Indication	Brentuximab vedotin in combination with bendamustine for CD30-positive relapsed or refractory classical Hodgkin lymphoma following failure of at least two prior lines of therapy or relapsed following autologous stem cell transplant. Patients must have not received any previous treatment with bendamustine and not had a less than partial or complete response to previous treatment with brentuximab vedotin. NB the use of bendamustine is unlicensed for this indication. Trust policy regarding the use of unlicensed (off-label) treatments must be followed.
Treatment Intent	Disease Modification,
Frequency and number of cycles	Repeat every 21 days. Continue treatment for up to a maximum of 6 cycles, unacceptable toxicity or patient choice whichever occurs first. A full assessment should occur by cycle 3, if response assessment demonstrates a response status of less than a partial or a complete response treatment should be discontinued.

Monitoring Parameters	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion.
	• **Ensure Irradiated blood products are used for future transfusions in Hodgkins Lymphoma patients.**
	• Patients with previous cardiac disease require an **ECG** before each cycle of bendamustine, potassium levels closely monitored and supplements prescribed when K^+ <3.5mmol/L.
	• **FBC**, **U&Es** and **LFTs** must be measured before each dose. Proceed with next cycle once ANC >/=1.0x 10^9/l and platelets >/=75 x 10^9/l.
	• **Blood pressure, pulse, temperature** and **O2 saturation** must be measured and recorded at baseline, at end of brentuximab infusion, and 30 minutes post brentuximab infusion end time.
	• **Hepatic impairment:**
	  ○ **Brentuximab Vedotin:** In patients with any degree of hepatic impairment, starting dose is 1.2mg/kg. Monitor patient closely for adverse events.
	  ○ **Bendamustine:** No dose adjustment in mild hepatic impairment (Bilirubin < 21µmol/L). A 30% dose reduction is recommended for moderate hepatic impairment (Bilirubin 21-51µmol/L). Contraindicated in severe hepatic impairment (Bilirubin> 51µmol/L).
	• **Renal impairment:**
	  ○ **Brentuximab vedotin:** If CrCl < 30ml/min then dose at 1.2mg/kg. Use with caution and monitor patient carefully.
	  ○ **Bendamustine:** No dose reduction is required if CrCl >10ml/min.
	• **Infusion-related reactions:**
	• **Brentuximab:** If a patient suffers an infusion-related reaction, the infusion should be interrupted and appropriate management given. The infusion may be re-started at a slower rate after symptom resolution. For these patients, all subsequent doses of brentuximab should be pre-medicated with paracetamol, chlorphenamine and hydrocortisone.
	• **Bendamustine:** Infusion related reactions are generally mild, although severe anaphylaxis has been reported. Measures to prevent severe reactions, including antihistamines, antipyretics and corticosteroids must be considered in subsequent cycles in patients who have previously experienced infusion reactions.
	Patients who experienced Grade 3 or worse allergic-type reactions should continue with treatment at the clinician's decision.

- **Management of adverse reactions and dose adjustments:**
- **Brentuximab:**
  - If neutropenia develops during treatment it should be managed by dose delays. If Grade 1 or Grade 2 neutropenia, continue with same dose and schedule. If Grade 3 or 4 neutropenia, withhold dose until toxicity returns to </= Grade 2 or baseline then resume treatment at the same dose and schedule. Consider G-CSF support in subsequent cycles for patients who develop Grade 3 or Grade 4 neutropenia.
  - **Peripheral sensory or motor neuropathy**: If peripheral sensory or motor neuropathy emerges or worsens during treatment see Table 1 for dose modification of brentuximab.
  - **Progressive multifocal leukoencephalopathy (PML):** Use of brentuximab has been associated with increased risk of progressive risk of progressive multifocal leukoencephalopathy (PML). Patient must be monitored for new or worsening neurological, cognitive, or psychiatric symptoms which may be suggestive of PML.
  - **Pancreatitis:** Acute pancreatitis has been observed in patients treated with brentuximab. Patients should be closely monitored for new or worsening abdominal pain, which may be suggestive of acute pancreatitis. Treatment should be held for any suspected case of acute pancreatitis and should be discontinued if acute pancreatitis is confirmed.
  - **Pulmonary toxicity:** Interstitial lung disease (ILD), pneumonitis, and acute respiratory distress syndrome. Patients should be advised to report any new or worsening respiratory symptoms. Full investigation should be performed and consider withholding treatment until cause established.
  - **Steven Johnsons syndrome (SJS) and Toxic epidermal necrolysis (TEN**): Cases of SJS and TEN have been observed. If symptoms or signs of SJS or TEN appear, treatment with brentuximab should be discontinued and the patient referred to a specialised unit for assessment and treatment. If the patient has developed SJS or TEN with the use of brentuximab permanent discontinuation of treatment is recommended.
- **Bendamustine:**
  - If grade 4 haematological toxicity, or grade 3 or 4 non-haematological toxicity occur – delay treatment and reduce dose by 25% once resolved.
  - **Tumour lysis syndrome** has been reported with bendamustine treatment. Preventive measures such as adequate hydration, close monitoring of blood chemistry, particularly potassium and uric acid levels, and the use of hypouricemic agents (allopurinol and rasburicase) should be considered prior to therapy. There have been a few cases of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis reported when bendamustine and allopurinol are administered concomitantly.
  - **Stevens – Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)** has been report. Patients should be advised to report signs and symptoms immediately, if skin reactions are progressive, bendamustine should be withheld or discontinued.
- **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:**
  - **Brentuximab** is not to be combined with bleomycin. Co-administration of brentuximab with a strong CYP3A4 and P-gp inhibitors (e.g. Clarithromycin, itraconazole, ketoconazole, ritonavir, amiodarone) should be avoided due to increased risk of neutropenia, if azole anti-fungals are used, use with caution and monitor for neutropenia.
  - **Bendamustine:** Caution with concomitant use of Allopurinol – risk of Stevens Johnson Syndrome and toxic epidermal necrolysis
- **Missed dose:** If a planned dose of brentuximab is missed, the next dose should be administered as soon as possible. The administration schedule must be adjusted to maintain a 3-week interval between doses**.**
- **Driving and machinery:** Brentuximab can potentially cause fatigue/dizziness in some patients and therefore use caution when driving or using machines. Patients should be advised that bendamustine has a major influence on the ability driving or using machines, if ataxia, peripheral neuropathy or somnolence experienced by patient these tasks should be avoided.
- **Pregnancy and contraception:** Please refer to the brand specific SPC for full guidance. Women of childbearing potential should use effective contraception and not consider pregnancy during treatment

	and for a period after. Men should be advised to use effective contraception and not to conceive children during treatment and for a period after.
References	CDF list V1.406 accessed online 09.09.2026 SPC accessed online 11.09.2026 https://www.england.nhs.uk/wp-content/uploads/2026/07/2404-commissioning-policy-bvb-for-hodgkin-lymphoma.pdf

NB for funding information, refer to CDF and NICE Drugs Funding List

Table 1: Brentuximab dosing recommendations for new or worsening peripheral sensory or motor neuropathy

Severity of peripheral sensory or motor neuropathy signs and symptoms [abbreviated description of CTCAE[a]])	**Modification of dose and schedule**
Grade 1 (paraesthesia and/or loss of reflexes, with no loss of function)	Continue with the same dose and schedule.
Grade 2 (interfering with function but not with activities of daily living)	Withhold dose until toxicity returns to ≤ Grade 1 or baseline, then restart treatment at a reduced dose of 1.2 mg/kg up to a maximum of 120 mg every 3 weeks.
Grade 3 (interfering with activities of daily living)	Withhold dose until toxicity returns to ≤ Grade 1 or baseline, then restart treatment at a reduced dose of 1.2 mg/kg up to a maximum of 120 mg every 3 weeks.
Grade 4 (sensory neuropathy that is disabling or motor neuropathy that is life threatening or leads to paralysis)	Discontinue treatment.

Repeat every 21 days to a maximum of 6 cycles

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Paracetamol	1gm	PO		Only give if required for prevention or treatment of brentuximab infusion related reactions. If required give 30 minutes before Brentuximab infusion.
	Chlorphenamine	10mg	IV	stat	
	Hydrocortisone	100mg	IV	stat	
	BRENTUXIMAB VEDOTIN	**1.8mg/kg (max dose 180mg)**	IV	30mins	in 100-250ml sodium chloride 0.9% Final concentration must be between 0.4mg/mL to 1.2mg/mL Flush with sodium chloride 0.9% or 5% glucose after administration
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	Sodium chloride 0.9% 50ml
	BENDAMUSTINE	**90mg/m^2**	IV	30-60 mins	Sodium chloride 0.9% 500ml
2	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	Sodium chloride 0.9% 50ml
	BENDAMUSTINE	**90mg/m^2**	IV	30-60 mins	Sodium chloride 0.9% 500ml

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone	6mg	PO	OM for 4 days starting on day 2. Day 2 dose to be taken before bendamustine.
	Allopurinol	300mg	PO	OD For the first month then prescribe continuing supply if required from cycle 2 onwards.
	Co-Trimoxazole	480mg	PO	BD on Mondays, Wednesdays and Fridays.
	Loperamide	2mg-4mg	PO	4 mg initially then 2 mg after each loose stool when required for diarrhoea (maximum dose of 16mg in 24hrs).
	Metoclopramide	10mg	PO	Take 10mg TDS for three days, then take 10mg up to TDS when required. Do not take for more than 5 days continuously
	Aciclovir	400mg	PO	BD