SMC2762

brentuximab vedotin powder for concentrate for solution for infusion (Adcetris®)

Takeda UK Ltd

04 July 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission under the orphan equivalent medicine process

brentuximab vedotin (Adcetris®) is accepted for use within NHSScotland.

Indication under review: for adult patients with previously untreated CD30+ Stage III or IV Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD).

In an open-label, phase III study, six cycles of brentuximab vedotin (in combination with AVD) compared with six cycles of ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine), significantly improved modified progression-free survival in adults with previously untreated CD30+ Stage III or IV HL.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Co-Vice Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Brentuximab vedotin is an antibody drug conjugate that binds to and enters CD30-expressing tumour cells, where proteolysis releases monomethyl auristatin E (MMAE), a cytotoxic that disrupts the tubulin microtubule network, inducing cell death. Brentuximab vedotin is given by intravenous infusion, 1.2 mg/kg (to a maximum of 120 mg) on days 1 and 15 of 28-day cycles for six cycles in combination with doxorubicin, vinblastine and dacarbazine (AVD).[1-3]

1.2. Disease background

Hodgkin lymphoma is characterised by malignant Hodgkin and Reed Sternberg cells surrounded by non-malignant inflammatory cells. The two main types are classical and nodular lymphocyte predominant, based on malignant cell immunohistology and microscopic appearance. The classical subtype expresses CD30, and accounts for 95% of all cases. Clinical symptoms, which are present in about two thirds of patients, include B symptoms (fever, night sweats, and unexplained weight loss >10% in 6 months), fatigue, pruritus and alcohol-induced pain.[2]

1.3. Treatment pathway and relevant comparators

In Scotland, adults with previously untreated Stage III or IV CD30+ Hodgkin lymphoma who are less than 60 years old and have a good performance status generally initiate treatment with one of two chemotherapy regimens. Patients can receive ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) given via the RATHL study protocol, in which patients with positive disease (Deauville score 4 or 5) on positron emission tomography (PET) after the second cycle, escalate to receive a further four cycles of escBEACOPDac (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, dacarbazine and prednisolone) and patients with negative disease (Deauville score 1 to 3) de-escalate to receive four further cycles of AVD. Alternatively, patients can commence treatment with escBEACOPDac given via the HD18 / AHL 2011 study protocols, where those with positive disease on PET after the second cycle receive a further four cycles and those with negative disease receive a further two cycles or switch to four cycles of AVD or ABVD. The choice between these routes is a complex clinical decision influenced by patient and disease factors.[4]

1.4. Category for decision-making process

Eligibility for a PACE meeting

Brentuximab vedotin meets SMC orphan equivalent criteria in this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence is from the ECHELON-1 study, detailed in Table 2.1.[2, 3, 5]

Table 2.1. Overview of relevant study

Criteria	ECHELON-1[2, 5]
Study design	International, open-label, phase III study.
Eligible patients	Adults (≥18 years) with classical Hodgkin lymphoma (Ann Arbour Stage III or IV) not previously treated with systemic chemotherapy or radiotherapy, who have an ECOG performance status of 0 to 2.
Treatments	Six 28-day cycles of IV treatment on day 1 and day 15 with A+AVD (brentuximab vedotin 1.2mg/kg plus AVD: doxorubicin 25 mg/m^2, vinblastine 6 mg/m^2 and dacarbazine 375 mg/m^2) or ABVD (bleomycin 10 units/m^2 plus AVD).
Randomisation	Randomisation was stratified by IPFP risk factors (0 to 1 versus 2 to 3 versus 4 to 7), and region (Americas versus Asia versus Europe). Patients were equally assigned.
Primary outcome	Modified progression-free survival (mPFS), assessed by independent review using Revised Response Criteria for Malignant Lymphoma, and defined as time to disease progression, death from any cause, or modified progression (non-complete response after completion of frontline therapy followed by new anticancer therapy). In intention-to-treat population, which included all randomised patients.
Secondary outcomes	Overall survival, defined as time from randomisation to death from any cause. Complete response and objective response at the end of study treatment. Negative disease on PET scan after Cycle 2.
Statistical analysis	The key secondary outcome, overall survival, was included in a hierarchical testing strategy and assessed only if the primary outcome was significant. Other secondary outcomes were not controlled for multiplicity.

Abbreviations: ECOG = Eastern Cooperative Oncology Group; IPFP = International Prognostic Factor Project; IV = intravenous; PET = positron emission tomography.

At the primary analysis (20 April 2017), the primary outcome, modified progression-free survival (mPFS), significantly improved with A+AVD (brentuximab vedotin plus AVD) compared with ABVD. At an interim analysis (1 June 2021), overall survival (OS) was significantly improved with A+AVD compared with ABVD as the p-value, 0.009, crossed the pre-specified boundary (0.0365). The final OS analysis (11 March 2023) was descriptive. Results are detailed in Table 2.2.[2, 5]

Table 2.2: Results of ECHELON-1 study.[2, 3, 5-7]

	A+AVD (n=664)	ABVD (n=670)
Modified progression-free survival assessed by IRF; cut-off 20 April 2017		
mPFS events, n	117	146
Hazard ratio (95% CI), p-value	0.77 (0.60 to 0.98), p=0.035	
KM estimated mPFS at 3 years	79%	75%
Complete response at end of study treatment by IRF; cut-off 20 April 2017		
Percentage of patients	73%	70%
Relative risk (95% CI)	1.04 (0.97 to 1.11)	
Objective response at end of study treatment by IRF; cut-off 20 April 2017		
Percentage of patients	86%	83%
Relative risk (95% CI)	1.04 (0.99 to 1.09)	
PET negative after cycle 2		
Percentage of patients	89%	86%
Relative risk (95% CI)	1.03 (0.99 to 1.07)	
Overall survival; cut-off 1 June 2021		
Deaths	39	64
Hazard ratio (95% CI), p-value	0.59 (0.40 to 0.88), p=0.009	
KM estimated OS at 6 years	94%	89%

Overall survival; cut-off 11 March 2023		
Deaths	46	69
Hazard ratio (95% CI)	0.62 (0.42 to 0.90)	
KM estimated OS at 8 years	93%	88%

Abbreviations: A+AVD = brentuximab vedotin, doxorubicin, vinblastine and dacarbazine; ABVD = doxorubicin, bleomycin, vinblastine and dacarbazine; CI = confidence interval; KM = Kaplan-Meier; IRF = independent review facility; mPFS = modified progression-free survival; OS = overall survival; PET = positron emission tomography.

2.2. Health-related quality of life outcomes

During study treatment, quality of life was assessed using the following questionnaires: European Organisation for Research and Treatment of Cancer (EORTC) core quality of life (QLQ-C30), Functional Assessment of Chronic Illness Therapy (FACIT) Dyspnoea 10, EQ-5D-3L, and Functional Assessment of Cancer Therapy/Gynaecologic Oncology Group Neurotoxicity subscale (FACT/GOG-NTx). All were assessed at baseline and day 1 of each cycle. During post-treatment follow-up, quality of life was assessed for a further 36 months using EORTC QLQ-C30 and EQ-5D-3L. Compliance was generally high in both groups, ranging from 85% to 98% across the different quality of life instruments.[2, 8]

The European regulator noted that there was no clinically meaningful difference between treatment arms for quality of life outcomes but a trend of unfavourable scores on various subscales and symptom measures of EORTC QLQ-C30/FACIT-Dyspnoea 10 in the A+AVD group compared with ABVD, consistent with the higher frequency of adverse events, including serious adverse events, in the A+AVD group. In post-treatment follow-up, EORTC QLQ-C30 scores returned to at least baseline levels.[2]

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

There were indirect comparisons of six cycles of ABVD in ECHELON-1 study[5-7] versus the RATHL study regimen[9, 10], which commences with two cycles of ABVD and then de-escalates to four cycles of AVD in patients with negative disease on PET or escalates to four cycles of escBEACOPP (which is the same as the escBEACOPDac regimen with dacarbazine replaced by procarbazine). This supports an assumption of equivalent efficacy in the economics analyses. See Table 2.3 for details.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Unanchored indirect comparisons: unadjusted and adjusted
Population	Newly diagnosed adults (≥18 years) with advanced (Stage III or IV) classical Hodgkin lymphoma
Comparators	Six cycles of ABVD versus RATHL protocol (i.e. PET-adapted ABVD)
Studies included	ECHELON-1 (six cycles of ABVD)[5-7]; RATHL Stage III or IV subgroup (two cycles of ABVD then, if disease negative on PET, four cycles of AVD or, if disease positive, four cycles of escBEACOPP)[9, 10]
Outcomes	PFS and OS
Results	**Unadjusted:** Kaplan-Meier curves of PFS and OS of the regimens are similar with some overlap. **Adjusted:** PFS HR 1.01 (95% CI: 0.80 to 1.27); OS HR 0.88 (95% CI: 0.61 to 1.27)

Abbreviations: ABVD = doxorubicin, bleomycin, vinblastine and dacarbazine; AVD = doxorubicin, vinblastine and dacarbazine; CI = confidence interval; escBEACOPP = bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisolone; HR = hazard ratio; OS = overall survival; PET = positron emission tomography; PFS = progression-free survival.

3. Summary of Safety Evidence

The European regulator noted that toxicity of the medicines in the A+AVD and ABVD regimens is established, and no new safety concerns were identified in ECHELON-1. At the 20 April 2017 cut-off, 95% of patients had completed the six-cycle regimens per protocol and median follow-up was 24.6 months. In the respective groups, almost all patients had a treatment-related adverse event: 97% (641/662) and 94% (617/659). Within the A+AVD group, compared with ABVD, there were higher rates of adverse events that were at least grade 3 severity (83% and 66%; treatment-related in 79% and 59%); serious (43% and 27%; treatment-related in 36% and 19%); and associated with a dose modification (64% and 44%).[2, 5]

At the 20 April 2017 cut-off, there were higher rates in the A+AVD group compared with the ABVD of the haematological events: neutropenia (58% versus 45%; grade ≥3, 54% versus 39%), febrile neutropenia (19% versus 7.9%; grade ≥3, 19% versus 7.9%) and anaemia (21% versus 10%; grade ≥3, 8.1% versus 3.8%); and other events: diarrhoea (27% versus 18%; grade ≥3, 2.9% versus 0.8%); abdominal pain (21% versus 10%; grade ≥3, 3.2% versus 0.6%), decreased weight (22% versus 6.1%), decreases appetite (18% versus 12%), bone pain (19% versus 10%) and insomnia (19% versus 12%).[2, 5]

In ECHELON-1, granulocyte colony stimulating factor (G-CSF) was allowed to manage neutropenia. However, after enrolment of about 70% of the study population, the independent data monitoring committee recommended that patients randomised to A+AVD be given prophylactic G-CSF from Cycle 1. In the 83 patients within the A+AVD group who received G-CSF primary prophylaxis, compared with the 579 patients who did not, there were lower rates of febrile neutropenia during the whole study (11% versus 21%) and during Cycle 1 (1% versus 11%); neutropenia of any grade (35% versus 73%) and grade ≥3 (29% versus 70%); grade ≥3 infections (11% versus 18%); and serious adverse events of febrile neutropenia, neutropenia, sepsis, neutropenic sepsis, pyrexia and infection-related events (24% versus 33%).[2]

Peripheral neuropathies are established adverse effects of brentuximab vedotin. At the 20 April 2017 cut-off, within the A+AVD and ABVD groups, 67% versus 43% reported these as adverse events, including peripheral sensory neuropathy (27% versus 16%) and peripheral neuropathy (26% versus 13%). Patients with peripheral neuropathy at the end of frontline treatment were followed up and, at the 1 June 2021 cut-off, within the respective groups, this remained ongoing at grade 1 for 16% and 14%, at grade 2 for 8.6% and 5.6%, and at grade 3 for 3.4% and 1.4%. One patient had a grade 4 polyneuropathy (in A+AVD group) and this was ongoing at their death.[3]

In contrast, at the 20 April 2017 cut-off, interstitial lung disease was reported less frequently in the A+AVD group compared with ABVD, 1.8% (12/662) versus 6.7% (44/659), with the most frequent being pneumonitis. Pulmonary toxicity is an established adverse effect of bleomycin, which is part of the ABVD regimen, but not A+AVD.[2] Exposure to bleomycin in the ECHELON-1 ABVD six-cycle regimen is greater than in the RATHL protocol used in NHSScotland, where patients who have negative disease on PET after the second cycle omit it and receive AVD for the next four cycles.[4]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In a phase III study, six cycles of A+AVD compared with six cycles of ABVD, significantly improved mPFS, with hazard ratio (HR) of 0.77 and about 4% difference in Kaplan-Meier (KM) estimated three-year mPFS and OS, with HR of 0.62 and about 5% difference in KM estimated eight-year OS.[2, 3 5] At the final analysis of OS, which was descriptive, median follow-up was around 7.5 years.[7]
- Brentuximab vedotin is the first medicine that is an antibody drug conjugate licensed for first-line treatment of advanced Stage III or IV Hodgkin lymphoma.

4.2. Key uncertainties

- The comparator in ECHELON-1, six cycles of ABVD, is not representative of Scottish practice where patients less than 60 years old and with good performance status can commence treatment with ABVD following the RATHL study protocol or with escBEACOPDac.
- An indirect comparison was provided to support an assumption of equivalent efficacy in terms of PFS and OS for six cycles of ABVD and the PET-adapted ABVD via the RATHL protocol. Despite the limitations characteristic of unanchored and unadjusted indirect comparisons, this is accepted and is supported by key outcomes of the RATHL study.[9]
- The indirect comparisons of six cycles of ABVD and the PET-adapted ABVD did not assess safety. In the RATHL study, omission of bleomycin (switching from ABVD to AVD after the second cycle) reduced toxicity, in particular, there were lower incidences of fatigue and respiratory events and better preservation of lung diffusing capacity for carbon monoxide. In practice, any differences in pulmonary toxicity between A+AVD and the RATHL protocol are likely to be smaller than those observed between A+AVD and six cycles of ABVD in ECHELON-1. It is not clear whether the increase in rates of adverse events with A+AVD compared with six cycles of ABVD in ECHELON-1 (such as peripheral neuropathies and neutropenia) would be greater, in practice, compared with the RATHL protocol.[9-11]
- The submission did not include a comparison with the alternative first-line treatment option, escBEACOPDac recommended in Scottish guidelines.[4] Clinical experts consulted by SMC confirm that the choice between this and the RATHL protocol is a complex clinical decision. They note that A+AVD is likely to be used in place of ABVD, that is, replacing bleomycin in that regimen with brentuximab vedotin. They believe that it is unlikely to be given to patients who would receive escBEACOPDac. However, it was suggested that there may be uncertainty around the impact of A+AVD on choice of treatment pathway.
- The majority of the A+AVD group did not receive G-CSF primary prophylaxis, which was associated with lower levels of neutropenia, including febrile neutropenia.[2] The summary of product characteristics (SPC) recommends G-CSF primary prophylaxis.[1] In practice, the rates of these adverse events may be lower than observed in ECHELON-1.

4.3. Clinical expert input

Clinical experts consulted by SMC note that the brentuximab vedotin-containing regimen is a therapeutic advance in the first-line treatment of Stage III or IV classical Hodgkin lymphoma due to its improved efficacy relative to one of the current first-line treatment options, ABVD. However, they noted its potential increase in toxicity, particularly peripheral neuropathy. They considered that it is likely to be used in place of treatment that commences with ABVD (that is, the RATHL protocol).

5. Summary of Patient and Carer Involvement

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of brentuximab vedotin, as an orphan equivalent medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Stage III or IV CD30-positive Hodgkin lymphoma is a rare blood cancer commonly diagnosed in young people aged 15 to 25 years and in older people over the age of 60 years. Symptoms include fatigue, weight loss and night sweats, as well as the emotional burden of a cancer diagnosis. It is curable for most patients with first-line chemotherapy, but this has side effects that limit the patient's ability to care for themselves and may persist life-long; infertility is particularly distressing. The patient's family may be required to help with the patient's previous work or caring responsibilities and support them to attend frequent hospital appointments. A minority are not cured and require intensive high-dose salvage chemotherapy with stem cell transplant if feasible, which is associated with additional side effects, particularly infertility.
- The choice of first-line therapy (which is the best chance of cure) is a complex clinical decision balancing cure rates, side effects that may persist life-long, and desire to start a family in the future. There is an unmet need for safer, more personalised first-line treatments that maintain high cure rates whilst reducing toxicities.
- The availability of brentuximab vedotin would increase the range of possible treatment options and allow the first-line regimen to be tailored to patients' circumstances, for example patients who have lung problems may avoid bleomycin-containing regimens (AVBD and escBEACOPDac) and patients with nerve damage may avoid brentuximab vedotin.
- By increasing the proportion of patients achieving a cure with first-line treatment compared to AVBD, brentuximab vedotin may spare some patients and their family from the difficulties and psychological impact associated with additional intensive salvage therapy.
- Clinical experts advise that brentuximab vedotin would not increase the number of hospital visits for administration of chemotherapy but may increase contact with medical services to manage side effects such as neutropenia and neuropathy. They note that national clinical management guidelines currently support decision-making for patients with Hodgkin lymphoma and that, if brentuximab vedotin is accepted for use in Scotland, it would be included in these.

Additional Patient and Carer Involvement

We received a patient group submission from Lymphoma Action, which is a registered charity. Lymphoma Action has received 7.65% pharmaceutical company funding in the past two years, including from the submitting company. A representative from Lymphoma Action participated in the PACE meeting. The key points of the submission from Lymphoma Action have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Details of the economic case is included below in Table 6.1

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	The analysis was a cost-utility analysis using a partitioned survival approach.
Time horizon	60 years was adopted in the base case analysis, with 50 and 70 years explored in scenario analysis.
Population	Adult patients with previously untreated CD30+ Stage III or IV Hodgkin lymphoma in combination with AVD.
Comparators	Combination chemotherapy with ABVD
Model description	The model included three mutually exclusive health states: progression-free, progressed disease and death. Cycle length was 7 days. If patients remained progression-free for 24 months after the end of treatment they were assumed to be cured, experiencing the same costs and utilities as the general population. A standardised mortality ratio (SMR) was applied to all-cause mortality to account for the possibility that patients surviving long-term do not experience average general population life expectancies, with a different rate applied in each arm.
Clinical data	The main source of clinical evidence was the ECHELON-1 study.[5] However, as the comparator group received six cycles of ABVD, whereas in clinical practice this is PET scan dependent after cycle 2, data from the RATHL study[10] were also used. In terms of efficacy, equivalent efficacy between the RATHL approach and ECHELON-1 approach was assumed based on the indirect treatment comparison (ITC) analysis. In terms of safety, the RATHL study estimates were used to inform probabilities associated with adverse events for the 90% of patients in the ABVD arm who are assumed to receive PET-adapted ABVD. ECHELON-1 was used to inform rates for A+AVD, and the remaining 10% of patients in the ABVD arm who are assumed to receive six cycles of ABVD. The ITC did not include a comparison of these approaches to ABVD treatment in terms of safety, only clinical efficacy.
Extrapolation	For PFS, a mixture cure model was applied, whereby separate distributions were fitted to the A+AVD and ABVD data from ECHELON-1. For OS, mixture cure models did not yield results that the submitting company's clinical experts deemed plausible, so one-knot (hazards) splines were fitted separately to the A+AVD and ABVD data.
Quality of life	Quality of life data were collected from participants in ECHELON-1 via the EQ-5D-3L. A regression analysis identified the covariates that the utility scores were sensitive to, namely baseline score, age, whether the patient was on/off treatment and whether the patient had a grade 3 or above adverse event. Few alternative data sources were available for utilities generally, but adverse event utilities were available and tested in scenario analysis.
Costs and resource use	Costs included in the model were medicine acquisition costs, administration (outpatient setting assumed), concomitant medications, follow-up care, the cost of adverse events, and the costs of subsequent treatments.

PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price.

6.2. Results

SMC would wish to present the with-PAS cost-effectiveness results that were used for decision-making. However, SMC is unable to publish these results due to commercial in confidence concerns regarding the PAS.

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in table 6.3. The analysis suggested that varying the parameters such as use of brentuximab vedotin monotherapy, dosing and subsequent therapy had an impact on the economic outcomes.

Table 6.3 Scenario analyses

	Parameter	**Base case**	**Scenario**
1	Time horizon	60 years	50 years
2	PFS distribution and method	Independent MCMs log logistic for A+AVD and ABVD	Independent MCMs Gompertz for A+AVD and ABVD
3			Independent one-knot splines (hazard) for A+AVD and ABVD
4	OS distribution and method	One-knot (hazards) splines	Independent MCMs (log logistic) applied to each arm separately
5			Dependent Weibull distribution applied to both arms
6			Independent MCMs Gompertz for A+AVD and ABVD
7	PFS and OS distribution and method	Independent MCMs log logistic for PFS and one-knot (hazards) splines for OS	Independent MCM (Gompertz) for PFS and Independent MCM (Loglogistic) for OS
8	Proportion receiving PET-adapted ABVD in the comparator group	PET-adapted ABVD: 90% of ABVD-based comparator	100% of ABVD-based comparator
9			95% of ABVD-based comparator
10	Varying SMR	SMR 1.05 for A+AVD and 1.10 for ABVD	1.10 for A+AVD and 1.15 for ABVD
11	Cure timepoint	Cure timepoint: 24 months	60-months
12	AE disutilities	AE disutilities: Regression	Literature
13			Excluded
14	Second malignancies	Second malignancies: Excluded	Included
15	Subsequent therapy distribution	Subsequent therapy distribution: ECHELON-1	UK clinical opinion
16	Primary prophylaxis with G-CSF	100% patients receiving A+AVD and escBEACOPDac receive primary prophylaxis with G-CSF, otherwise 0%	As per ECHELON-1 study
17	Testing the ITC conclusion	Hazard ratio of 1	0.8 for PET-adapted RATHL (both PFS and OS)
18			1.2 for PET-adapted RATHL (both PFS and OS)
19	Equalising SMR		Both set to 1.10

	Parameter	Base case	Scenario
20		1.05 for A+AVD and 1.10 for ABVD	Both set to 1.15
21	Subsequent therapies	Proportions of patients receiving each therapy based on ECHELON-1 in each arm	Proportions of patients receiving therapy applied midpoint between arms used across both treatments
22			Proportions of patients receiving therapy applied midpoint between arms (originally estimated by clinicians separately for each treatment group)
23	Health state utilities	Health state utilities informed by ECHELON-1 study	Health state utilities informed by SMC2525
24			Health state utilities informed by NICE TA641

Abbreviations: A+AVD = brentuximab vedotin, doxorubicin, vinblastine, dacarbazine; ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine; AE = adverse events; ITC = indirect treatment comparison; MCM = mixture cure model; OS = overall survival; PFS = progression-free survival; SMR = standardised mortality ratio.

6.4. Key strengths

- The model uses a partitioned survival structure which is common to many oncology indications.
- The model included EQ-5D-3L quality of life data collected in the ECHELON-1 study.

6.5. Key uncertainties

- The ITC analysis considered equivalence in efficacy between six cycles of ABVD and the PET-adapted RATHL approach for the comparator, but it did not include safety outcomes. The economic analysis had applied PET-adapted RATHL adverse event data to the comparator arm, so this was tested with the ECHELON-1 comparator data in a scenario analysis. However this did not have a material change in the base case result.
- A different SMR was applied in each arm to patients considered cured at 24 months after the end of treatment. While there was some testing of this in scenario analysis, further consideration was warranted including testing of the base case SMR for ABVD of 1.10 or 1.15 to be applied to both arms (see scenarios 19 and 20).
- Second malignancies were assumed to be incorporated into the SMR. Separate consideration of second malignancies is included as an exploratory scenario analysis, although the submitting company noted that it was difficult to find information on this issue in the literature. It is unclear how second malignancies were taken into consideration when clinicians were determining the SMR.
- The search for alternative utility data was quite specific to the population of interest (CD30+ patients with Stage IIIb/Stage IV disease), but potentially relevant data sources from a more broadly defined patient group may be useful to test in scenario analysis. Specifically, analyses using the utilities from relevant SMC and NICE Technology Assessments were requested (see scenarios 23 and 24).

7. Conclusion

The Committee considered the benefits of brentuximab vedotin in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as brentuximab vedotin is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted brentuximab vedotin for use in NHSScotland.

8. Guidelines and Protocols

In 2022, the British Society for Haematology (BSH) published 'Guideline for the first-line management of classical Hodgkin lymphoma – a British Society for Haematology guideline.'[11]

In 2018, the European Society for Medical Oncology (ESMO) published 'Hodgkin lymphoma: EMSO clinical practice guidelines for diagnosis, treatment and follow-up.'[12]

9. Additional Information

9.1. Product availability date

17 September 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per six-cycle course (£)
Brentuximab vedotin Doxorubicin Vinblastine Dacarbazine	1.2 mg/kg on Day 1 and 15 of 28-day cycle 25mg/m^2 on Day 1 and 15 of 28-day cycle 6 mg/m^2 on Day 1 and 15 of 28-day cycle 375 mg/m^2 on Day 1 and 15 of 28-day cycle	£64,233

Costs from BNF online on 28 February 2025 based on a weight of 70kg and body surface area of 1.8m^2. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

SMC is unable to publish the with-PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 11 April 2025.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises

NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.