ability.

Current treatment guidelines from the American Academy of Neurology (AAN) do not address Qalsody, or other newer treatment options, Relyvrio™‡ or Radicava®‡. The parameter states that riluzole, the only other disease-modifying agent approved for ALS, is safe and effective for slowing disease progression to a modest degree and should be offered to patients with ALS. All other pharmacologic recommendations center on symptomatic management and palliative care.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Qalsody was approved for the treatment of amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (*SOD1*) gene. This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with Qalsody. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Qalsody 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. One hundred eight (108) patients were randomized 2:1

to receive treatment with either Qalsody 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-randomized ALS Functional Rating Scale-Revised (ALSFRS-R) decline slope and *SOD1* mutation type. The non-mITT population (n=48) had an 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 Qalsody and patients who received placebo, with slightly shorter time from symptom onset and higher plasma NfL at baseline in the Qalsody 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 Qalsody treatment group and 37.3 (5.8) in the placebo group. Median time from symptom onset was 11.4 months in the Qalsody 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 Qalsody experienced less decline from baseline in the ALSFRS-R compared to placebo, but the results were not statistically significant (Qalsody-placebo adjusted mean difference [95% CI]: 1.2 [-3.2, 5.5]). 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.

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References

1. Qalsody [package insert]. Biogen, Inc. Cambridge, MA. Updated April, 2023

Policy History

Original Effective Date: 11/13/2023
Current Effective Date: 11/11/2024
10/05/2023 Medical Policy Committee review
10/11/2023 Medical Policy Implementation Committee approval. New policy.
12/12/2023 Coding update
10/03/2024 Medical Policy Committee review
10/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 10/2025

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice

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medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No code
HCPCS	J1304 Delete code effective 01/01/2024: C9157
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.