Indication	For the treatment of untreated CD30+ systemic anaplastic large cell lymphoma (sALCL) in combination with cyclophosphamide, doxorubicin and prednisolone (CHP)
Treatment Intent	Disease modification
Frequency and number of cycles	Repeat every 3 weeks for up to a maximum of 6 or 8 cycles of chemotherapy, 6 cycles being the usual maximum. A formal medical review must occur by the end of the first 6 weeks of treatment to establish whether to continue treatment.
Monitoring Parameters pre-treatment	• **Check virology status prior to cycle 1** • FBC, U&Es, LFTs and random blood glucose before each cycle. • Pre-treatment bloods: Neuts >/= 1 and platelets >/= 50. • Pre-Doxorubicin ECG check and ECHO if clinically indicated. • **Hepatic Impairment:** ○ **Brentuximab:** In mild hepatic impairment (bilirubin </=1.5 x ULN and AST/ALT </= 3) the starting dose of brentuximab should be reduced to 1.2mg/kg. There is limited data in patients with hepatic impairment, where total bilirubin is > 1.5 times the upper limit of normal (ULN) (unless due to Gilbert syndrome), or aspartate aminotransferase (AST) or alanine aminotransferase (ALT) are > 3 times the ULN therefore brentuximab in combination with chemotherapy should be avoided in moderate to severe hepatic impairment. ○ **Doxorubicin:** Bilirubin 20-51µmol/L give 50%, bilirubin 52-85µmol/L, give 25%, bilirubin > 85µmol/L omit. If AST 2-3 x normal, give 75% dose. If AST >3x ULN, give 50% dose • **Renal Impairment:** This regimen is not recommended in severe renal impairment (CrCl <40ml/min). • Maximum cumulative dose of Doxorubicin = 450-550mg/m². Check previous exposure to anthracyclines • **Haematological toxicity:** If neutrophil count < 1.0 x 10^9/l, delay treatment until neutrophils have recovered to ≥ 1.0 x 10^9/l. Then continue treatment at the same doses. If Platelets <50 d/w consultant. • **Infusion related reaction**: 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 an IRR occurs, the infusion should be interrupted and appropriate medical management instituted. The infusion may be restarted at a slower rate after symptom resolution. Patients who have experienced a prior IRR should be premedicated for subsequent infusions. Premedication may include paracetamol, chlorphenamine and hydrocortisone (hydrocortisone only to be given if prednisolone has been withheld, not in addition to). • **Common Adverse reactions:** ○ **Peripheral sensory or motor neuropathy:** If peripheral sensory or motor neuropathy emerges or worsens during treatment see Table 1 for dose modification of brentuximab. ○ **Pulmonary toxicity:** Interstitial lung disease (ILD), pneumonitis, and acute respiratory distress syndrome have been reported in patients treated with brentuximab. Patients should report any new or worsening respiratory symptoms and evaluation performed. Consider withholding treatment during evaluation and until symptomatic improvement. ○ **Progressive multifocal leukoencephalopathy (PML):** Use of brentuximab has been associated with increased 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. ○ **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. ○ **Pancreatitis**: Acute pancreatitis has been observed in patients treated with brentuximab. • **Common drug interactions:** Brentuximab is not to be combined with bleomycin. Co-administration of brentuximab with a strong CYP3A4 and P-gp inhibitors (eg 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. • Patients should be advised that brentuximab may affect their ability to drive or operate machinery.
References	KMCC proforma HAEM-NHL-007v3 KMCC proforma HAEM-HL-010v2 https://clinicaltrials.gov/ct2/show/NCT01777152 SPC accessed online 13.07.20 St Lukes protocol BRENTUXIMAB VEDOTIN – CHP "Response package for interaction 00176366" response from Takeda received via email 15.04.21

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)	Sensory neuropathy: Continue treatment at same dose level. Motor neuropathy: Reduce dose to 1.2 mg/kg, up to a maximum of 120 mg every 3 weeks.
Grade 3 (interfering with activities of daily living)	Sensory neuropathy: Reduce dose to 1.2 mg/kg up to a maximum of 120 mg every 3 weeks. Motor neuropathy: Discontinue treatment.
Grade 4 (sensory neuropathy which 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) v4.03; see neuropathy: motor; neuropathy: sensory; and neuropathic pain.

Repeat every 21 days.

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15min	Sodium chloride 0.9% 50ml
	Non EC PREDNISOLONE	**100mg**	PO	stat	
	DOXORUBICIN	**50mg/ m²**	IV	bolus	Through the side of a fast running sodium chloride 0.9% infusion.
	CYCLOPHOSPHAMIDE	**750mg/m²**	IV	bolus	For doses >1500mg give in 250-500ml sodium chloride over 30-60mins.
	BRENTUXIMAB	**1.8mg/kg Maximum dose 180 mg**	IV	30 min	In 100-250ml sodium chloride 0.9% Final concentration must be between 0.4mg/mL to 1.2mg/mL NB for dose calculation purposes the weight should be capped at 100kg

TTO	Drug	Dose	Route	Directions
	Non EC PREDNISOLONE	**100mg**	PO	OM days 2-5 Take with or after food.
	Omeprazole	20mg	PO	OM
	Metoclopramide	10mg	PO	Up to TDS PRN Do not take for more than 5 days continuously.
	Loperamide	2mg	PO	4 mg initially then 2 mg after each loose stool when required for diarrhoea (maximum dose of 16mg in 24hrs) Dispense with cycle 1 only and then only when required.
	Allopurinol	300mg	PO	OD. For the first cycle only and then review.
	Chlorhexidine Mouthwash	10ml	topical	Use topically as a mouthwash, rinsing mouth for at least 1 minute four times a day.
	Filgrastim	300 micrograms or consider dose of 480 micrograms if patient > 80kg	SC	Daily from day 8 for 5 days
	Aciclovir	400mg	PO	BD
	Co-trimoxazole	480mg	PO	BD on Mondays, Wednesday and Fridays
	Consider the use of prophylactic anti-fungals (see interactions)			