Anmodning om vurdering av legemiddel i Nye metoder

En leverandør som ønsker et legemiddel vurdert i Nye metoder skal rette en henvendelse til sekretariatet for Nye metoder ved å bruke dette skjemaet. Ved å sende en anmodning signaliserer leverandøren at de vil sende inn dokumentasjon for vurdering av et nytt legemiddel eller en indikasjonsutvidelse for et eksisterende legemiddel.

Utfylt anmodningsskjema sendes via e-post til Nye metoder nyemetoder@helse-sorost.no.

Informasjon om Nye metoder finnes på https://nyemetoder.no. Kontakt sekretariatet ved spørsmål.

Anmodningen sendes tidligst ved dag 120 i vurderingsprosessen hos European Medicines Agency (EMA) for nye legemidler i normal godkjenningsprosedyre og tidligst ved dag 1 for indikasjonsutvidelser og for nye legemidler i akselerert godkjenningsprosedyre.

Hele anmodningsskjemaet skal fylles ut. Nye metoder bruker anmodningen om vurdering til å planlegge vurderingsprosessen.

Leverandøren skal på anmodningstidspunktet ha en plan for når de skal levere dokumentasjon.

Merk: Skjemaet vil bli publisert i sin helhet. Eventuell informasjon som ifølge lovverket kan unntas offentligheten kan sendes inn som vedlegg merket «unntatt offentlighet».

Innsender er klar over at skjemaet vil bli publisert i sin helhet **(Må krysses av):** ☑

1 Kontaktopplysninger	
Dato:	June 23th 2023
Leverandør:	Biogen Norway AS
Navn:	Mónica Gómez Castañeda
Stilling:	Market Access Manager
Telefon:	46561765
E-post:	monica.gomezcastaneda@biogen.com
Ekstern representasjon *OBS: Ved ekstern representasjon, vedlegg fullmakt*	
Navn/virksomhet	
Telefon/e-post	

2 Legemiddelinformasjon	
Gjelder anmodningen et nytt virkestoff?	Yes
Handelsnavn	Qalsody
Generisk navn (virkestoff(er))	Tofersen

Innehaver av markedsføringstillatelse i Norge	Currently evaluated for marketing authorisation at EMA. Biogen Norway AS will be MA holder if approved.
ATC-kode	Not classified as of yet
Administrasjonsform	Intrathecal injection by lumbar puction
Farmakoterapeutisk gruppe og virkningsmekanisme. *Skriv kort*	Tofersen is an antisense oligonucleotide for the treatment of amyotrophic lateral sclerosis in adults with mutations in the superoxide dismutase 1 (SOD1) gene. Tofersen prevents the production of mutated SOD1 protein by binding to SOD1 mRNA and inducing its degradation by RNAse-H induction. Tofersen reduces the synthesis of mutated SOD1 protein and its accumulation resulting in slowing disease progression.
Hvilken indikasjon gjelder anmodningen?	Amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the SOD1 gene.

3 Historikk

Er legemidlet vurdert til andre indikasjoner tidligere i Nye metoder? *Hvis ja, oppgi ID-nummer i Nye metoder*	No
Er du kjent med om andre legemidler er vurdert i Nye metoder til samme indikasjon? *Hvis ja, oppgi ID-nummer i Nye metoder*	No

4 Forventet tidslinje

Prosedyrenummer for MT-saken i EMA	EMEA/H/C/005493/0000
Forventet tidspunkt (måned/år) for CHMP positive opinion i EMA	Q4 2023
Forventet tidspunkt (måned/år) for markedsføringstillatelse (MT) i Norge	January-February 2024
Forventet tidspunkt (kvartal/år) for levering av dokumentasjon til Statens legemiddelverk *Tidspunkt må oppgis*	November 2023

5 Diagnostikk og ressursbruk

Fyll inn der det er relevant

Vil anvendelse av legemidlet kreve diagnostisk test for analyse av biomarkør?	Yes. Treatment with Tofersen requires a confirmed SOD1 mutation through genetic testing which is a established procedure in Norway. Further measurement of neurofilment light chains levels in plasma are relevant for disease progression and follow-up of treatment response.
Hvilken biomarkør(er) er aktuell og hvilke publikasjoner beskriver dette?	SOD1 mutation and levels of neurofilament light chains.
Henvis til publikasjoner	Miller TM, Cudkowicz ME, Genge A, Shaw PJ, Sobue G, Bucelli RC, Chiò A, Van Damme P, Ludolph AC, Glass JD, Andrews JA, Babu S, Benatar M, McDermott CJ, Cochrane T, Chary S, Chew S, Zhu H, Wu F, Nestorov I, Graham D, Sun P, McNeill M, Fanning L, Ferguson TA, Fradette S; VALOR and OLE Working Group. Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS. N Engl J Med. 2022 Sep 22;387(12):1099-1110. doi: 10.1056/NEJMoa2204705. PMID: 36129998.

Kjenner dere til om diagnostikk kan utføres i offentlig helsetjeneste eller om den må utføres av ekstern leverandør?	Yes, genetic testing for SOD1 mutation can be performed in the public sector. Olsen, C. G., et al. (2022). "Genetic Epidemiology of Amyotrophic Lateral Sclerosis in Norway: A 2-Year Population-Based Study." Neuroepidemiology 56(4): 271-282.
Kjenner dere til om innføring vil kreve etablering av annen/ny infrastruktur? *For eksempel tilpasset analysemaskin, digital patologi/AI-basert analyse, proteomikk, funksjonelle tester m.m.?*	No. Genetic testing and measurement of plasma levels of neurofilament can be performed with current infrastructure. The low number of patients will not affect hospitals' capacity or require any uptake of new infrastructure. Moreover, we have contacted clinicians who confirm that Ahus has plans to purchase new infrastructure that can analyze neurofilament levels among other markers.
Pre-analytiske forhold *F.eks. kreves biopsering, annen prøvetakning, prøveprosessering m.m.*	Testing for the SOD-1 gene requires a blood sample.
Testutførelse: er det behov for etablering av én spesifikk test eller er biomarkør allerede etablert i helsetjenesten (f.eks. i genpanel)?	Genetic testing for SOD1 mutations has already been performed for research purposes in Norway. We have been in contact with clinicians who can confirm that SOD1 testing is performed in various sites such as Skien, OUS and Haukeland. Olsen, C. G., et al. (2022). "Genetic Epidemiology of Amyotrophic Lateral Sclerosis in Norway: A 2-Year Population-Based Study." Neuroepidemiology 56(4): 271-282. Lenken til genetikkportalen: https://genetikkportalen.no/find-analysis [genetikkportalen.no]
Beskrivelse av avlesning av resultat inkl. dataanalyseprogram dersom det er nødvendig.	Results must be interpreted by a neurologist and a geneticist.
Hvilke pasientgrupper må testes og hva er forventet andel funn som gir behandlingsmulighet?	The patient group is adult patients with ALS due to an underlying SOD1 mutation. The fraction of patients with ALS-SOD1 is approximately 4% of the total of ALS patients in Norway (Olsen,2022). Olsen, C. G., et al. (2022). "Genetic Epidemiology of Amyotrophic Lateral Sclerosis in Norway: A 2-Year Population-Based Study." Neuroepidemiology 56(4): 271-282.

6 Sykdommen og eksisterende behandling

Sykdomsbeskrivelse *<u>Kort</u> beskrivelse av sykdommens patofysiologi og klinisk presentasjon / symptombilde, eventuelt inkl. referanser*	Amyotrophic lateral sclerosis (ALS) is a rare neurodegenerative disorder characterized by spontaneous and progressive degeneration of motor neurons (11). ALS symptom onset typically begins in the limbs, but bulbar onset can be present in approximately 20%-30% of cases affecting speech and swallowing. In rare cases, the respiratory muscles are involved leading to breathing difficulty and respiratory failure (2,11). ALS causes progressive disability and most patients die from respiratory failure within 3 to 5 years from symptom onset (2,3). ALS has been divided into familial and sporadic ALS. Globally, patients with sporadic ALS (no family history of ALS) account for 90%-95% of cases and classified genetic mutations are present in approximately 10% of cases. Familial ALS cases account for the remaining 5%-10% of cases and genetic mutations are found in approximately 70% of cases (13,15). ALS ethiology is multifactorial but the end result is always axonal injury and neurodegeneration (3,15) . Mutations in key cellular genes result in the accumulation of toxic proteins and RNA aggregates, which in turn disrupts cellular processing (3,4,9,10,15). The end result of this process is loss of neuromuscular junction viability and motor neuron dysfunction or death (5). Olsen et al. found that the superoxide dismutase 1 (SOD1) mutation is the second most frequent genetic cause of ALS in Norway with a prevalence of 3.6%. A SOD1 mutation was found in 28% of the familial ALS cases (n=22), and in 0.4% of the sporadic ALS cases (n=247) (7)
Fagområde *Angi hvilket fagområde som best beskriver metoden*	Nevrologi Psykiske lidelser og ruslidelser Radiologi og nukleærmedisin
Kreftområde *Hvis metoden gjelder fagområdet Kreftsykdommer, angi hvilket kreftområde som er aktuelt*	* Ingen Kreftsykdom Bein- og bløtvevskreft Blod- beinmargs- og lymfekreft
Dagens behandling *Nåværende standardbehandling i Norge, inkl. referanse*	Riluzol Beslutningsforum for Nye Metoder 20.06.2022 under sak 083-2022. ID-number: ID2022_095

Prognose *Beskriv prognosen med nåværende behandlingstilbud, inkl. referanse*	ALS causes progressive disability and most patients die from respiratory failure within 3 to 5 years from symtom onset(1,2). The current standard of care, Riluzol, is thought to exert neuroprotective effects by preventing the accumulation of toxic concentrations of glutamic acid in the CNS of ALS patients . Riluzol is well tolerated by patients but its efficacy is modest as it increases the median ventilation-free survival by approximately 2-3 months without noticeable improvement in strength or disability; it is not a genetically targeted treatment (3,4). References 1.Brown, R. H. and A. Al-Chalabi (2017). "Amyotrophic Lateral Sclerosis." N Engl J Med 377(2): 162-172. 2.Bunton-Stasyshyn, R. K., et al. (2015). "SOD1 Function and Its Implications for Amyotrophic Lateral Sclerosis Pathology: New and Renascent Themes." Neuroscientist 21(5): 519-529. 3.Doble, A. (1996). "The pharmacology and mechanism of action of riluzole." Neurology 47(6 Suppl 4): S233-241. 4.Saitoh, Y. and Y. Takahashi (2020). "Riluzole for the treatment of amyotrophic lateral sclerosis." Neurodegener Dis Manag 10(6): 343-355.
Det nye legemidlets innplassering i behandlingsalgoritmen	Once a ALS diagnosis is confirmed, genetic testing is performed to investigate whether a SOD1 is the underlying cause. If the SOD1 mutation is confirmed, the patient is candidate to receive Tofersen. In the case that a patient is already diagnosed with ALS and treated with Riluzol, the patient can undergo genetic testing to clarify whether a SOD1 mutation is the underlying cause, in which case tofersen treatment can be started as an add-on therapy.
Pasientgrunnlag *Beskrivelse, insidens og prevalens av pasienter omfattet av aktuell indikasjon* i Norge, inkl. referanse.* *Antall norske pasienter antatt aktuell for ny behandling* ** Hele pasientgruppen som omfattes av aktuell indikasjon skal beskrives*	In Norway, the yearly incidence of ALS is reported to be 3 new cases per 100,000 inhabitants (i.e., approximately 165 patients for the year 2022) (2,3), while the prevalence lies around 6.9-7.6 cases per 100,000 inhabitants (i.e., approximately 417 patients for the year 2022) (2,3). Based on the Reseptregisteret database, for the period 2016-2020, an average of 88% of the total ALS patient population was receiving treatment with Riluzol (1). Approximately 4% of ALS cases in Norway are caused by an underlying SOD1 mutation. Thus, taking into account an annual incidence of approximately 165 patients, we estimate that around 7 patients would be considered for treatment with Tofersen each year (3). 1.Folkehelseinstituttet (2023). Riluzol bruk. Resepregisteret. http://www.reseptregisteret.no 2.Nakken, O., et al. (2018). "Assessing amyotrophic lateral sclerosis prevalence in Norway from 2009 to 2015 from compulsory nationwide health registers." Amyotroph Lateral Scler Frontotemporal Degener 19(3-4): 303-310. 3.Olsen, C. G., et al. (2022). "Genetic Epidemiology of Amyotrophic Lateral Sclerosis in Norway: A 2-Year Population-Based Study." Neuroepidemiology 56(4): 271-282.

7 Kan legemidlet vurderes som sammenlignbart med andre legemidler og inngå i anbud?

Er det eksisterende anbud på terapiområdet?	No
Finnes det andre legemidler med lignende virkningsmekanisme og /eller tilsvarende effekt (for samme indikasjon)?	No
Vurderer leverandøren at legemidlet er sammenlignbart med andre legemidler?	No

8 Studiekarakteristika for relevante kliniske studier

	Studie 1	Studie 2	Studie 3
Studie ID *Studienavn, NCT-nummer, hyperlenke*	Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS (VALOR Study and its Open Label Extension), NCT02623699 and NCT03070119, DOI: 10.1056/NEJMoa2204705	Phase 1–2 Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS, NCT02623699, DOI: 10.1056/NEJMoa2003715	
Studietype og -design	VALOR: 28- week, Phase 3, double-blind, randomized, placebo-controlled (n=108) OLE: the ongoing non-randomized open-label extension enrolled 95 of the 108 participants in VALOR; all participants received tofersen (participants remained unaware of their trial-group assignment in VALOR)	Phase 1-2 ascending-dose, randomized, double-blind, placebo-controlled trial	
Formål	Evaluate the clincial efficacy of tofersen administered to adults with ALS and a confirmed SOD1 mutation	Evaluate the safety, pharmacokinetics, and tolerability of ascending doses of tofersen in adults with ALS and a documented SOD1 mutation.	
Populasjon *Viktige inklusjons- og eksklusjonskriterier*	Adults with SOD1-ALS (n=108). Recognizing the heterogeneity in SOD1-ALS, criteria anchored in SOD1 mutation type and pre-study Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) slope were defined to enrich the primary analysis (28-weeks VALOR) population with participants predicted to experience faster disease progression during the study period (faster-progressing subgroup). Those in this subgroup who received at least one dose of study treatment comprised the faster-progressing population (N=60), in which the primary and key secondary endpoints were formally tested. The study also enrolled participants who did not meet these enrichment criteria and thus were predicted to progress more slowly. This "slower-progressing" population	Adults with SOD1-ALS. Participants were assigned to one of four dose cohorts (20,40,60, or 100mg) which were assessed sequentially. Each dose-level cohort included 12 participants who had been randomly assigned to receive tofersen or placebo. Inclusion criteria: -Weakness attributalble to ALS and documented SOD1 mutation at Screening Visit 2. -A forced vital capacity (FVC) ≥50% of predicted value as adjusted for sex, age, and height (from the sitting position). Participants with stable FVC <50% but	

	Studie 1	Studie 2	Studie 3
Intervensjon (n) *Dosering, doseringsintervall, behandlingsvarighet*	Tofersen: intrathecal bolus injection through a lumbar puncture of a 15-ml solution (100mg) administered over a period of 24 weeks- 3 loading doses once every 2 weeks, followed by 5 maintenance doses once every 4 weeks.	Tofersen: intrathecal bolus injection through a lumbar punction. Each dose cohort (20mg,40mg,60mg, or 100mg) receive 5 doses of tofersen administered over a period of 12 weeks. Tofersen was administered on days 1, 15, 29, 57, and 85. Participants were followed for up to 31 weeks, which comprised a screening period of up to 7 weeks followed by the 12- week intervention period and a 12- weeks follow- up (final follow-up visit at Day 169).	
Komparator (n) *Dosering, doseringsintervall, behandlingsvarighet*	Placebo: 15ml of artificial cerebrospinalfluid, administered over the same time period and at the same dose as tofersen.	Placebo: 15ml of artificial cerebrospinalfluid, administered over the same time period and at the same dose as tofersen	
Endepunkter *Primære, sekundære og eksplorative endepunkter, herunder definisjon, målemetode og ev. tidspunkt for måling*	The VALOR and the ongoing OLE consist of a 28-and 52 weeks analysis, respectively. Patients who received placebo in the VALOR study were offered to receive tofersen during the OLE. A total of 95 participants out of the 108 from VALOR, were enrolled in the OLE and all received tofersen. The 28-week (6 months), Phase 3 randomized VALOR study did not meet the primary endpoint of change from baseline to Week 28 in the ALSFRS-R total score. However, significant reduction in CSF SOD1 protein and plasma NfL suggested a slowing of clinical decline in faster-progressing patients receiving tofersen. Moreover, trends favoring tofersen were seen across multiple secondary and exploratory measures of clinical function. The 52 weeks (12 months) analyses integrating data from VALOR and the OLE (data cut January 2022) compared early initiation of tofersen (at the start of VALOR) to delayed initiation of tofersen (six months later, in the OLE). For this analyses, baseline NfL was incorporated as a covariate to controll for heterogeneity of disease progression. This allowed the analysis of the overall population, rather than relying on subgroups to enrich for faster progression.	Primary endpoints: -Incidence of Adverse Events (AEs) and Serious Adverse Events (SAEs) up to Day 169. (An AE is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. A SAE is any untoward medical occurrence that at any dose results in death, life-threatening event, requires inpatient hospitalization, significant disability/incapacity or congenital anomaly). -Abnormalities in clinical laboratory assessments and vital signs up to Day 169. -Abnormalities in Electrocardiogram, physical and neurological examination up to Day 169. -Pharmacokinetic measures in plasma up to Day 169: Maximum Observed Concentration (Cmax); Time to Reach Maximum Observed Concentration (Tmax); Area Under the Concentration-time Curve From Time Zero to Infinity (AUCinf); Area Under the Concenration-time Curve From Time Zero to the Time of the Last Measurable Concentration (AUClast); Apparent Terminal	
Relevante subgruppeanalyser *Beskrivelse av ev. subgruppeanalyser*	Faster-progressing: comprised participants who met the prognostic enrichment criteria for rapid disease progression defined according to SOD1 mutation type and prerandomization ALSFRS-R slope (n=60): -SOD1 mutation historically associated with shorter survival OR another SOD1 mutation AND -Pre-randomization ALSFRS-R slope decline ≥0.2 points/month OR ≥0.9 points/month AND -SVC ≥ 65% predicted Slower-progressing: all other participants who did not meet the enrichment criteria for rapid disease progression (n=48).	A fast-progression subgroup was defined post hoc. It comprised participants who had: -SOD1 mutation historically associated with shorter survival OR another SOD1 mutation AND -Pre-randomization ALSFRS-R slope decline ≥0.2 points/month OR ≥0.9 points/month. Participants who did not meet these criteria were included in the "other" subgroup for post hoc analysis.	
Oppfølgingstid *Hvis pågående studie, angi oppfølgingstid for data som forventes å være tilgjengelige for vurderingen i Legemiddelverket samt den forventede/planlagte samlede oppfølgingstid for studien*	VALOR: the study included a 24-week treatment period and a follow-up period of 4 to 8 weeks followed by an ongoing extension phase. OLE: after compeltion of VALOR, participants were offered to enroll in an open-label extension for up to 236 weeks. A combined analysis at 52 weeks of VALOR and its OLE is the most recent data cut to this date and these are the results presented in the study.	Participants were followed for up to 31 weeks, which comprised a screening period of up to 7 weeks followed by a 12-week intervention period and a 12-week follow-up.	
Tidsperspektiv resultater *Pågående eller avsluttet studie? Tilgjengelige og fremtidige datakutt*	The open label extension (OLE) is ongoing. Data analysis is planned when all participants have completed at least 3.5 years of follow-up, which at the moment has not been reached. The OLE is expected to last 3 to 7 years.	Study completed. Data is available for up to Day 169 (End of study visit or final follow-up visit) equivalent to approximately 6 months.	
Publikasjoner *Tittel, forfatter, tidsskrift, årstall. Ev. forventet tidspunkt for publikasjon*	Miller TM, Cudkowicz ME, Genge A, Shaw PJ, Sobue G, Bucelli RC, Chiò A, Van Damme P, Ludolph AC, Glass JD, Andrews JA, Babu S, Benatar M, McDermott CJ, Cochrane T, Chary S, Chew S, Zhu H, Wu F, Nestorov I, Graham D, Sun P, McNeill M, Fanning L, Ferguson TA, Fradette S; VALOR and OLE Working Group. Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS. N Engl J Med. 2022 Sep 22;387(12):1099-1110. doi: 10.1056/NEJMoa2204705. PMID: 36129998.	Miller T, Cudkowicz M, Shaw PJ, Andersen PM, Atassi N, Bucelli RC, Genge A, Glass J, Ladha S, Ludolph AL, Maragakis NJ, McDermott CJ, Pestronk A, Ravits J, Salachas F, Trudell R, Van Damme P, Zinman L, Bennett CF, Lane R, Sandrock A, Runz H, Graham D, Houshyar H, McCampbell A, Nestorov I, Chang I, McNeill M, Fanning L, Fradette S, Ferguson TA. Phase 1-2 Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS. N Engl J Med. 2020 Jul 9;383 (2):109-119. doi: 10.1056/NEJMoa2003715. PMID: 32640130.	

9 Igangsatte og planlagte studier

Er det pågående eller planlagte studier for legemidlet innenfor samme indikasjon som kan gi ytterligere informasjon i fremtiden? *Hvis ja, oppgi forventet tidspunkt*	Yes. Benatar M, Wuu J, Andersen PM, Bucelli RC, Andrews JA, Otto M, Farahany NA, Harrington EA, Chen W, Mitchell AA, Ferguson T, Chew S, Gedney L, Oakley S, Heo J, Chary S, Fanning L, Graham D, Sun P, Liu Y, Wong J, Fradette S. Design of a Randomized, Placebo-Controlled, Phase 3 Trial of Tofersen Initiated in Clinically Presymptomatic SOD1 Variant Carriers: the ATLAS Study. Neurotherapeutics. 2022 Jul;19(4):1248-1258. doi: 10.1007/s13311-022-01237-4. Epub 2022 May 18. Erratum in: Neurotherapeutics. 2022 Sep 29;: PMID: 35585374; PMCID: PMC9587202. Expected completion: August 2027
Er det pågående eller planlagte studier for legemidlet for andre indikasjoner?	No.

10 Forventet helseøkonomisk dokumentasjon

Angi informasjon om den forventede helseøkonomiske analysen

Type helseøkonomisk analyse *F.eks. kostnad-per-QALY analyse eller kostnadsminimeringsanalyse (Begrunn forslaget)*	A cost-utility analysis will be performed to assess the cost per QALY/LY. This type of cost-effectiveness analysis is chosen due to the availability of data input for the comparison of tofersen with standard of care, and to best reflect its cost-effectiveness in terms of quality and quantity of life.
Pasientpopulasjonen som den helseøkonomiske analysen baseres på, herunder eventuelle subgrupper. *Grunnanalysen (basecase) skal omfatte hele pasientpopulasjonen omfattet av ansøkt indikasjon.*	The modelled patient population are based on the VALOR trial population, which included patients of at least 18 years of age with a diagnosis of ALS and confirmed SOD1 mutation. Subgroup analyses in both "Slow-progressors" and "Fast-progressors" will be performed.
Hvilken dokumentasjon skal ligge til grunn for relativ effekt? *(H2H studie, ITC, konstruert komparatorarm)*	Phase 3, double-blind, randomized, placebo-controlled trial: Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS (VALOR Study and its Open Label Extension), NCT02623699 and NCT03070119, DOI: 10.1056/NEJMoa2204705
Hvilken dokumentasjon skal ligge til grunn for helserelatert livskvalitet?	Health utilities were obtained from literature where health outcomes were assessed mainly by the EQ-5D-5L but other assessment measures such as the Amyotrophic Lateral Sclerosis Utility Index and the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised were used. Furthermore, health state utilitities from the VALOR study were included in the model and reported data collected by the EQ-5D-5L questionnaire. Stenson, K., et al. (2022). "POSB356 Health-Related Quality of Life across King's and Mitos Stages Among Amyotrophic Lateral Sclerosis Patients: Results from a Real-World Point-in-Time Survey." Value in Health 25(1): S229-S230. Thakore NJ, Pioro EP, Udeh BL, Lapin BR, Katzan IL. A Cost-Effectiveness Framework for Amyotrophic Lateral Sclerosis, Applied to Riluzole. Value Health. 2020 Dec;23(12):1543-1551. doi: 10.1016/j.jval.2020.06.012. Epub 2020 Oct 9. PMID: 33248509. Jones AR, Jivraj N, Balendra R, Murphy C, Kelly J, Thornhill M, Young C, Shaw PJ, Leigh PN, Turner MR, Steen IN, McCrone P, Al-Chalabi A. Health utility decreases with increasing clinical stage in amyotrophic lateral sclerosis. Amyotroph Lateral Scler Frontotemporal Degener. 2014 Jun;15(3-4):285-91. doi: 10.3109/21678421.2013.872149. Epub 2014 Feb 7. PMID:
Forventet legemiddelbudsjett i det året med størst budsjettvirkning i de første fem år.	It is expected that the introduction of tofersen will not have a significant budget impact due to the small number of ALS patients who could be candidates for treatment.

11 Aktuelt for FINOSE?

Kan legemidlet være aktuelt for utredning i FINOSE (ja/nei) *Dersom nei, hvorfor ikke?*	We do not think so as this is a very small patient population and might not be evaluated in the same manner in other countries.

12 Andre relevante opplysninger *Opplys om andre forhold som Nye metoder bør være oppmerksomme på.*	
Angi eventuelle konkrete spørsmål eller emner som ønskes drøftet med Nye metoder før innsending av dokumentasjon.	-
Har dere vært i kontakt med klinikere ved norske helseforetak om dette legemidlet/indikasjonen? Ja/nei Hvis ja, hvem har dere vært i kontakt med og hva har de bidratt med? *(Relevant informasjon i forbindelse med rekruttering av fagekspertер i Nye metoder)*	Biogen is planning an Adboard Communication Meeting for September 6th 2023. We had contact with the specialists Ole-Bjørn Tysnes (Haukeland US) and Trygve Holmøy (Akershus US). They provided input on the availability of infrastructure to perform SOD1 testing in the public sector.
Anser leverandør at det kan være spesielle forhold ved dette legemidlet som gjør at en innkjøpsavtale ikke kan basere seg på flat rabatt for at legemidlet skal kunne oppfylle prioriteringskriteriene (ja/nei)? Hvis ja, skal eget skjema fylles ut og sendes nyelegemidler@sykehusinnkjop.no samtidig med at dokumentasjon sendes til Statens legemiddelverk for metodevurdering. Informasjon og skjema: https://sykehusinnkjop.no/informasjon-og-opplering#rammeverk-for-alternative-prisavtaler	-
Andre relevante opplysninger?	-