7.05 TOFERSEN, Solution for intrathecal injection 100 mg in 15 mL, Qalsody™, BIOGEN AUSTRALIA PTY LTD

1 Purpose

1.1 The early re-entry resubmission sought a Section 100 (Highly Specialised Drugs Program) Authority Required (telephone/electronic) listing for tofersen for the treatment of amyotrophic lateral sclerosis (ALS) associated with a mutation in the superoxide dismutase 1 (SOD1) gene.

1.2 The resubmission was based on the PBAC decision to not recommend tofersen for this indication at the November 2025 PBAC meeting. How the resubmission addressed the issues raised by PBAC is presented in the table below.

Table 1: Summary of key matters to be addressed from November 2025 minutes

Matter of concern	Response	Addressed?
Restriction		
The PBAC advised that: - Treatment should be limited to registered specialist clinics equipped to adequately support patients and manage ongoing lumbar punctures; - Suggested wording changes suggested by the Secretariat should be adopted; - Initial supply should be amended to 3 vials with 0 repeats to cater for the loading doses (paragraph 7.16).	The resubmission: - Limited initial treatment to specialists with expertise in the diagnosis and management of ALS, with continuation treatment by a specialist or in consultation with a specialist. The resubmission considered that restricting treatment to registered specialist clinics may create equity of access issues; - Accepted the wording changes suggested by the Secretariat; - Did not amend the initial supply as recommended as separate listings were required in the context of the proposed pay for performance framework.	Partially Yes No, but may be reasonable.

Matter of concern	Response	Addressed?
Clinical evidence		
The PBAC considered it was reasonable to conclude that tofersen provided some clinical benefit to patients, but that the magnitude of the benefit and longer-term effects were uncertain (paragraph 7.8).	The resubmission provided the final VALOR OLE dataset, extending follow up from 104 weeks to 148 weeks. Most of the final VALOR OLE data were presented in the November 2025 pre-Sub-Committee Response.	No
Economic model		
The PBAC considered that the ICER was very high and unreliable….The PBAC considered that the value proposition was difficult to assess given the uncertainty in the ICER which reflected the limited clinical data, the small number of patients included in the studies and the individualised nature of ALS-SOD1 progression. The PBAC considered that the uncertainty in the ICER was unlikely to be adequately resolved with further revision to the model structure and inputs (paragraph 7.11, Nov minutes).	The resubmission provided an updated economic analysis that included the reduced price of tofersen. This resulted in an ICER of $[redacted][1] per QALY gained (reduced from $[redacted][2] per QALY in the November 2025 submission).	-
The PBAC considered that tofersen would be acceptably cost-effective with a price reduction that would results in a cost per year that aligned with other treatments for rare diseases funded on the PBS. The PBAC noted that the cost per year in the original submission was $[redacted] and considered that a substantial price reduction would be required (paragraph 7.12).	The resubmission proposed a [redacted]% price reduction for the initiation and response phases compared to the November 2025 submission. A further [redacted]% price reduction was offered for the first continuation phase. This resulted in a cost of tofersen in Year 1 of $[redacted] and in Years 2+ of $[redacted].	PBAC to advise
Financial estimates and RSA		
The PBAC noted that the estimated ALS-SOD1 population was somewhat uncertain….as Australian estimates are not available. The PBAC noted that: - The estimates were based on a prevalence approach, without incorporating incident patients in each year; - The duration of treatment, extension of survival and additional loading doses for incident patients were not appropriately modelled; - Uptake may be limited by suitableness for ongoing lumbar punctures and geographical access to treatment centres; - The duration of treatment in patients who respond to treatment was uncertain; - Compliance and discontinuation rates would be affected by response to treatment, especially as administration was via lumbar puncture (paragraph 7.13).	The resubmission made the following changes to the financial estimates: - Incident/prevalent approach was adopted; - Continuation of incident patients was modelled; - Uptake was adjusted; - Continuation rates were updated and aligned with the economic model. - As above.	 Yes Yes Minor changes Yes
The PBAC considered that a RSA based on the revised financial estimates would be required, with higher rebate levels over the Deed term (submission offered [redacted]% rebate [redacted]) (paragraph 7.15).	The resubmission proposed a [redacted] RSA, with a [redacted]% rebate on expenditure up [redacted]	Yes

Source: Compiled from the November 2025 PBAC minutes and the March 2026 early re-entry submission
ALS = amyotrophic lateral sclerosis; ALS-SOD1 = amyotrophic lateral sclerosis-superoxide dismutase 1; ICER = incremental cost-effectiveness ratio; OLE = open-label extension; QALY = quality-adjusted life year; RSA = risk sharing arrangement
The redacted values correspond to the following ranges:
[1] *$755,000 to < $855,000*
[2] *$955,000 to < $1,055,000*

2 Background

2.1 Tofersen was granted orphan drug status on 5 July 2024, on the basis that it is intended to treat a rare disease, and was considered by the TGA via the Provisional Pathway. The TGA Delegate's Overview recommended the provisional registration of tofersen for:

> 'the treatment of adults with amyotrophic lateral sclerosis (ALS) associated with a mutation in the superoxide dismutase 1 (SOD1) gene'

2.2 The PICO from the previous submission is presented below.

Table 2: Key components of the clinical issue addressed by the November 2025 submission

Component	Description
Population	People with amyotrophic lateral sclerosis (ALS) who have a superoxide dismutase 1 (SOD1) gene pathogenic variant.
Intervention	Tofersen in addition to best supportive care with or without riluzole. Tofersen is administered at a dose of 100 mg (15 mL) via intrathecal injection: 3 loading doses at 14-day intervals (day 0, 14, 28) and maintenance doses every 28 days thereafter.
Comparator	Placebo, as a proxy for best supportive care (BSC) with or without riluzole.
Outcomes	VALOR (Phase 3, Study 101, Part C) - 28 weeks • change from baseline in ALS Functional Rating Scale-Revised (ALSFRS-R) total score (primary) • change from baseline in total SOD1 protein concentration in CSF • change from baseline in total plasma neurofilament light chain (NfL) • change from baseline in percent predicted slow vital capacity (SVC) • change from baseline in handheld dynamometry (HHD) megascore to assess muscle strength • time to death or permanent ventilation (PV) (≥22 hours of mechanical ventilation [invasive or non-invasive] per day for ≥21 consecutive days) • time to death • quality of life (change from baseline in ALSAQ-5, EQ-5D-5L, Fatigue severity scale (FSS)) VALOR open label extension (Study 102) - up to 104 weeks AEs and SAEs (in patients completing Part A/B/C of Study 101) (primary) Integrated efficacy analysis comparing early-tofersen vs delayed -tofersen (patient completing Part C, Study 101) - all outcomes listed above
Clinical claim	In people with SOD1-ALS, tofersen is superior in terms of efficacy and inferior in terms of comparative safety, compared to best supportive care with or without riluzole.

Source: Table 1, p1 November 2025 minutes.
AE = adverse event; ALS = amyotrophic lateral sclerosis; CSF = cerebrospinal fluid; NfL = neurofilament light chain; SAE = serious adverse event; SOD1 = superoxide dismutase 1; SVC = slow vital capacity

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

3.1 The resubmission proposed the restrictions presented below. The resubmission did not present a separate restriction for the loading doses, as suggested by the PBAC in November 2025, instead it proposed an initiation phase (6 months supply), a first continuation phase (6 months supply) and a response phase (after 1 year of treatment) restriction. The resubmission stated that the separate listings were required in the context of the proposed pay for performance framework (see paragraph 3.2 and 4.20).

3.2 The resubmission stated the listing structure was in response to the PBAC's concerns regarding implementing a rebate for non-response. The price proposed for the first continuation phase (for 6 to 12 months treatment) was [redacted]% lower than for the other treatment phases, reflecting the expected proportion of non-responders at 12 months. Patients who meet the pre-defined response criteria (i.e. any improvement or stabilisation) defined as no more than 20% decline from baseline in the ALS Functional Rating Scale-Revised (ALSFRS-R) at 12 months continue treatment using the response phase listing at the full effective price.

3.3 The proposed listing, with changes suggested by the Secretariat, is shown below.

Name, restriction, manner of administration and form	Maximum quantity (packs)	Maximum quantity (units)	Number of repeats	Dispensed price for maximum quantity	Proprietary name and manufacturer	
INITIATION PHASE[1]						
tofersen, 100 mg/ 15 mL injection, 15 mL vial	1	1	7	Published: Public: [redacted] Private: $[redacted] Effective: Public: $[redacted] Private: $[redacted]	QALSODY™	Biogen Australia Pty Ltd
FIRST CONTINUATION PHASE[2]						
tofersen, 100 mg/ 15 mL injection, 15 mL vial	1	1	6	Published: Public: $[redacted] Private: $[redacted] Effective: Public: $[redacted] Private: $[redacted]	QALSODY™	Biogen Australia Pty Ltd
RESPONSE PHASE						
tofersen, 100 mg/ 15 mL injection, 15 mL vial	1	1	5	Published: Public: $[redacted] Private: $[redacted] Effective: Public: $[redacted] Private: $[redacted]	QALSODY™	Biogen Australia Pty Ltd

Source: Table 1.2 of the March 2026 early re-entry resubmission

[1] This item can be used only once

[2] The maximum number of item(s) to be used is 2 to allow for the 3-month confirmation period, which may be utilised prior to discontinuing due to non-response, or continuing as a responder

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public) MP	1	1	7	Qalsody

Concept ID (For Dept. use}	**Category / Program:** Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)
Prescribing rule level:	
	Administrative Advice: *No increase in the maximum quantity or number of units may be authorised.*
	Administrative Advice: *No increase in the maximum number of repeats may be authorised.*
	Administrative Advice: *Special Pricing Arrangements apply.*
	Administrative Advice: *Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.*

	Administrative Advice: *The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/*
Restriction Summary [new1] / Treatment of Concept: [new1A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: Initial treatment ~~phase~~
	Clinical criteria:
	Patient must not have previously received PBS-subsidised treatment with this drug for this condition.
	AND
	Clinical criteria:
	Patient must have/have had a clinical symptom(s) of amyotrophic lateral sclerosis prior to commencing treatment with this drug,
	AND
	Clinical criteria:
	The condition must have been diagnosed by a neurologist,
	AND
	Clinical criteria:
	The condition must have a confirmed pathogenic (class 5) or likely pathogenic (class 4) superoxide dismutase 1 (SOD1) gene variant,
	AND
	Clinical criteria:
	Patient must not have undergone a tracheostomy,
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria:
	Patient must not be receiving concomitant treatment with edaravone for this condition.
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis.
	Prescribing Instructions: *The following must be documented in the patient's medical records:* *a)* ~~The d~~ *D*ate and details of the patient's genetic testing confirming the presence of the SOD1 gene mutation ~~must be documented in the patient's medical record.~~ b) ~~The b~~ *B*aseline *score of* Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised (ALSFRS-R) ~~score~~ at treatment initiation
	~~**Administrative Advice:**~~ ~~**Note**~~ ~~Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.~~ ~~**Note**~~ ~~No increase in the maximum quantity or number of units may be authorised.~~ ~~**Note**~~ ~~No increase in the maximum number of repeats may be authorised.~~ ~~**Note**~~

	~~The maximum number of items to be used is 1.~~ ~~**Note**~~ ~~Special Pricing Arrangements apply.~~

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public) MP	1	1	6	Qalsody

Concept ID (For Dept. use}	**Category / Program:** Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)
Prescribing rule level:	
	Administrative Advice: *No increase in the maximum quantity or number of units may be authorised.*
	Administrative Advice: *No increase in the maximum number of repeats may be authorised.*
	Administrative Advice: *Special Pricing Arrangements apply.*
	Administrative Advice: *Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.*
	Administrative Advice: *The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/*
Restriction Summary [new2] / Treatment of Concept: [new2A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: First continuing treatment ~~phase~~
	Clinical criteria
	Patient must have previously received PBS-subsidised treatment with this drug for this condition *under the initial treatment restriction,*
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria
	Patient must not be receiving concomitant treatment with edaravone for this condition.

	AND
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis, **OR**
	Must be treated by a medical practitioner in consultation with a specialist with expertise in the management of patients with amyotrophic lateral sclerosis.
	~~**Administrative Advice:**~~ ~~**Note**~~ ~~Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.~~ ~~**Note**~~ ~~No increase in the maximum quantity or number of units may be authorised.~~ ~~**Note**~~ ~~No increase in the maximum number of repeats may be authorised.~~ ~~**Note**~~ ~~The maximum number of items to be used is 2.~~ ~~**Note**~~ ~~Special Pricing Arrangements apply.~~
	Prescribing Instructions: *Assessment of response must be conducted after 6 months of the first continuing treatment, (i.e. at 12 months from treatment initiation).* *If a response to treatment cannot be demonstrated at this assessment, prescribers may apply for up to a maximum of three months (i.e. 2 repeats) of additional continuing treatment under the extended first continuing treatment phase to verify non-response.* *Reassessment of response must be conducted after the additional three months of therapy to determine the patient's eligibility for further treatment.* *If this reassessment is not undertaken, the patient will not be eligible for ongoing treatment.*
	Prescribing Instructions: *All the assessments of response must be documented in the patient's medical records.*
	Prescribing Instructions: *Adequate response to treatment is defined as any improvement or stabilisation (no more than 20% decline) from baseline score of ALSFRS-R.*

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public) MP	1	1	2	Qalsody

Concept ID (For Dept. use}	**Category / Program:** Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)
Prescribing rule level:	
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/
Restriction Summary [new5] / Treatment of Concept: [new5A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: Extended first continuing treatment (additional 3 doses)
	Clinical criteria
	Patient must have not demonstrated an adequate response to treatment under the first continuing restrictions
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis, **OR**
	Must be treated by a medical practitioner in consultation with a specialist with expertise in the management of patients with amyotrophic lateral sclerosis.
	Prescribing Instructions: Reassessment of response must be conducted after the additional three months of therapy to determine the patient's eligibility for further treatment. If this reassessment is not undertaken, the patient will not be eligible for ongoing treatment.

	Prescribing Instructions: *All the assessments of response must be documented in the patient's medical records.*
	Prescribing Instructions: *Patient may qualify for this treatment phase once only.*
	Prescribing Instructions: *Adequate response to treatment is defined as any improvement or stabilisation (no more than 20% decline) from baseline score of ALSFRS-R.*

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public) MP	1	1	5	Qalsody

Concept ID (For Dept. use}	**Category / Program:** Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)
Prescribing rule level:	
	Administrative Advice: *No increase in the maximum quantity or number of units may be authorised.*
	Administrative Advice: *No increase in the maximum number of repeats may be authorised.*
	Administrative Advice: *Special Pricing Arrangements apply.*
	Administrative Advice: *Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.*
	Administrative Advice: *The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/*
Restriction Summary [new3] / Treatment of Concept: [new3A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: *Subsequent continuing* Treatment ~~response phase~~
	Clinical criteria
	Patient must have previously received PBS-subsidised treatment *with this drug for this condition under the first continuing treatment, the extended first continuing treatment or the grandfather treatment restriction.* ~~or treatment from the sponsor's early access program with this drug for this condition,~~
	AND
	Clinical criteria:
	~~Patients who previously received PBS-subsidised treatment must demonstrate treatment response once at 12 months as described below,~~ *Patient must have demonstrated adequate response to treatment if they have received PBS-subsidised treatment under the first continuing treatment or the extended first continuing treatment restriction.*
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,

	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria:
	Patient must not be receiving concomitant treatment with edaravone for this condition.
	AND
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis, **OR**
	Must be treated by a medical practitioner in consultation with a specialist with expertise in the management of patients with amyotrophic lateral sclerosis.
	~~**Prescribing Instructions:**~~ ~~For patients who previously received PBS-subsidised treatment under the first continuation phase, the Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised (ALSFRS-R) score at 12 months must be documented in the patient's medical record. This requirement does not apply to patients transitioning from the sponsor's early access program.~~ ~~Treatment response is defined as any improvement or stabilisation (no more than 20% decline) from baseline ALSFRS-R at 12 months. If a patient does not meet the continuation criteria at 12 months, a confirmation period of up to three months allows re-measurement before discontinuation to verify non-response.~~
	Prescribing Instructions: *Adequate response to treatment is defined as any improvement or stabilisation (no more than 20% decline) from the baseline score of ALSFRS-R.*
	~~**Administrative Advice:**~~ ~~**Note**~~ ~~Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.~~ ~~**Note**~~ ~~No increase in the maximum quantity or number of units may be authorised.~~ ~~**Note**~~ ~~No increase in the maximum number of repeats may be authorised.~~ ~~**Note**~~ ~~Special Pricing Arrangements apply.~~

MEDICINAL PRODUCT ***medicinal product pack***	***PBS item code***	***Max. qty packs***	***Max. qty units***	***№.of Rpts***	***Available brands***
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	*NEW (Private)* *NEW (Public)* *MP*	*1*	*1*	*5*	*Qalsody*
Concept ID (For Dept. use}	***Category / Program:*** *Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)*				
	Prescriber type: ☒ *Medical Practitioners*				

	Benefit type: ☒ *Authority Required (Telephone/ Online PBS Authorities System)*
Prescribing rule level:	
	Administrative Advice: *No increase in the maximum quantity or number of units may be authorised.*
	Administrative Advice: *No increase in the maximum number of repeats may be authorised.*
	Administrative Advice: *Special Pricing Arrangements apply.*
	Administrative Advice: *Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.*
Restriction Summary [new4] / Treatment of Concept: [new4A]	
	Indication: *Amyotrophic lateral sclerosis*
	Treatment Phase: *Transitioning from non-PBS to PBS-subsidised treatment – 'Grandfather' arrangements*
	Clinical criteria:
	Patient must have been receiving non-PBS-subsidised treatment with this drug for this condition prior to [date of listing]
	AND
	Clinical criteria:
	Patient must have had a clinical symptom(s) of amyotrophic lateral sclerosis prior to commencing treatment with this drug,
	AND
	Clinical criteria:
	The condition must have been diagnosed by a neurologist,
	AND
	Clinical criteria:
	The condition must have a confirmed pathogenic (class 5) or likely pathogenic (class 4) superoxide dismutase 1 (SOD1) gene variant,
	AND
	Clinical criteria:
	Patient must not have undergone a tracheostomy,
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria:
	Patient must not be receiving concomitant treatment with edaravone for this condition.
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis.
	Prescribing Instructions:

	The date and details of the patient's genetic testing confirming the presence of the SOD1 gene mutation must be documented in the patient's medical records.
	Prescribing Instructions: *A patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a grandfathered patient must qualify under the Subsequent continuing treatment criteria.*
	Prescribing Instructions: *This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.*

3.4 In the November 2025 submission the requested effective ex-manufacturer price (EMP) for tofersen was $[redacted] per vial; whereas the effective EMP in the March 2026 resubmission is $[redacted] per vial ([redacted]% reduction). The effective EMP is reduced by a further [redacted]% in the first continuation phase (see paragraph 3.2) to $[redacted] per vial to reflect the proportion of non-responders.

3.5 The resubmission accepted the majority of the Secretariat's proposed wording changes. The resubmission stated that restricting treatment to registered specialist clinics may inadvertently create equity of access issues, particularly for rural and remote patients. Instead, the resubmission proposed that treatment must be initiated by a specialist with expertise in the diagnosis and management of ALS, with continuation treatment by a specialist or in consultation with a specialist. The PBAC considered that treatment should be by a specialist only for both initial and continuing treatment.

3.6 The submission proposed that patients are treated under the initial listing for 6 months (3 loading doses on day 0, 14, and 28 followed by dosing every 4 weeks). The proposed 7 repeats would allow for up to 28 weeks of treatment (approximately 7 months). Patients would then receive an additional 6 months of treatment under the first continuing listing, after which they would be assessed for response to treatment. The proposed 6 repeats would allow for another 28 weeks of treatment (i.e. up to 56 weeks in total until the first assessment of response at 12 months).

3.7 If a patient does not meet the response criteria, the submission proposed they receive an additional 3 months of treatment under the first continuing listing, before reassessment. Where patients meet the response criteria they would continue treatment under the treatment response phase listing. The resubmission suggested that a prescriber note (e.g. Patient will be eligible for a maximum of one PBS-subsidised prescription as initial phase, and a maximum number of two PBS-subsidised prescriptions as a first continuation phase) could be included to ensure clinicians progress the patients through in the correct sequence and ensure that the correct item is used in the case that a confirmation period of 3 months is required for discontinuation due to non-response. This would also be necessary to ensure that patients are not able to continue treatment indefinitely under the first continuation phase without the need to demonstrate treatment response. As it would be

administratively difficult to approve an additional 3 supplies under the same first continuing treatment, the Secretariat has proposed a separate listing with 2 repeats, to be accessed only where a patient does not demonstrate response at the initial 12 months.

3.8 The resubmission defined a treatment response in the response phase restriction as any improvement or stabilisation (no more than 20% decline) from baseline ALSFRS-R at 12 months. The resubmission noted that ALSFRS-R is an ordinal, non-linear scale (its scores indicate rank order of function but do not represent equal intervals across the range). As such, the resubmission stated that because the impact of a point change varies significantly depending on the baseline score, a percentage change provides a more clinically relevant measure of progression. Further, there is currently no universal consensus on how to define a clinically meaningful change in ALSFRS-R. The resubmission noted that during consideration of edaravone for all ALS patients, the ESC proposed the clinically minimally important difference (MCID) reported of 3.24 points by Fournier 2023 (edaravone Public Summary Document [PSD], November 2023 PBAC meeting). Importantly, the same publication acknowledges that "the [minimal important difference] for ALSFRS-R in reality is likely not a rigidly fixed value across the range of the scale" (Fournier et al., 2023). The proportional impact of a 3.24-point change varies across the full ALSFRS-R scale range. For instance, a 3.24-point decline from a score of 48 corresponds to a 7% change, while a decline from a score of 20 corresponds to a 16% change. When applied across the range of 4–48, this MCID corresponds to an average proportional decline of 19%. Therefore, the resubmission stated that a 20% cut-off reflects the average proportional equivalent of the MCID across disease stages, ensuring that the definition of response is anchored in patient-perceived meaningful change. Further, resubmission noted that the average decline in the VALOR studies after 12 months was 21% and that Australian clinicians involved in the early access program (3) supported the definition of response. The submission proposed that continuing treatment after 12 months will depend on meeting predefined response criteria, i.e. any improvement or stabilisation (no more than 20% decline) from baseline ALSFRS-R at 12 months. However, it did not clearly explain if patients should maintain the response for ongoing PBS access. The pre-PBAC response stated that the 12 month assessment of response provides a clinically meaningful interval to evaluate treatment effect while also allowing sufficient time for stabilisation of disease trajectory to be observed. The pre-PBAC response clarified that remeasuring response is not proposed given the progressive nature and high burden of ALS, the nonlinearity of ALSFRS-R trajectories and increasing measurement limitations in later disease stages. The pre-PBAC response stated that it is anticipated that patients not continuing to benefit from treatment will discontinue given the monthly intrathecal injections. The Secretariat has added online reference to the ALSFRS-R tool (consistent with the edaravone restriction).

3.9 The resubmission requested a grandfather restriction that aligns with the initiation phase restriction. However, the resubmission also requested that the grandfather patients transitioning directly from the early access program (opened since [redacted]) commence PBS subsidised treatment under the responder phase listing. The resubmission requested that for these grandfathered patients, a measurement of ALSFRS-R at 12 months is not required. The Secretariat has proposed a separate grandfather phase to provide a pathway for these patients. The pre-PBAC response stated that the proposed grandfather restriction was appropriate.

3.10 Potential flow-on changes to the edaravone PBS listing will be required to prevent concomitant use with tofersen if recommended for listing.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer input

4.2 Although no consumer inputs were received for the early re-entry resubmission, the PBAC recalled the input received from individuals (33), health care professionals (1) and organisations (1) via the Office of Health Technology Assessment Consultation Hub in November 2025. The comments highlighted the high and urgent clinical need for treatments for SOD1-ALS, the progressive nature of the disease and that any slowing of disease progression or retention of functional capacities was a crucial factor in improving patient quality of life.

Comparative effectiveness

4.3 The resubmission presented the final VALOR OLE dataset, which had a follow-up of 148 weeks, as compared to 104 weeks in the previous submission. Much of the final VALOR OLE data was presented in the November 2025 pre-Sub-Committee response. The additional data was not used to revise any inputs to the economic evaluation.

4.4 The November 2025 submission was based on (i) one randomised control trial (RCT) comparing tofersen versus placebo (VALOR – Part C; N = 108) and (ii) an ongoing open-label extension (VALOR OLE; N = 95). Patients who completed VALOR-Part C could enter the VALOR-OLE, while remaining unaware of their trial-group assignment in VALOR. Patients treated with tofersen in VALOR for the first 24 weeks and continued on tofersen in VALOR-OLE (n=63) were referred as "early-start", and patients treated with placebo for the first 24 weeks in VALOR who initiate on tofersen in VALOR-OLE (n=32) were referred as "delayed start patients".

4.5 The primary outcome in VALOR was change from baseline in ALSFRS-R at Week 28 in the modified intention to treat (mITT) population, an "enriched" subgroup of the ITT population who were fast progressing based on ALSFRS-R slope decline or SOD1 variant. In November 2025, the ESC considered that the ITT population was the most relevant and consistent with the proposed PBS population.

Table 3: Change from baseline in ALSFRS-R at Week 28 (VALOR, completed 16 July 2021)

Outcome[a,b]	ITT		mITT		Non-mITT	
	TOF (N=72)	PBO (N=36)	TOF (N=39)	PBO (N=21)	TOF (N=33)	PBO (N=15)
ALSFRS-R score: change from VALOR baseline to Week 28						
Covariates: baseline disease duration, baseline ALSFRS-R score, and riluzole/edaravone use						
Adjusted LS mean (SE)	-4.5 (NR)	-5.8 (NR)	-6.98 (NR)	-8.14 (NR)	-1.33 (NR)	-2.73 (NR)
Difference (95% CI) vs PBO	1.4 (-1.34, 4.09)		1.2 (-3.2, 5.5)		1.4 (-1.1, 3.9)	
p-value JRT+MI	0.9130[c]		0.9689		NR	
p-value ANCOVA+MI	0.3218[c]		0.5998[d]		0.2726[c]	
Covariates: baseline plasma NfL, baseline ALSFRS-R score, and riluzole/edaravone use						
Adjusted LS mean (SE)	-4.1 (NR)	-6.2 (NR)	NR	NR	NR	NR
Difference (95% CI) vs PBO	2.1 (-0.33, 4.54)		2.2 (-1.82, 6.16)		NR	
p-value JRT+MI	0.5015[c]		0.5842[c]		NR	
p-value ANCOVA+MI	0.0904[d]		0.2858[c]		NR	

Source: Table 4, p15 November 2025 minutes

ALSFRS-R = amyotrophic lateral sclerosis functional rating scale–revised; ANCOVA = analysis of covariance; CI = confidence interval; ITT = intention-to-treat; mITT = modified ITT; JRT = joint rank test; LS = least square; MI = multiple imputation; NfL = neurofilament light chain; NR = not reported; PBO = placebo; SE = standard error; SOD1 = superoxide dismutase 1

a MI model included treatment group, baseline disease duration since symptom onset, relevant baseline score, and riluzole or edaravone use. Analyses adjusting for baseline plasma NfL included baseline plasma NfL in the MI model.

b Adjusted means, ratios to baseline, treatment differences (or ratios) and 95% CIs and nominal p-values were obtained from the ANCOVA model for change from baseline. JRT p-values obtained from the ANCOVA model for ranked scores where deaths were ranked lowest, in conjunction with MI for handling missing data due to withdrawals other than death.

c *Post hoc* analysis.

d Sensitivity analysis.

Blue = data presented in November 2025 submission

4.6 In November 2025, the PBAC considered that the claim of superior comparative effectiveness was not well-supported by the data, which was limited by the small patient population and the short duration of the comparative phase of the trial. However, on balance, the PBAC considered that tofersen was likely to provide a clinically meaningful benefit to some patients, but that the magnitude of the benefit and longer-term effects were uncertain (paragraph 6.37 tofersen PSD, November 2025 PBAC).

4.7 Change from baseline in ALSFRS-R total score at Weeks 76, 104 and 148 from the VALOR OLE study are presented in Table 4 and Figure 1.

Table 4: ALSFRS-R total score - change from baseline (Week 76, Week 104, Week 148; ITT population)

	VALOR OLE (Week 76) Early-start tofersen (n=72) vs. Placebo/delayed-start tofersen (n=36)	**VALOR OLE (Week 104)** Early-start tofersen (n=72) vs. Placebo/delayed-start tofersen (n=36)	**VALOR OLE (Week 148)** Early-start tofersen (n=72) vs. Placebo/delayed-start tofersen (n=36)
Original Multiple Imputation[a]			
Adjusted Means: TOF; PBO	-7.6; -11.0	-9.5; -13.2	-9.9, -13.5
TOR-PBO: Adjusted Mean Difference (95% CI)	3.4 (-0.3, 7.1)	3.7 (-0.7, 8.2)	3.6 (-1.2, 8.4)
p-Value (ANCOVA+MI)	p=0.0686	p=0.1004	p = 0.1432
p-Value (original JRT+MI)	p=0.0860	p=0.0835	p = 0.1064
p-Value (alter. JRT+MI)	p=0.0375	p=0.0335	p = 0.0541
Multiple Imputation and Imputation Zero After Death[a,b]			
Adjusted Means: TOF; PBO	-9.0; -14.5	-10.6; -16.2	-11.8; -16.7
TOF-PBO: Adjusted Mean Difference (95% CI)	5.6 (1.0,10.1)	5.6 (0.6,10.5)	4.9 (-0.4, 10.1)
p-Value (ANCOVA+MI)	p=0.0160	p=0.0280	p = 0.0711

Source: Table 2.1, p31 of the March 2026 early re-entry resubmission

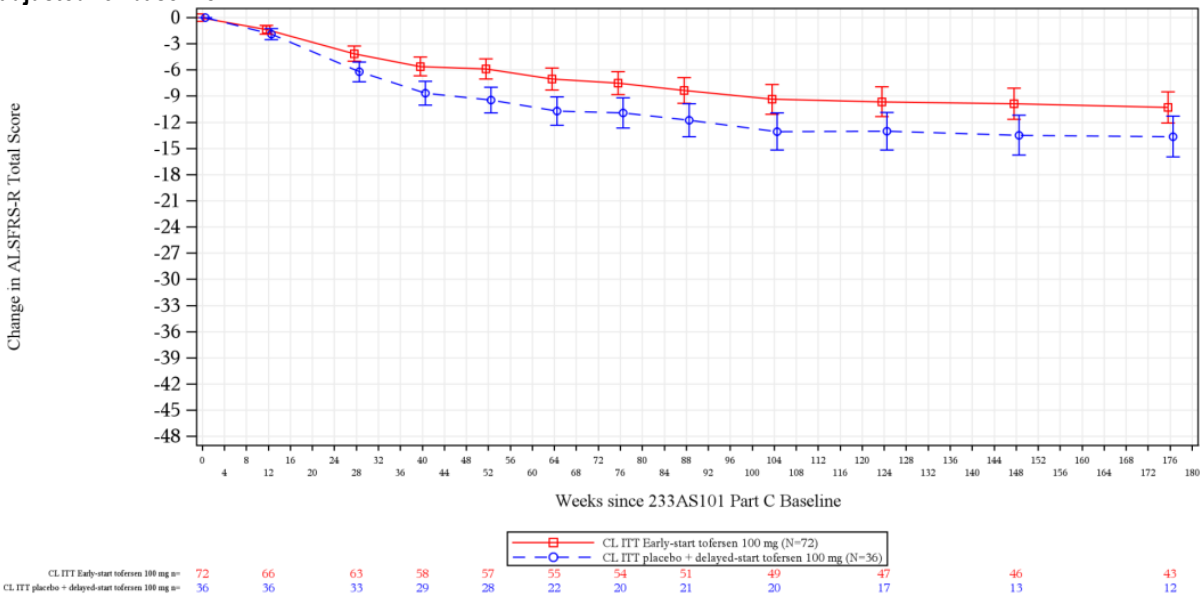
ALSFRS-R = amyotrophic lateral sclerosis functional rating scale–revised; ANCOVA = analysis of covariance; CI = confidence interval; ITT = intention to treat; JRT = joint rank test; MI = multiple imputation; NfL = neurofilament light chain; OLE = open-label extension; PBO = placebo; TOF = tofersen

A Joint rank p-value was calculated from the rank ANCOVA model based on the change of the ranked score pre- and post-treatment, i.e., the ranked score with ALSFRS-R total score at Week 76 or Week 104, where deaths were ranked the lowest, minus the rank of baseline ALSFRS-R total score, and in conjunction with multiple imputation for handling missing data due to withdrawals other than death. The rank ANCOVA model includes treatment as a fixed effect and adjusts for the following ranked covariates: ranked baseline plasma NfL, ranked baseline ALSFRS-R total score, and use of riluzole or edaravone.

B Multiple imputation including the treatment group, use of riluzole or edaravone, baseline plasma NfL, and relevant baseline and postbaseline values for the endpoint was used for missing data. The missing data after death were imputed with zero.

Blue = data presented in November 2025 submission

Figure 1: ALSFRS-R total score LS mean change from baseline (ITT), early vs delayed tofersen from VALOR OLE, adjusted for baseline nfL



Source: Figure 2.1, p32 of the March 2026 early re-entry resubmission
ALSFRS-R = amyotrophic lateral sclerosis functional rating scale–revised; ITT = intention to treat; NfL = neurofilament light chain; OLE = open-label extension

4.8 Consistent with the data presented in the November 2025 submission, the submission stated that over the longer-term, the early-start tofersen group experienced a significantly slower decline in ALSFRS-R total score from baseline at Week 76 (3.4 points), Week 104 (3.7 points) and Week 148 (3.6 points) compared to the placebo/delayed-start group.

4.9 The resubmission also presented ALSFRS-R, percent-predicted slow vital capacity (%SVC) and handheld dynamometry (HHD) megascore responder analyses, change from baseline in cerebrospinal fluid (CSF) SOD1, plasma neurofilament light change (NfL), %SVC and HHD megascore, time to event and patient-reported outcome data from the VALOR OLE at Week 148. As noted in paragraph 6.28 of the November 2025 PSD, the ESC considered that the results from Week 148 were consistent with those presented at Week 104. The ESC noted that there was no difference between early-start and delayed-start tofersen patients at Week 148 in the improvement from baseline in function and survival. Reduction in NfL was also similar between early-start and delayed-start patients at Week 148. The ESC agreed that there was a trend towards slower decline in ALSFRS-R score, %SVC and HDD.

Comparative harms

4.10 The resubmission noted that the second Period Safety Update Report (PSUR) was available. No new safety findings were noted.

Clinical claim

4.11 The resubmission did not provide new clinical claims, rather it appeared to accept the PBAC's considerations in November 2025 that:

- the claim of superior comparative effectiveness was not well-supported by the data, which was limited by the small patient population and the short duration of the comparative phase of the trial. However, on balance, tofersen was likely to provide a clinically meaningful benefit to some patients, but that the magnitude of the benefit and longer-term effects were uncertain (paragraph 6.37, tofersen PSD, November 2025).
- the claim of inferior comparative safety was reasonable (paragraph 6.38, tofersen PSD, November 2025).

Economic analysis

4.12 The resubmission presented an updated economic model which included the revised prices of tofersen (see paragraph 3.4 and Table 5). There were no other changes applied to the economic model in the resubmission.

Table 5: Updated effective DPMQs of tofersen (assuming 50% of tofersen use would be in private hospitals)

Treatment phase	Description	Effective EMP per vial	Effective DPMQ (weighted)[a]	Model cycles applied
Initiation phase	Tofersen 100 mg vial	$[redacted]	$[redacted]	1-6
First continuation phase	Tofersen 100 mg vial	$[redacted]	$[redacted]	7-13
Response phase	Tofersen 100 mg vial	$[redacted]	$[redacted]	14+

Source: Table 3.3, p53 of the March 2026 early re-entry resubmission
DPMQ = dispensed price per maximum quantity; EMP = ex-manufacturer price;
a 50% public/private weighting is unchanged from initial submission.

4.13 The results for the revised economic evaluation are presented in Table 6.

Table 6: Results of the revised economic evaluation

	Tofersen	BSC	Increment
Costs	$[redacted]	$25,202	$[redacted]
QALYs gained	1.39	0.69	0.70
Incremental cost/extra QALY gained			**$[redacted][1]**
November 2025 economic model			
Costs	$[redacted]	$33,901	$[redacted]
QALYs	1.39	0.69	0.70
Incremental cost/extra QALY gained			**$[redacted][2]**

Source: Table 10, p34 of the November 2025 minutes and Table 3.12, p 57 of the March 2026 early re-entry resubmission
BSC = best supportive care; QALY = quality adjusted life year
The redacted values correspond to the following ranges:
[1] *$755,000 to < $855,000*
[2] *$955,000 to < $1,055,000*

Tofersen cost/patient/year

Table 7: Cost of tofersen per patient per year

	Economic model [a]	Financial estimates
Number of administrations – Year 1[b]	Initiation phase: 6.57 First continuation phase: 6.61 Total: 13.18	Initiation phase: 7.50 First continuation: 6.57 Total: 14.07
Cost per patient – Year 1[c]	Initiation phase: $[redacted] First continuation phase: $[redacted] Total: $[redacted]	Initiation phase: $[redacted] First continuation phase: $[redacted] Total: $[redacted]
Number of administrations – Year 2+	Response phase: 6.12 x 2 = 12.24	Response phase: 6.12 x 2 = 12.24
Cost per patient – Year 2+[c]	$[redacted][d]	$[redacted]
November 2025 submission		
Cost per patient per year	$[redacted]	$[redacted]

Source: Table 3.4, p53 of the March 2026 early re-entry resubmission
DPMQ = dispensed price for maximum quantity
a Estimated assuming approximately 6 months of treatment per treatment phase. Includes loading doses in the initiation phase
b Number of administrations includes compliance (93.8%) in both the economic model and financial estimates.
c Assumed 50% public/private weighting and DPMQs as per Table 5 to give a weighted DMPQ of $[redacted] (economic model) and $[redacted] (financial estimates) for the initiation and response phase and $[redacted] (economic model) and $[redacted] (financial estimates). Differences are due to dispensing fees applied in the model ($8.88) and financial estimates ($8.67).
d Corrected from Table 3.4 to exclude riluzole costs.

4.14 Differences between the model and financial cost per patient per year are due to differences in the number of administrations in Year 1. The number of administrations for the initiation phase in the financial estimates appears overestimated as it would be expected that the total number of administrations per year would be 14.04 (including one additional loading dose at day 14; ((365.25/28) + 1)). With compliance applied this would be 13.17 ((365.25/28 +1) x 93.8%). There were also slight differences in the DPMQs applied in the economic evaluation and financial estimates as mark-ups were updated in the financial estimates but not the economic evaluation. The pre-PBAC response stated that the number of administrations/vials in the first year is 15, but also noted that this would include treatment coverage to 1 year + 28 days. The pre-PBAC response noted that the difference in approaches is marginal and has limited impact on the overall expenditure.

Estimated PBS usage & financial implications

4.15 The November 2025 submission presented a prevalence model which did not appropriately account for newly diagnosed patients. The March 2026 resubmission has presented a mixed incidence/prevalence model.

4.16 Table 8 summarises the parameters and data sources applied in the revised financial analysis.

Table 8: Key inputs for utilisation and financial impact estimates

Input	Value and source	Comment
Australian population	28,372,315 in Year 1 (2026) to 30,314,335 in Year 6 (2031) (ABS, Series B)	Unchanged.
ALS incidence	2.9 per 100,000 (Vucic 2020)	New. Based on advice in the November 2025 submission.
ALS prevalence	6.22 per 100,000 (Meta analysis: Brown 2021)	Unchanged.
SOD1 proportion	4.2% (Average % of relevant countries (Australia, Europe, New Zealand, UK, World) – Battistini 2010; Brown 2021; Gromicho 2018; McCann 2017; Mrkela 2024; Van Es 2010; Zou 2017)	Unchanged. The DUSC previously noted that the estimates were highly sensitive to the proportion and that there was substantial geographic heterogeneity in this proportion.
Grandfathered patients	[redacted] in Year 1 (Biogen early access program)	Unchanged.
Uptake	Year 1: [redacted]% Year 2: [redacted]% Year 3: [redacted]% Year 4: [redacted]% Year 5: [redacted]% Year 6: [redacted]% (Assumption)	Updated from November 2025 ([redacted]% in Year 1 to [redacted]% in Year 6). The resubmission stated that there was anticipated demand from patients and clinicians. The PBAC maintained that some patients will elect not to receive treatment due to ongoing lumbar punctures and may be limited by geographical access to treatment centres. The PBAC considered that a maximum uptake of [redacted]% should be applied.
Continuation rate	Year 1: [redacted]% Year 2: [redacted]% Year 3: [redacted]% Year 4: [redacted]% Year 5: [redacted]% Year 6: [redacted]% (Economic model, 'Markov Trace' sheet)	Updated from November 2025 ([redacted]% applied at the end of each year). The resubmission aligned the continuation rates with the economic model. The DUSC previously considered that the continuation rate may be overestimated and may be affected by voluntary assisted dying. The PBAC previously noted that this may be affected by response to treatment.
Compliance	93.8% (VALOR Part C trial)	Unchanged. Aligned with the economic model. The PBAC previously noted that this rate may be affected by response to treatment.
Beneficiary type	99% PBS and 1% RPBS; (PBS item reports of riluzole and edaravone combined from October 2024 to September 2025) 50% / 50% split for public / private hospital (Assumption)	Updated, based on DUSC advice. Was 100% PBS in November 2025. Unchanged.
Administration and adverse events	Administration: MBS item 18216 Adverse events: MBS item 105	Unchanged.

Source: Table 4.1, p59 of the March 2026 early re-entry resubmission and Table 12, p37 of the November 2025 minutes

ABS = Australian Bureau of Statistics; ALS = amyotrophic lateral sclerosis; MBS = Medicare Benefits Schedule; SOD1 = superoxide dismutase 1

The redacted values correspond to the following ranges:

[1] *< 500*

Table 9: Estimated use and financial implications of listing tofersen on the PBS/RPBS

	2026	2027	2028	2029	2030	2031
Estimation of number of treated patients						
Incident patients with SOD1	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Prevalent patients with SOD1	[redacted][1]	-	-	-	-	-
Total eligible patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Uptake rate	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Grandfathered population on treatment	[redacted][1]	-	-	-	-	-
Total patients initiating tofersen	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated number of tofersen scripts (PBS/RPBS)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated effective cost of tofersen to PBS/RPBS						
Total cost of tofersen	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
PBS copayments	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]
Net cost to PBS/RPBS (excluding copayments)	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Total cost to MBS	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]
Net cost to PBS/RPBS/MBS	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**
November 2025 submission						
Estimation of number of treated patients						
Total patients initiating tofersen	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated number of tofersen scripts (PBS/RPBS)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated effective cost of tofersen to PBS/RPBS						
Net cost to PBS/RPBS (excluding copayments)	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**
Total cost to MBS	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]
Net cost to PBS/RPBS/MBS	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**

Source: Tables 4.6, 4.7, 4.11, 4.12, 4.14 of the submission

MBS = Medicare Benefits Scheme; SOD1 = superoxide dismutase 1

[a] Net change in authorities likely underestimated. Submission assumed 5 repeats for both initial loading and subsequent doses. Initial loading dose should have 2 repeats.

The redacted values correspond to the following ranges:

[1] *< 500*

[2] *500 to < 5,000*

[3] *$10 million to < $20 million*

[4] *net cost saving*

[5] *$0 to < $10 million*

4.17 The total cost to the PBS/RPBS of listing tofersen was estimated to be $10 million to < $20 million in Year 1, and a total of $100 million to < $200 million in the first 6 years of listing. This compared to a total cost of $90 million to < $100 million in the first 6 years of listing in the November 2025 submission. However, the number of doses under the initiation and first continuation phases appear to be overestimated (see

paragraph 4.14). Financial Management – Risk Sharing Arrangement and Pay for Performance Framework

4.18 The resubmission proposed a [redacted] risk sharing arrangement based on estimated net cost to PBS/RPBS in Table 9. [redacted] rebate of [redacted] on expenditure [redacted] rebate of [redacted]

4.19 The pre-PBAC response proposed a simpler, alternative approach in which the expenditure caps are reduced by [redacted]% for the duration of the deed, with a rebate of [redacted]% for use beyond the caps.

Table 10: Risk share arrangement proposed in the pre-PBAC response

Year	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated PBS expenditure	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Expenditure caps (estimated PBS expenditure – [redacted]%)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]

Source: pre-PBAC response, p2
ALS-SOD1 = amyotrophic lateral sclerosis – superoxide dismutase 1

4.20 Noting that there are no additional studies planned for tofersen in ALS-SOD1 and the regulatory pathway recommended by the TGA is provisional due to the uncertainty of the clinical data from the VALOR trial, the resubmission has also proposed a "pay for performance" framework, with an additional [redacted]% discount to the price in the first continuation phase restriction (i.e. months 6 to 12 of treatment), assuming that [redacted]% of patients will be non-responders (see paragraph 3.2). The resubmission notes that the proposal applies to incident patients, with those enrolled in the early access program grandfathered into the response phase. This [redacted]% reduction in the cost for scripts under the first continuation phase listing is included in the values in Table 10. The resubmission stated that the first continuation phase accounts for uncertainty in response and provides an upfront discount to reflect the expected proportion of non-responders before formal assessment at 12 months and ensures consistency with the trial evidence, administrative simplicity and value delivery. This is not strictly a pay for performance framework, but rather a price reduction to address uncertainty in the overall cost-effectiveness.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 PBAC Outcome

5.1 The PBAC recommended tofersen for the treatment of patients with amyotrophic lateral sclerosis (ALS) who have a superoxide dismutase 1 (SOD1) gene pathogenic variant. The PBAC noted the high unmet need for targeted treatments for this rare subtype of ALS. The PBAC recalled that it had previously considered that tofersen was likely to be associated with a meaningful clinical benefit (maintaining function for longer and increasing overall survival) compared with the current standard of care (riluzole) but that the longer-term effects remained uncertain. The PBAC considered the resubmission addressed the Committee's previous concerns. The PBAC considered

that the cost-effectiveness of tofersen was uncertain due to the limited data informing the economic model, but that in the context of this life-limiting disease in a rare sub-group of ALS patients, and considering the expected level of improvement in quality of life and survival, the tofersen was cost-effective at the price proposed in the resubmission, in the context of the proposed Risk Sharing Arrangement (RSA). The PBAC noted that this recommendation was in line with other treatments for rare diseases funded on the PBS, accounting for clinical need, available evidence, nature of the benefits and size of the patient population. The PBAC also considered that some minor changes to the financial estimates were required and that the proposed RSA was appropriate to manage the uncertainty associated with the long-term clinical benefit for tofersen and the uncertain duration of therapy.

5.2 In terms of the proposed restrictions, the PBAC considered that they were generally appropriate, noting that:

- a Section 100 HSD program Authority required (telephone/online) listing was appropriate for all treatment phases, given that the drug is required to be administered intrathecally in a hospital setting;
- the initial supply restriction should have 6 repeats (to provide 7 doses, approximately 5.5 months of therapy including 2 doses in the first month) as should the first continuing supply (to provide 7 doses, approximately 6.5 months of therapy). This would result in the assessment of response occurring after approximately 12 months of therapy;
- the extended first continuing treatment restriction, which allows non-responding patients to access an additional 3 doses of treatment (3 months) at the lower price, was appropriate. A reassessment of response would be required for non-responding patients (i.e., after approximately 15 months of therapy), to determine eligibility for ongoing treatment. The PBAC considered that the inclusion of a Prescribing Instruction to ensure clinicians progress patients through the restrictions in the correct sequence was reasonable;
- in the subsequent continuing restriction, reassessment of response for responding patients was not required beyond 12 months as ALS is a progressive disease with limited life-expectancy, and ongoing treatment is likely to be limited due to the intrathecal administration;
- restricting treatment to registered specialist clinics, as recommended in November 2025, could inadvertently create equity of access issues. Therefore, the PBAC advised that the restrictions should allow tofersen to be prescribed only by a specialist with expertise in the diagnosis and management of ALS in all treatment phases. The PBAC considered it was not appropriate to allow treatment in any phase by non-specialist medical practitioners in consultation with a specialist;

- the proposed grandfather restriction was appropriate and assessment of response for access to continued treatment for grandfathered patients should occur within 12 months of treatment initiation and would be based on clinical judgement as grandfathered patients would not necessarily have a recorded baseline ALSFRS-R score.

5.3 The PBAC noted that no new comparative clinical evidence was presented in the early re-entry resubmission. The PBAC recalled that it had previously considered that compared to best supportive care in terms of (i) efficacy, tofersen was likely to provide a clinically meaningful benefit to some patients, but that the magnitude of the benefit and the longer-term effects were uncertain; and (ii) safety, tofersen was inferior.

5.4 The PBAC recalled that it had previously considered that the economic model was uninformative and not reliable for decision making. Therefore, in November 2025 it had advised that tofersen would be acceptably cost-effective with a substantial price reduction that resulted in a patient cost per year consistent with the expected clinical benefit for tofersen and aligned with other treatments for rare diseases funded on the PBS, accounting for clinical need, available evidence, nature of the benefits and size of the patient population. The PBAC noted that the early re-entry resubmission proposed a [redacted]% price reduction for the initiation and response treatment phases, with an additional [redacted]% price reduction for the first continuation phase. The PBAC considered that tofersen was cost-effective at the price proposed in the resubmission, in the context of the proposed RSA (see paragraph 5.6).

5.5 The PBAC considered that the structure of the revised utilisation estimates presented in the resubmission, which were based on a mixed incidence/prevalence model, was generally acceptable. The PBAC noted that changes were also made to the modelling of continued treatment and the uptake rate. The PBAC considered that the number of doses of tofersen in the financial estimates should be revised to be consistent with the economic model and with the listings as per paragraph 5.2 (14 doses total in year 1, before accounting for compliance/discontinuation). The PBAC noted that the uptake rates applied ([redacted]% in Year 1 increasing to [redacted]% in Year 6) remained high for a drug that was administered intrathecally and considered that a maximum uptake rate of [redacted]% would be more reasonable. The PBAC recommended that the utilisation of tofersen should be reviewed after 3 years.

5.6 The PBAC considered that the RSA proposed in the pre-PBAC response would manage the uncertainty associated with the long-term clinical benefit of tofersen and the uncertain duration of therapy. The PBAC noted that the expenditure caps, which were set [redacted]% below the estimated financial impact aimed to manage the uncertainty regarding the cost-effectiveness of tofersen (see paragraph 5.4). The PBAC considered that the proposed rebate of [redacted]% for use that exceeded the caps was appropriate.

5.7 The PBAC advised that tofersen should be exempt from the Early Supply Rule.

5.8 The PBAC advised that tofersen was not suitable for prescribing by nurse practitioners as it is administered intrathecally.

5.9 The PBAC advised that under section 101(3BA) of the *National Health Act 1953*, tofersen should not be treated as interchangeable on an individual patient basis with any other drug.

5.10 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were met. Specifically, the PBAC found that in the circumstances of its recommendation for tofersen:

a) The treatment is expected to provide a substantial and clinically relevant improvement in efficacy, over best supportive care;

b) The treatment is expected to address a high and urgent unmet clinical need;

c) It would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A on the basis of the preceding findings.

5.11 The PBAC noted that this submission was not eligible for an Independent Review, as it received a positive recommendation.

Outcome:
Recommended

6 Recommended listing

6.1 Add new item:

Initial

MEDICINAL PRODUCT **medicinal product pack**		**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
TOFERSEN						
tofersen 100 mg/ 15 mL injection, 15 mL vial		NEW (Private) NEW (Public)	1	1	6	Qalsody
Concept ID (For Dept. use}	**Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)					
	Prescriber type: ☒ Medical Practitioners					
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)					
Prescribing rule level:						
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.					
	Administrative Advice: No increase in the maximum number of repeats may be authorised.					
	Administrative Advice: Special Pricing Arrangements apply.					

	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/
Restriction Summary [new1] / Treatment of Concept: [new1A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: Initial treatment
	Clinical criteria:
	Patient must have/have had a clinical symptom(s) of amyotrophic lateral sclerosis prior to commencing treatment with this drug,
	AND
	Clinical criteria:
	The condition must have been diagnosed by a neurologist,
	AND
	Clinical criteria:
	The condition must have a confirmed pathogenic (class 5) or likely pathogenic (class 4) superoxide dismutase 1 (SOD1) gene variant,
	AND
	Clinical criteria:
	Patient must not have undergone a tracheostomy**,**
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition
	AND
	Clinical criteria:
	Patient must not be receiving concomitant treatment with edaravone for this condition.
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis.
	Prescribing Instructions: The following must be documented in the patient's medical records: a) date and details of the patient's genetic testing confirming the presence of the SOD1 pathogenic gene variant b) baseline score of Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised (ALSFRS-R) at treatment initiation

First continuing treatment

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public)	1	1	6	Qalsody

Concept ID (For Dept. use}	**Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)
Prescribing rule level:	
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/
Restriction Summary [new2] / Treatment of Concept: [new2A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: First continuing treatment
	Clinical criteria
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the initial treatment restriction,
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria

	Patient must not be receiving concomitant treatment with edaravone for this condition.
	AND
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis
	Prescribing Instructions: Assessment of response must be conducted after 6 months of the first continuing treatment, (i.e. at 12 months from treatment initiation). If a response to treatment cannot be demonstrated at this assessment, prescribers may apply for up to a maximum of three months (i.e. 2 repeats) of additional continuing treatment under the extended first continuing treatment phase to verify non-response. Reassessment of response must be conducted after the additional three months of therapy to determine the patient's eligibility for further treatment. If this reassessment is not undertaken, the patient will not be eligible for ongoing treatment.
	Prescribing Instructions: All the assessments of response must be documented in the patient's medical records.
	Prescribing Instructions: Adequate response to treatment is defined as any improvement or stabilisation (no more than 20% decline) from baseline score of ALSFRS-R.

Extended first continuing treatment

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public)	1	1	2	Qalsody

Concept ID (For Dept. use}	**Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)
Prescribing rule level:	
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/
Restriction Summary [new3] / Treatment of Concept: [new3A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: Extended first continuing treatment (additional 3 doses)
	Clinical criteria
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the first continuing restriction
	AND
	Clinical criteria
	Patient must **not** have demonstrated an adequate response to treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:

	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria
	Patient must not be receiving concomitant treatment with edaravone for this condition.
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis
	Prescribing Instructions: Reassessment of response must be conducted after the additional three months of therapy to determine the patient's eligibility for further treatment. If this reassessment is not undertaken, the patient will not be eligible for ongoing treatment.
	Prescribing Instructions: All the assessments of response must be documented in the patient's medical records.
	Prescribing Instructions: Patient may qualify for this treatment phase once only.
	Prescribing Instructions: Adequate response to treatment is defined as any improvement or stabilisation (no more than 20% decline) from baseline score of ALSFRS-R.

Subsequent continuing treatment (response phase)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public)	1	1	5	Qalsody

Concept ID (For Dept. use}	**Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)

Prescribing rule level:	
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: The ALS Functional Rating Scale - Revised (ALSFRS-R) can be accessed online at: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/
Restriction Summary [new4] / Treatment of Concept: [new4A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: Subsequent continuing treatment
	Clinical criteria
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the first continuing treatment, the extended first continuing treatment or the grandfather treatment restriction.
	AND
	Clinical criteria:
	Patient must have demonstrated an adequate response to treatment defined as any improvement or stabilisation in the ALSFRS-R score (i.e. no more than a 20% decline from the baseline ALSFRS-R score), if they have received treatment under the first continuing or extended first continuing restriction; or.
	Patient must have demonstrated a clinical benefit from treatment, based on clinician judgment, within 12 months of treatment initiation, if they have received treatment under the grandfather listing.
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria:
	Patient must not be receiving concomitant treatment with edaravone for this condition.
	AND
	Treatment criteria:

	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis

Grandfather treatment

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TOFERSEN					
tofersen 100 mg/ 15 mL injection, 15 mL vial	NEW (Private) NEW (Public)	1	1	5	Qalsody

Concept ID (For Dept. use}	**Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (Telephone/ Online PBS Authorities System)
Prescribing rule level:	
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
Restriction Summary [new4] / Treatment of Concept: [new4A]	
	Indication: Amyotrophic lateral sclerosis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised treatment – 'Grandfather' arrangements
	Clinical criteria:
	Patient must have been receiving non-PBS-subsidised treatment with this drug for this condition prior to [date of listing]
	AND
	Clinical criteria:
	Patient must have had a clinical symptom(s) of amyotrophic lateral sclerosis prior to commencing non-PBS subsidised treatment with this drug,
	AND
	Clinical criteria:
	The condition must have been diagnosed by a neurologist,
	AND
	Clinical criteria:
	The condition must have a confirmed pathogenic (class 5) or likely pathogenic (class 4) superoxide dismutase 1 (SOD1) gene variant,
	AND

	Clinical criteria:
	Patient must not have undergone a tracheostomy**,**
	AND
	Clinical criteria:
	Patient must not have experienced respiratory failure,
	AND
	Clinical criteria:
	Patient must not be receiving palliative care,
	AND
	Clinical criteria:
	The treatment must be given concomitantly with best supportive care (including riluzole where appropriate) for this condition,
	AND
	Clinical criteria:
	Patient must not be receiving concomitant treatment with edaravone for this condition.
	Treatment criteria:
	Must be treated by a specialist with expertise in the diagnosis and management of amyotrophic lateral sclerosis.
	Prescribing Instructions: The date and details of the patient's genetic testing confirming the presence of the SOD1 pathogenic gene variant must be documented in the patient's medical records.
	Prescribing Instructions: A patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a grandfathered patient must qualify under the Subsequent continuing treatment criteria.
	Prescribing Instructions: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.

6.2 Flow on changes

1 Flow-on changes to edaravone PBS listings (item codes 14804E, 14805F, 14806G) for amyotrophic lateral sclerosis to prevent concomitant use with tofersen:

	Clinical criteria:
	Patient must not be receiving concomitant treatment with tofersen for this condition.

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

8 Sponsor's Comment

Biogen welcomes the PBAC's positive recommendation for tofersen (QALSODY) for people with amyotrophic lateral sclerosis (ALS) who have a superoxide dismutase 1 (SOD1) mutation.

Biogen is working collaboratively with the Department to progress PBS listing and enable timely equitable access.

Biogen would like to take this opportunity to thank the ALS community and healthcare professionals who supported the submission.