

7.09 EDARAVONE, Solution concentrate for injection I.V infusion 30 mg in 20 mL, Radicava[®], Teva Pharma Australia Pty Ltd.

1 Purpose

- 1.1 The early re-entry resubmission requested Section 100 Highly Specialised Drugs Authority Required (telephone/electronic) listing of edaravone solution for intravenous (IV) infusion as adjunct treatment to current standard of care (SOC) with or without riluzole in patients with amyotrophic lateral sclerosis (ALS).
- 1.2 The resubmission was based on the PBAC decision to not recommend edaravone for this indication at its November 2023 meeting. Table 1 outlines the issues raised by the PBAC in November 2023 and how these issues were addressed in the resubmission.

Table 1 Summary of key matters to be addressed

Matter of concern	Response	Addressed?
Revision of the restrictions to align the PBS population with patients included in the Study 19 as described in paragraphs 7.4-7.6 November 2023 PSD.	Recommendation adopted	Yes
Revision of the economic model to remove the mortality adjustment (see paragraph 7.13 November 2023 PSD) and reduce the discontinuation rate to 15% (see paragraph 7.13 November 2023 PSD).	Recommendation adopted The discontinuation rate was maintained at 30%. The justification presented in the submission was the change to delivery via infusion centres, which, the resubmission argued, is more likely to result in higher discontinuation rates than the sponsor-funded home delivery proposed in the November 2023 submission.	Yes No
Reduce the price for edaravone to result in an ICER of less than \$ [redacted] ¹ per QALY gained.	[redacted] % price reduction proposed with an ICER of \$ [redacted] ¹ /QALY gained. Reduced from \$ [redacted] to \$ [redacted] per ampoule.	Partially
Reduction of the patient numbers as outlined in paragraph 7.16 of November 2023 PSD. The PBAC noted that estimated patient numbers as outlined in paragraph 7.16 remain uncertain and may require further consideration.	Recommendations adopted for calculation of eligible patient numbers, however additional changes to uptake and duration were also applied, increasing the number of patients accessing treatment and total cost for edaravone.	Partially
Proposal of an RSA	No RSA was proposed in the resubmission.	No

ICER = incremental cost-effectiveness ratio; PSD = Public Summary Document; QALY = Quality adjusted life years; RSA = risk sharing arrangement

The redacted values correspond to the following ranges

¹ \$95,000 to < \$115,000

2 Background

2.1 Edaravone was registered by the TGA on 15 February 2023 for the following indication:

“RADICAVA is indicated in adults with a diagnosis of amyotrophic lateral sclerosis who are independent in activities of daily living with normal respiratory function and where treatment is initiated within two years of disease onset. Efficacy has not been demonstrated in patients outside of this defined population.”

2.2 The PICO from the previous submission is presented below.

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

Component	Description
Population	Patients with amyotrophic lateral sclerosis (ALS).
Intervention	Edaravone (Radicava®) as 30 mg/20 mL concentrated solution for injection to be diluted before use as an intravenous (IV) infusion.
Comparator	Current standard of care with or without riluzole
Outcomes	ALS functional rating scale (ALSFRS-R) after 6 cycles (6 months).
Clinical claim	Edaravone plus current standard of care with or without riluzole is superior in terms of effectiveness and has similar (non-inferior) safety compared to standard of care with or without riluzole.

Source: Table 1-1, p3 of the November 2023 submission.

ALS=amyotrophic lateral sclerosis; ALSFRS-R=ALS Functional Rating Scale – Revised

For more detail on PBAC’s view, see section 5 PBAC outcome.

3 Requested listing

3.1 The resubmission proposed amendments to the previously considered PBS restriction, to include the following criteria in the restriction, in addition to the proposed forced vital capacity (FVC)/ slow vital capacity (SVC) requirements, to better align the PBS population with the key trial population:

- patients must have had symptoms of ALS for less than 2 years
- patients must not require assistance for eating or ambulation
- patients must have at least two points on each item of the ALSFRS-R (paragraph 7.4, edaravone Public Summary Document (PSD), November 2023 PBAC meeting).

3.2 The PBAC previously considered that use of the Gold Coast criteria for diagnosis of ALS was reasonable but noted that a broader patient population would be captured, and the impact of this difference on the efficacy of edaravone in the PBS population compared with the trial population was uncertain (paragraph 7.5, edaravone PSD, November 2023 PBAC meeting). In addition, the PBAC considered that given the high treatment burden, and regular assessment by clinicians, discontinuation criteria regarding tracheostomy and respiratory failure were considered sufficient (paragraph 7.6, edaravone PSD, November 2023 PBAC meeting). The PBAC noted that in the clinical trials, the criteria for discontinuing treatment also included other functional decline (including tube feeding, loss of useful speech) and signs of continued respiratory decline (%FVC≤50% and/or PaCO₂ (blood gas) ≥45 mmHg and all-day

Public Summary Document – March 2024 PBAC Meeting

respiratory support), or adverse events. The PBAC acknowledged that this approach to the restriction discontinuation criteria may result in continuing treatment of some patients where efficacy has not been demonstrated. The PBAC considered that uncertainty in the rate of discontinuation and in the cost-effectiveness of continuing treatment for patients with functional or respiratory decline could be addressed through an RSA with subsidisation caps.

3.3 The proposed listing is shown below.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max Qty	Max. qty packs	Max. qty units	No. of Rpts	Available brands
EDARAVONE					
edaravone 30 mg/20 mL injection, 10 x 20 mL ampoules	\$ [REDACTED] (public) \$ [REDACTED] (private)	3	28	0	Radicava
Restriction Summary [new 1] / ToC: [new 2]					
Category / Program: Section 100 – Highly Specialised Drugs Program (Public Hospital, Private Hospital)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
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 Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.					
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.					
Indication: Amyotrophic lateral sclerosis (ALS)					
Treatment Phase: Initial treatment					
Clinical criteria:					
The condition must be/have been diagnosed by a neurologist					
AND					
Clinical criteria:					
Patient must not have had symptoms for more than 2 years prior to commencing therapy with this drug					
AND					
Clinical criteria:					
Patient must have at least 80 per cent of predicted forced vital capacity (FVC) or slow vital capacity (SVC) within the 2 months prior to commencing therapy with this drug					
AND					
Clinical criteria:					
Patient must not require assistance for eating or ambulation					
AND					
Clinical criteria:					
Patient must have at least two points on each individual item of the ALS Functional Rating Scale – Revised (ALSFRRS-R) score prior to commencing therapy with this drug					

Public Summary Document – March 2024 PBAC Meeting

AND
Clinical criteria:
Patient must not have undergone a tracheostomy
AND
Clinical criteria:
Patient must not have experienced respiratory failure
Prescribing Instructions:
The date of diagnosis, the date and results of spirometry (in terms of percent of predicted forced vital capacity or slow vital capacity) must be supplied with the initial authority application.

Additional criteria proposed as per PBAC advice are shaded blue

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max Qty	Max. qty packs	Max. qty units	No. of Rpts	Available brands
EDARAVONE					
edaravone 30 mg/20 mL injection, 10 x 20 mL ampoules	\$ [REDACTED] (Public) \$ [REDACTED] (Private)	2	20	2	Radicava
Restriction Summary [New 3] / ToC: [New 4]					
Category / Program: Section 100- Highly Specialised Drugs Program (Public Hospital, Private Hospital and Community Access)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (Telephone/Electronic)					
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: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.					
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.					
Indication: Amyotrophic lateral sclerosis (ALS)					
Treatment Phase: Continuing treatment					
Clinical criteria:					
Patient must have previously received PBS-subsidised treatment with this drug for this condition					
AND					
Clinical criteria:					
Patient must not have undergone a tracheostomy					
AND					
Clinical criteria:					
Patient must not have experienced respiratory failure					

3.4 The resubmission proposed a lower AEMP for edaravone (reduced from \$ [REDACTED] to \$ [REDACTED] per ampoule).

- 3.5 The resubmission noted that a reduction in price was possible (in part) because it is now proposed that infusions take place in infusion centres (hospital based or dedicated infusion centres, and via private insurance provided home infusions, or in GP clinics) rather than a home-based program funded by the sponsor. The resubmission stated that some private health insurers offer patients assistance with home-based infusions for a range of chemotherapies and other infused medications via third party nursing services providers. The resubmission estimated that these programs would be available to 53.1% of patients (the proportion with hospital cover).
- 3.6 The resubmission noted that the sponsor is working towards providing a 14-syringe pack to reduce wastage during initiation. However, the DPMQ in the proposed listing above was based on a maximum quantity of 28 units, assuming one broken pack and potential wastage of 2 units. The PBAC considered that the 14-syringe pack was preferable but assuming current pack sizes the maximum quantity (packs) for initiation has been revised to 2.8 to account for the broken pack.
- 3.7 The diagnostic tool (ALS Functional Rating Scale – Revised (ALSFRS-R)) in the revised restrictions is a document incorporated by reference (DIBR). As such, an explanatory statement will need to be added to describe the ALSFRS-R and how it may be freely accessed. The pre-PBAC response noted that the ALSFRS-R questionnaire is routinely administered to patients with ALS by neurologists at every clinic visit, typically 3 monthly. It is not proprietary and can be accessed online, being reproduced on multiple medical websites (e.g. <https://www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r>). There are also websites that allow the neurologist to input a patient's ratings to obtain a printable or digital copy of their score (<https://neurotoolkit.com/alsfrs-r/>). An ALSFRS-R calculator is available via the MiNDAUS ALS registry https://www.mindaus.org/wp-content/uploads/2023/09/22094546/DataDictionaryPROMMindausHansenJuly2023_V01.1.pdf.
- 3.8 Currently Community Access on the Highly Specialised Drugs (HSD) program allows authorised community-based practitioners to prescribe treatments for hepatitis B, HIV/AIDS, opioid dependence and schizophrenia (continuing treatment only), plus lanreotide and octreotide (continuing treatment only), without the need to be affiliated with a hospital. For prescribers to be able to prescribe Community Access medicines for the treatment of hepatitis B, hepatitis C, HIV/AIDS and schizophrenia, prescribers are required to be accredited which usually requires a state-based training and accreditation program. This is not required for lanreotide and octreotide, noting these are listed as Community Access for continued treatment only. The pre-PBAC response noted that MND patients are managed within multidisciplinary teams, ensuring that neurologists are always part of the decision-making process. The PBAC considered it would be appropriate for HSD Community Access arrangements to apply to edaravone for treatment of ALS for continuing treatment, without requiring additional accreditation for prescribers. The PBAC considered it would be appropriate for edaravone to be administered by infusion nurses (under instruction from a

neurologist). The PBAC considered nurse prescribing for continuing treatment would not be appropriate.

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 In addition to the comments already received for the November 2023 consideration of edaravone, the PBAC noted and welcomed the input from individuals (54), health care professionals (2) and an organisation via the Consumer Comments facility of the PBS website.
- 4.3 Motor Neurone Disease Australia noted that edaravone has been shown to be clinically effective and safe and has been approved for use in motor neurone disease (MND) in several other countries including the United States, Canada and Japan. The comments noted that subsequent real-world data analysis has shown a material improvement in overall survival with edaravone, as has a systematic review and meta-analysis. The organisation pointed to the use of edaravone by Australian patients, through a Special Access Scheme, who have experienced minimal side effects and reported of improvements in their disease. The comments noted the flexibility to receive edaravone with riluzole, or without it in those patients unsuitable for riluzole.
- 4.4 Two health care professionals noted the current lack of effective treatment options for ALS and emphasised the importance of slowing disease progression with edaravone at an early stage of the disease. The health care professionals noted the effect of ALS on patients and families, stating that edaravone allowed patients to remain well for longer rather than living with advanced disability.
- 4.5 The comments from individuals to support edaravone listing were received from ALS patients (both current/potential edaravone patients) and family members/carers. In addition to the comments provided by health care professionals, individual comments focused on the hope that edaravone will slow ALS disease progression and reduce symptoms. Individuals particularly commented on quality-of-life issues associated with ALS, such as pain, loss of mobility, loss of independence, inability to talk, and difficulty breathing. The comments portrayed the devastating nature of the disease and the urgent need for treatment options.

Clinical evidence

- 4.6 The resubmission presented additional clinical data relevant to the revised model inputs (discontinuation rate and long-term effect on survival).

Treatment duration

- 4.7 In the economic model a discontinuation rate of 30% per three 28-day cycles is applied, resulting in a median edaravone treatment duration of 9.0 months (7.2 months mean duration). The resubmission presented a search for long-term edaravone studies reporting treatment duration to help inform the likely duration of use in practice.
- 4.8 The median edaravone treatment duration for most studies identified ranged from 8.6 to 11.8 months. The mean treatment duration tended to be shorter (6.5 to 8.7 months) with the exception of one small study in Japan (Houzen et al 2021, n=22, mean 26.6 months). The resubmission argued that the assumption of approximately 9.0 cycles median treatment (7.2 months mean duration) in the economic model is therefore likely reasonable.

Long term survival

- 4.9 The PBAC previously considered that, overall, edaravone was superior to placebo in slowing the rate of decline in terms of motor impairment and functional deterioration, however the level of long-term benefit and effect on survival is uncertain (paragraph 7.10 edaravone PSD, November 2023 PBAC Meeting). The resubmission noted that as patients enrolled in the pivotal studies (Study 19 and Study 16) were newly diagnosed with good function, and the studies were not powered to detect a difference in survival, real-world evidence was required to assess relative survival in the modelled evaluation.
- 4.10 The resubmission presented results of a meta-analysis of long-term use of edaravone (Nourelden 2023). This meta-analysis included 11 studies, including randomised controlled trials and observational studies, with 5 of these studies contributing to long term survival outcomes with outcomes reported at timepoints from 6 to 30 months (Brooks 2022, Houzen 2021, Lunetta 2020, Okada 2018, Witzel 2022).
- 4.11 The overall risk ratio (RR) reported in Nourelden (2023) was 1.11 (95% CI 1.05, 1.18) for edaravone vs. control across all timepoints. Edaravone was associated with significantly improved survival outcomes compared with control at each timepoint:
- 18 months: RR 1.13¹ (1.02, 1.24); p=0.02
 - 24 months: RR 1.22 (1.06, 1.41); p=0.007
 - 30 months: RR 1.17 (1.01, 1.34); p=0.03
- 4.12 Two of the studies (Brooks 2022 and Witzel 2022) both used propensity-matching of key characteristics (including age, riluzole use, disease duration and site of onset),

¹ This value was reported as 1.03 in the abstract of the publication but 1.13 in the body of the publication. The correct value appears to be 1.13 based on Figure 3.

resulting in balance across the groups of these key prognostic variables. Three of the included studies (Houzen 2021, Lunetta 2020 and Okada 2018) did not use matching techniques to select the control group and Houzen 2021 and Okada 2018 had more favourable outcomes for edaravone compared with the matched studies. Overall, the resubmission concluded that the meta-analysis supported the inclusion of a mortality benefit in the edaravone modelled evaluation.

Economic analysis

- 4.13 The base case incremental cost-effectiveness ratio (ICER) for the revised model was \$95,000 to < \$115,000 per QALY. The PBAC previously considered that in the context of the high clinical need an ICER of up to \$95,000 to < \$115,000 per QALY gained would be considered acceptable (paragraph 7.15, edaravone PSD, November 2023 PBAC meeting).
- 4.14 In the base case model presented, the resubmission removed the mortality calibration as requested by the PBAC. The removal of the mortality calibration reduced the discounted incremental QALY gain from 0.76 QALYs to 0.34 QALYs. The base case economic evaluation included an overall survival benefit of 0.52 years (undiscounted) over a 10-year time horizon. The resubmission also provided a sensitivity analysis using a calibration factor of 0.925 (compared with 0.67 in the November 2023 submission). The resubmission noted that this value (0.925) was chosen to result in a mean survival benefit of 0.67 year, which is the estimate of mean survival benefit from Brooks 2022 using the best fitting extrapolation function for each arm. Application of the mortality calibration in the resubmission's sensitivity analysis increased the survival benefit to 0.62 years (undiscounted), resulting in a reduction of the ICER to \$95,000 to < \$115,000 per QALY.
- 4.15 For the base case the submission did not reduce the discontinuation rate applied in the model from 30% to 15% per model cycle in King's stage 1-3, as requested by the PBAC. The resubmission's justification for retaining the higher discontinuation rate was the change from sponsor-funded home-based administration to infusion centres (hospital based or dedicated infusion centres, or in GP clinics) or via private insurance provided home infusions for some patients. The resubmission argued that this change will result in higher rates of discontinuation, due to the requirement for some patients to travel for ongoing administration of treatment. Due to the time and effort required for patients to receive treatment, at a time of increasing functional limitations, the resubmission considered that a discontinuation rate of 30% every 3 months was conservative. The ICER increased to \$155,000 to < \$255,000 per QALY in the sensitivity analysis using a 15% per cycle discontinuation rate.
- 4.16 In addition to the changes requested by PBAC (paragraphs 4.13 and 4.15) the sponsor updated PBS and MBS costs in the model to reflect December 2023 prices. The resubmission also added a cost of \$27.11 per infusion (a cost of \$57.80 (MBS item code 14221) applied to 46.9% of patients) to reflect the withdrawal of sponsor-funded

home-based administration. This value was not consistent with the additional cost of infusions included in the financial estimates, see also paragraph 4.26.

- 4.17 For the base case to reach an ICER of \$95,000 to < \$115,000 per QALY a [REDACTED] % reduction in price from \$[REDACTED] mean cost per infusion to \$[REDACTED] per infusion would be required.
- 4.18 For the sensitivity analysis applying a discontinuation rate of 15% every 3 months to reach an ICER of \$95,000 to < \$115,000 per QALY a [REDACTED] % reduction in price from \$[REDACTED] to \$[REDACTED] per infusion would be required.
- 4.19 The resubmission also presented a range of alternative sensitivity analyses. The ICER ranged from \$95,000 to < \$115,000 per QALY to \$155,000 to < \$255,00 per QALY for these sensitivity analyses.

Cost/patient/course

- 4.20 The resubmission stated that the estimated drug cost/patient per course would be \$[REDACTED], based on a treatment duration of 8.6 cycles and AEMP price of \$[REDACTED] per ampoule (see Table 3). The estimated drug cost/patient per course in the November 2023 submission was \$[REDACTED], based on a treatment duration of 7.8 cycles and \$[REDACTED] AEMP per ampoule. The average cost per infusion used in the economic model (\$[REDACTED]) was based on the calculations in Table 3. The treatment duration of 8.6 cycles used in the resubmission appears to be based on the median duration of treatment in Brooks et al 2022 (8.6 months), however the mean treatment duration is likely to be shorter. The total cost per patient may be overestimated if mean treatment duration is less than 8.6 months. The PBAC noted that the calculations in Table 3 may underestimate the average cost per infusion if the number of cycles of continuation is overestimated as the relative price of initiation is higher due to the additional initiation doses required.

Table 3: DPMQ and average cost per infusion as presented in the resubmission

Use	Value	Initiation		Continuation	
		Private	Public	Private	Public
Section 4 financials	Ex-man. price (AEMP) per ampoule	\$[REDACTED]			
	Max Qty	28		20	
	Max Qty AEMP	\$[REDACTED]		\$[REDACTED]	
	DPMQ price	\$[REDACTED]	\$[REDACTED]	\$[REDACTED]	\$[REDACTED]
	Assumed Weighting	50%	50%	50%	50%
	Weighted Avg DPMQ	\$[REDACTED]		\$[REDACTED]	
Section 3 modelling	Infusions	14		10	
	Cycles	1		7.6	
	Total Infusions	90			
	Total cost per patient	\$[REDACTED]			
	Average cost per Infusion (DPMQ)	\$[REDACTED]			

Source: Table 3-1 pf the resubmission

- 4.21 The median duration of treatment in the economic model (assuming 30% per cycle discontinuation) was 9.0 months, whereas the mean duration of treatment in the model was 7.2 months (7.8 28-day treatment cycles). The total undiscounted

edaravone cost per patient in the base case economic model was \$¹. As shown in Table 4 this was inconsistent with the treatment duration applied in the financial estimates (9.4 28-day treatment cycles) and the cost per patient in the financial estimates was therefore substantially higher than the in the economic model. The PBAC considered that the inconsistency between the duration in the economic model and financial estimates was not appropriate and considered the financial estimates should be aligned to the duration in the economic model.

Table 4: Drug cost per patient for edaravone

	Edaravone Trial dose and duration	Edaravone Model	Edaravone Financial estimates
Mean dose	60mg/day	60mg/day	60mg/day
Mean duration	10.2 treatment cycles (76% of patients received 12/12 cycles during the 48- week trial period)	7.2 months (7.8 treatment cycles)	8.6 months (9.4 treatment cycles)
Cost/patient/course	-	\$ ^a	\$ ^b

^a Undiscounted total costs for edaravone (Edaravone – Radicava – TEVA- Section 3 – Economic Model – March 2024 (Final), “Markov edaravone” worksheet, cell BM3)

^b Net cost of edaravone divided by total initiating patients (Edaravone – Radicava – TEVA – Section 4 – Base Case – March 2024 (Final) “3b. Impact – proposed (pub)”).

Estimated PBS usage & financial implications

- 4.22 The PBAC previously considered that there was a high level of uncertainty regarding the estimates of incidence and prevalence and potential double-counting of patients in the year 1 estimates in the November 2023 submission (paragraph 7.16, edaravone PSD, November 2023 PBAC meeting). The PBAC noted that the riluzole patient numbers provided by the DUSC Secretariat reflect the actual number of patients treated with riluzole in Australia (1,200-1,400 per year) and considered this was a more reliable estimate of ALS patient numbers than the submission’s estimates. The resubmission’s estimates assumed 500 to < 5,000 ALS incident patients per year, with an annual growth rate of 2.05%. The submission stated that the growth rate was based on advice from Motor Neurone Disease Australia that the prevalence of MND is anticipated to increase globally, with a 69% increase forecast in the next 25 years. The estimate of 500 to < 5,000 patients per year (based on riluzole utilisation) includes both incident and prevalent patients, therefore applying this value in each year may overestimate the number of incident patients. However, the PBAC noted that the mean treatment duration for riluzole was less than 12 months, therefore the patient numbers would approximate the total population in each year.
- 4.23 The PBAC also considered that with the narrower restriction criteria (as per the trial criteria and revised proposed restrictions), there is likely to be few eligible prevalent patients (paragraph 7.16, edaravone PSD, November 2023 PBAC meeting). The PBAC considered that it would be reasonable to include a small number of additional prevalent patients in year 1, the PBAC considered this would be no more than 17.5% of patients treated with riluzole from the year prior to listing (approximately 210-245 patients) (paragraph 6.68, edaravone PSD, November 2023 PBAC meeting). The

resubmission retained the prevalent patient pool, assuming 500 to < 5,000 prevalent patients from the prior year, with an uptake rate of 1%, resulting in < 500 eligible prevalent patients in year 1 of the estimates. It may not be reasonable to assume that prevalent patients, who would have been diagnosed up to 2 years prior, would receive the same duration of treatment as newly diagnosed patients. The prevalent patient population would also include any grandfathered patients. The PBAC considered that prevalent patients (including grandfather patients) should be assumed to receive at most, half the treatment duration of incident patients as these patients would be less recently diagnosed.

- 4.24 The PBAC previously noted that around 35% of patients enrolled in Study 16 fit the dpEESP2y criteria. The PBAC considered that the proportion of patients meeting the revised PBS eligibility criteria is likely to be no more than 35% of incident patients (< 500 of < 500 patients in year 1 based on the incidence in Vucic 2020, or up to < 500-< 500 patients based on riluzole patient numbers) (paragraph 7.16, edaravone PSD, November 2023 PBAC meeting). For the resubmission the 35% eligibility rate is applied in the forward estimates for the incident population representing < 500 patients in the first forward year.
- 4.25 The resubmission noted that the median number of cycles was based on the Brooks 2022 analysis showing patients received 8.6 cycles (median). The resubmission stated that it had applied a 70% continuation rate (consistent with the economic model) at the end of the first 28-day cycle of edaravone in the financial estimates, whereas it is applied at the end of the first 3-month model cycle in the economic model. The financial estimates applied a 70% continuation rate to incident and prevalent patient numbers electing continuing treatment on worksheets “2a. patients - incident” and “2b. patients - prevalent” (rather than per 3-month treatment cycle in the model). The estimates assumed 1 initiating script and 12 continuing scripts (see worksheet “3.a Scripts - proposed”). This resulted in an average of 9.4 28-day cycles per initiating patient. In the November 2023 submission financial estimates, the time on edaravone was assumed to be 7.8 treatment cycles, based on the median time on treatment of 8.6 months in Brooks 2022, with a 15% discontinuation rate after the first treatment cycle. The reason for this change was unclear and it is inconsistent with the claim that fewer patients will continue treatment due to the removal of the sponsor-funded home-based administration program. The pre-PBAC response noted the number of modelled edaravone treatment cycles can be adjusted in the forward estimates to better reflect the 7.8 mean cycles of the economic modelling, resulting in a 7.1% reduction in the net cost to Government for the proposed listing. The PBAC considered that it would be appropriate to adjust the financial estimates such that the duration of treatment reflects the mean treatment duration in the economic model of 7.8 cycles (7.2 months). The PBAC noted that this decreased the financial estimates by approximately 22%.
- 4.26 The resubmission provided updated estimates of the MBS costs associated with installing and removing a porta catheter and added MBS costs for infusions. The cost

to the MBS increased substantially in the resubmission estimates from less than \$0 to < \$10 million per year to more than \$0 to < \$10 million in each year (see Table 5). The cost per patient increased from \$| per initiating patient to \$| per initiating patient. This cost was inconsistent with the administration costs included in the economic model (\$| per patient) as the economic model only applied infusion costs to 46.9% of patients, see paragraph 4.16). The PBAC considered that these costs should be adjusted to be consistent with the economic model as proposed in the pre-PBAC response. The PBAC noted that after adjusting the treatment duration and administration costs, the net cost to the MBS was reduced by 62%.

- 4.27 The PBAC previously noted DUSC considered that the uptake rates applied in the submission are likely to have been underestimated, given the level of patient and clinician awareness of edaravone and the lack of new alternative treatments (paragraph 7.16, edaravone PSD, November 2023 PBAC meeting). The resubmission increased the uptake rates from |% to |% in year 1, rising to |% by year 3 (|% in the November 2023 submission). The substantial increase in uptake rates resulted in increased patient and script numbers compared with the November 2023 submission. The PBAC considered the proposed increases to uptake rates in the resubmission were not reasonable and considered that they should be reduced as shown in Table 6. The PBAC noted that uptake rates in Table 6 for years 1-4 were higher than those in the November 2023 submission (consistent with DUSC advice), but the revised estimated number of patients treated with edaravone, and scripts of edaravone, were similar to the November 2023 submission estimates.
- 4.28 The resubmission estimated a net cost to the PBS of \$20 million to < \$30 million in Year 6 of listing, with a total net cost to the PBS of \$100 million to < \$200 million over the first 6 years of listing. With revised duration of treatment (to align with the economic evaluation), reduced duration in the prevalent population, and reduced uptake estimates, the net cost to the PBS/RPBS was \$10 million to < \$20 million in Year 6 of listing, with a total net cost to the PBS/RPBS of \$70 million to < \$80 million over the first 6 years of listing.

Public Summary Document – March 2024 PBAC Meeting

Table 5: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Incident population						
Estimated incident ALS population (riluzole treated)	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Proportion of patients eligible	35%	35%	35%	35%	35%	35%
Total incident patients eligible	█ ²	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Patients electing treatment	80%	90%	95%	95%	95%	95%
Total incident patients initiate edaravone	█ ²	█ ²	█ ²	█ ²	█ ¹	█ ¹
Total incident patients continue edaravone ^a	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Prevalent population						
Prevalent ALS population (incident patients from previous year)	█ ¹					
Proportion of patients eligible	█ ⁶					
Total prevalent patients eligible	█ ²					
Patients electing treatment	80%					
Total prevalent patients initiate with edaravone	█ ²					
Total prevalent patients continue with edaravone	█ ²					
Total patients initiate edaravone	█ ¹	█ ²	█ ²	█ ²	█ ¹	█ ¹
Number of scripts dispensed ^b	█ ³	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Estimated financial implications						
Cost to PBS/RPBS edaravone	█ ⁴	█ ⁵	█ ⁴	█ ⁴	█ ⁴	█ ⁴
Cost to PBS/RPBS additional riluzole	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶
Net cost to PBS/RPBS	█ ⁴	█ ⁵	█ ⁴	█ ⁴	█ ⁴	█ ⁴
Cost to MBS for administration	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶
Net cost to PBS/RPBS/MBS	█ ⁴	█ ⁴	█ ⁴	█ ⁴	█ ⁴	█ ⁴
Previous submission November 2023						
Patients electing treatment	30%	50%	60%	70%	80%	80%
Total patients	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Total scripts	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Net cost to PBS/RPBS edaravone	█ ⁵	█ ⁵	█ ⁵	█ ⁵	█ ⁴	█ ⁴
Net cost to PBS/RPBS	█ ⁵	█ ⁵	█ ⁵	█ ⁴	█ ⁴	█ ⁴
Net cost to MBS for administration	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶
Net cost to PBS/RPBS/MBS	█ ⁵	█ ⁵	█ ⁵	█ ⁴	█ ⁴	█ ⁴

ALS = amyotrophic lateral sclerosis

^a revised estimates assume 100% of patients continue treatment, with duration of treatment set on worksheet "3a. Scripts-proposed"

^b assumes 9.4 months treatment for incident and prevalent patients.

Source: Table 4-2 of the resubmission

Cells in blue are values from the previous submission.

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² < 500

³ 5,000 to < 10,000

⁴ \$20 million to < \$30 million

⁵ \$10 million to < \$20 million

⁶ \$0 to < \$10 million

Public Summary Document – March 2024 PBAC Meeting

Table 6: Estimated use and financial implications – PBAC revised values

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Incident population						
Estimated incident ALS population (riluzole treated)	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Proportion of patients eligible	35%	35%	35%	35%	35%	35%
Total incident patients eligible	█ ²	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Patients electing treatment	50%	60%	70%	75%	80%	80%
Total incident patients initiate edaravone	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Total incident patients continue edaravone ^a	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Prevalent population						
Prevalent ALS population (incident patients from previous year)	█ ¹					
Proportion of patients eligible	█ ² %					
Total prevalent patients eligible	█ ²					
Patients electing treatment	40%					
Total prevalent patients initiate with edaravone ^a	█ ²					
Total prevalent patients continue with edaravone	█ ²					
Total patients initiate edaravone	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Number of scripts dispensed^b	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Estimated financial implications						
Revised cost to PBS/RPBS for edaravone	█ ³	█ ⁴	█ ⁴	█ ⁴	█ ⁴	█ ⁴
Revised net cost to PBS/RPBS	█ ⁴	█ ⁴	█ ⁴	█ ⁴	█ ⁴	█ ⁴
Revised cost to MBS for administration	█ ³	█ ³	█ ³	█ ³	█ ³	█ ³
Revised Net cost to PBS/RPBS/MBS	█ ⁴	█ ⁴	█ ⁴	█ ⁴	█ ⁴	█ ⁴

ALS = amyotrophic lateral sclerosis

^a revised estimates assume 100% of patients continue treatment, with duration of treatment set on worksheet “3a. Scripts-proposed”

^b assumes 7.2 months treatment for incident patients and 3.6 months treatment for prevalent patients.

Source: Table 4-2 of the resubmission, calculated based on corrected Section 4 worksheet.

Cells in green are revised values reflecting PBAC advice.

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² < 500

³ \$0 to < \$10 million

⁴ \$10 million to < \$20 million

Financial Management - Risk Sharing Arrangements

4.29 The PBAC specified that the resubmission should include proposal of a risk sharing arrangement (RSA) (paragraph 7.18, edaravone PSD, November 2023 Meeting). The resubmission noted this request but did not propose an RSA. The resubmission considered that the wording of the restriction clearly articulates the eligible patient

population and therefore that there is unlikely to be significant residual financial risk in the forward estimates.

- 4.30 The PBAC noted that the economic model in the resubmission relied on a discontinuation rate of 30% every 3 months to maintain an ICER of approximately \$95,000 to < \$115,000 per QALY. In addition, the PBAC noted that the approach to the discontinuation criteria may result in continuing treatment of some patients where efficacy has not been demonstrated (see paragraph 3.2). The PBAC considered that uncertainty in the rate of discontinuation and in the resulting cost-effectiveness of edaravone should be addressed through an RSA with subsidisation caps and 10% rebate for expenditure above the caps. The PBAC considered the revised costs in Table 5 would be a reasonable basis for the RSA subsidisation caps.

5 PBAC Outcome

- 5.1 The PBAC recommended the listing of edaravone, for treatment of amyotrophic lateral sclerosis (ALS) in patients who are independent in activities of daily living and where treatment is initiated within two years of disease onset, on the basis that it should be available only under special arrangements under Section 100. The PBAC recommended Community Access on the HSD program for continuing treatment only. The PBAC acknowledged the high clinical need for effective treatments for amyotrophic lateral sclerosis (ALS). The PBAC recalled that in November 2023 it did not recommend edaravone for this indication, noting that edaravone was not cost-effective at the price proposed in the submission and that the economic model included a number of optimistic assumptions that were likely to underestimate the incremental cost-effectiveness ratio. The PBAC considered that the majority of the outstanding issues were satisfactorily resolved in the resubmission, including changes to the restriction, economic model and financial estimates and advised that edaravone would be acceptably cost-effective at the price proposed in the resubmission. The PBAC noted that the submission did not reduce the discontinuation rate in the economic model as requested but considered that the remaining uncertainty regarding the treatment duration and the potential for ongoing use in a broader population than in the trial could be addressed via an RSA with subsidisation caps.
- 5.2 The PBAC was satisfied that edaravone provides, for some patients, a significant improvement in efficacy over standard of care.
- 5.3 The PBAC acknowledged the high clinical need for effective treatments for ALS, the most common phenotype of motor neuron disease (MND). The PBAC acknowledged the devastating nature of ALS and the lack of treatment options. The PBAC noted that consumers remained supportive of making edaravone accessible to patients in Australia based on its demonstrated clinical benefit, potential for survival benefit and minimal safety concerns.
- 5.4 The PBAC noted that the resubmission had revised the requested listing to better reflect the trial population, for whom there is evidence of clinical benefit. The PBAC

previously considered that use of the Gold Coast criteria for diagnosis of ALS was reasonable but noted that a broader patient population would be captured, and the impact of this difference on the efficacy of edaravone in the PBS population compared with the trial population was uncertain. In addition, the PBAC noted that in the clinical trials, the criteria for discontinuing treatment also included other functional decline and signs of continued respiratory decline or adverse events. The PBAC remained of the view that given the high treatment burden, and regular assessment by clinicians, discontinuation criteria regarding tracheostomy and respiratory failure were considered sufficient. However, the PBAC acknowledged that this approach to the discontinuation criteria may result in continuing treatment of some patients where efficacy has not been demonstrated.

- 5.5 The PBAC noted from the pre-PBAC response that the sponsor is working towards the provision of a 14-vial pack size to reduce potential wastage during the initiation phase (which requires 14 consecutive daily doses, requiring 28 vials). The PBAC considered the preferred initiation phase listing would be the new pack size (14 ampoules), however, if the new pack size wasn't available at the time of listing, edaravone would be listed with the pack size of 10. As the maximum quantity (units) PBS-subsidised is 28 ampoules, the maximum quantity (packs) would be 2.8, with possible broken pack fees.
- 5.6 The PBAC noted that the submission presented additional clinical data relevant to the revised model inputs (discontinuation rate and long-term effect on survival). The PBAC noted that there was substantial variability in the treatment duration in the studies identified. The PBAC noted that persistence with treatment is likely to depend on various factors that may be specific to local treatment practices. Overall, the PBAC considered that the treatment duration for the PBS population remains uncertain. The PBAC considered that the meta-analysis of long-term use of edaravone in 11 randomised controlled trials and observational studies, together with the evidence presented in the November 2023 submission, supported a survival gain for patients treated with edaravone, though the magnitude of benefit was uncertain as the observational studies had a high risk of bias.
- 5.7 The PBAC noted that the base case model presented in resubmission removed the mortality calibration as requested by the PBAC, resulting in a reduced overall survival benefit of 0.52 years (undiscounted) over a 10-year time horizon. The resubmission also provided a sensitivity analysis using a reduced calibration factor of 0.925 to result in a mean survival benefit of 0.67 years (the estimate of mean survival benefit from Brooks 2022 using the best fitting extrapolation function for each arm). The PBAC noted this sensitivity analysis increased the survival benefit to 0.62 years (undiscounted), resulting in a reduction of the incremental cost effectiveness ratio (ICER) to \$95,000 to < \$115,000 per QALY.
- 5.8 The PBAC noted that the base case economic model did not reduce the discontinuation rate from 30% to 15% per model cycle in King's stage 1-3, as requested by the PBAC. The resubmission's justification for retaining the higher discontinuation

rate was the change from sponsor-funded home-based administration to infusion centres (hospital based or dedicated infusion centres, or in GP clinics) or via private insurance provided home infusions for some patients. The PBAC considered that this change to administration may have an impact on treatment compliance and rates of continuation, however considered that the discontinuation rate in the model may still be overestimated based on the low rate of discontinuation observed in Study 19 and because the proposed PBS restriction specifies few stopping criteria. The PBAC considered that in practice, patients are likely to want to continue treatment for as long as they feel it is slowing progression. The PBAC noted that the ICER increased to \$155,000 to < \$255,000 per QALY in the sensitivity analysis using a 15% per cycle discontinuation rate. The PBAC considered that the rate of treatment discontinuation was uncertain but the risk of it being lower than assumed in the model could be addressed through the RSA as outlined in paragraph 5.13.

- 5.9 The PBAC noted that the resubmission proposed a [REDACTED] % lower AEMP for edaravone compared with the previous submission (reduced from \$| to \$| per ampoule). This resulted in an ICER of \$95,000 to < \$115,000 per QALY for the base case revised model. The PBAC previously considered that in the context of the high clinical need an ICER of up to \$95,000 to < \$115,000 per QALY gained would be considered acceptable (paragraph 7.15, edaravone PSD, November 2023 PBAC meeting). Noting a plausible estimate of the ICER was between \$95,000 to < \$115,000 and \$95,000 to < \$115,000 per QALY, depending on the survival assumptions, the PBAC considered that edaravone would be acceptably cost-effective at the price proposed in the resubmission.
- 5.10 The PBAC noted that the financial estimates in the resubmission had revised the patient numbers as requested. The PBAC noted that the uptake rates were substantially increased in the resubmission, based on DUSC advice that uptake was underestimated in the November 2023 submission. The PBAC considered that the extent of the proposed increase to the uptake rates in the resubmission was not justified and that, overall, the number of patients treated would not be expected to be substantially higher than that estimated in the November 2023 submission as the proposed patient population was narrower in the resubmission. The PBAC considered that uptake rates for years 1-4 should be higher than proposed in the November 2023 submission but reduced from those proposed in the resubmission (see Table 6).
- 5.11 The PBAC noted that there were errors in the financial estimates worksheet in application of the treatment duration. The PBAC considered that it would be appropriate to adjust the financial estimates such that the mean duration of treatment is the same as in the economic model (7.8 cycles; 7.2 months). The PBAC noted that when the errors were corrected and the mean treatment duration of 7.2 months applied for incident patients, the cost to the PBS/RPBS decreased by approximately 22%. The PBAC also considered that prevalent patients should be assumed to receive at most, half the treatment duration of incident patients as these patients would be less recently diagnosed.

Public Summary Document – March 2024 PBAC Meeting

- 5.12 The PBAC noted that with the revisions as per paragraphs 5.10-5.11 to uptake and treatment duration, the estimated number of patients treated with edaravone in each year, and scripts of edaravone, were similar to the November 2023 submission estimates, and the PBAC considered the revised estimates were reasonable. The PBAC considered that costs for administration should be adjusted to apply to only 46.9% of patients (where administration costs are not funded via private insurance home infusion programs).
- 5.13 The PBAC considered that there was remaining uncertainty in the cost-effectiveness of treating a potentially broader population than included in the trials and treatment continuing in patients with functional or continuing respiratory decline. In addition, there was uncertainty in the treatment duration applied in the economic model, and a discontinuation rate of 30% every 3 months was required to maintain an ICER of approximately \$95,000 to < \$115,000 per QALY (paragraph 5.8). The PBAC considered that the uncertainty in the discontinuation rate and treatment of a potentially broader population than in the trials, and in the resulting cost-effectiveness of edaravone, should be addressed through an RSA with subsidisation caps with a 1% rebate for expenditure above the caps. The PBAC considered the revised costs in Table 6, which reflect the changes as described in paragraphs 5.10-5.11, would be a reasonable basis for the RSA subsidisation caps.
- 5.14 The PBAC recommended that edaravone should not be treated as interchangeable with any other drugs.
- 5.15 The PBAC advised that edaravone is not suitable for prescribing by nurse practitioners.
- 5.16 The PBAC recommended that the Early Supply Rule should apply.
- 5.17 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for edaravone:
- a) The magnitude of the overall survival benefit, if any, is uncertain and therefore the treatment does not meet the criteria of providing a substantial and clinically relevant improvement in efficacy over standard of care;
 - b) The treatment is expected to address a high and urgent unmet clinical need;
 - c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.
- 5.18 The PBAC noted that this submission is not eligible for an Independent Review as it is a positive recommendation.

Outcome:

Recommended

6 Recommended listing

Add new item:

MEDICINAL PRODUCT medicinal product pack	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Edaravone 30 mg/20 mL injection, 10 x 20 mL ampoules	2.8	28	0	Radicava
Restriction Summary [new 1] / ToC: [new 2]				
Category / Program: Section 100 – Highly Specialised Drugs Program (Public Hospital, Private Hospital)				
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
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.				
Indication: Amyotrophic lateral sclerosis (ALS)				
Treatment Phase: Initial treatment				
Clinical criteria:				
The condition must be/have been diagnosed by a neurologist				
AND				
Clinical criteria:				
Patient must not have had symptoms for more than 2 years prior to commencing therapy with this drug				
AND				
Clinical criteria:				
Patient must have at least 80 per cent of predicted forced vital capacity (FVC) or slow vital capacity (SVC) within the 2 months prior to commencing therapy with this drug				
AND				
Clinical criteria:				
Patient must not require assistance with eating or ambulation				
AND				
Clinical criteria:				
Patient must have at least two points on each individual item of the ALS Functional Rating Scale – Revised (ALSFRRS-R) score prior to commencing therapy with this drug				
AND				
Clinical criteria:				
Patient must not have undergone a tracheostomy				
AND				
Clinical criteria:				
Patient must not have experienced respiratory failure				
Prescribing Instructions:				
The date of diagnosis, the date and results of spirometry (in terms of percent of predicted forced vital capacity or slow vital capacity) must be supplied with the initial authority application.				
Prescribing Instructions:				
The ALSFRS-R can be accessed online: www.mdcalc.com/calc/10166/revised-amyotrophic-lateral-sclerosis-functional-rating-scale-alsfrs-r or https://neurotoolkit.com/alsfrs-r/ .				

Public Summary Document – March 2024 PBAC Meeting

Additional criteria proposed as per PBAC advice are shaded blue

MEDICINAL PRODUCT medicinal product pack	Max. qty packs	Max. qty units	No. of Rpts	Available brands
EDARAVONE				
edaravone 30 mg/20 mL injection, 10 x 20 mL ampoules	2	20	2	Radicava
Restriction Summary [New 3] / ToC: [New 4]				
Category / Program: Section 100- Highly Specialised Drugs Program (Community Access)				
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
Restriction type: <input checked="" type="checkbox"/> Authority Required (Telephone/Electronic)				
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.				
Indication: Amyotrophic lateral sclerosis (ALS)				
Treatment Phase: Continuing treatment				
Clinical criteria:				
Patient must have previously received PBS-subsidised treatment with this drug for this condition				
AND				
Clinical criteria:				
Patient must not have undergone a tracheostomy				
AND				
Clinical criteria:				
Patient must not have experienced respiratory failure				

This restriction 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

Teva Pharma is committed to working across the Department of Health to bring Radicava to Australian patients with ALS in the most rapid manner possible.