

QALSODY- tofersen injection

Biogen Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use QALSODY™ safely and effectively. See full prescribing information for QALSODY.

QALSODY (tofersen) injection, for intrathecal use
Initial U.S. Approval: 2023

----- **INDICATIONS AND USAGE** -----

QALSODY is an antisense oligonucleotide indicated 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 observed in patients treated with QALSODY. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s). (1)

----- **DOSAGE AND ADMINISTRATION** -----

QALSODY is administered intrathecally (2.1)

Dosing Information (2.1)

- Recommended dose: 100 milligrams (15 mL) per administration
- Initiate QALSODY treatment with 3 loading doses administered at 14day intervals. A maintenance dose should be administered once every 28 days thereafter.

Preparation and Administration Instructions (2.2)

- Allow to warm to room temperature prior to administration
- Administer within 4 hours of removal from vial
- Prior to administration, remove approximately 10 mL of cerebrospinal fluid
- Administer as an intrathecal bolus injection over 1 to 3 minutes

----- **DOSAGE FORMS AND STRENGTHS** -----

Injection: 100 mg/15 mL (6.7 mg/mL) solution in a single-dose vial (3)

----- **CONTRAINDICATIONS** -----

None (4)

----- **WARNINGS AND PRECAUTIONS** -----

- *Myelitis and/ or Radiculitis*: Serious events of myelitis and radiculitis have been reported. Monitor for symptoms; diagnostic workup and treatment should be initiated according to the standard of care. (5.1)
- *Papilledema and Elevated Intracranial Pressure*: Serious events of papilledema and elevated intracranial pressure have been reported. Monitor for symptoms; diagnostic workup and treatment should be initiated according to standard of care. (5.2)
- *Aseptic Meningitis*: Serious events of aseptic meningitis have been reported. Monitor for symptoms; diagnostic workup and treatment should be initiated according to standard of care. (5.3)

----- **ADVERSE REACTIONS** -----

The most common adverse reactions (≥ 10% of patients treated with QALSODY and greater than placebo) were pain, fatigue, arthralgia, cerebrospinal fluid white blood cell increased, and myalgia. (Section 6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Biogen at 1-877-725-7639 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 4/2023

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1. Dosing Information
- 2.2. Preparation and Administration Instructions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1. Myelitis and/or Radiculitis
- 5.2. Papilledema and Elevated Intracranial Pressure
- 5.3. Aseptic Meningitis

6 ADVERSE REACTIONS

- 6.1. Clinical Trials Experience

8 USE IN SPECIFIC POPULATIONS

- 8.1. Pregnancy
- 8.2. Lactation
- 8.4. Pediatric Use
- 8.5. Geriatric Use

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1. Mechanism of Action
- 12.2. Pharmacodynamics
- 12.3. Pharmacokinetics
- 12.6. Immunogenicity

13 NONCLINICAL TOXICOLOGY

- 13.1. Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

- 16.1. How Supplied
- 16.2. Storage and Handling

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

QALSODY is indicated 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 [see *Clinical Studies (14)*]. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1. Dosing Information

Recommended Dosage

Administer QALSODY intrathecally using a lumbar puncture by, or under the direction of, healthcare professionals experienced in performing lumbar punctures.

The recommended dosage is 100 mg (15 mL) of QALSODY per administration.

Initiate QALSODY treatment with three (3) loading doses administered at 14-day intervals.

Administer a maintenance dose every 28 days thereafter.

Missed Dose

If the second loading dose is missed, administer QALSODY as soon as possible, and administer the third loading dose 14 days later.

If the third loading dose or a maintenance dose is missed, administer QALSODY as soon as possible, and administer the next dose 28 days later.

2.2. Preparation and Administration Instructions

Use aseptic technique when preparing and administering QALSODY intrathecally. Prepare and administer QALSODY according to the following steps:

Preparation

Vial preparation instructions

- Allow refrigerated QALSODY vial to warm to room temperature (25°C/77°F) prior to administration without using external heat sources [see *Storage and Handling (16.2)*].
- Inspect the solution in the QALSODY vial prior to administration. Do not administer if particles are observed or the liquid in the vial is not clear and colorless to slightly yellow.
- Do not shake the QALSODY vial.

Procedural preparation instructions

- If indicated by the clinical condition of the patient, consider sedation.
- If indicated by the clinical condition of the patient, consider imaging to guide intrathecal administration of QALSODY.
- Prior to removing the vial's cap on the aluminum overseal, confirm readiness of the patient. An unopened QALSODY vial can be returned to the refrigerator [see *Storage and Handling (16.2)*].
- Evaluate patients prior to and after intrathecal injection for the presence of potential conditions related to lumbar puncture, to avoid serious procedural complications.

Administration

Prior to administration, remove approximately 10 mL of cerebrospinal spinal fluid (CSF) using a lumbar puncture needle.

Prior to administration, remove the plastic cap and attach a needle to the syringe, for the purpose of withdrawing QALSODY from the vial. Insert the needle into the vial through the center of the overseal and withdraw the required dose of 15 mL (equivalent to 100 mg) from the vial.

- Do not dilute QALSODY.
- External filters are not required.

Administer QALSODY using a lumbar puncture needle as an intrathecal bolus injection over 1 to 3 minutes.

- QALSODY contains no preservatives. Once drawn into the syringe, the solution should be administered immediately (within 4 hours of removal from the vial) at room temperature; otherwise, it must be discarded.

Any unused contents of the single-dose vial should be discarded.

3 DOSAGE FORMS AND STRENGTHS

Injection: 100 mg/15 mL (6.7 mg/mL) as a clear and colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1. Myelitis and/or Radiculitis

Serious adverse reactions of myelitis and radiculitis have been reported in patients treated with QALSODY. Six patients treated with QALSODY experienced myelitis or radiculitis in the clinical studies. Two patients discontinued treatment with QALSODY and required symptomatic management with full resolution of symptoms. In the remaining 4 patients, symptoms resolved without discontinuation of QALSODY. If symptoms consistent with myelitis or radiculitis develop, diagnostic workup and treatment should be initiated according to the standard of care. Management may require interruption or discontinuation of QALSODY.

5.2. Papilledema and Elevated Intracranial Pressure

Serious adverse reactions of papilledema and elevated intracranial pressure have been reported in patients treated with QALSODY. Four patients developed elevated intracranial pressure and/or papilledema. All patients received treatment with standard of care with resolution of symptoms, and no events led to discontinuation of QALSODY. If symptoms consistent with papilledema or elevated intracranial pressure develop, diagnostic workup and treatment should be initiated according to the standard of care.

5.3. Aseptic Meningitis

Serious adverse reactions of aseptic meningitis (also called chemical meningitis or drug-induced aseptic meningitis) have been reported in patients treated with QALSODY. One patient experienced a serious adverse reaction of chemical meningitis, which led to discontinuation of QALSODY. One patient experienced a serious adverse reaction of aseptic meningitis, which did not lead to discontinuation of QALSODY. In addition, nonserious adverse drug reactions of CSF white blood cell increased, and CSF protein

increased have also been reported with QALSODY [see *Adverse Reactions (6.1)*]. If symptoms consistent with aseptic meningitis develop, diagnostic workup and treatment should be initiated according to the standard of care.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed elsewhere in the labeling:

- Myelitis and/or Radiculitis [see *Warnings and Precautions (5.1)*]
- Papilledema and Elevated Intracranial Pressure [see *Warnings and Precautions (5.2)*]
- Aseptic Meningitis [see *Warnings and Precautions (5.3)*]

6.1. Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of QALSODY cannot be directly compared to rates in clinical trials of other drugs and may not reflect the rates observed in practice.

The safety of QALSODY 100 mg was evaluated in 147 patients with SOD1-ALS. The median patient exposure was 119.4 weeks (range from 4 to 212 weeks). QALSODY was evaluated in the placebo-controlled Study 1 and in the open label extension Study 2. In Study 1 Part C, approximately 43% were female; 57% were male; 64% were White and 8% were Asian. The mean age at entry in Study 1 Part C was 49.8 years (range from 23 to 78 years).

The most common adverse reactions ($\geq 10\%$ of patients treated with QALSODY and greater than placebo) were pain, fatigue, arthralgia, CSF white blood cell increased, and myalgia. Table 1 shows the common adverse reactions that occurred in at least 5% of patients treated with QALSODY and at a 5% or higher frequency than placebo.

Table 1: Adverse Drug Reactions That Occurred in At Least 5% of Patients Treated with QALSODY and at >5% Higher Frequency Than Placebo

Adverse Reaction	Study 1 Part C	
	QALSODY 100 mg (n = 72) %	Placebo (n = 36) %
Pain ^{‡‡}	42	22
Fatigue	17	6
Arthralgia	14	6
CSF white blood cell increased*	14	0
Myalgia	14	6
CSF protein increased	8	3
Musculoskeletal stiffness	6	0
Neuralgia	6	0

^{‡‡} Pain includes preferred terms of pain, back pain, and pain in extremity.

* CSF white blood cell increased includes preferred terms of CSF white blood cell increased and pleocytosis.

Less Common Adverse Reactions

Serious adverse reactions of myelitis and radiculitis; papilledema and elevated intracranial pressure; and aseptic meningitis have occurred in patients treated with QALSODY [see *Warnings and Precautions (5.1, 5.2, 5.3)*].

In the long-term extension study, nonserious adverse reactions of pyrexia have occurred with repeat administration of QALSODY.

8 USE IN SPECIFIC POPULATIONS

8.1. Pregnancy

Risk Summary

There are no adequate data on developmental risks associated with the use of QALSODY in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data

Animal Data

Subcutaneous administration of tofersen (0, 3, 10, 30 mg/kg) every other day to pregnant mice during the period of organogenesis resulted in no adverse effects on embryofetal development. Plasma exposure at the highest dose tested (30 mg/kg) was approximately 4 times that in humans at the recommended human dose (RHD) of 100 mg.

Subcutaneous administration of tofersen (0, 3, 10, 30 mg/kg) every other day to pregnant rabbits during the period of organogenesis resulted in no adverse effects on embryofetal development. Plasma exposure at the highest dose tested (30 mg/kg) was approximately 20 times that in humans at the RHD.

Subcutaneous administration of tofersen (0, 3, 10, or 30 mg/kg) every other day to male and female mice prior to and during mating and continuing in females throughout organogenesis resulted in no adverse effects on pre- or postnatal development. Plasma exposures at the highest dose tested (30 mg/kg) were approximately 4 times that in humans at the RHD.

8.2. Lactation

Risk Summary

There are no data on the presence of tofersen or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Tofersen was detected in the milk of lactating mice following subcutaneous administration. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for QALSODY and any potential adverse effects on the breastfed infant from QALSODY or from the underlying maternal condition.

8.4. Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

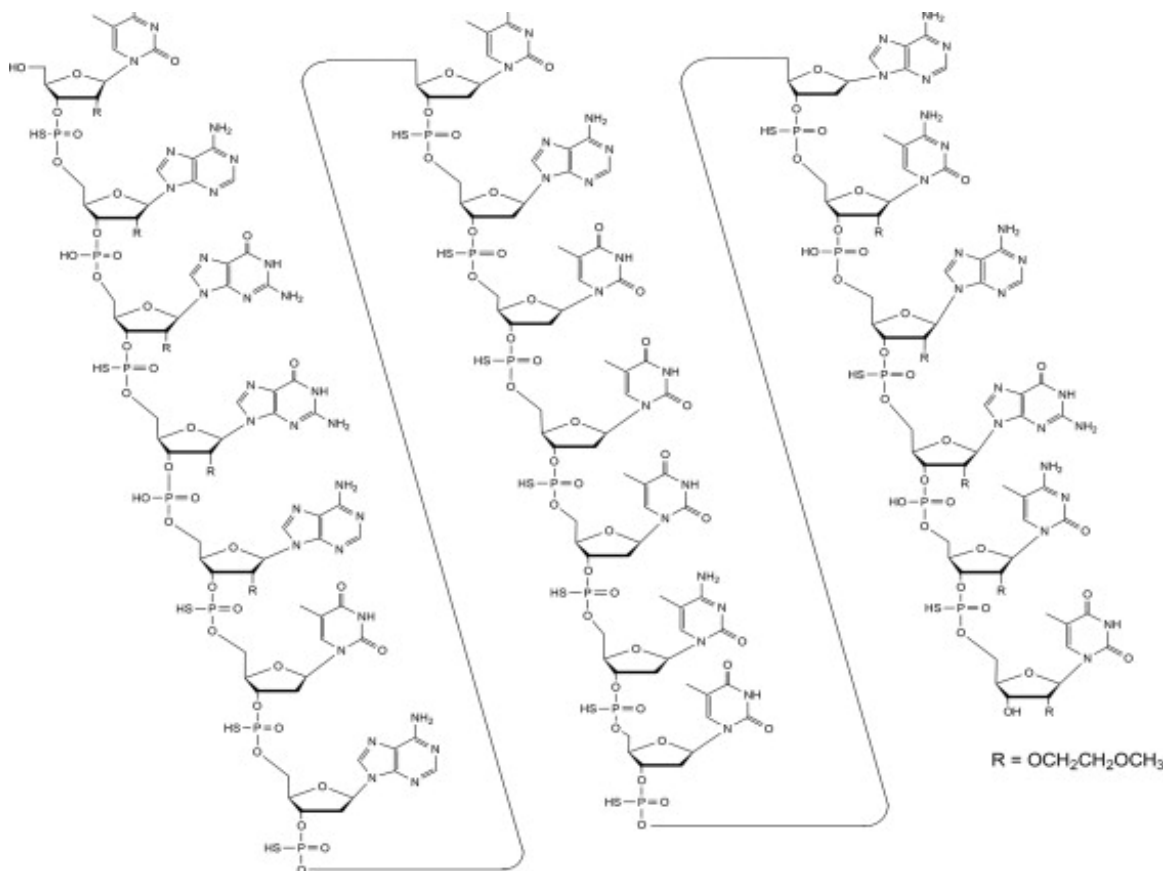
8.5. Geriatric Use

A total of 13.5% (22/162) patients were 65 years of age and older and 1.2% (2/162) patients were 75 years of age and older at initiation of treatment in clinical studies for ALS in patients who have a mutation in the superoxide dismutase 1 (*SOD1*) gene [see *Clinical Studies (14)*]. No overall differences in safety or effectiveness were observed between these patients and younger patients, but a greater sensitivity of some older individuals cannot be ruled out. There is no evidence for special dosage considerations based on age when QALSODY is administered.

11 DESCRIPTION

Tofersen, an antisense oligonucleotide, is a 20-base residue (20-mer) 5-10-5 MOE gapmer mixed backbone oligonucleotide. Of the nineteen internucleotide linkages, fifteen are 3'-O to 5'-O phosphorothioate diesters, and four are 3'-O to 5'-O phosphate diesters. Ten of the twenty sugar residues are 2-deoxy-D-ribose and the remainder are 2'-O-(2-methoxyethyl)-D-ribose (MOE). The residues are arranged so that there are five MOE nucleosides at the 5' and 3'-ends of the molecule flanking a gap of ten 2'-deoxynucleosides. The cytosine and uridine bases are methylated at the 5-position. The structural formula is:

Figure 1: Structural Formula for Tofersen



The molecular formula is C₂₃₀ H₃₁₇ N₇₂ O₁₂₃ P₁₉ S₁₅ and the molecular weight is

7127.86 atomic mass units (amu).

QALSODY is supplied as a sterile, preservative-free, clear, and colorless to slightly yellow solution in a Type I glass vial to be administered by intrathecal administration. Each vial of drug product contains a single dose of 100 mg tofersen at a concentration of 6.7 mg/mL in a formulation containing 0.21 mg/mL calcium chloride dihydrate, 0.11 mg/mL dibasic sodium phosphate, 0.16 mg/mL magnesium chloride hexahydrate, 0.03 mg/mL monobasic sodium phosphate, 0.22 mg/mL potassium chloride, 8.77 mg/mL sodium chloride, and water for injection. The pH of QALSODY is approximately 7.2 (range 6.7 to 7.7).

12 CLINICAL PHARMACOLOGY

12.1. Mechanism of Action

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.

12.2. Pharmacodynamics

Effect of Tofersen on Total CSF SOD1 Protein

Total CSF SOD1, an indirect measure of target engagement, was evaluated in Study 1 Part C in SOD1-ALS patients [see *Clinical Studies (14)*].

At Week 28 in Study 1 Part C, a reduction in total CSF SOD1 protein of 35% (geometric mean ratio to baseline) in the tofersen-treated group versus a 2% decrease from baseline in the corresponding placebo subjects in the ITT population was observed (difference in geometric mean ratios for tofersen to placebo: 34%; nominal $p < 0.0001$).

Effect of Tofersen on Neurofilament Proteins

Plasma NfL, a blood-based biomarker of axonal injury and neurodegeneration, was evaluated in Study 1 Part C in SOD1-ALS patients [see *Clinical Studies (14)*].

At Week 28 in Study 1 Part C, mean plasma NfL was reduced 55% (geometric mean ratio to baseline) in the QALSODY-treated subjects, compared to a 12% increase with placebo in ITT population (difference in geometric mean ratios for QALSODY to placebo: 60%; nominal $p < 0.0001$). Plasma NfL declined until approximately Day 113, after which the reductions were sustained. The reductions in phosphorylated neurofilament heavy chain (pNfH) were similar compared to reductions in NfL, as were reductions in CSF compared to plasma.

Cardiac Electrophysiology

At the maximum approved recommended dosing regimen, QALSODY does not prolong the QTc interval to any clinically relevant extent.

12.3. Pharmacokinetics

Absorption

Intrathecal administration of QALSODY into the CSF allows tofersen to be distributed from the CSF to central nervous system tissues. The maximum CSF trough concentration occurred at the third dose, which was the last dose of the loading period.

There was little to no accumulation for CSF tofersen with monthly dosing after the loading phase. Tofersen is transferred from CSF into the systemic circulation, with median time to maximum concentration (T_{max}) plasma values ranging from 2 to 6 hours. There was no accumulation in plasma tofersen exposure following monthly maintenance dosing.

Distribution

Autopsy tissue from patients treated with tofersen (n=3) showed that tofersen administered intrathecally was distributed within the central nervous system tissues.

Elimination

Metabolism

Tofersen is expected to be metabolized through exonuclease (3'- and 5')-mediated hydrolysis and is not a substrate for, or inhibitor or inducer of CYP450 enzymes.

Excretion

The primary route of elimination has not been characterized. The effective half-life in CSF is estimated to be 4 weeks.

Drug Interaction Studies

No clinical drug interaction studies have been performed. In vitro, QALSODY is not a substrate or inhibitor/inducer of major CYP enzymes or a substrate or inhibitor of major transporters.

Specific Populations

Effect of sex, race, age, and body weight on tofersen exposure in plasma was not clinically significant. The effect of these factors on tofersen exposure in CSF is unknown.

Patients with Renal or Hepatic Impairment

No clinical studies have been conducted to evaluate the pharmacokinetics of tofersen in patients with renal or hepatic impairment. Tofersen is not expected to undergo metabolism by hepatic enzymes.

12.6. Immunogenicity

As with all therapeutic oligonucleotides, there is a potential for immunogenicity.

Immunogenicity assay results are highly dependent on the sensitivity and specificity of the assay and may be influenced by several factors such as: assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to tofersen with the incidence of antibodies to other products may be misleading.

The immunogenic response to QALSODY was evaluated in 166 patients with post-baseline plasma samples for anti-drug antibodies (ADAs). Overall, 97 QALSODY-treated patients (58.4%) developed treatment-emergent ADAs, of which 14 were transient and 83 were persistent. The presence of anti-drug antibodies (ADA) appeared to decrease plasma tofersen clearance by 32%. Effects of ADA on CSF tofersen clearance is unknown. No discernible effects of ADAs on total SOD1 protein reduction or plasma NfL reduction have been observed. No discernible effects of ADAs on safety (incidence of AEs including hypersensitivity, anaphylactic reaction, and angioedema) have been

observed. Medical review of individual cases of serious neurological events also showed no association with ADA status.

13 NONCLINICAL TOXICOLOGY

13.1. Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Studies to assess the carcinogenic potential of tofersen have not been conducted.

Mutagenesis

Tofersen was negative in *in vitro* (bacterial reverse mutation and mammalian cell chromosomal aberration) and *in vivo* (mouse micronucleus) assays.

Impairment of Fertility

In a study to assess effects on fertility and reproductive function, tofersen (0, 3, 10, 30 mg/kg) was administered every other day to male and female mice prior to and during mating and continuing in females to gestation day (GD) 7. Adverse effects on male reproductive organs (seminiferous tubular degeneration, seminiferous tubule dilatation, spermatid retention, apoptosis of epithelial cells, increased cellular debris in the testes, and hypospermia in the epididymis) were observed at the highest dose tested; however, there were no adverse effects on functional endpoints. Plasma exposure at the no-effect dose (10 mg/kg) for adverse effects on male reproductive organs was approximately 2 times that in humans at the recommended human dose of 100 mg.

14 CLINICAL STUDIES

The efficacy of QALSODY was assessed in a 28-week randomized, double-blind, placebocontrolled 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 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) \geq 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) \geq 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 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 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 (see Table 2). NfL reduction was consistently observed for all subgroups based on sex, disease duration since symptom onset, site of onset, and riluzole/edaravone use.

Table 2: Biomarker Results of QALSODY in Study 1 Part C at Week 28

Biomarker Endpoints	QALSODY	Placebo
Plasma NfL		
ITT population	N=72	N=36
Adjusted geometric mean ratio to baseline	0.45	1.12
QALSODY to placebo difference in geometric mean ratio (95% CI)	0.40 (0.33, 0.49)	
Nominal p-value (ANCOVA+MI)	<0.0001	
mITT population	N=39	N=21
Adjusted geometric mean ratio to baseline	0.40	1.20
QALSODY to placebo difference in geometric mean ratio (95% CI)	0.33 (0.25, 0.45)	
Nominal p-value (ANCOVA+MI)	<0.0001	
CSF SOD1 Protein		
ITT population	N=72	N=36
Adjusted geometric mean ratio to baseline	0.65	0.98
QALSODY to placebo difference in geometric mean ratio (95% CI)	0.66 (0.57, 0.77)	
Nominal p-value (ANCOVA+MI)	<0.0001	
mITT population	N=39	N=21
Adjusted geometric mean ratio to baseline	0.71	1.16
QALSODY to placebo difference in geometric mean ratio (95% CI)	0.62 (0.49, 0.78)	
Nominal p-value (ANCOVA+MI)	<0.0001	

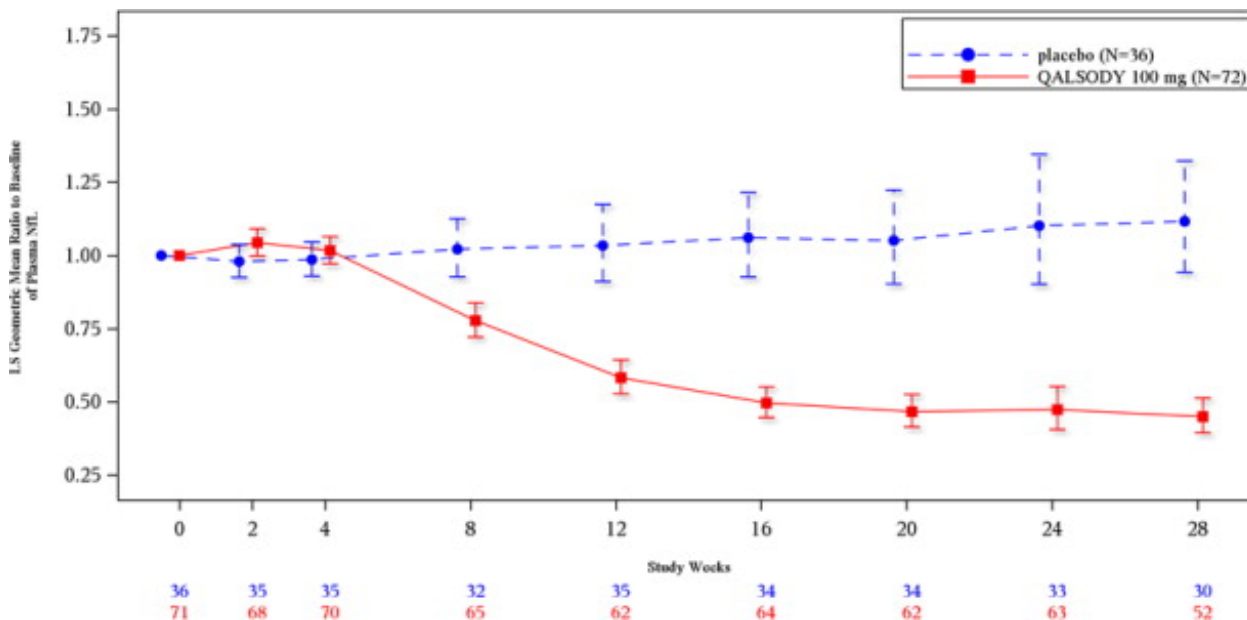
Note 1: N is the number of patients with baseline value.

Note 2: MI was used for missing data. Model included treatment, use of riluzole or edaravone, relevant baseline score and postbaseline values (natural log transformed data). Separate models for mITT and nonmITT were used and combined for ITT analyses.

Note 3: Adjusted geometric mean ratios to baseline, treatment differences in adjusted geometric mean ratios to baseline and corresponding 95% CIs and nominal p-values were obtained from the

ANCOVA model for change from baseline including treatment as a fixed effect and adjusting for the following covariates: baseline disease duration since symptom onset, relevant baseline score, and use of riluzole or edaravone. The analysis was based on natural log transformed data.

Figure 2: Plasma NfL Adjusted Geometric Mean Ratio to Baseline Values in Study 1 Part C by Study Week for the ITT Population



After completion of Study 1, patients had the option to enroll in an open-label extension study. At an interim analysis at 52 weeks, reductions in NfL were seen in patients previously receiving placebo who initiated QALSODY in the open-label extension study, similar to the reductions seen in patients treated with QALSODY in Study 1. Earlier initiation of QALSODY compared to placebo/delayed initiation of QALSODY was associated with trends for reduction in decline on ALSFRS-R, 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 QALSODY 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.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1. How Supplied

QALSODY injection is a sterile, clear and colorless to slightly yellow solution supplied as 100 mg/15 mL (6.7 mg/mL) solution in a single-dose glass vial free of preservatives.

The NDC is 64406-109-01.

16.2. Storage and Handling

Store refrigerated between 2°C to 8°C (36°F to 46°F) in the original carton to protect

from light. Do not freeze.

If no refrigeration is available, QALSODY may be stored in its original carton, protected from light at or below 30°C (86°F) for up to 14 days.

If removed from the original carton, unopened vials of QALSODY can be removed from and returned to the refrigerator, if necessary, for not more than 6 hours per day at or below 30°C (86°F) for a maximum of 6 days (36 hours).

17 PATIENT COUNSELING INFORMATION

Myelitis and/or Radiculitis

Inform patients and caregivers that QALSODY could cause myelitis and radiculitis. Instruct patients and caregivers to contact their healthcare provider if symptoms consistent with these adverse reactions develop [see *Warnings and Precautions (5.1)*].

Papilledema and Elevated Intracranial Pressure

Inform patients and caregivers that QALSODY could cause papilledema and elevated intracranial pressure. Instruct patients and caregivers to contact their healthcare provider if symptoms consistent with these adverse reactions develop [see *Warnings and Precautions (5.2)*].

Aseptic Meningitis

Inform patients and caregivers that QALSODY could cause aseptic meningitis. Instruct patients and caregivers to contact their healthcare provider if symptoms consistent with meningitis develop [see *Warnings and Precautions (5.3)*].

57294-01

Manufactured by:
Biogen MA Inc.
Cambridge, MA 02142

QALSODY is a trademark of Biogen MA Inc.
© Biogen Inc.

Principal Display Panel - Carton Label

1 vial

NDC: 64406-**109**-01

QALSODY™
(tofersen) Injection

100 mg/15 mL
(6.7 mg/mL)

Sterile solution for
Intrathecal Injection Only

Rx only

Biogen®



Principal Display Panel - Vial Label

**QALSODY™
(tofersen) Injection**

**100 mg/15 mL
(6.7 mg/mL)**

Sterile solution for Intrathecal Injection Only

Rx only

1 vial NDC 64406-109-01

QALSODY™
(tofersen) Injection

100 mg/15 mL
(6.7 mg/mL)

Sterile solution for Intrathecal Injection Only **Rx only**

Recommended Dosage: See prescribing information.
Single-dose vial.
Discard unused portion.
Store Refrigerated: 2°C to 8°C (36°F to 46°F)
Do not freeze. Store in the original carton to protect from light.
Manufactured for: Biogen MA Inc.
Cambridge, MA 02142 USA
1-877-725-7639

Biogen®

LOT: 000080
EXP: MM/YYYY

ART05607

QALSODY

tofersen injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:64406-109
Route of Administration	INTRATHECAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
tofersen (UNII: 2NU6F9601K) (tofersen - UNII:2NU6F9601K)	tofersen	100 mg in 15 mL

Inactive Ingredients

Ingredient Name	Strength
sodium phosphate, monobasic, unspecified form (UNII: 3980JH2S W)	
sodium phosphate, dibasic, unspecified form (UNII: GR686LBA74)	
sodium chloride (UNII: 451W47IQ8X)	
potassium chloride (UNII: 660YQ98I10)	
calcium chloride (UNII: M4I0D6VV5M)	
magnesium chloride (UNII: 02F3473H9O)	
water (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64406-109-01	1 in 1 CARTON	04/25/2023	
1		15 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product		

Marketing Information

Marketing	Application Number or Monograph	Marketing Start	Marketing End
-----------	---------------------------------	-----------------	---------------

Category	Citation	Date	Date
NDA	NDA215887	04/25/2023	

Labeler - Biogen Inc. (121376230)

Revised: 4/2023

Biogen Inc.