Indication	For the treatment of relapsed / refractory CD30-positive Hodgkin lymphoma ➢ following autologous stem cell transplant (ASCT) ➢ following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option ➢ re-use after ASCT as bridge to allogenic stem cell transplant or donor lymphocyte infusion after a previous partial/ complete response to brentuximab vedotin For the treatment of relapsed / refractory systemic anaplastic large cell lymphoma (sALCL). For the treatment of relapsed / refractory CD30+ cutaneous T cell lymphoma after at least 1 line of systemic therapy.
Treatment Intent	Curative/Non-Curative/Remission.
Frequency and number of cycles	Repeat every 21 days. Treatment should be continued until disease progression or unacceptable toxicity up to a maximum of 16 cycles. NB for re-use after ASCT, maximum of 16 cycles includes cycles administered pre ASCT.
Monitoring Parameters pre-treatment	• **Virology status checked and negative prior to cycle 1.** • FBC, U&Es and LFTs must be measured before each dose. Proceed with next cycle once ANC >/=1.0x 10^9/l and platelets >/=50 x 10^9/l. • Blood pressure, pulse, temperature and O2 saturation must be measured and recorded at baseline, at end of infusion, and 30 minutes post infusion end. • 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. • Neuropathy: If Grade 2 (interfering with function but not ADL) or Grade 3 (interfering with ADL) withhold dose until toxicity resolves to </=Grade 1, then re-start treatment at 1.2mg/kg (maximum dose 120mg) every 3 weeks. If Grade 4 (sensory neuropathy which is disabling or motor neuropathy which is life-threatening or leads to paralysis) discontinue brentuximab. • **<u>Infusion related reactions</u>** • 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. • **Renal impairment**: If CrCl < 30ml/min then dose at 1.2mg/kg. Use with caution and monitor patient carefully. • **Hepatic impairment:** In patients with any degree of hepatic impairment, starting dose is 1.2mg/kg. Monitor patient closely for adverse events. • **Common Adverse reactions:** o **Peripheral sensory or motor neuropathy:** If peripheral sensory or motor neuropathy emerges or worsens during treatment see Table 1 for dose modification of brentuximab. o **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. ○ **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. • **Ensure Irradiated blood products are used for future transfusions in Hodgkins Lymphoma patients.** • **Common drug interactions (for comprehensive list refer to BNF/SPC):** 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. • **Missed dose:** If a planned dose 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. • Brentuximab can potentially cause fatigue/dizziness in some patients and therefore use caution when driving or using machines.
References	KMCC proforma HAEM-HL-010v2 SPC accessed online 05.05.2022 cdf list v1.210

NB For funding information, refer to the SACT funding spread sheet

Table 1: 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.

[a.] Grading based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v3.0; see neuropathy: motor; neuropathy: sensory; and neuropathic pain.

Repeat every 21 days

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	**1.8mg/kg (max 180mg)**	IV	Over 30 mins	in 100-250ml sodium chloride 0.9% Final concentration must be between 0.4mg/mL to 1.2mg/mL
TTO	Drug	Dose	Route		Directions
	Allopurinol	300mg	PO	OD For the first month then review	
	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)	