

6.02 BRENTUXIMAB VEDOTIN

50 mg injection: powder for;

Adcetris®, Takeda Pharmaceuticals Australia Pty Ltd.

1 Purpose of Application

- 1.1 The submission requested Section 100 – Efficient Funding of Chemotherapy – listing for brentuximab vedotin for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin Lymphoma following autologous stem cell transplant (ASCT). The submission also requested that the PBAC consider whether the Rule of Rescue is applicable.

2 Requested listing

- 2.1 The submission requested listing in patients with Hodgkin Lymphoma who have relapsed or refractory disease after a primary ASCT procedure, and who are suitable for systemic curative intent salvage therapy.
- 2.2 The requested listing is outlined below, with suggestions and additions proposed by the Secretariat 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	Proprietary Name and Manufacturer
BRENTUXIMAB VEDOTIN 50mg injection, 1 x 50 mg vial	200mg	3	<i>Published:</i> \$ [REDACTED] <i>Effective:</i> \$ [REDACTED]	Adcetris Takeda

Category / Program	Section 100 – Efficient Funding of Chemotherapy Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Severity:	<i>Relapsed or Refractory</i>
Condition:	<i>Hodgkin Lymphoma</i>
PBS Indication:	<i>Relapsed or Refractory Hodgkin Lymphoma</i>
Treatment phase:	Initial
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" 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 type="checkbox"/> Streamlined
Clinical criteria:	The treatment must be for curative intent; AND

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	<p>The patient must have undergone appropriate prior front-line curative intent chemotherapy; and a first autologous stem cell transplant</p> <p>AND</p> <p><i>The patient must have undergone a first curative intent autologous stem cell transplant;</i></p> <p>The patient must demonstrate relapsed or <i>chemotherapy</i> refractory Hodgkin Lymphoma disease after their ASCT autologous stem cell transplant.</p>
<p>Prescriber Instructions</p>	<p>Applications for authorisation of initial treatment must be in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Hodgkin lymphoma Brentuximab vedotin PBS Authority Application - Supporting Information Form (may be downloaded from the Medicare Australia website (www.medicareaustralia.gov.au)) which includes the following:</p> <ol style="list-style-type: none"> I. A histology report including evidence of the tumour's CD30 positivity from a biopsy at time of diagnosis or subsequent to the most recently delivered prior treatment with radiation, chemotherapy, biologics, immunotherapy or other agents; II. The date of initial diagnosis of Hodgkin lymphoma; III. Dates of commencement and completion of front-line curative intent chemotherapy, all lines of curative intent salvage chemotherapy and ASCT procedure; IV. A declaration of whether the patient's disease is relapsed or refractory, and the date and means by which the patient's disease was assessed as being relapsed or refractory subsequent to the patient's first ASCT; V. A declaration that the patient has not had a second stem cell transplant (SCT). VI. A declaration of whether the patient is planned to have a second SCT, and the type of transplant procedure planned. <p>A maximum quantity and number of repeats to provide for an initial course of brentuximab vedotin of 4 cycles will be authorised as part of the initiating restriction</p>
<p>Administrative Advice</p>	<p>No increase in the maximum number of repeats may be authorised.</p> <p>No increase in the maximum quantity or number of units may be authorised.</p> <p><i>Special pricing arrangement apply</i></p> <p><i>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</i></p> <p><i>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</i></p> <p><i>Applications for authority to prescribe should be forwarded to:</i> <i>Department of Human Services</i> <i>Prior Written Approval of Complex Drugs</i> <i>Reply Paid 9826</i> <i>GPO Box 9826</i> <i>HOBART TAS 7001</i></p>

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Category / Program	Section 100 – Efficient Funding of Chemotherapy Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Severity:	<i>Relapsed or Refractory</i>
Condition:	<i>Hodgkin Lymphoma</i>
PBS Indication:	<i>Relapsed or Refractory Hodgkin Lymphoma</i>
Treatment phase:	Continuing
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	Patient must not have progressive disease AND Patient must have previously been issued with an Authority prescription for this drug <i>for this indication.</i>
Prescriber Instructions	The maximum number of cycles for any individual patient is 16 cycles <i>The treatment must not exceed a lifetime total of 16 cycles.</i> The following information is to be provided at time of request for continuation of treatment: <ul style="list-style-type: none"> - The date of initial treatment with brentuximab vedotin; - The date and means by which the patient's disease was assessed as being responsive or not to brentuximab vedotin treatment; - A declaration of the patient's response to initial treatment (categorised by type of response), and - A declaration of whether the patient has had, or is planned to have, a <i>second</i> transplant. Patients should be assessed for response after 4 cycles of brentuximab vedotin treatment. Patients should not be continued on brentuximab vedotin treatment if they are in a progressive disease state after the first assessment of response.

Administrative Advice	<p>No increase in the maximum number of repeats may be authorised.</p> <p>No increase in the maximum quantity or number of units may be authorised.</p> <p><i>Special pricing arrangement apply</i></p> <p>Authority applications for continuing treatment may be made by telephone to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p>
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- 2.3 The submission, Pre-Sub-Committee Response (PSCR) and Pre-PBAC response outlined options for different restrictions including limiting use to first-line post ASCT, limiting use to patients who are intended for an allogeneic SCT and/or requiring patients to have a Complete Response in order to continue treatment beyond the fourth cycle.
- 2.4 The submission presented a cost-utility analysis that compared brentuximab vedotin to salvage chemotherapy (represented by gemcitabine+vinorelbine).

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

3 Background

- 3.1 TGA status: Brentuximab vedotin was TGA registered on 19 December 2013 for:
- Treatment of adult patients with relapsed or refractory CD30+ Hodgkin Lymphoma:
 - o Following ASCT or
 - o Following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option.
 - Treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma.
- 3.2 Brentuximab vedotin was recommended for listing by the PBAC in March 2014 for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma.

4 Clinical place for the proposed therapy

- 4.1 Hodgkin Lymphoma is a neoplasm characterised by the presence of clonal malignant Reed-Sternberg cells. Brentuximab vedotin is an antibody-drug conjugate that targets the cell membrane protein CD30 that is expressed on the surface of such cells.
- 4.2 The proposed algorithm and requested restriction would allow Hodgkin Lymphoma patients to receive brentuximab vedotin as first post ASCT salvage or as second post ASCT salvage. However, the base case economic model only included the effectiveness in the first-line post ASCT setting.

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

5 Comparator

- 5.1 The submission nominated salvage chemotherapy consisting of gemcitabine+vinorelbine as the main comparator. The ESC agreed that this was the appropriate comparator.

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

6 Consideration of the evidence

Sponsor hearing

- 6.1 The sponsor requested a hearing for this item. The sponsor reiterated its request for consideration under the Rule of Rescue. The sponsor acknowledged the limitations of the naïve indirect comparison presented, but outlined that no further data are likely to become available.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (13), health care professionals (3) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with brentuximab vedotin including improved quality of life, the ability to be well enough for an allogeneic SCT, long term disease control and better tolerability than other chemotherapies.
- 6.3 Representatives of the PBAC met with Lymphoma Australia prior to the PBAC meeting, and reported the following key points to the PBAC:
- The current submission requested brentuximab vedotin for a small group of patients who have a high clinical need. Given the limited treatment options available, brentuximab vedotin provides patients with a sense of hope.
 - Patients do not view brentuximab vedotin as a cure, but rather as a highly effective treatment option that may provide a "bridge" to enable some patients to undergo a SCT.
 - The current options for accessing brentuximab vedotin are seen as inequitable because of the high cost of the drug and the variable nation-wide access to the drug through clinical trials or public hospitals.
 - Patients understand the importance of high quality clinical evidence, and that while large clinical trials are not always possible in conditions that affect small patient populations, better trials would have been possible.
 - Brentuximab vedotin may offer greater benefits to the Hodgkin Lymphoma patient population if it were used at an earlier stage of treatment (eg it could change the overall patient lifetime treatment algorithm if used in the first-line setting).

The PBAC noted and welcomed this input.

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

Clinical trials

- 6.4 No direct randomised trials were identified. The submission was based on one naïve comparison:
- Brentuximab vedotin: Study 0003 was a single-arm prospective cohort study (N=102); a subgroup of 45 patients received brentuximab vedotin as first-line treatment post ASCT.
 - Salvage chemotherapy: Data from the Kaloyannidis study and British Columbia registry; patients received salvage chemotherapy in first-line post ASCT.
- 6.5 Details of the studies presented in the submission are provided in the table below.

Trials and associated reports presented in the submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Brentuximab vedotin - observational study		
Study 0003	A pivotal study of SGN-35 in treatment of patients with relapsed or refractory Hodgkin lymphoma. Clinical study report Addendum 1. Key publication Younes A, Gopal AK, et al. "Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma."	20 December 2010. 30 November 2011. <i>Journal of Clinical Oncology</i> 2012; 30(18): 2183-2189.
Salvage chemotherapy – observational studies		
Kaloyannidis 2012	Kaloyannidis P, Voutiadou G, et al. "Outcomes of Hodgkin's lymphoma patients with relapse or progression following autologous hematopoietic cell transplantation."	<i>Biol Blood Marrow Transplant</i> (2012) 18(3): 451-457.
Connors 2013 (British Columbia registry)	Connors JM, MD. Clinical Director, BC Cancer Agency Centre for Lymphoid Cancer, Acting Head, Division of Medical Oncology, University of British Columbia. "Clinical Characteristics and Outcome for Patients with Relapse of Hodgkin Lymphoma after High Dose Chemotherapy and Autologous Hematopoietic Stem Cell Transplantation (ASCT) in British Columbia", unpublished report dated 5 February 2014.	Unpublished report dated 5 February 2014.
Crump 2008	Crump M. Management of Hodgkin lymphoma in relapse after autologous stem cell transplant.	<i>Hematology Am Soc Hematol</i> ; 2008:326 –333.
Martinez 2013	Martinez C, et al. "Identification of prognostic factors predicting outcome in Hodgkin's lymphoma patients relapsing after autologous stem cell transplantation."	<i>Ann of Oncology</i> (2013) 24: 2430-2434.
Moskowitz, 2009	Moskowitz AJ, Perales MA, Kewalramani T, et al. "Outcomes for patients who fail high dose chemoradiotherapy and autologous stem cell rescue for relapsed and primary refractory Hodgkin lymphoma."	<i>British Journal of Haematology</i> (2009), 146 (2): 158–163.
Arai 2013	Arai S, Fanale M, et al. "Defining a Hodgkin Lymphoma Population for Novel Therapeutics after Relapse from Autologous Hematopoietic Cell Transplantation"	<i>Leukemia & Lymphoma</i> . (2013); 54(11): 2531-2533

Source: Table Bi.2-2, ppB-15 – B-19 of the submission.

- 6.6 The key features of the studies are summarised in the following table.

Key features of the included evidence – naïve comparison

Trial	N	Design/ median follow-up or study period	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
Brentuximab vedotin						
Study 0003	102	Prospective single-arm cohort; MC / 37months <i>Recruitment: 2009</i>	High	Relapsed HL post ASCT, any line	OS, PFS	Sub-group used (n=45)
Salvage chemotherapy						
Kaloyannidis dataset	87	IPD; R; MC / 17 months <i>Relapse post ASCT: 1997-2010</i>	High	Relapsed HL post ASCT, 1 st -line	OS; PFS	Used
British Columbia registry	22	IPD; R. / 36 months <i>First ASCT: 1996-2012</i>	High	Relapsed HL post ASCT, 1 st line	OS; PFS	Used
Supportive salvage chemotherapy						
Crump 2008	118	R; O; 1986-2006	High	Relapsed HL post ASCT	OS; PFS	X
Martinez 2013	462	R; O; 1996-2005	High	Relapsed HL post ASCT	OS	X
Moskowitz 2009	71	R; O; 1994-2005	High	Relapsed HL post HDT-ASCT	OS	X
Arai 2013	756	R; O; 1981-2007	High	Relapsed HL post AHCT	PPS; OS	X

Source: compiled during the evaluation

AHCT = autologous hematopoietic cell transplant; ASCT = autologous stem cell transplant; HDT-ASCT = high dose chemoradiotherapy with ASCT; HL = Hodgkin lymphoma; IPD = individual patient data; MC=multi-centre; O=observational; OS=overall survival; PD = disease progression; PFS=progression-free survival; PPS = post progression survival; R = retrospective.

- 6.7 The ESC noted the differences between the studies and the years in which patient data were collected as outlined in the table above. The ESC considered that it was difficult to interpret the comparative treatment effect given the heterogeneity of the data because of:
- confounding in relation to the participant population. The patients recruited into the studies may have received different first-line chemotherapy prior to the primary ASCT.
 - different treatments in the intervention groups. The ESC noted the improvements over time in transplant outcomes and the changes in therapies used post ASCT and supportive care. The PBAC considered that this may bias the estimates of effect in favour of the comparator.
- 6.8 The definition of overall survival in the British Columbia registry was different from that in the other two datasets used in the naïve comparison (Study 003 and Kaloyannidis).
- 6.9 Study 0003 collected data from 2009-2010 and this may limit its applicability to the intended PBS population. The ESC considered that newer first-line treatments for Hodgkin Lymphoma may be more effective than older treatments, and therefore the patients who currently meet the criteria for brentuximab vedotin may be different (with a different risk profile) to those who were recruited to Study 0003.

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

Comparative effectiveness

- 6.10 The table below presents the key results from Study 0003 used for the brentuximab vedotin arm. These were extracted from the Clinical Study Report of Study 0003.

Results of clinically relevant outcomes in Study 0003 (Brentuximab vedotin only) (CSR data)

	ITT	Number of tx post ASCT		1 st post ASCT	
		1 st post ASCT	≥2 nd post ASCT	+2 nd SCT	No 2 nd SCT
N	102	45	57	7	38
PFS					
Events, n (%)					
Median, months (95% CI)					
OS					
Events, n (%)					
Median, months (95% CI)					

Source: Table 14.2.27.1, p258; Table 14.2.27.4, p261; Table 14.2.33.1, p279; Table 14.2.33.4, p282; Table 14.2.33.7, p285; Table 14.2.33.8, p286; Table 14.2.27.7, p264 of Study 0003 CSR;

ASCT = autologous stem cell transplant; CSR = clinical study report; IPD = individual patient dataset; mths = months; NR = not reported; PFS = progression free survival; SCT = stem cell transplant; tx = treatment; wks = weeks.

- 6.11 These data suggested that brentuximab vedotin might be more effective in first-line post ASCT than in later lines of treatment. The comparison between patients with or without allogeneic SCT consolidation was more difficult to interpret, due to the small size of the subgroups and the risk of selection bias. Analyses to estimate the effect size were not possible during evaluation.
- 6.12 The table below presents the key results from the non-randomised studies used in the submission. These were extracted from the individual patient datasets.

Key results across the non-randomised studies for first-line post ASCT- IPD

Study	BV (IPD Sept 2014)	Salvage chemotherapy			HR (95% CI)
		Kaloyannidis	British Columbia	Combined	
N					
Median follow-up (months)					
median PFS (months)					a
median OS (months)					

Source: Comparator IPD efficacy datasets – ICON final-2014.xlsx; Data_request_Sept2014.xls; Table Bi.3-5, pB-27 of the submission; Table Bi.3-10, ppB-33 to B-34 of the submission.

ASCT = autologous stem cell transplant; BV = brentuximab vedotin; CI = confidence interval; IPD = individual patient dataset; PFS = progression free survival; OS = overall survival.

^a The dataset for the British Columbia did not specify if patient had progressed, therefore the median PFS was not computed during evaluation. The HR for PFS was based on brentuximab vedotin and the Kaloyannidis study only.

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

Comparative harms

- 6.13 The table below presents the key adverse events from Study 0003.

Summary of grade 3 or 4 key adverse events in Study 0003 (CSR for ITT, IPD for 1st line treatment)

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Study	ITT (CSR)	ITT (IPD Sept 2014)	1 st line post ASCT	1 st line post ASCT	
				With 2 nd SCT	No 2 nd SCT
N	102	102	45	7	38
Peripheral neuropathy					
Neutropenia					
Thrombocytopenia					
Anaemia					

Source: Table Bi.6-12, pB-82 of the submission, Table 12-6 of the Clinical study report.

ASCT = autologous stem cell transplant; CSR= clinical study report; IPD = individual patient data; ITT = intention to treat; SCT = stem cell transplant.

- 6.14 The ESC noted that brentuximab vedotin is associated with a rare risk of Progressive Multifocal Leukoencephalopathy (PML).
- 6.15 The submission did not present a comparative safety analysis because safety endpoints were not available from the two comparator group datasets (Kaloyannidis and the British Columbia registry). However, the PSCR provided safety data from several cohorts of different treatments for Hodgkin Lymphoma and other cancers. This is presented in the table below.

Safety comparison of BV versus older post ASCT salvage chemotherapy

Adverse event	% patients who experienced at least 1 event				Incidence per cycles delivered Spencer 2007 (116 cycles)****
	Gemcitabine/ Vinorelbine Product information*	Venkatesh 2004 (N=27)***	Czyz 2013%	BV study 0003*	
Thrombocytopenia, gr 4	NR	11.1% (3/27)	NR	████████	Comparative results for BV study 0003 were extracted from the IPD data based on █████ cycles of BV delivered in the N=45 subgroup. The following 2 comparisons were able to be undertaken: Thrombocytopenia, gr 4: BV: █████ Gem-vino: 15% Neutropenia, gr 4: BV: █████ Gem-vino: 13% Infection gr 3/4: Gem-vino: 6% (no comparable term in BV study)
Thrombocytopenia, gr 3	NR	22.2% (6/27)	NR	████████	
Subtotal		33%	35.1%	████████	
Neutropenia, gr 4	6% / 28.4%	3.7% (1/27)	NR	████████	
Neutropenia, gr 3	19.3% / 25.2%	25.9% (7/27)	NR	████████	
Subtotal	25.3% / 54%	30%	40.5%	████████	
Leukopenia, gr 4	NR	0.0% (0/27)	NR	████████	
Leukopenia, gr 3	NR	14.8% (4/27)	NR	████████	
Subtotal		15%	NR	████████	
Anaemia, gr 4	NR	0.0% (0/27)	NR	████████	
Anaemia, gr 3	NR	7.4% (2/27)	NR	████████	
Subtotal		7%	35.1%	████████	
Febrile neutropenia, gr 3/4	NR	3.7% (1/27) (cycle 2)	11%	████████	
PS neuropathy, gr 3	NR	0.0% (0/27)	NR	████████	
Elevated ALT, gr 3	NR	3.7% (1/27)	NR	████████	
Venous thrombosis gr 3	NR	0.0% (0/27)	NR	████████	
Reduced cardiac func. gr 3	NR	3.7% (1/27)	NR	████████	

Source: PSCR, Table 2, p6.

Notes:

‡ For the N=45 subgroup.

* PI data collected in NSCLC, pancreatic, breast, bladder, and ovarian cancer trials.

*** US study: 62% of HL patients in the study were relapsed or refractory after primary ASCT, thus relevant to the requested PBS-listing.

% Czyz Poland 2006-2011 used gemcitabine, cisplatin (n=16) and gemcitabine, vinorelbine (n=21).

**** Australian pilot study: HL/NHL relapsed or refractory after at least 1 line of chemo; but only 12/40 had undergone prior ASCT; results not reported separately. Thus this study included mainly patients earlier in the treatment algorithm than the requested PBS population.

- 6.16 In the absence of safety data being available from Kaloyannidis and the British Columbia registry, the submission's economic evaluation used adverse event data from Czyz 2013 to inform the comparator group in the economic evaluation (for safety only). However the PSCR stated: "the sponsor noted during the preparation of this PSCR that the Venkatesh 2004 population is a better match to the BV Study 0003 population", and the PSCR used the adverse event rates from Venkatesh 2004 in its revised economic evaluation. Evidence was not provided to support the claim that the Venkatesh 2004 population is a better match to the Study 0003 population than Czyz 2013. The comparability of both population and drug use need to be considered. Patients in the study by Venkatesh used only gemcitabine, while those in Czyz used gemcitabine plus cisplatin or gemcitabine plus vinorelbine.

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

Benefits/harms

6.17 A summary of the comparative benefits for brentuximab vedotin versus salvage chemotherapy is presented in the table below. The redacted table below shows a comparison of brentuximab vedotin compared to the main comparator. The size of the OS and PFS benefit was uncertain due to the naïve comparison methodology and the small patient numbers in the subgroups relevant to the comparison, and as a result the superiority claim is not adequately supported.

Summary of comparative benefits for brentuximab vedotin and salvage chemotherapy

Study	BV (IPD Sept 2014)	Salvage chemotherapy			Absolute difference	HR (95% CI)
		Kaloyannidis	BC registry	Combined		
N						
Median follow-up (months)						
median PFS (months)					a	a
median OS (months)						

Source: Comparator IPD efficacy datasets – ICON final-2014.xlsx; Data_request_Sept2014.xls; Table Bi.3-5, pB-27 of the submission; Table Bi.3-10, ppB-33 to B-34 of the submission.

BC = British Columbia; BV = brentuximab vedotin; CI = confidence interval; NC = not calculable; PFS = progression free survival; OS = overall survival.

^a The dataset for the British Columbia did not specify if patient had progressed, therefore the median PFS was not computed during evaluation. The HR for PFS was based on brentuximab vedotin and the Kaloyannidis study only.

6.18 Based on a naïve indirect comparison with no common comparator, the comparison of brentuximab vedotin and salvage chemotherapy resulted in:

- An estimated 14.4 months additional median PFS (based on the Kaloyannidis study only for the comparator group). The ESC considered that this estimate was unreliable due to the lack of comparability in the studies used to provide this estimate.
- The ESC noted that the impact on OS was unknown.
- Unknown difference in adverse events. The ESC noted that adverse event rates will vary significantly depending on the type of salvage chemotherapy used.

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

Clinical claim

6.19 The submission claimed that brentuximab vedotin was superior in terms of comparative effectiveness and superior in terms of comparative safety over salvage chemotherapy. The evaluation considered that this was not adequately supported. There was no direct evidence available for the comparative efficacy of brentuximab vedotin and the nominated comparator. Therefore, the submission used a naïve indirect comparison using individual patient data. There could have been bias favouring brentuximab vedotin, and the effect size may be smaller than that presented in the submission.

6.20 In particular, the ESC noted that there were several key systematic differences between the studies including differences in exposure to pre-primary ASCT salvage

chemotherapy, baseline performance status, age, sex and time to relapse post primary ASCT. The ESC considered that these significant imbalances in key prognostic factors made it difficult to isolate the true treatment effect from the many sources of differential confounding. Further, the studies used different definitions for the clinically relevant outcomes. The PSCR argued that the overall cumulative bias favours the comparator, suggesting that the efficacy advantage of brentuximab vedotin is likely to be conservative. The ESC considered that whilst data for some prognostic factors and confounders were available from the individual patient datasets, the imbalance and overall direction of the bias associated with these differences was unclear as some confounders were not common to all trials whilst others were not collected.

- 6.21 The primary efficacy evaluation was based on the subgroup of patients from Study 0003 who received treatment in the first-line post ASCT setting, while the requested PBS listing would allow use in the second- or later-line post ASCT patient populations.
- 6.22 The ESC considered that the comparative safety was difficult to determine:
- The submission did not present any safety outcomes for the comparator arm on the basis that no safety endpoints were available from Kaloyannidis or the British Columbia registry.
 - The PSCR provided a safety comparison using data from Venkatesh 2004, Czyz 2013 and Spencer 2007. These studies were not included in the submission's assessment of comparative efficacy. Further, the PSCR didn't assess the exchangeability of these studies with Study 0003. The ESC considered that the safety information from these small cohorts was difficult to compare in view of patients, treatment type, time and place.

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

Economic analysis

- 6.23 The submission presented a stepped economic analysis based on a naïve comparison of non-randomised studies. The economic evaluation was a cost-utility analysis.

Summary of model structure and rationale

Component	Summary
Time horizon	13 years in the base case versus a maximum of 56 months in trial
Outcomes	LYG and QALYs
Methods used to generate results	Kaplan Meier estimates
Health states	Model used 3 health states of Progression free; progressive disease; death
Cycle length	Month
Transition probabilities	Kaplan Meier estimates from individual patient datasets.

Source: compiled during the evaluation.

LYG = life years gained; QALY = quality adjusted life years.

- 6.24 The economic model only considered evidence in first-line post ASCT. This was inconsistent with the proposed listing.

- 6.25 The comparator arm of the economic evaluation relied on data combined from the Kaloyannidis and British Columbia registries. The ESC considered that the British Columbia registry should not have been included in the base-case of the economic evaluation because it defined overall survival differently to Study 0003 and Kaloyannidis. Further, this method aggregated patients with different baseline prognoses who differed with regards to key prognostic confounders of treatment effect and had differences in their overall treatment of Hodgkin Lymphoma.
- 6.26 The ESC noted that the model was very sensitive to the time horizon used. The maximum follow-up of Study 0003 was 56 months (median follow-up of 37 months). This was extrapolated to 13 years using Kaplan Meier estimates from the two registries (Kaloyannidis and British Columbia, which both had 13 year follow-up data available). The extrapolation of brentuximab vedotin efficacy was not conservative because even though the rate of decline of PFS was assumed to be the same as the comparator after 56 months, the starting point was higher – mathematically this implied a continuing treatment effect beyond the study duration though the model curves do eventually merge. This was tested in sensitivity analyses of the time horizon.
- 6.27 The ESC noted that the submission used utilities that were derived from direct elicitation (Time Trade-Off) based on 9 health state descriptions. These health states were condensed into 3 states for the purpose of the economic model. The ESC considered this reasonable.
- 6.28 Whilst the cost utility model has been adjusted for some of the prognostic factors that are not balanced between the studies used in the naïve comparison, the ESC noted that this does not control for other differences that were either partially collected or not observed at all.
- 6.29 The table below presents the key drivers of the economic model.

Key drivers of the model

Description	Method/Value	Impact
% patients consolidated with SCT	Assumption made in the submission, base case = 30%	High, favoured brentuximab vedotin
% receiving concomitant G-CSF with brentuximab vedotin	Based on Study 0003, base case = 30% (100% for salvage chemotherapy)	Medium, favoured brentuximab vedotin
Proportion of patients treated in public/private	Submission assumed 80/20	Low, favoured brentuximab vedotin

Source: compiled during the evaluation.

G-CSF = granulocyte-colony stimulating factor; SCT = stem cell transplant.

- 6.30 The table below outlines the results of the stepped economic evaluation presented in the submission.

Results of the submission's stepped economic evaluation

Step and component	Brentuximab vedotin	Salvage chemotherapy	Increment
Step 1: trial-based costs and outcomes			
With SCT consolidation (30%)			
Costs	\$ [REDACTED]	\$19,717	\$ [REDACTED]
Life years gained	2.77	2.09	0.68
ICER SCT consolidation			\$ [REDACTED]
Without SCT consolidation (70%)			
Costs	\$ [REDACTED]	\$19,717	\$ [REDACTED]
Life years gained	2.21	1.79	0.42
ICER without SCT consolidation			\$ [REDACTED]
Step 1 weighted			
Costs	\$ [REDACTED]	\$19,717	\$ [REDACTED]
Life years gained	2.38	1.88	0.50
Incremental cost/extra life year gained			\$ [REDACTED]
Step 2: drug-related costs only; timeframe = 13 years			
Costs	\$ [REDACTED]	\$19,717	\$ [REDACTED]
Life years gained	5.03	3.40	1.64
Incremental cost/extra life year gained			\$ [REDACTED]
QALY	2.85	1.85	1.00
Incremental cost/extra QALY			\$ [REDACTED]
Step 3: modelled evaluation (all costs & full timeframe)			
With SCT consolidation (30%)			
Costs	\$ [REDACTED]	\$138,463	\$ [REDACTED]
Life years gained	6.70	4.20	2.50
QALY	4.62	2.39	2.22
ICER, with SCT consolidation			
ICER/LY gained			\$ [REDACTED]
ICER/QALY			\$ [REDACTED]
Without SCT consolidation (70%)			
Costs	\$ [REDACTED]	\$60,850	\$ [REDACTED]
Life years gained	4.32	3.05	1.27
QALY	2.09	1.62	0.47
ICER, without SCT consolidation			
ICER/LY gained			\$ [REDACTED]
ICER/QALY			\$ [REDACTED]
Step 3: Weighted			
Costs	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
LY gained	5.03	3.4	1.64
Incremental cost/extra life year gained			\$ [REDACTED]
QALY	2.85	1.85	1.00
Incremental cost/extra QALY			\$ [REDACTED]

Source: Table D.5.3, pD-32 of the submission, Section_D_brentuximab vedotin_Adcetris_RR_HL post ASCT_CE Model_March2015 PBAC.xlsm.

ICER = incremental cost effectiveness ratio; LY = life year; QALY = quality adjusted life year; SCT = stem cell transplant.

6.31 The submission estimated that the brentuximab vedotin would result in an incremental cost of \$75,000 – \$105,000 and 1.64 incremental discounted life years and 1.0 incremental discounted quality adjusted life years (QALY), resulting in a cost per life year of \$45,000 – \$75,000 and a cost per QALY of \$75,000 – \$105,000.

6.32 The submission included a scenario analysis in which patients only continue

treatment beyond four cycles if they have a Complete Response, rather than a Partial Response as proposed in the restriction. This scenario analysis resulted in an ICER of \$45,000 – \$75,000, using the submission’s model (compared with \$105,000 – \$200,000 in the submission’s base case). However, in the economic model, only the costs of treatment were adjusted when the continuation rule was applied, not the outcomes. The submission stated that survival outcomes were not adjusted because it was assumed that the clinical benefit is experienced within those patients who had a Complete Response. The Pre-PBAC response further stated that the continuation rule is unlikely to materially alter the outcomes because patients with Complete Response contribute the majority of the PFS benefit and substantial OS benefit. However, the evaluation considered that it was inappropriate for the cost impacts of the continuation rule to be modelled but not the QALYs. The PBAC considered that the information in the Pre-PBAC response did not adequately justify the claim that the benefit of brentuximab vedotin was primarily confined to patients who achieved a Complete Response after 4 cycles.

6.33 The submission’s model assumed that 30% of patients in both treatment groups would receive allogeneic SCT consolidation. However in Study 0003, 15.5% of patients in the first-line post ASCT sub-group received allogeneic SCT consolidation. Further, in the combined comparator dataset 16% of patients who were treated with salvage chemotherapy received allogeneic SCT consolidation. The justification provided for using a higher rate in the model was:

- A Victorian medical records study in which 52% of patients (9/17) who received systemic salvage treatment underwent a second SCT. Four of the 17 patients (24%) underwent immediate allogeneic SCT consolidation following first-line salvage chemotherapy post ASCT. It was unclear to the evaluators when the second SCT took place for the remaining patients.
- 23 face-to-face interviews in which specialists stated that the estimate from the Victorian medical records is “roughly application to the rest of Australia”.
- An advisory board meeting in which it was noted that 25-30% of patients would have a second SCT, and that a “higher proportion (was) expected with brentuximab vedotin”.

The evaluation considered that the model’s assumption that 30% of patients in both treatment groups would receive allogeneic SCT consolidation was not adequately justified. The ICER is sensitive to this assumption. If the rate of second SCT from Study 0003 (15.5%) is applied to both treatment arms, the ICER increases from \$75,000 – \$105,000 (per step 3 from table below) to \$105,000/QALY – \$200,000/QALY.

6.34 A revised economic model was presented in the PSCR. The changes to the model are outlined in the table below.

Comparison of the base case presented in the submission and the PSCR

Step	Submission	PSCR	ICER
Base case ICER from submission			\$ [REDACTED]
1. Clinical data included	Individual patient datasets	Individual patient dataset; 4 patients excluded. The ESC considered that this was appropriate.	\$ [REDACTED]
2. Source of adverse events for the comparator group	Czyz 2013	Venkatesh 2004. The PSCR argued that the population from Venkatesh 2004 is a better match to Study 0003 population. Small impact, but the ESC considered that it was unclear whether this is reasonable in view of the different chemotherapy regimens used, which clearly influences ADEs	from \$ [REDACTED] to \$ [REDACTED]
3. Comparator	Multi-agent chemotherapy regimens only (n=109)	Multi-agents regimens and single-agent chemotherapy. 12 patients with single agent gemcitabine, vinorelbine or lomustine are now included. (n = 121). The ESC considered that this was reasonable.	from \$ [REDACTED] to \$ [REDACTED]
4. Proportion of patients receiving SCT consolidation	30% in both treatment groups	35% of BV patients would receive SCT consolidation vs. 25% in patients receiving salvage chemotherapy. The ESC considered that this may not be reasonable.	from \$ [REDACTED] to \$ [REDACTED]
Cumulative total of all 4 changes – PSCR's revised base case			\$ [REDACTED]

Source: extracted during evaluation.

PSC = Pre-Sub-Committee response; BV = brentuximab vedotin; BSC = best supportive care.

6.35 The submission's base case ICER of \$75,000 – \$105,000 was revised in the PSCR to \$75,000 – \$105,000. The main reason for this reduction was an optimistic assumption regarding the proportion of patients who would receive an allogeneic SCT. The submission assumed that 30% of patients in both groups would receive an allogeneic SCT consolidation, while the PSCR used differential rates between the two groups, which were:

- 35% of patients in the brentuximab vedotin group. The PSCR stated this was based on Advisory Board advice.
- 25% in the comparator group. The Pre-PBAC response outlined that this was based on Victorian medical records, advisory board advice and interviews with haematologists.

The ESC considered that these assumptions were not conservative, were based on very small numbers and were not adequately justified in the PSCR. Further, the higher efficacy of brentuximab vedotin in patients who receive SCT consolidation was based on a sub-group of 7 patients, and this sub-group analysis may have been highly confounded.

6.36 The submission presented different scenario analyses and some univariate sensitivity analyses, as shown in the table below. The table below also presents sensitivity analyses based on a scenario in which the first three of the PSCR's proposed changes are accepted, but not the differential proportion of patients receiving SCT consolidation. This results in an ICER of \$75,000 – \$105,000 (SA 1). In addition to these three changes, if the comparator group were based on data from Kaloyannidis only, the ICER would be \$75,000 – \$105,000 (SA 2). The information based on the PSCR's revised base case is shaded grey.

Results of sensitivity analyses based on the submission's model and PSCR's revised economic model (shaded grey)

	Δ costs	Δ QALY	ICER	
Base case (30% patients consolidated with 2 nd SCT)	\$ [REDACTED]	0.995	\$ [REDACTED]	
Sensitivity analyses – using submission's model				
100% patients consolidated with 2 nd SCT	\$ [REDACTED]	2.22	\$ [REDACTED]	
0% patients consolidated with 2 nd SCT	\$ [REDACTED]	0.469	\$ [REDACTED]	
Time horizon = 8 years (base case = 13 years)	\$ [REDACTED]	0.877	\$ [REDACTED]	
% of BV patients receiving G-CSF = 100% (base case = 30%)	\$ [REDACTED]	0.957	\$ [REDACTED]	
Sensitivity analyses - performed based on the PSCR's first 3 changes being accepted, but with the rate of 2nd SCT remaining at 30% in both arms per the submission's base case				
SA 1 (PSCR1+2+3)	2 nd SCT rates: 30% both arms (i.e. first three of the PSCR's changes accepted)	\$ [REDACTED]	1.06	\$ [REDACTED]
SA 2	2 nd SCT rates: 30% both arms + Kaloyannidis data only	\$ [REDACTED]	1.11	\$ [REDACTED]
SA 3	2 nd SCT rates: 30% both arms + Kaloyannidis data only, 8 year time horizon	\$ [REDACTED]	0.99	\$ [REDACTED]
SA 4	2 nd SCT rates: 30% both arms + Kaloyannidis data only, 5 year time horizon	\$ [REDACTED]	0.70	\$ [REDACTED]
SA 5	2 nd SCT rates: 30% both arms + Kaloyannidis data only, 3 year time horizon	\$ [REDACTED]	0.47	\$ [REDACTED]

Source: Table D.5.4, pD-33; Table D.5.5, pD-34 of the submission Table 2, p5 of the PSCR, and calculated.

BV = brentuximab vedotin; G-CSF = granulocyte-colony stimulating factor; SCT = stem cell transplant; SA = sensitivity analysis; PSCR = Pre Sub Committee Response; QALY = quality adjusted life years; ICER = incremental cost effectiveness ratio; CR = complete response.

6.37 Along with analyses performed during evaluation, the results showed that the key influences on the model were the proportion of patients being consolidated with an allogeneic SCT, the time horizon of the model and the proportion of patients receiving G-CSF. While it appeared that consolidation with an allogeneic SCT resulted in more favourable outcomes, and as a result meant that brentuximab vedotin was more cost-effective in this patient population, the low patient numbers that were used to inform efficacy in this sub-group limited the reliability of this conclusion.

6.38 While the costs of adverse events and SCT treatment may have been underestimated by the model, variation in these parameters did not substantially alter the ICER. Utility variations also made little difference to the ICER.

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

6.39 The drug cost was estimated to be \$ [REDACTED] per patient per course based on 2.86 x 50 mg vials per cycle (using an average body weight of 73.8 kg) and 9.8 cycles per treatment course and 80% of patients being treated in a public hospital.

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

Estimated PBS usage & financial implications

6.40 This submission was not considered by DUSC. The submission followed an epidemiological approach and forecasted the number of eligible patients using the number of ASCTs conducted in Australia for Hodgkin Lymphoma. The submission accounted for the use of brentuximab vedotin in the prevalent population and assumed an uptake rate of 80%.

Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated extent of use					
Number treated					
Vials ^a					
Estimated net cost to PBS/RPBS/MBS					
Net cost to PBS/RPBS	\$	\$	\$	\$	\$
Net cost to MBS	\$	\$	\$	\$	\$
Estimated total net cost					
Net cost to PBS/RPBS/MBS	\$	\$	\$	\$	\$

^a Assuming ■ vials per cycle and ■ cycles per treatment course as estimated by the submission.

Source: Table E-6, p14 of the submission; Table E-12, p22 of the submission.

- 6.41 The redacted table above shows that the number of patients treated with brentuximab vedotin is estimated to be less than 10,000 per year at a net cost to the PBS of less than \$10 million per year.
- 6.42 There was potential for the net cost/year for the PBS to be greater or less than the estimate in the submission due to the:
- Unclear number of eligible patients (higher or lower),
 - Possible underestimate of number of patients likely to be treated in private hospitals; this would underestimate the cost per vial, and
 - Incorrect inclusion of aciclovir in cost offsets (small impact on overall cost).

Rule of Rescue

- 6.43 The submission stated that the patient population was likely to be small (<■ per year) and requested the PBAC consider whether the Rule of Rescue is applicable. Four factors must apply concurrently in order for the Rule of Rescue to be relevant. The first factor is that no alternative exists in Australia to treat patients with the specific condition. The evaluation considered that brentuximab vedotin may not meet this factor because alternative therapies are available, including salvage therapy with gemcitabine and vinorelbine. The PSCR stated that this was not a suitable alternative due to the cumulative toxicity of gemcitabine and vinorelbine in addition to the poor long term survival and cure rate seen with this therapy. The PSCR therefore argued that brentuximab vedotin does fulfil factor one of the Rule of Rescue.

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

7 PBAC Outcome

- 7.1 The PBAC did not recommend extending the listing of brentuximab vedotin to the treatment of relapsed or refractory Hodgkin Lymphoma following ASCT because the clinical place was not adequately defined and the submission’s estimate of cost-effectiveness was not reliable. The PBAC was also concerned that the proposed range of restrictions would exclude some patient groups who could derive significant benefit from this drug.
- 7.2 The PBAC welcomed the input received from individuals and organisations in support

of the submission, including at the consumer hearing. The comments highlighted the sense of hope that an active treatment can provide, and that brentuximab vedotin improves quality of life during remission.

- 7.3 The PBAC considered that there is a high clinical need for treatments for Hodgkin Lymphoma, including in parts of the treatment algorithm other than that applied for by the sponsor. Specifically the PBAC noted that:
- a) brentuximab vedotin is also TGA registered for use in relapsed or refractory Hodgkin Lymphoma following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option. The PBAC considered this to be an area of high clinical need. However, the sponsor did not seek listing in this patient population.
 - b) there are on-going trials of brentuximab vedotin earlier in the Hodgkin Lymphoma treatment algorithm. For example, the PBAC noted the Aethera trial, an on-going phase 3 study in patients at risk of progression following a primary ASCT.¹ This trial was designed to evaluate whether early treatment with brentuximab vedotin post ASCT can prevent progression. There are also on-going trials in first-line treatment of Hodgkin Lymphoma.² The PBAC considered that use in these earlier settings may: result in greater overall benefit than use in later lines; reduce the need for SCT and re-treatment; and enable more patients to be treated. Therefore the PBAC considered that the treatment algorithms for patients with poor prognosis Hodgkin lymphoma are likely to change over the next few years as new trial data emerge.
- 7.4 With regard to the patient population requested in the submission, the PBAC considered that the restriction should allow use in relapsed/refractory patients at any line post ASCT. The PBAC noted that use in later-lines will diminish once the prevalent population has been treated.
- 7.5 Further, the PBAC considered that the restriction could include a ‘continuation rule’ whereby only patients with a Complete Response can continue to use brentuximab vedotin after the fourth cycle (presented as Option 1b in the pre-PBAC response). To pursue this option, the sponsor would need to justify the claim that the benefit of brentuximab vedotin was primarily confined to patients who achieved complete response after 4 cycles. The PBAC considered that such a strict continuation rule would disadvantage patients who achieved a partial response with brentuximab but who have no allogeneic SCT option.
- 7.6 The PBAC considered that the restriction should not limit use to patient’s whose treatment has a curative intent, noting that this would be ambiguous and would preclude use in some patients who would derive improvements in quality of life. The

¹ Moskowitz CH, et al. The Aethera trial: results of a randomized, double-blind, placebo-controlled phase 3 study of brentuximab vedotin in the treatment of patients at risk of progression following autologous stem cell transplant for Hodgkin lymphoma. Program and abstracts of the 56th ASH Annual Meeting and Exposition, December 6-9, 2014; San Francisco, California. Abstract 673.

² A randomized, open-label, phase 3 trial of A+AVD Versus ABVD as frontline therapy in patients with advanced classical Hodgkin Lymphoma (ECHELON-1). NCT01712490.

A randomized phase III study of brentuximab vedotin for newly diagnosed high-risk classical Hodgkin Lymphoma (cHL) in children and adolescents. NCT02166463.

PBAC recommended that the Authority application should include the following information:

- a histology report including evidence of the tumour's CD30 positivity;
- the date of the primary ASCT; and
- a declaration about whether the disease is relapsed or refractory.

The PBAC considered that many of the prescriber instructions in the requested restriction were unnecessary (eg. timing of biopsy, dates of diagnoses, dates of chemotherapy, dates of assessment of relapsed/refractory). Further, the PBAC considered that it may be desirable to include a requirement for prescribers to declare whether the patient is planned to have an allogeneic SCT.

- 7.7 The PBAC agreed that salvage therapy consisting of gemcitabine plus vinorelbine was the appropriate comparator.
- 7.8 The PBAC considered that the data presented in the submission were of poor quality with a high risk of bias. The submission was based on a naïve comparison of datasets with small sample sizes and sparse event data
- 7.9 The PBAC considered that brentuximab vedotin is an effective treatment, but that the magnitude of the gains in PFS and overall survival were difficult to quantify given the poor quality of the data. The PBAC considered that brentuximab vedotin is not a cure, but rather provides a “bridge” to enable some patients to undergo a potentially curative allogeneic SCT. It also provides palliative benefit to responding patients who do not have an allogeneic SCT option.
- 7.10 The PBAC considered that brentuximab vedotin is less toxic than salvage therapy, particularly if some patients only use 4 cycles given that the neurotoxicity associated with brentuximab vedotin can develop after longer exposure to the drug. The PBAC noted that 18% of patients enrolled in the study (Study 0003) completed 16 cycles of treatment and considered that this supported the overall safety claim of the submission.
- 7.11 The PBAC considered that the submission's estimate of the cost-effectiveness of brentuximab vedotin was not reliable. The PBAC considered that an 8 year time horizon, rather than the submission's 13 year time horizon, would be more appropriate. The PBAC also considered that the proportion of patients assumed to receive allogeneic SCT consolidation in the model was not adequately justified in the submission or the Pre-PBAC response.
- 7.12 The PBAC considered that the Rule of Rescue is not relevant to this submission because alternative therapies are available. The PBAC considered that a therapy with a lower response rate is still a treatment alternative. Further, the PBAC did not consider that brentuximab vedotin provides a ‘worthwhile clinical improvement sufficient to qualify as a rescue from the medical condition’. Therefore, the submission does not meet two of the four factors that are required to apply concurrently in order for the Rule of Rescue to be relevant.
- 7.13 The PBAC considered that utilisation estimates in the submission were reasonable for the restriction proposed in the submission, except that uptake was likely to be higher than 80%.

7.14 The PBAC considered that the following would need to be addressed in a major re-submission:

- incorporate changes to the restriction as outlined in paragraph 7.5.
- use the combined data from the Kaloyannidis and British Columbia registries to inform the effectiveness of the comparator arm in the economic model, per the submission. The PBAC noted the issues raised by the ESC about combining the two datasets, but considered that the combined data were more informative.
- use an 8 year time horizon in the base case of the economic model.
- provide more reliable data on the rates of consolidation with an allogeneic SCT.
- The PBAC considered that an ICER, derived from the re-specified base case, should be between \$50,000 and \$60,000/QALY in order for brentuximab vedotin to be acceptably cost-effective.
- update the financial estimates to include a more appropriate uptake rate. .

Should the sponsor wish to pursue the inclusion of a continuation rule in the restriction, the claim that the benefit of brentuximab vedotin was primarily confined to patients who achieved complete response after 4 cycles would need to be strongly justified. Further the financial estimates would need to be updated.

7.15 A major re-submission would be required to present the data adequately to allow evaluation.

7.16 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:

Rejected

8 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.

9 Sponsor's Comment

The sponsor is disappointed with the PBAC's decision but remains committed to working with the PBAC, the clinical community and the patient organisations to enable the listing of brentuximab vedotin on the PBS for patients with relapsed or refractory CD30+ Hodgkin Lymphoma following ASCT.