MEDISON

We are Always Ahead | We Grow as One | We Care

אוגוסט 2026

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

הריני להודיעכם כי העלון לרופא של התכשיר עודכן:

Qalsody **קלסודי**

INTRATHECAL

מרכיב פעיל : tofersen

להלן העדכונים בעלון לרופא (מסומן באדום**):**

התוויה מאושרת :

Qalsody is indicated for the treatment of adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (SOD1) gene.

4.8 Undesirable effects

Summary of safety profile

The serious adverse reactions in tofersen-treated participants were myelitis (4.1%), increase intracranial pressure and/or papilloedema (2.7%), radiculitis (1.4%) and aseptic meningitis (1.4%). The most common adverse reactions reported in tofersen-treated participants who received 100 mg (n=147) were pain (68.7%), arthralgia (36.7%), fatigue (30.6%), CSF white blood cell increased (27.9%), CSF protein increased (26.5%), myalgia (22.4%) and pyrexia (20.4%).

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Myelitis and/or radiculitis

In the clinical studies, 6 participants receiving tofersen 100 mg reported serious reactions of myelitis (4.1%). The number of tofersen doses received before the onset of myelitis ranged from 5 to 58 doses. Four participants were symptomatic and 2 participants were asymptomatic. All 6 participants had abnormal magnetic resonance imaging (MRI) findings related to the event. Two participants discontinued treatment, and the event resolved. In the remaining 4 participants, the event did not lead to discontinuation of treatment (see section 4.4).

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5.1 Pharmacodynamic properties

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To allow for long-term follow up, participants that completed Study 101 Part C had the opportunity to enrol in an open-label extension (Study 102), wherein all participants received tofersen 100 mg. In total, 95 (88%) participants, n = 63 in the early-start group (ES group: those randomised to tofersen in Study 101 Part C) and n = 32 in the placebo/delayed-start group (DS group: those randomised to placebo in Study 101 Part C) enrolled in Study 102. At the time of the final integrated analysis 33.3% (12/36) of participants in the placebo/delayed-start group and 47.2% (34/72) of participants in the early-start group completed Study 102, with a median opportunity for follow-up across the

two studies of 4.9 years (range: 3.6 to 5.4 years). Earlier initiation of tofersen (ES group) was associated with trends for reduction in decline on ALSFRS-R, SVC percent-predicted, and HHD megascore as compared to placebo/delayed initiation of tofersen (DS group), although the differences were not statistically significant.

Earlier initiation of tofersen (ES group) was associated with an apparent reduction in the risk of death or permanent ventilation (HR [95% CI]: 0.64 [0.28, 1.46]) and risk of death (HR [95% CI]: 0.52 [0.20, 1.36]). Median time-to-event was not estimable due to the limited number of events observed. Among participants in the integrated analysis of Study 101 Part C and Study 102, who were more likely to experience faster disease progression (based on higher plasma NfL levels at baseline), the median time to death or permanent ventilation in the ES group was 253.6 weeks compared with 76.0 weeks in the placebo/delayed-start group.

5.2 Pharmacokinetic properties

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Distribution

Tofersen administered intrathecally was extensively distributed within the CNS, achieving therapeutic levels in the target spinal cord tissues. The median plasma AUC at 100 mg (Study 101 Part C data) after first dose was 13973.1 ng/mL*h; median maximum plasma concentration (Cmax) was 824.3 ng/mL, which occurred at between 4-6 hours post dose. The median plasma volume of distribution was estimated at 48.7L (124% CV) in study 101 and 102; and was 43.0 L (123% CV) in the 100 mg dose group. Pharmacokinetic (PK) analysis demonstrates that intrathecally administered tofersen is widely distributed into central nervous system (CNS) tissues and is rapidly transferred from CSF to the systemic circulation.

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Elimination

The primary route of elimination is expected via urinary excretion of unchanged tofersen and its metabolites. Although CNS tissue half-life cannot be measured in humans, the mean terminal elimination half-life was measured in the CNS tissue of cynomolgus monkeys and found to be 31 to 40 days. The median plasma clearance was in study 101 and 102 participants estimated at 8.20 L/hr (47.3% CV); and was 6.02 L/hr (48.2% CV) at 100 mg dose.

Linearity/non-linearity

In CSF, the pharmacokinetics of tofersen administered IT increase less than dose proportional for dose ranging from 20 mg to 100 mg.

In plasma, the pharmacokinetics of tofersen administered IT increase more than dose proportional for dose ranging from 20 mg to 100 mg.

Immunogenicity

The presence of anti-drug antibodies (ADAs) appeared to decrease plasma clearance by 37.9%.

העלון לרופא והעלון לצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בברכה,

מדיסון פארמה בע"מ

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