

**6.02 ERIBULIN,  
1 mg/2 mL (as mesilate) injection, 1 x 2 mL vial,  
Halaven<sup>®</sup>,  
Eisai Australia Pty Ltd.**

**1 Purpose of Application**

1.1 The submission requested a Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital), Authority Required (STREAMLINED) listing for the treatment of advanced or metastatic liposarcoma who have failed prior chemotherapy, including an anthracycline.

**2 Requested listing**

2.1 The requested restriction is provided below. Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Amt	Nº. of Rpts	Dispensed Price for Max. Amount (published)	Proprietary Manufacturer	Name and Manufacturer
ERIBULIN 1 mg/2 mL (as mesilate) injection, 1 x 3 mg 2 mL vial		13	Public: \$ [REDACTED] Private: \$ [REDACTED]	Halaven <sup>®</sup>	Eisai Australia Pty Ltd

<b>Category / Program</b>	Section 100 – Efficient funding of Chemotherapy
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Severity:</b>	<i>Advanced (unresectable and/or metastatic)</i> <del>Advanced, defined as locally recurrent, locally advanced or metastatic</del>
<b>Condition:</b>	<del>Soft tissue sarcoma (STS)-Liposarcoma</del>
<b>PBS Indication:</b>	<i>Advanced (unresectable and/or metastatic) liposarcoma</i>
<b>Treatment phase:</b>	<del>initial</del>
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Must be treated by an oncologist.

<b>Clinical criteria:</b>	<p>Patient must have a WHO ECOG performance status of 2 or less,</p> <p>AND</p> <p>Patient must have received prior chemotherapy treatment including an anthracycline with doxorubicin and ifosfamide (unless contraindicated),</p> <p>AND</p> <p>The treatment must be the sole PBS-subsidised therapy for this condition.</p>
<b>Prescriber instructions</b>	<p><i>Patient must have not any of the following disease subtypes: Well-differentiated liposarcoma</i></p>
<b>Population criteria:</b>	<p>Patient must be aged 18 years or older.</p>
<b>Administrative Advice</b>	<p><i>No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.</i></p>

- 2.2 The requested PBS listing was for patients with unresectable or metastatic liposarcoma who have received prior chemotherapy.
- 2.3 The submission requested PBS listing of eribulin for second-line treatment of advanced or metastatic liposarcoma, while the clinical evidence was in the third- and further line setting. The submission argued that there was a substantial clinical need, and a precedent was set with the PBAC recommendation of pazopanib for second-line treatment in patients with soft tissue sarcoma (July 2013 PBAC meeting). The assumption that pazopanib provided a precedent was inappropriate. The key clinical data for pazopanib included patients who had failed at least one prior therapy or were contraindicated for an anthracycline ( $\leq 44\%$ ), while less than 1% of the patients in the key eribulin trial had received only one prior therapy. The submission also argued that for patients who would require doxorubicin plus ifosfamide as first-line treatment, a clinician might delay ifosfamide treatment to meet the eligibility criteria for eribulin treatment, if eribulin was only listed as a third-line treatment.
- 2.4 The submission sought listing on the basis of a cost-effectiveness analysis of eribulin compared to dacarbazine. Dacarbazine is not PBS-subsidised and therefore the cost-effectiveness of dacarbazine has not been established in the context of the Australian health care setting. The ESC noted that dacarbazine was widely available via hospital formularies.
- 2.5 The Pre-PBAC response (p2) proposed that the clinical criterion for eribulin be changed to, “The patient must have received prior treatment with an anthracycline and ifosfamide (unless contraindicated)”. The PBAC considered that second-line use of eribulin is acceptable, however, was concerned that the risk of leakage to other subtypes of sarcoma was high.

*For more detail on PBAC’s view, see section 7 “PBAC outcome”.*

### **3 Background**

- 3.1 TGA status at time of the PBAC consideration: the submission was made under the TGA-PBAC parallel process. At the time of the PBAC consideration, the Delegate's Overview and Resolution of the Advisory Committee on Prescription Medicines (ACPM) were available. The ACPM considered that eribulin had an overall positive benefit-risk profile for the proposed indication, "(eribulin) is indicated for the treatment of patients with unresectable liposarcoma who have received prior chemotherapy for advanced or metastatic disease".
- 3.2 Eribulin is a first-in-class halichondrin B-based, microtubule dynamics inhibitor, and has not previously been considered by the PBAC for the treatment of liposarcoma. Eribulin is PBS-subsidised for the treatment of locally advanced or metastatic breast cancer in patients with progressive disease who have failed at least two prior chemotherapeutic regimens.
- 3.3 The PBAC recommended the PBS listing of pazopanib, a multi-targeted tyrosine kinase inhibitor, in July 2013. Pazopanib is PBS-subsidised for second-line treatment in patients with advanced soft tissue sarcoma, however the PBS restriction excludes patients with adipocytic soft tissue sarcoma, which includes liposarcomas.

### **4 Clinical place for the proposed therapy**

- 4.1 Soft tissue sarcomas are rare malignancies. There are more than 50 histological subtypes of sarcoma, with US data from the Surveillance, Epidemiology, and End Results (SEER) Program indicating the most common sarcomas were liposarcomas (17.1%), leiomyosarcomas (13.6%), and malignant fibrous histiocytoma (8.2%). The five-year survival rate for patients with liposarcoma was approximately 25%; in patients with metastatic relapse, the five-year survival rate was as low as 16%.
- 4.2 Liposarcomas are a specific type of malignant adipocytic tumour. Many other forms of adipocytic tumours, such as lipomas, are benign. Liposarcomas can be further classified into the following subtypes: well-differentiated, myxoid, pleomorphic and dedifferentiated. The inclusion criteria in the pivotal trial (Study 309) included myxoid, pleomorphic, dedifferentiated and round cell subtypes of liposarcomas, or leiomyosarcoma; no specification (to include or exclude from trial entry) was made with regards to well-differentiated liposarcoma.
- 4.3 The clinical practice guidelines for the management of adult onset sarcoma (Cancer Council Australia, 2016) reported that doxorubicin, alone or in combination with ifosfamide, is standard first-line treatment for patients with advanced or metastatic liposarcoma. For patients where doxorubicin is considered inappropriate, ifosfamide as a single agent had the second highest objective response rate (Cancer Council Australia 2016). For patients who have not received ifosfamide as first-line treatment, ifosfamide monotherapy might be considered for second-line use. Dacarbazine, with or without gemcitabine, is a reasonable third-line therapy after exposure to doxorubicin and ifosfamide in advanced soft tissue sarcomas. Dacarbazine is not PBS subsidised, while doxorubicin, ifosfamide and gemcitabine are PBS-subsidised for the treatment of patients with advanced or metastatic liposarcoma.

- 4.4 The submission stated that if eribulin was recommended for PBS listing for patients with advanced or metastatic liposarcoma (including dedifferentiated, myxoid, round cell and pleomorphic subtypes), eribulin would replace ifosfamide (if doxorubicin was used as first-line treatment) or dacarbazine (if the patient had received prior ifosfamide).

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

## **5 Comparator**

- 5.1 The submission nominated dacarbazine as the main comparator, with ifosfamide as a supplementary comparator. These were the appropriate comparators. Dacarbazine is registered in the Australian Register of Therapeutic Goods (ARTG) for the treatment of soft tissue sarcoma; however, it is not PBS listed for this indication. Dacarbazine is mostly supplied in a hospital setting.
- 5.2 For patients treated with doxorubicin monotherapy as a first-line treatment, eribulin was likely to be used as an alternate second-line treatment in place of ifosfamide if listed on the PBS. The submission provided a naïve comparison of the clinical evidence. However, the submission did not include ifosfamide in the economic evaluation or financial estimates. The ESC considered that there were insufficient data to inform a robust comparison of eribulin with ifosfamide, and as such, the submission's proposal for eribulin to be listed as a second-line therapy was not adequately justified.
- 5.3 The PBAC agreed with the ESC that there were limited data to draw a conclusion on the comparison between ifosfamide and eribulin, however, considered that use of eribulin in the second-line setting, after prior chemotherapy, was acceptable for metastatic disease.

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

## **6 Consideration of the evidence**

### ***Sponsor hearing***

- 6.1 There was no hearing for this item.

### ***Consumer comments***

- 6.2 The PBAC noted the letter of support received from Rare Cancers Australia for the eribulin submission. Rare Cancers Australia stated that, based on anecdotal experience, outcomes for liposarcoma are often poor, treatment options are limited and there is a high unmet clinical need for additional therapies.

### ***Clinical trials***

6.3 The submission was based on one randomised head-to-head trial comparing eribulin and dacarbazine in patients with advanced soft tissue sarcomas (Study 309, N = 452). For the supplementary comparator, ifosfamide, the submission identified one trial comparing two ifosfamide dose regimens as first- and second-line therapies in patients with advanced soft tissue sarcoma (van Oosterom 2002, N = 182). Only patients who received ifosfamide as a second-line therapy were considered in the evaluation (n = 76).

6.4 Details of the trials presented in the submission are provided in Table 1.

**Table 1: Trials and associated reports presented in the submission**

Trial ID	Protocol title/Publication title	Publication citation
<b>Main comparator: dacarbazine</b>		
Study 309	A randomised, open-label, multicentre, phase 3 study to compare the efficacy and safety of eribulin with dacarbazine in subjects with soft tissue sarcoma. Clinical Study Report.  Analysis of patient-reported outcomes for Eisai's E789-G000-309 "a randomised, open-label, multicentre, phase 3 study to compare the efficacy and safety of eribulin with dacarbazine in subjects with soft tissue sarcoma." Report Version 6.0.  Schöffski P, Chawla S, Maki R.G. <i>et al.</i> , Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicenter, phase 3 trial.	22 June 2015  8 July 2015  Lancet. 2016; 387(10028):1629-37.
<b>Supplementary comparator: ifosfamide</b>		
van Oosterom (2002)	Van Oosterom AT, Mouridsen HT, Nielsen OS, <i>et al.</i> 2002. Results of randomised studies of the EORTC Soft Tissue and Bone Sarcoma Group (STBSG) with two different ifosfamide regimens in first- and second-line chemotherapy in advanced soft tissue sarcoma patients.	Eur J Cancer 2002; 38(18), 2397-2406.

Source: Table B-4, p43 of the submission

6.5 The key features of the randomised trials are summarised in Table 2.

**Table 2: Key features of the included evidence**

Trial	N	Design/duration	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
<b>Main comparison: Eribulin vs. dacarbazine</b>						
Study 309	452 <sup>a</sup> 143 <sup>b</sup>	R, OL Median: 31 mths	Low	Unresectable/metastatic STS, failed ≥ 2 prior Tx, subgroup with liposarcoma	OS, PFS, safety, QoL	Used
<b>Supportive comparator: ifosfamide vs. ifosfamide</b>						
van Oosterom (2002)	76 <sup>c</sup>	R, OL Duration: NR	High	Unresectable/metastatic STS, subgroup 2 <sup>nd</sup> line	ORR, OS, PFS, safety	Not used

Source: compiled during the evaluation

mths = months; NR = not reported; OL = open-label; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; QoL = quality of life; R = randomised; STS = soft tissue sarcoma; Tx = treatment

<sup>a</sup> Intention-to-treat population

<sup>b</sup> Patients with liposarcoma (including dedifferentiated, myxoid, round cell and pleomorphic subtypes)

<sup>c</sup> Patients treated in the second-line setting

- 6.6 The proposed PBS population differed from the Study 309 population as the requested PBS listing:
- limited eribulin to patients with liposarcoma (Study 309 [N=452] included patients with liposarcoma [n=143] and leiomyosarcoma [n=309]); and
  - required patients to have failed at least one prior therapy, including an anthracycline, whereas Study 309 required patients to have failed at least two prior treatments.
- 6.7 The submission presented the subgroup of patients with liposarcoma for efficacy outcomes and the whole trial population for safety outcomes. No safety outcomes were provided for the subgroup of patients with liposarcoma.
- 6.8 The PBAC noted that Study 309 was not powered to identify a difference in survival across the treatment arms for the liposarcoma subgroup, and that results require caution in interpretation.

### Comparative effectiveness

- 6.9 The results for overall survival from Study 309 are presented in Table 3 and Figures 1 and 2 for the intention-to-treat (ITT) population and subgroup of patients with liposarcoma.

**Table 3: Summary of the overall survival (OS) – median follow-up 31 months (Study 309) <sup>a</sup>**

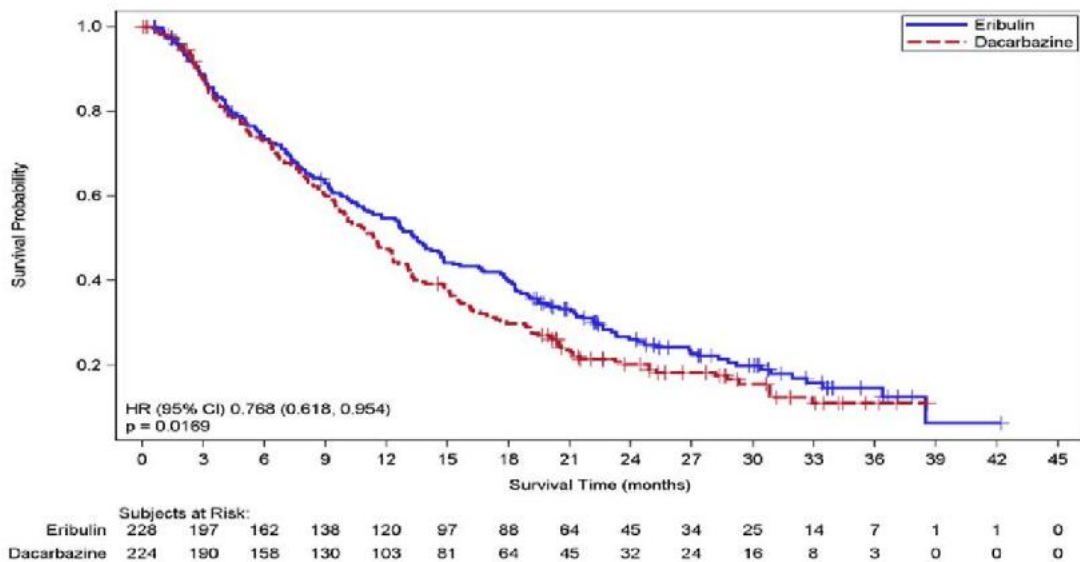
	ITT analysis N = 452		Liposarcoma n = 143, (31.6% ITT)		Leiomyosarcoma N = 309, (68.4% ITT)	
	Eribulin	Dacarbazine	Eribulin	Dacarbazine	Eribulin	Dacarbazine
N	228	224	71	72	157	152
Patients with events, n (%)	176 (77%)	181 (81%)	52 (73%)	63 (88%)	124 (79%)	118 (78%)
Censored, n (%)	52 (23%)	43 (19%)	-	-	-	-
Median OS, months (95% CI)	13.5 (10.9, 15.6)	11.5 (9.6, 13.0)	15.6 (10.2, 18.6)	8.4 (5.2, 10.1)	12.7 (9.8, 14.8)	13.0 (11.3, 15.1)
HR (95% CI)	0.77 (0.62, 0.95) p=0.0115		0.51 (0.35, 0.75) p=0.0006		0.93 (0.71, 1.20) p=0.5730	

Source: Table B-16, p61, Table B-24, p71, Figure B-3, p66, Figure B-5, p72 of the submission

<sup>a</sup> Within the clinical study report the test for interaction was not presented.

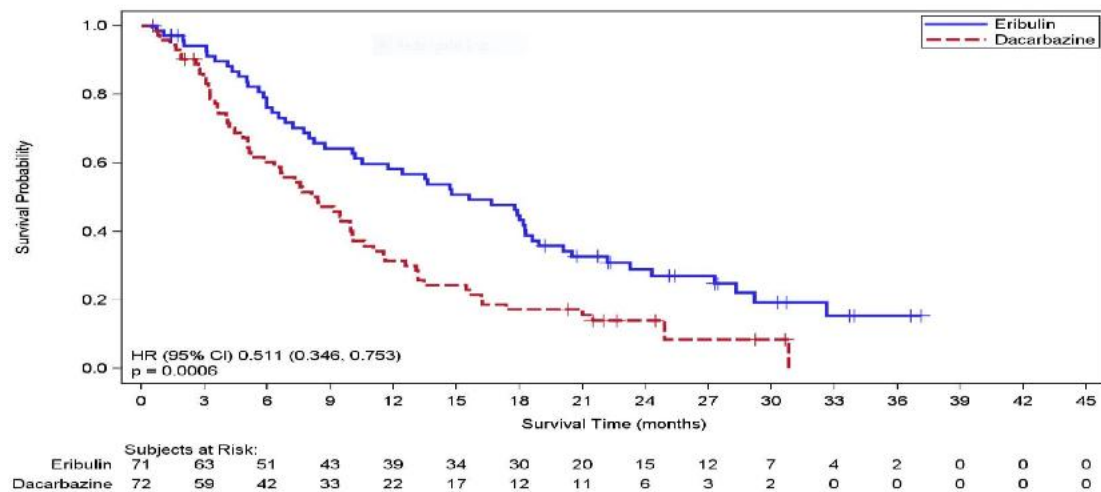
CI = confidence interval; HR = hazard ratio; ITT = intention to treat; OS = overall survival

Figure 1: Overall survival in the intention to treat population of Study 309 – median follow-up 31 months



Source: Figure B-1, p62 of the submission  
 CI = confidence interval; HR = hazard ratio

Figure 2: Overall survival in patients with liposarcoma of Study 309 – median follow-up 31 months



Source: Figure B-4, p72 of the submission  
 CI = confidence interval; HR = hazard ratio

6.10 In the ITT population of Study 309, the median overall survival with eribulin was 13.5 months compared with 11.5 months for patients treated with dacarbazine (hazard ratio (HR): 0.77; 95% confidence interval (CI): 0.62 to 0.95). The effect was more pronounced in patients with liposarcoma (pre-specified subgroup), with a median survival of 15.6 months for eribulin compared with 8.4 months for dacarbazine (HR: 0.51; 95% CI: 0.35 to 0.75). In contrast, eribulin did not improve overall survival in patients with leiomyosarcoma compared with dacarbazine, with a similar median overall survival reported in both treatment groups of 12.7 months for eribulin, versus 13.0 months for dacarbazine (HR: 0.93; 95% CI: 0.71 to 1.20). The submission stated that the difference in prognosis between liposarcoma and leiomyosarcoma

might offer an explanation for the difference in efficacy of eribulin treatment by subgroup.

6.11 The PBAC noted that the median overall survival in the dacarbazine arm was 11.5 (95% CI: 9.6 to 13.0) months in the ITT population, 8.4 (95% CI: 5.2 to 10.1) months in the liposarcoma subgroup, and 13.0 (95% CI: 11.3 to 15.1) months in the leiomyosarcoma subgroup. Therefore, the PBAC considered that the larger incremental survival gain observed in eribulin vs dacarbazine patients in the liposarcoma subgroup (7.2 months) compared to the ITT population (2.0 months), was partly due to the reduced survival in the dacarbazine arm of the liposarcoma subgroup rather than being solely due to an increased survival in the eribulin arm. The PBAC also noted that although the subgroups were pre-specified in Study 309, the submission did not make any adjustments for multiplicity or present a formal test of interaction for subgroup effects. Therefore, the PBAC considered that the observed difference in median overall survival between the eribulin and dacarbazine arms in the liposarcoma subgroup, compared to the leiomyosarcoma subgroup and the ITT population, was not a robust result. The PBAC further noted that the median overall survival difference between the eribulin and dacarbazine arms in the ITT population was 2 months, and considered that this may be more reflective of the true efficacy of eribulin, rather than the 7.2 months observed in the liposarcoma subgroup.

6.12 The results for progression free survival are presented in Table 4.

**Table 4: Summary of the progression free survival (PFS) results from Study 309 – median follow-up 31 months<sup>a</sup>**

	ITT analysis		Liposarcoma		Leiomyosarcoma	
	Eribulin	Dacarbazine	Eribulin	Dacarbazine	Eribulin	Dacarbazine
N	228	224	71	72	157	152
Patients with events, n (%)	197 (86%)	188 (84%)	57 (80%)	59 (82%)	140 (89%)	129 (85%)
Median PFS, months (95% CI)	2.6 (1.9, 2.8)	2.6 (1.8, 2.7)	2.9 (2.6, 4.8)	1.7 (1.4, 2.6)	2.2 (1.5, 2.7)	2.6 (2.4, 2.9)
HR (95% CI)	0.88 (0.71, 1.09) p=0.1773		<b>0.52 (0.35, 0.78)</b> <b>p=0.0015</b>		1.07 (0.84, 1.38) p=0.5848	

Source: Table B-20, p67 of the submission, and extracted from Table 14.2.3.1.1, p291 of the CSR

<sup>a</sup> Within the clinical study report the test for interaction was not presented.

CI = confidence interval; HR = hazard ratio; ITT = intention to treat; PFS = progression free survival; **Bold** = statistically significant

6.13 No differences were observed in progression free survival in the ITT population, with median progression free survival being 2.6 months for both treatments (HR 0.88; 95% CI: 0.71 to 1.09). A 1.2 month improvement in median progression free survival was observed in the liposarcoma subgroup (HR: 0.52; 95% CI: 0.35 to 0.78). No difference in progression free survival was observed for patients with leiomyosarcoma.

6.14 The PBAC noted the inconsistency in the incremental difference between eribulin and dacarbazine for progression free survival compared to overall survival for the ITT population (nil PFS vs 2 months OS), liposarcoma subgroup (1.2 month PFS vs 7.2 months OS) and leiomyosarcoma subgroup (-0.4 month PFS vs -0.3 month OS). The PBAC considered that this added further uncertainty to estimating eribulin's treatment

effect, and that the true magnitude of survival benefit was likely to be less than 7.2 months. The PBAC also noted that the majority of the survival gain in the liposarcoma subgroup was post-progression, and considered that the magnitude of post-progression survival was neither consistent with the known disease prognosis nor consistent with results demonstrated by other trials in this disease area.

- 6.15 A naive comparison of the efficacy of the key outcomes for the supportive comparator ifosfamide is presented in Table 5.

**Table 5: Side by side comparison of the key efficacy outcomes for the supportive comparator, ifosfamide**

	Study 309 - ITT		Van Oosterom (2002) - 2 <sup>nd</sup> line	
	Eribulin	Dacarbazine	Ifosfamide 5 g/m <sup>2</sup> x 1 day	Ifosfamide 3 g/m <sup>2</sup> x 3 day
<b>N</b>	<b>228</b>	<b>224</b>	<b>36</b>	<b>40</b>
Median OS, months (95% CI)	13.5 (10.9, 15.6)	11.5 (9.6, 13.0)	10.4 (NR)	8.3 (NR)
Median PFS, months (95% CI)	2.6 (1.9, 2.8)	2.6 (1.8, 2.7)	1.4 (NR)	3.2 (NR)

Source: Tables 9-11, pp11-13 of Appendix 1 to the submission

CI = confidence interval; ITT = intention to treat; NR = not reported; OS = overall survival; PFS = progression free survival

- 6.16 The submission summarised the results for the comparison of eribulin with ifosfamide (supportive comparator), rather than making a formal comparison, due to the heterogeneity between the two trials and the lack of a common treatment arm. This was considered reasonable during the evaluation. The submission noted that the overall survival for ifosfamide (5 g/m<sup>2</sup> x 1 day) was similar to that reported for dacarbazine. It was difficult to formally compare eribulin and ifosfamide due to the differences in trial design, included histological subtypes, prior treatments and the lack of common comparator.

### Comparative harms

- 6.17 The submission noted that the number of treatment-emergent adverse events (TEAEs) was slightly higher for eribulin compared with dacarbazine. However, the submission argued that the analysis did not support a conclusion that there were significant differences between the rates of key adverse events (AEs) relevant for PBAC decision making. This might not have been reasonable, as the number of Grade 3 or 4 adverse events was statistically significantly higher in the eribulin treatment arm compared with dacarbazine treatment arm (152/226 (67%) versus 126/224 (56%), relative risk: 1.20; 95% CI: 1.03 to 1.39).
- 6.18 The ESC noted that the TGA Delegate's Overview stated eribulin was 'moderately more toxic than dacarbazine with a higher incidence of Grade ≥ 3 AEs (67.3% vs. 56.3%) and AEs leading to withdrawal (7.5% vs. 4.9%)'.
- 6.19 Treatment-emergent adverse events (all Grades) that occurred with a statistically significantly higher incidence in the eribulin arm included: neutropenia, alopecia, peripheral sensory neuropathy, headache, stomatitis, pyrexia, urinary tract infection and hypokalaemia. Thrombocytopenia was the only TEAE that occurred with a statistically significantly higher incidence in the dacarbazine arm.

- 6.20 For Grade 3 or 4 adverse events, eribulin was associated with statistically significantly more TEAEs (any type), blood and lymphatic system disorders (total), neutropenia and leukopenia, while dacarbazine was associated with more thrombocytopenia.

### Benefits/harms

- 6.21 A summary of the comparative benefits and harms for eribulin versus dacarbazine is presented in Table 6.

**Table 6: Summary of comparative benefits and harms for eribulin and dacarbazine from Study 309**

Benefits – subgroup of patients with liposarcoma						
Trial	Eribulin		Dacarbazine	Absolute Difference		HR (95% CI)
<b>OS: median follow-up 31 months</b>						
Deaths, n/N	52/71		63/72	-		<b>0.51 (0.35, 0.75)</b>
Median, months (95% CI)	15.6 (10.2, 18.6)		8.4 (5.2, 10.1)	7.2		-
<b>PFS: median follow-up 31 months</b>						
Progressed, n/N	57/71		59/72	-		<b>0.52 (0.35, 0.78)</b>
Median, months (95% CI)	2.9 (2.6, 4.8)		1.7 (1.4, 2.6)	1.2		-
<b>Harms – safety population (liposarcoma and leiomyosarcoma) <sup>a</sup></b>						
	Eribulin	Dacarbazine	RR (95% CI)	Event rate/100 patients <sup>b</sup>		RD (95% CI)
				Eribulin	Dacarbazine	
<b>All Grade TEAE (non-haematological), n/N</b>						
Pyrexia	63/226	31/224	<b>2.01 (1.37, 2.97)</b>	28	14	<b>0.14 (0.07, 0.21)</b>
Peripheral sensory neuropathy	46/226	8/224	<b>5.70 (2.75, 11.8)</b>	20	4	<b>0.17 (0.11, 0.23)</b>
Alopecia	79/226	6/224	<b>13.1 (5.81, 29.3)</b>	35	3	<b>0.32 (0.26, 0.39)</b>
<b>Grade 3/4 TEAE (haematological), n/N</b>						
Neutropenia	80/226	35/224	<b>1.30 (1.01, 1.69)</b>	35	16	<b>0.20 (0.12, 0.28)</b>
Leukopenia	23/226	10/224	<b>1.11 (0.63, 1.96)</b>	10	4	<b>0.06 (0.01, 0.11)</b>
Thrombocytopenia	1/226	34/224	<b>1.47 (0.81, 2.69)</b>	0.4	15	<b>-0.15 (-0.20, -0.10)</b>

Source: Compiled during the evaluation and calculated during evaluation

CI = confidence interval; HR = hazard ratio; OS = overall survival; PFS = progression free survival; RD = risk difference; RR = relative risk; TEAE = treatment-emergent adverse event; **Bold** = statistically significant

<sup>a</sup> Two patients in the eribulin arm were not treated and therefore excluded from the safety population.

<sup>b</sup> Median follow-up in Study 309 = 31 months

- 6.22 On the basis of the direct evidence presented by the submission, in the liposarcoma subgroup (which represented 31.6% of the ITT population and was not powered to detect a difference in survival between treatment arms), approximately a 7.2 month increase in median overall survival was observed in patients treated with eribulin in comparison with dacarbazine. However, the PBAC considered that the true survival benefit with eribulin would likely be less than 7.2 months, given that the subgroup results were not adjusted for multiplicity. Therefore the PBAC considered that results of the ITT population, which demonstrated a 2.0 month increase in median overall survival in patients treated with eribulin in comparison with dacarbazine, was a more reliable estimate of the true benefit of treatment with eribulin.

- 6.23 On the basis of the direct evidence presented for the ITT population, for every 100 patients treated with eribulin in comparison with dacarbazine, over a median follow-up of around 31 months:
- Approximately 14 additional patients would have pyrexia (fever, any Grade);
  - Approximately 17 additional patients would have peripheral sensory neuropathy (loss of feeling in extremities, any Grade);
  - Approximately 32 additional patients would have alopecia (hair loss, any Grade);
  - Approximately 20 additional patients would have Grade 3 or 4 neutropenia (very low white blood cell count);
  - Approximately 6 additional patients would have Grade 3 or 4 leukopenia (very low white blood cell count); and
  - Approximately 15 fewer patients would have Grade 3 or 4 thrombocytopenia (very low platelet count).

***Clinical claim***

- 6.24 The submission described eribulin as superior in terms of comparative effectiveness and different in terms of comparative safety over dacarbazine.
- 6.25 The claim of different safety compared with dacarbazine was not adequately supported. A more appropriate claim would be that eribulin is inferior to dacarbazine in terms of comparative safety for the treatment of patients with locally unresectable or metastatic soft tissue sarcoma, as:
- the proportion of patients with Grade 3 or 4 TEAEs was significantly higher with eribulin;
  - eribulin was associated with statistically significant higher rates of any Grade neutropenia, alopecia, peripheral sensory neuropathy, headache, stomatitis, pyrexia, urinary tract infection and hypokalaemia, while dacarbazine was associated with a statistically significant higher incidence of thrombocytopenia; and
  - eribulin was associated with statistically significant higher rates of Grade 3 or 4 TEAEs (any type), blood and lymphatic system disorders (total), neutropenia and leukopenia; dacarbazine was associated with a higher incidence of thrombocytopenia.
- 6.26 The PSCR acknowledged that it might have been reasonable to consider eribulin as inferior to dacarbazine with regards to comparative safety, however, the PSCR also stated that the development of serious haematological AEs could be mitigated through implementation of dose delay/reduction protocols. The ESC noted that the impact of dose delay/reduction protocols on the efficacy and safety of eribulin had not been demonstrated and therefore considered that it was unknown if such strategies would mitigate the risk of developing serious AEs. The ESC agreed with the commentary that a more appropriate claim would be that eribulin is inferior to dacarbazine in terms of comparative safety.

- 6.27 The submission made no claims of comparative efficacy or safety for the comparison with ifosfamide due to the substantial differences in the clinical characteristics of patients enrolled across the identified trial, the lack of a common intervention, and the heterogeneity in the nature of outcomes reported. This was considered reasonable during the evaluation.
- 6.28 The PBAC accepted the submission’s claim of superior comparative effectiveness of eribulin over dacarbazine, however, considered that the magnitude of the overall survival benefit of 7.2 months in the liposarcoma subgroup was implausibly large. The PBAC considered that a difference in prognosis between liposarcoma and leiomyosarcoma was not a clinically robust rationale to explain a difference in treatment effect. The PBAC noted that if the results of the liposarcoma subgroup analysis were accepted, eribulin achieved an additional 1.2 months of progression free survival, and thus the remaining survival gain (6 months) represented post-progression survival. The PBAC considered that the magnitude of the post-progression survival was not biologically plausible.
- 6.29 The PBAC considered that the claim of different comparative safety was not adequately supported by the data, and that eribulin was of inferior safety to dacarbazine.

**Economic analysis**

- 6.30 The submission presented a modelled economic analysis comparing eribulin and dacarbazine (main comparator). This was consistent with the clinical evidence. The submission did not consider ifosfamide as a supplementary comparator for the economic evaluation. A summary of the model structure and rationale is presented in Table 7.

**Table 7: Summary of model structure and rationale**

Component	Summary
Time horizon	The submission stated that the model had a 5 year time horizon, however the economic model was a trial-based analysis whereby the full Kaplan-Meier curves for OS from the liposarcoma subgroup were applied. In the model it was assumed that all patients died in the cycle following the end of the curves. As a consequence, all patients in the eribulin arm had died at 40 months and in the dacarbazine arm, at 32 months. As such, the time horizon in effect was 40 months.
Outcomes	LYG and QALYs
Methods used to generate results	Expected value analysis, directly trial based
Health states	Stable disease, progressed disease, death.
Cycle length	One month
Transition probabilities	Kaplan-Meier curve.

Source: compiled during the evaluation and calculated during evaluation  
 LYG = life years gained; OS = overall survival; QALY = quality-adjusted life year

- 6.31 The ESC considered that the economic model was only applicable to patients who had previously received two or more systemic therapies prior to receiving eribulin.
- 6.32 The submission’s method for estimating the cost per infusion for eribulin and dacarbazine was inappropriate. For eribulin, the submission calculated the number of 2 mL or 3 mL vials required (including wastage). The inclusion of the 3 mL vial in

these calculations was inappropriate, as it was not requested in the submission or included in the TGA application. The submission then estimated the cost per vial (including dispensing fees and mark-ups). This was inappropriate. According to the Efficient Funding of Chemotherapy Remuneration Arrangements, dispensing fees and mark-ups should be calculated per infusion/dispensing rather than per vial. During evaluation these two errors (inclusion of 3 mL vial and incorrect application of dispensing fees and mark-ups) were corrected, resulting in a monthly eribulin cost of \$█████ compared with the estimated cost in the submission of \$█████. A similar error was made for dacarbazine, resulting in a higher estimated monthly cost (\$█████ versus \$█████ using the same methodology for applying dispensing fees and mark-up as for eribulin). Further, it should be noted that as dacarbazine is not PBS-subsidised, inclusion of dispensing fees and mark-ups may or may not be appropriate.

- 6.33 Patients in the progressed disease health state received one cycle of post-progression chemotherapy. The submission calculated the average cost for post-progression treatment incorrectly, similar to that done for eribulin and dacarbazine. The ESC however noted that a substantial proportion of the liposarcoma subgroup did not have another course of chemotherapy post-progression (35.2% and 45.8% respectively in the eribulin and dacarbazine groups) (Table C-4, p108 of the submission), and considered that such progression costs may have been overestimated.
- 6.34 The ESC noted that the submission excluded dacarbazine as a third-line treatment option in the estimation of post-progression treatment costs. The ESC considered that this was inappropriate, as patients may receive dacarbazine after experiencing disease progression with eribulin. The PBAC noted that 69.3% of eribulin patients and 62.9% of dacarbazine patients in the ITT population received at least one post-trial chemotherapy.
- 6.35 The revised base case included the appropriate dispensing fees and mark-ups for eribulin, dacarbazine and post-progression treatments and excluded the use of the 3 mL vial for eribulin (the 3 mL vial was not requested by the submission).
- 6.36 The key drivers of the economic model are presented in Table 8.

**Table 8: Key drivers of the model**

Description	Method/Value	Impact
Time horizon	After the end of the OS KM curve, patients were assumed to have died; this resulted in different duration for both treatment arms.	Low, favours eribulin
Utility value progressed disease	Values from Study 309 (EQ-5D-3L, US or UK weights) for stable disease and post-progression were applied. The value for post-progression might not reflect the accelerated decline in health related QoL prior to death. In Villa (2015), using a health related vignette study, the mean change in utility from progression free to progressed disease was -0.239.	Low, favours eribulin
Cost of dacarbazine	Submission used quoted price for a clinical trial, while a lower price is published in eMIMS. Hospital prices may be even lower than the eMIMS price.	Low, favours eribulin

Source: compiled during the evaluation, eMIMS (accessed 23 August, 2016) and calculated during evaluation  
 eMIMS = electronic Monthly Index of Medical Specialties; EQ-5D-3L = Euroqol 5-dimension 3-level instrument; KM = Kaplan-Meier; OS = overall survival; QoL = quality of life; UK = United Kingdom; US = United States

- 6.37 The submission did not provide details as to whether the utility values were specific for the subgroup of patients with liposarcoma, and no details were provided on the number of patients providing values for progressed disease. Further, EQ-5D-3L measurements for the progressive disease state were taken immediately following progression; therefore, this utility value might not have been representative for the more advanced progressed disease state.
- 6.38 The PSCR acknowledged that the utility value applied in the ‘progressive disease’ health state was based on EQ-5D data collected at the first off-treatment visit following disease progression and may therefore not fully capture the decline in quality of life prior to death. However, the PSCR argued that the application of more conservative utility values in the commentary resulted in an ICER that was still cost-effective.
- 6.39 The ESC noted that the submission applied disutilities for adverse events. The ESC considered that this may be inappropriate, as the EQ-5D-3L data from the trial should already capture the impact of adverse events. Applying additional disutilities in the economic model may double count the impact of adverse events.
- 6.40 The PBAC noted that utility values were not a major driver in the economic model and had a relatively small impact on the incremental cost-effectiveness ratio (ICER).
- 6.41 The results of the economic evaluation are presented in Table 9.

**Table 9: Results of the economic evaluation – discounted**

Component	Eribulin	Dacarbazine	Increment
Costs			
Revised base case <sup>a</sup>	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
LYG	1.33	0.81	0.52
<b>Incremental cost/extra LYG</b>			\$ [REDACTED]
Revised base case <sup>a</sup>			\$ [REDACTED]
QALYs	0.91	0.55	0.36
<b>Incremental cost/extra QALY gained</b>			\$ [REDACTED]
Revised base case <sup>a</sup>			\$ [REDACTED]

Source: Table D-23, p140 of the submission and calculated during evaluation

LYG = life years gained; QALY = quality-adjusted life year

<sup>a</sup> For the revised base case, dispensing fees and mark-ups were applied per infusion, rather than a weighted cost per vial (per the 1 August 2016 Efficient Funding for Chemotherapy). Further the 3 mL eribulin vial was excluded from the calculations.

- 6.42 The submission estimated an ICER of \$15,000 - \$45,000 per life year gained and \$15,000 - \$45,000 per quality-adjusted life year (QALY) gained. Using the revised values, the ICER increased to \$15,000 - \$45,000 per life year gained and \$15,000 - \$45,000 per QALY gained.
- 6.43 The key sensitivity analyses using the revised base case are presented in Table 10.

**Table 10: Results of univariate and multivariate sensitivity analyses – using the revised base case <sup>a</sup>**

	Δ costs	Δ QALY	ICER
<b>Revised base case <sup>a</sup></b>	\$ [REDACTED]	0.36	\$ [REDACTED]
<b>Univariate sensitivity analyses</b>			
Duration of treatment (base case: until progression for both arms of model, eribulin = 6.2 months; dacarbazine = 3.4 months )			
6 cycles for both arms	\$ [REDACTED]	0.36	\$ [REDACTED]
11 cycles for both arms	\$ [REDACTED]	0.36	\$ [REDACTED]
Cost of dacarbazine, 200 mg (base case AEMP = \$ [REDACTED]) \$ [REDACTED] (eMIMS)	\$ [REDACTED]	0.36	\$ [REDACTED]
Model duration (base case = 5-years) 31 months (i.e. longest follow-up in dacarbazine arm)	\$ [REDACTED]	0.31	\$ [REDACTED]
Utility values (base case: SD = 0.73; PD = 0.67) From Villa (2015): SD = 0.67; PD = 0.44	\$ [REDACTED]	0.28	\$ [REDACTED]
Percentage of patients receiving post-progression treatment (base case 100%) From Study 309: eribulin 65%, dacarbazine 54%	\$ [REDACTED]	0.28	\$ [REDACTED]
<b>Multivariate sensitivity analyses</b>			
Model duration = 31 months, and utility values from Villa (2015)	\$ [REDACTED]	0.24	\$ [REDACTED]
Model duration = 31 months, and dacarbazine price = \$ [REDACTED]	\$ [REDACTED]	0.31	\$ [REDACTED]
Model duration = 31 months, utility values from Villa (2015), and dacarbazine price = \$ [REDACTED]	\$ [REDACTED]	0.24	\$ [REDACTED]

Source: Table D-24, p141 and Table D-27, p143 of the submission and calculated during evaluation using the economic model  
 AE = adverse event; AEMP = Australian ex-manufacturer price; CT = computed tomography; eMIMS = electronic Monthly Index of Medical Specialties; ICER = incremental cost effectiveness ratio; PD = progressive disease; QALY = quality-adjusted life year; SD = stable disease

<sup>a</sup> For the revised base case, dispensing fees and mark-ups were applied per infusion, rather than a weighted cost per vial (per the 1 August 2016 Efficient Funding for Chemotherapy). Further the 3 mL eribulin vial was excluded from the calculations.

- 6.44 The results of the sensitivity analyses indicated the model was most sensitive to the utility value applied for progressive disease and model duration. Under all scenarios the ICER remained below approximately \$45,000 - \$75,000 per QALY gained.
- 6.45 The PBAC noted that the submission presented a trial-based economic analysis using results for overall survival from the liposarcoma subgroup, which produced a favourable ICER. However, the PBAC was concerned that the magnitude of survival gain observed in the liposarcoma subgroup was not reflective of and likely exaggerated the true efficacy of eribulin. The PBAC further noted that if the survival gain observed in the ITT population was applied (2 months), the incremental cost per QALY gained would increase substantially. On this basis, the PBAC considered that a price reduction would be required to ensure the cost-effective PBS listing of eribulin.

**Drug cost/patient/course: \$ [REDACTED]**

- 6.46 The eribulin cost per patient per course was based on assumptions presented in the submission to estimate the financial impact. The submission assumed that every patient would receive 2.19 vials (1 mg in 2 mL) per infusion (based on the recommended eribulin dose of 1.40 mg/m<sup>2</sup>, using an average body surface area of 1.82 m<sup>2</sup>, and a dose intensity of 86% from Study 309; but excluded potential wastage). On the basis of Study 309, it was also assumed each patient would receive 10.62 infusions. Based on doxorubicin prescribing patterns, the submission assumed that 31% would be treated in the public hospital and the remaining in a

private hospital. The costs included the effective price of \$[redacted] ex-manufacturer per vial (1 mg in 2 mL) and dispensing fees/mark-ups per infusion of \$82.67 for the public hospital setting and \$123.62 for the private hospital setting (1 April 2016 PBS Schedule).

### Estimated PBS usage & financial implications

6.47 This submission was not considered by DUSC. The estimated use and financial implications are presented in Table 11.

**Table 11: Estimated use and financial implications (italics = Australian epidemiological sources)<sup>a</sup>**

	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Estimated extent of use</b>					
Number treated Revised <sup>a</sup>	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Market share	[redacted] %	[redacted] %	[redacted] %	[redacted] %	[redacted] %
Vials <sup>b</sup> Revised <sup>a</sup>	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
<b>Estimated net cost to PBS/RPBS/MBS</b>					
Net cost to PBS/RPBS	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]
Net cost to MBS	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]
<b>Estimated total net cost</b>					
Net cost PBS/RPBS & MBS Revised <sup>a</sup> patient numbers	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]

Source: Tables E-3 to E-6, pp149-153 and Table E-9, p158 of the submission; and Eribulin Liposarcoma\_Section E Workbook.xlsx and calculated during evaluation

MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme

<sup>a</sup> The estimated use and financial implications were revised during the evaluation. The following assumptions were included: 1) Incidence of soft tissue sarcoma is 3.56 in the adult population (AIHW 2016); 2) The 1-year prevalence of soft tissue sarcoma is 321 patients (based on AIHW 2014 and ABS population projections); 3) 17% of the soft tissue sarcomas are liposarcomas (submission, Howlader 2015); and 4) 80% of incident and prevalent patients with liposarcoma will have advanced/metastatic disease and received prior treatment

<sup>b</sup> Assuming 2.19 vials (2 mL) per infusion and 10.62 infusions per patient.

6.48 The submission estimated that in the first year of listing less than 10,000 patients would be eligible and treated with eribulin, decreasing to less than 10,000 patients in Year 2 and then slowly increasing to less than 10,000 patients in Year 5 of listing. There might be potential for the number of eligible patients to be lower in the first year of listing and greater from Year 2 onwards than the estimate in the submission, because:

- The estimated incidence rate for soft tissue sarcoma (2.11 per 100,000 population) may have been underestimated, as rates reported more recently by the Australian Institute of Health and Welfare (AIHW) for the adult population were higher (3.56 per 100,000 population).
- The percentage of soft tissue sarcomas that were liposarcomas was unknown, as the submission used data from a US data set which might not be applicable to Australia.
- The submission assumed that all patients with liposarcoma would be eligible and treated with eribulin. The utilisation of eribulin may be overestimated, as some patients might not have advanced or metastatic disease and some may not have failed prior treatment.

- The submission calculated the prevalent population based on outdated US data (1960-1999) and 5-year survival (US data 2008-2012) and the estimated incidence rates which might not be applicable to the Australian setting. It may have been more appropriate to use Australian 1-year prevalent population data for the basis of estimating the number of eligible patients.
- 6.49 During evaluation, Australian data were applied to estimate the total eligible and treated population, using the following assumptions:
- Incidence of soft tissue sarcoma was 3.56 per 100,000 in the adult population (AIHW 2016);
  - The 1-year prevalence of soft tissue sarcoma was 321 patients (based on AIHW 2014 and Australian Bureau of Statistics population projections);
  - 17% of soft tissue sarcomas were liposarcomas (submission, Howlader 2015); and
  - 80% of incident and prevalent patients with liposarcoma will have advanced or metastatic disease and will have received prior treatment.
- 6.50 The submission estimated that in the first five years of listing the cost to the PBS/RPBS and MBS would be less than \$10 million. This cost was uncertain as:
- The submission may have overestimated the number of patients in Year 1 and underestimated the number of patients in Years 2-5;
  - The submission did not consider potential wastage;
  - Cost offsets may have been overestimated as the submission did not account for replacement of PBS/RPBS listed chemotherapy were excluded ;
  - The submission did not include additional costs to the PBS/RPBS and MBS for the increased incidence of certain adverse events (underestimate); and
  - The submission applied the full MBS fee for the cost of administration – private patients (MBS 13915) and cost of monitoring – all patients (MBS 56801); it would have been more appropriate to use the 85% MBS fee.
- 6.51 Using updated patient numbers estimated during evaluation, the cost to the PBS/RPBS and MBS over the first five years of listing was estimated to be less than \$10 million.
- 6.52 The PBAC accepted the revised estimated use and financial implications presented by the evaluation.

### **Quality Use of Medicines**

- 6.53 The submission did not discuss quality use of medicines initiatives. The submission requested listing of the 2 mL (1 mg) vial only; however, for the economic evaluation both the 2 mL (1 mg) and 3 mL (1.5 mg) vials were used to estimate the mean number of vials per infusion. Including the 3 mL vial would result in less wastage. Using the distribution of number of vials per infusion as used in the economic model, the use of the 2 mL and 3 mL vials would result in a mean eribulin dose of 2.38 mg compared with a mean dose of 2.73 mg if only the 2 mL vials would be used.

## Financial Management – Risk Sharing Arrangements

- 6.54 The submission proposed a special pricing arrangement similar to the current arrangement for use in patients with breast cancer. In the Pre-PBAC response, the sponsor indicated a willingness to negotiate a risk sharing arrangement to mitigate additional concerns raised by the PBAC.
- 6.55 The PBAC considered that a risk sharing agreement with a financial cap based on the submission's patient numbers may be appropriate to address uncertainty in the utilisation and financial estimates. The financial estimates should be updated following the Committee's recommendations.

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

## 7 PBAC Outcome

- 7.1 The PBAC recommended the listing of eribulin, on the basis that it should be available only under special arrangements under Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital).
- 7.2 The PBAC is satisfied that eribulin provides, for some patients, a significant improvement in efficacy over dacarbazine.
- 7.3 The PBAC acknowledged the high unmet clinical need for treatment options in liposarcoma patients. The PBAC accepted the submission's proposal for eribulin to be used in the second-line setting for the treatment of unresectable or metastatic liposarcoma, after prior treatment with an anthracycline and ifosfamide (unless contraindicated). However, the PBAC was concerned that given the limited treatment options available for sarcoma patients, that there was a risk of leakage of using PBS-subsidised eribulin for subtypes of sarcoma other than liposarcoma.
- 7.4 The PBAC accepted dacarbazine as the primary comparator, and ifosfamide as a supplementary comparator, and noted that dacarbazine is not listed on the PBS.
- 7.5 The PBAC accepted the submission's claim that eribulin was of superior comparative effectiveness over dacarbazine. However, the PBAC did not accept the results of the liposarcoma subgroup analysis as being representative of eribulin's true extent of clinical benefit, on the basis that:
- although the liposarcoma subgroup was a pre-specified subgroup in Study 309, the trial was not statistically powered to detect a difference in survival between the eribulin and dacarbazine treatment arms in the liposarcoma subgroup;
  - the ITT population, which was statistically powered to compare overall survival in patients treated with eribulin versus dacarbazine, showed a median overall survival benefit of 2.0 months;
  - the results of the liposarcoma subgroup showed a median progression free survival gain of 1.2 months and a median overall survival gain of 7.2 months: the PBAC considered that 6 months of post-progression survival gain was not biologically plausible;
  - differences in post-trial treatments may have accounted for the marked

- differences in post-progression survival between the treatment arms;
  - the submission's proposal that the difference in prognosis between liposarcoma and leiomyosarcoma might explain for the difference in efficacy of eribulin by subgroup was not sufficient justification and was of limited biological plausibility;
  - the subgroup results were not adjusted for multiplicity; and
  - a formal test of interaction for subgroup effects was not presented.
- 7.6 The PBAC considered that eribulin was of inferior safety compared to dacarbazine. The PBAC noted that additional patients would experience treatment related adverse events including pyrexia, peripheral sensory neuropathy, alopecia, neutropenia or leukopenia, and that fewer patients would experience thrombocytopenia, when treated with eribulin, compared to dacarbazine.
- 7.7 The PBAC considered that the structure of the submission's economic model was reasonable, however, noted that the model was driven by the overall survival results from the liposarcoma subgroup. As the PBAC did not accept the claim of a 7.2 month survival gain for patients in the eribulin arm, the PBAC did not accept the submission's base case ICER of \$15,000 - \$45,000 per QALY gained. The PBAC considered that a more conservative and clinically plausible approach would have been to use the overall survival results from the ITT population of Study 309 (2 months). The PBAC noted that changing this input would substantially increase the base case ICER.
- 7.8 The PBAC considered that the submission underestimated the incidence of sarcomas and liposarcoma in Australia, and accepted the revised estimates presented in the commentary. The PBAC noted that the revised estimates had a minor impact on the five-year financial implications.
- 7.9 The PBAC considered that, on the basis of uncertain extent of clinical benefit and inferior safety of eribulin versus dacarbazine and risk of leakage of eribulin use in sarcomas subtypes other than liposarcoma, that further discussions with the sponsor would be required to achieve a cost effective PBS listing for eribulin for liposarcoma. The PBAC considered that a price reduction will be required to ensure the cost effective PBS listing of eribulin.
- 7.10 The PBAC noted that grandfathering of patients receiving non-PBS subsidised eribulin for liposarcoma onto PBS subsidised treatment was not requested by the sponsor.
- 7.11 The PBAC advised that eribulin is not suitable for prescribing by nurse practitioners.
- 7.12 The PBAC noted the Early Supply Rule cannot be applied to Section 100 drugs.
- 7.13 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**  
Recommended

## 8 Recommended listing

### 8.1 Amend existing listing as follows:

Name, Restriction, Manner of administration and form	Max. Amt	No. of Rpts	Proprietary Name and Manufacturer	
ERIBULIN 1 mg/2 mL (as mesilate) injection, 1 x 3 mg 2 mL vial		13	Halaven®	Eisai Australia Pty Ltd
<b>Category / Program</b>	Section 100 – Efficient funding of Chemotherapy			
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives			
<b>Severity:</b>	<i>Advanced (unresectable and/or metastatic)</i> <del>Advanced, defined as locally recurrent, locally advanced or metastatic</del>			
<b>Condition:</b>	<del>Soft tissue sarcoma (STS)</del> liposarcoma			
<b>PBS Indication:</b>	<i>Advanced (unresectable and/or metastatic) liposarcoma</i>			
<b>Treatment phase:</b>	initial			
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined			
<b>Treatment criteria:</b>	Must be treated by an oncologist.			
<b>Clinical criteria:</b>	Patient must have an ECOG performance status of 2 or less,  AND  Patient must have received prior chemotherapy treatment including an anthracycline and ifosfamide (unless contraindicated),  AND  The treatment must be the sole PBS-subsidised therapy for this condition.			
<b>Prescriber Instructions</b>	Patient must have the following conditions: Liposarcoma (dedifferentiated, myxoid, round-cell, or pleomorphic subtypes).			
<b>Population criteria:</b>	Patient must be aged 18 years or older.			
<b>Administrative Advice</b>	<i>No increase in the maximum number of repeats may be authorised.</i>  <i>Special Pricing Arrangements apply.</i>			

## 9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final

PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

**10 Sponsor's Comment**

The sponsor had no comment.