Indication	First line treatment of Mantle cell Lymphoma in patients fit enough for PBSCT
Treatment Intent	Disease Modification
Frequency and number of cycles	Every 3 weeks Maximum of 6 cycles. R-CHOP alternating with R-High Dose Cytarabine with additional Rituximab given on Day 9 of Cycle 6 for the purpose of stem cell mobilisation
Monitoring parameters pre-treatment	• **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. • Monitor FBC, U&Es and LFTs baseline and at each cycle. Monitor between cycles as clinically indicated. • ECG baseline. • A baseline MUGA scan/echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function. If ejection fraction is less than 50%, an alternative regimen should be given. • MUGA/echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment. • **Lifetime cumulative dose of doxorubicin 450-550mg/m^2. Check any previous anthracycline exposure.** • **Haematological:** o R-High Dose Cytarabine Proceed if neuts >/= 1.0 x 10^9/L and platelets >/= 100 x 10^9/L. Platelets < 100 x 10^9/L or neutrophils < 1 x 10^9/L - d/w consultant. o R-CHOP Neutrophils >/=1.0 x 10^9/L and platelets >/= 75 x 10^9/L - proceed with treatment. Neutrophils < 0.5 x 10^9/L or platelets < 50 x 10^9/L - delay by one week. Neutrophils 0.5 – 0.99 x 10^9/L – d/w consultant. Platelets 50 - 74 x 10^9/L – reduce cyclophosphamide and doxorubicin doses to 75%. • **Hepatic impairment:** o **Doxorubicin:** bilirubin 20-51umol/L give 50% dose; bilirubin 52-85umol/L give 25% dose; bilirubin > 85umol/L omit. Doxorubicin is contraindicated in patients with severe liver impairment (Child-Pugh C). **Vincristine:** A reduction of 50% recommended if bilirubin >50umol/L. o **Cytarabine:** If bilirubin >34µmol/l reduce cytarabine dose by 50%. o **Rituximab:** no recommended dose adjustment. • **Renal impairment:** o **Cyclophosphamide:** CrCl >/= 30 ml/min: no dose adjustment required. CrCl 10-29 ml/min, consider 75% of the original dose CrCl < 10 ml/min, not recommended, if unavoidable consider 50% of the original dose. o **Cytarabine:** o CrCl 46-60ml/min give 60% dose; o CrCl 30-45ml/min give 50% dose; o CrCl < 30ml/min omit Cytarabine. o No dose reductions required for **doxorubicin, rituximab or vincristine.** • **Dose Modification:** o Cytarabine: dose reduce 2g/m^2 if over 60 years of age. o Vincristine: If neuropathy symptoms occur discuss reducing or withholding vincristine dose with consultant. • **Infusion rates and Infusion-related reactions (IRRs):**

	Ensure pre-medication of rituximab with chlorphenamine, prednisolone or hydrocortisone & paracetamol. Monitor rituximab (complete monitoring form) infusions closely, watch for signs of dyspnoea, fever and rigors. If such symptoms occur stop infusion(s) and seek medical advice. Infusion may be recommenced at half the previous rate, once symptoms have subsided (see below for when to discontinue). Anaphylaxis drugs must be available. • **Rituximab:** Use rituximab infusion monitoring record. Consider withdrawing any anti-hypertensives 12 hours before treatment with rituximab. 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. Use rapid rituximab infusion chart. 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.
Reference(s)	KMCC protocol HAEM-NHL-078 V1 Lancet appendix *"Dose recommendations for anticancer drugs in patients with renal or hepatic impairment."* HOG 23.03.23: agreed standard dose R-Chop

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

Cycles 1, 3 and 5 R-CHOP

Day	Drug	Dose	Route	Infusion Duration	Administration Details
1	**Prednisolone**	**100mg**	PO		stat
	Paracetamol	1g	PO		stat
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	Chlorphenamine	10mg	IV	1min	By slow IV injection
	Commence rituximab 30 mins after pre-medication				
	RITUXIMAB	**375mg/m^2**	IV	as above	In 500ml sodium chloride 0.9%
	VINCRISTINE	**1.4mg/m^2 (Max 2mg)**	IV	5-10 mins	In 50ml sodium chloride 0.9%
	DOXORUBICIN	**50mg/m^2**	IV	bolus	Via fast running sodium chloride 0.9% infusion
	CYCLOPHOSPHAMIDE	**750mg/m^2**	IV	See admin details	Doses </=1500mg give as IV BOLUS through the side of a fast running Sodium Chloride 0.9% infusion Doses >1500mg give as IV INFUSION in 250-500ml Sodium Chloride 0.9% infusion over 30-60 minutes

TTO	Drug	Dose	Route	Directions
Cycle 1,3 & 5	Prednisolone	100mg	PO	OD from days 2-5 Take with or after food.
	Ondansetron	8mg	PO	BD for 5 days
	Metoclopramide	10mg	PO	10mg up to TDS PRN Do not take for more than 5 days continuously.
	Allopurinol	300mg	PO	OD Cycle 1 only
	Omeprazole	20mg	PO	OD
	Aciclovir	400mg	PO	BD
	Co-trimoxazole	480mg	PO	BD on Mondays, Wednesdays and Fridays
	Filgrastim	300micrograms **or consider dose of 480micrograms if patient >80kg**	SC	OD starting day …. For…. days
	Fluconazole	50mg	PO	OD

Cycle 2 and 4 R-HD Cytarabine

Day	Drug	Dose	Route	Infusion Duration	Administration Details
1 T0	Paracetamol	1g	PO		stat
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	Chlorphenamine	10mg	IV	1min	By slow IV injection
	Hydrocortisone	100mg	IV		stat
	Commence rituximab 30 mins after pre-medication				
	RITUXIMAB	**375mg/m²**	IV	as above	In 500ml sodium chloride 0.9%
	*** N.B. consider dose reduction of cytarabine to 2000mg/m² if patient >/= 60 years.**				
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%
T12	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%
2 T0	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%
T12	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%

TTO	Drug	Dose	Route	Directions
Cycles 2 & 4	Ondansetron	8mg	PO	BD for 3 days **starting on DAY 3.**
	Metoclopramide	10mg	PO	10mg up to TDS PRN Do not take for more than 5 days continuously.
	Prednisolone eye Drops 0.5%	1 drop	Both eyes	Four times a day starting before chemotherapy and for 5 days after cytarabine has stopped (day 7)
	Co-trimoxazole	480mg	PO	bd on Mondays, Wednesdays and Fridays
	Aciclovir	400mg	PO	BD
	Fluconazole	50mg	PO	OD
	Omeprazole	20mg	PO	OD
	Filgrastim	300micrograms **or consider dose of 480micrograms if patient > 80kg**	SC	OD starting day …. For…. days

Cycle 6 R-HD Cytarabine + additional Rituximab Day 9

Day	Drug	Dose	Route	Infusion Duration	Administration Details
1 T0	Paracetamol	1g	PO		stat
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	Chlorphenamine	10mg	IV	1min	By slow IV injection
	Hydrocortisone	100mg	IV		stat
	Commence rituximab 30 mins after pre-medication				
	RITUXIMAB	**375mg/m²**	IV	as above	In 500ml sodium chloride 0.9%
	*** N.B. consider dose reduction of cytarabine to 2000mg/m² if patient >/= 60 years.**				
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%
T12	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%
2 T0	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%
T12	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 mins	In 50ml sodium chloride 0.9%
	CYTARABINE*	**3000mg/m²**	IV	3 hours	In 500ml sodium chloride 0.9%
9	Paracetamol	1g	PO	stat	
	Chlorphenamine	10mg	IV	1min	By slow IV injection
	Hydrocortisone	100mg	IV	stat	
	Commence rituximab 30 mins after pre-medication				
	RITUXIMAB	**375mg/m²**	IV	as above	In 500ml sodium chloride 0.9%

Cycle 6 R-HD Cytarabine + additional Rituximab Day 9 continued

TTO	Drug	Dose	Route	Directions
Cycle 6	Ondansetron	8mg	PO	BD for 3 days **starting on DAY 3.**
	Metoclopramide	10mg	PO	10mg up to TDS PRN Do not take for more than 5 days continuously.
	Prednisolone eye Drops 0.5%	1 drop	Both eyes	Four times a day starting before chemotherapy and for 5 days after cytarabine has stopped (day 7)
	Co-trimoxazole	480mg	PO	BD on Mondays, Wednesdays and Fridays
	Fluconazole	50mg	PO	OD
	Aciclovir	400mg	PO	BD
	Omeprazole	20mg	PO	OD
	Filgrastim	300micrograms **or consider dose of 480micrograms if patient > 80kg**	SC	OD starting day 5 till stem cell harvest