Indication	Diffuse Large B Cell Lymphoma with contraindications to anthracyclines.
Treatment Intent	Curative
Frequency and number of cycles	Repeat every 21 days for 3-6 cycles

Monitoring Parameters pre-treatment	• Virology status to be checked prior to cycle 1.
	• ECG baseline.
	• Baseline MUGA/ECHO where clinically indicated.
	• FBC, U&E and LFTs at baseline and before each cycle. Monitor between cycles as clinically indicated.
	• Neuts <1 and PLT <80 delay cycle for 1 week and commence when levels have recovered to neuts >1 and plts 80.
	• After first neutropenic event, subsequent cycles should be given with prophylactic GCSF. For continued neutropenia even with GCSF support dose reduce cyclophosphamide and etoposide.
	• BP baseline and as clinically indicated.
	• Use rituximab infusion monitoring record.
	• Rituximab Infusion rates: First infusion – Initiate at 50 mg/hr. Increase at 50mg/hr increments every 30mins to 400mg/hr. max. Subsequent infusions – Initiate infusion at 100mg/hr. Increase rate at 100mg/hr increments every 30mins to 400mg/hr max. From cycle 2 onwards rapid infusion may be used if requested by clinician (patient must not have had a grade 3 or 4 reaction to previous rituximab treatment). In this case infuse first 100ml over 20 minutes, and if no reaction, infuse remaining 400ml over 60 minutes.
	• Ensure pre-medication of rituximab with chlorphenamine, prednisolone and paracetamol. Monitor rituximab infusion closely (complete monitoring form), watch for signs of dyspnoea, fever, rigors. If such symptoms occur stop infusion and seek medical advice. Infusion may be recommenced at half the previous rate, once symptoms have subsided. Anaphylaxis drugs must be available when treating with rituximab
	• Consider withdrawing any anti-hypertensives 12 hours before treatment with rituximab.
	• Consider reduction of cell load by other means prior to rituximab infusion if high tumour load and consider decreasing infusion speed.
	• Patients with a high tumour burden or with a high number of lymphocytes (>25 x 10^9/l) who may be at higher risk of especially severe cytokine release syndrome, should only be treated with extreme caution. These patients should be very closely monitored throughout the first infusion. Consideration should be given to the use of a reduced infusion rate for the first infusion in these patients or a split dosing over two days during the first cycle.
	• **Neurotoxicity** - Grade 2 motor and Grade 3 sensory toxicity give Vincristine 50% dose or Vinblastine 4-6mg/m2
	• **<u>Renal Impairment</u>**:
	  ○ **Cyclophosphamide:** CrCl 10–20 mL/min give 75%, CrCl <10mL/min give 50%.
	  ○ **Etoposide:** CrCl 15-50mL/min give 75%, CrCl < 15mL/min clinical decision, consider 50% dose reduction.
	• **<u>Hepatic Impairment:</u>**
	  ○ **Etoposide:** Bilirubin 26-51µmol/L or AST 60-180 units give 50%, bilirubin > 51µmol/L or AST > 180 units is a clinical decision.

	○ **Vincristine:** bilirubin 26-51µmol/L or AST/ALT 60-180 units give 50%, bilirubin >51µmol/L and AST/ALT normal give 50%, bilirubin >51µmol/L and AST/ALT >180 units omit.
References	ARIA regimen HAEM-NHL-044 CHOP R 21 days, Cheshire and Merseyside R-CEOP protocol, Derby-Burton local cancer network protocol R-CEOP No HCCPG B22 https://www.uhdb.nhs.uk/derby-burton-local-cancer-network Changes made in line with 'SOP for removal of ranitidine on KMCC protocols and on aria regimens'

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

Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15min	In 50ml Sodium chloride 0.9%
	Paracetamol	1000mg	PO		Stat Do not take more than 4000mg paracetamol each day.
	Chlorphenamine	10mg	IV	1 min	By slow IV injection
	Prednisolone	100mg	PO	Stat	Take with or just after food, or a meal
	Commence Rituximab at least 30 mins – 1 hour after pre-medication.				
	RITUXIMAB (Truxima®)	**375mg/m²**	IV	See notes	Sodium Chloride 0.9% 500ml
	VINCRISTINE	**1.4mg/m² Max dose 2mg**	IV	5-10 min	Sodium Chloride 0.9% 50ml
	CYCLOPHOSPHAMIDE	**750mg/m²**	IV	bolus	(Doses over 1500mg in 250-500ml NaCl 0.9% over 30mins – 1 hour.)
	ETOPOSIDE	**50mg/m²**	IV	1 hr	Sodium Chloride 0.9% 250ml-500ml

TTOs

TTO	Drug	Dose	Route	Directions
Dispense on Day 1	Prednisolone	100mg	PO	OM on days 2-5 only. Dispense on Day 1. Take with or just after food, or a meal.
	ETOPOSIDE	**100mg/m² Round to the nearest 50mg**	PO	OD on day 2 and 3 only. Take an hour before food or on an empty stomach.
	Allopurinol	300mg	PO	OD cycle 1 only and then review. Take with or just after food, or a meal. Take with a full glass of water
	Metoclopramide	10mg	PO	TDS regularly for 3 days, then 10mg up to TDS PRN (28 tabs). Do not take for more than 5 consecutive days
	Co-trimoxazole	480mg	PO	BD Mon, Wed and Fri only. Space the doses evenly throughout the day. Keep taking this medicine until the course is finished, unless you are told to stop.
	Aciclovir	400mg	PO	BD. Space the doses evenly throughout the day. Keep taking this medicine until the course is finished, unless you are told to stop.
	Omeprazole	20mg	PO	OD
	Chlorhexidine Mouthwash	10ml	mouth wash	QDS from Day 1 of chemotherapy.
	Filgrastim to be considered if clinical need arises.			