

Primary CNS Lymphoma
MATRIx

Height	
Weight	
BSA	
Infusion rate 125 x BSA Cap at 250ml/hour	

Patient Name Here

Cycle length:	21 days
Cycle no:	
Destination:	B6

CBC	Day 1	Limits
Date		
Neuts		> 1.5 x 10 ⁹ /L
Plts		> 100 x 10 ⁹ /L

Allergies/hypersensitivities

Antiemetics
Domperidone 10 mg PO QID PRN
± Cyclizine 25 mg – 50 mg PO/IV TDS PRN

Agent	Round
Rituximab	50mg
Methotrexate	100mg
Cytarabine	100mg
Thiotepa	5mg

DOSE MODIFIED: NO YES

Reference: Ferreri, A J M et al. Lancet Haematology 2016;
3(5):e217-227

Day	Date	Time	Agent	Dose	Route	Instructions	Rate	Doctor	Nurse	Check	Start	Stop	
0		T= -1 hr	# Methylprednisolone	100 mg	IV	In 100 mL sodium chloride 0.9 % over 15 minutes							
		T= -1 hr	Paracetamol	1000 mg	PO	Give 30-60 minutes prior to rituximab							
		T= -1 hr	Loratadine	20 mg	PO	Give 30-60 minutes prior to rituximab							
		T=0 hrs	Rituximab 375 mg/m² <i>See infusion chart page 8</i>		mg	IV	<input type="checkbox"/> Standard infusion: added to 500 mL sodium chloride 0.9 % <input type="checkbox"/> Rapid infusion: added to 500 mL sodium chloride 0.9 %						
		2200	Ural Sachet®	1		PO	Dissolved in 20mL water						
		2200	1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate				IV	Infuse at 125 mL/m ² /hr as above					

If no reaction to the first dose of rituximab, methylprednisolone may be omitted at the prescribers discretion

Consultant:
NZMC Reg. No:

Special Authority:
Rituximab
Pegfilgrastim

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1			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above						
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above						
		T = -1 hr	Dexamethasone	8 mg	PO	Give 1 hour prior to chemotherapy						
		T = -1 hr	Ondansetron	8 mg	PO/IV	Give 1 hour prior to chemotherapy						
		T = 0 hrs	Methotrexate 500 mg/m²		mg	IV	In 250 mL sodium chloride 0.9 % over 1 hour					
		T = +1 hr	Methotrexate 3000mg/m²		mg	IV	In 1000 mL sodium chloride 0.9% over 3 hours					
		2000	Ondansetron	8 mg	PO/IV							
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above						
	1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above								

- Measure serum creatinine and calculate CrCl prior to methotrexate infusion. Discuss with consultant if CrCl < 80mL/min.
- IV fluids run concurrently with chemotherapy. Check fluid balance at least 4 hourly, consider frusemide if urine output falls below 400mL/m² in any 4 hour period, or 1 kg weight increase
- Urine pH must be > 7.5 before starting methotrexate - adjust sodium bicarbonate and/or Ural sachets to keep pH between 7 and 8 during infusion and subsequent folinic acid rescue
- Stop proton pump inhibitors (omeprazole/lansoprazole/pantoprazole) the day prior to methotrexate infusion, restart once methotrexate has cleared
- It is recommended prophylactic trimethoprim/sulfamethoxazole (co-trimoxazole) be stopped 1 week before methotrexate therapy. Avoid concurrent high dose penicillins & nephrotoxic medications.
- See table on page 8 for guidance on adjusting fluid infusion rate and folinic acid dosage based on methotrexate levels.
- Acetazolamide 250mg PO QID, starting the night before methotrexate, and continued until methotrexate cleared, can alkalinise the urine and enhance methotrexate excretion—chart on MedChart.**

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2			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
		0800	Dexamethasone	8 mg	PO/IV						
		0800	Ondansetron	8 mg	PO/IV						
		T+24hrs	Methotrexate level (time _____, level_____)			Folinic acid rescue to commence at T+24hrs. Continue folinic acid until methotrexate level < 0.1 micromol/L. Notify lab if methotrexate levels will be required over a weekend. See page 7 for guidance on adjusting fluid infusion rate and folinic acid dosage based on methotrexate levels.					
		T+24hrs	Folinic acid	30 mg	PO	Give IV bolus if PO not tolerated					
		0900	Cytarabine 2000 mg/m²		mg IV	In 250mL sodium chloride 0.9% over 60 min					
		T+30hrs	Folinic acid	30 mg	PO	Give IV bolus if PO not tolerated					
		2000	Ondansetron	8 mg	PO/IV						
		2100	Cytarabine 2000 mg/m²		mg IV	In 250mL sodium chloride 0.9% over 60 min					
		T+36hrs	Folinic acid	30 mg	PO	Give IV bolus if PO not tolerated					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					

Prescribe on MedChart: prednisolone 1% eye drops - 1 drop into each eye TDS - starting 12 hours prior to first dose to cytarabine, and continue for 5 days after completion of cytarabine

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Day	Date	Time	Agent	Dose	Route	Instructions	Doctor	Nurse	Check	Start	Stop
3			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
		T+42hrs	Folinic acid	30 mg	PO	Give IV bolus if PO not tolerated					
		0800	Dexamethasone	8 mg	PO/IV						
		0800	Ondansetron	8 mg	PO/IV						
		T+48hrs	Methotrexate level (time _____, level _____)			Continue folinic acid until methotrexate level < 0.1 micromol/L. Notify lab if methotrexate levels will be required over a weekend. See page 7 for guidance on adjusting fluid infusion rate and folinic acid dosage based on methotrexate levels.					
		T+48hrs	Folinic acid	30 mg	PO	Give IV bolus if PO not tolerated					
		0900	Cytarabine 2000 mg/m²		mg IV	In 250mL sodium chloride 0.9% over 60 min					
		T+54hrs	Folinic acid	30 mg	PO	Give IV bolus if PO not tolerated					
		2000	Ondansetron	8 mg	PO/IV						
		2100	Cytarabine 2000 mg/m²		mg IV	In 250mL sodium chloride 0.9% over 60 min					
		T+60hrs	Folinic acid	30 mg	PO	Give IV bolus if PO not tolerated					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above					

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Day	Date	Time	Agent	Dose	Route	Instructions	Doctor	Nurse	Check	Start	Stop		
4			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above							
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above							
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above							
		T+66hrs	Folinic acid	30	mg	PO	Give IV bolus if PO not tolerated						
		0800	Dexamethasone	8	mg	PO/IV							
		0800	Ondansetron	8	mg	PO/IV							
		T+72hrs	Methotrexate level (time _____, level _____)					Continue folinic acid until methotrexate level < 0.1 micromol/L. Notify lab if methotrexate levels will be required over a weekend. See page 7 for guidance on adjusting fluid infusion rate and folinic acid dosage based on methotrexate levels.					
		T+72hrs	Folinic acid	30	mg	PO	Give IV bolus if PO not tolerated						
		0900	Thiotepa 30 mg/m²		mg	IV	In 50mL sodium chloride 0.9% over 60 min <i>(administer via 0.2 micron line filter)</i>						
		T+78hrs	Folinic acid	30	mg	PO	Give IV bolus if PO not tolerated						
		2000	Ondansetron	8	mg	PO/IV							
		T+84hrs	Folinic acid	30	mg	PO	Give IV bolus if PO not tolerated						
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above							
			1000 mL glucose 4 % & sodium chloride 0.18 % + 20 mmol potassium chloride + 50 mmol sodium bicarbonate		IV	Infuse at 125 mL/m ² /hr as above							

If necessary, continue folinic acid on Med Chart and IV fluids on QMR004B

Authorised by: Blake Hsu
Pharmacist: Timothy Vincent

Issued: July 2019
Review: July 2022

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Day	Date	Time	Agent	Dose	Route	Instructions	Rate	Doctor	Nurse	Check	Start	Stop
5		T= -60 mins	# Methylprednisolone	100 mg	IV	In 100 mL sodium chloride 0.9 % over 15 minutes						
		T= -60 mins	Paracetamol	1000 mg	PO	30-60 minutes prior to rituximab						
		T= -60 mins	Loratadine	20 mg	PO	30-60 minutes prior to rituximab						
			Rituximab 375 mg/m² <i>See infusion chart page 10</i>		mg	IV	<input type="checkbox"/> Standard infusion: added to 500 mL sodium chloride 0.9 % <input type="checkbox"/> Rapid infusion: added to 500 mL sodium chloride 0.9 %					
			Pegfilgrastim	6 mg	mg	subcut	Give at least 24 hours after chemotherapy – prescribe on Med Chart or Outpatient Prescription					

If no reaction to the first dose of rituximab, methylprednisolone may be omitted at the prescribers discretion

Methotrexate Monitoring Guide:

- Check methotrexate level and creatinine every 24 hours, starting 24 hours after the start of the methotrexate infusion
- Folinic acid rescue starts 24 hours after the start of the methotrexate infusion, and continues every 6 hours until methotrexate level is <0.1micromol/L. If required, folinic acid dose and frequency can be escalated as per guidelines below. If this occurs, the doses on the paper chemotherapy chart should be ceased and the new dose and frequency should be prescribed in MedChart.
- Do not reduce fluid infusion rate or folinic acid dose after they have been increased
- If methotrexate level is >0.08micromol/L at 96 hours, folinic acid must be continued until methotrexate level is <0.05micromol/L – continue folinic acid on MedChart and IV fluids on QMR0004B

	24 hours after methotrexate starts	48 hours after methotrexate starts	72 hours after methotrexate starts	96 hours after methotrexate starts	Action
Date and time:					
Methotrexate level:					
Creatinine					
Methotrexate level:		≤ 0.1 micromol/L	≤ 0.1 micromol/L	≤ 0.1 micromol/L	Stop IV fluids and folinic acid
	≤ 20 micromol/L	≤ 1 micromol/L	<0.1 AND >0.05micromol/L	<0.1 AND >0.05micromol/L	Continue current fluid infusion rate and folinic acid dose (30mg) until methotrexate level is <0.08micromol/L
	>20 and <50 micromol/L AND/OR creatinine rises 25 - 50%	>1 and <2 micromol/L AND/OR creatinine rises 25 - 50%	>0.5 and <5 micromol/L AND/ OR creatinine rises 25% - 50%	>0.5 and <5 micromol/L AND/ OR creatinine rises 25% - 50%	Increase fluid infusion rate to 250ml/m ² per hour AND increase folinic acid dose to 30mg IV q3h until next methotrexate level available. Do not reduce fluid infusion rate or folinic acid dose after it is increased.
	≥50 and <200 micromol/L AND/OR creatinine rises >50%	≥2 and <5 micromol/L AND/OR creatinine rises >50%	≥ 0.5 and <5 micromol/L AND/OR creatinine rises >50%	≥ 0.5 and <5 micromol/L AND/OR creatinine rises >50%	Increase fluid infusion rate to 250ml/m ² per hour AND increase folinic acid to 300mg IV q3h until next methotrexate level available. Do not reduce fluid infusion rate or folinic acid dose after they are increased.
	≥ 200 micromol/L	≥ 5 micromol/L	≥ 5 micromol/L	≥ 5 micromol/L	Increase fluid infusion rate to 250ml/m ² per hour AND increase folinic acid to 2000mg IV q6h until next methotrexate level available. Medical emergency – consider glucarpidase. Do not reduce fluid infusion rate or folinic acid dose after they are increased.

Rituximab 375 mg/m ² giving instructions		
	<i>Patient label</i>	
Date		
Standard infusion:	Commence infusion at 50 mg/hr for the first hour, if no side effects; increase the infusion rate in 50 mg increments every 30 minutes to a maximum rate of 400 mg/hr. Remember that the IV line will have been primed with saline therefore rituximab will not be infused immediately. To calculate 50mg in ____mL	
	<table border="1"> <tr> <td> $\frac{\text{Total volume of bag}}{\text{Total dose in bag}} \times 50 \text{ mg} = \text{____ mL}$ </td> </tr> </table>	$\frac{\text{Total volume of bag}}{\text{Total dose in bag}} \times 50 \text{ mg} = \text{____ mL}$
$\frac{\text{Total volume of bag}}{\text{Total dose in bag}} \times 50 \text{ mg} = \text{____ mL}$		
Rapid infusion:	If no previous toxicities, give 20% of the dose over 30 minutes and the remaining 80% over the following 60 minutes.	
If any adverse effects noted:	Discontinue infusion, evaluate severity of symptoms, and treat accordingly. If reactions settle, recommence at ½ the previous rate. Consider hydrocortisone 100 mg IV if required, plus chlorphenamine and paracetamol depending on time interval.	
Recordings:	Document T, P, R, B/P and EWS on adult observation chart (C280010) at baseline, 30 minutes, 60 minutes, and hourly thereafter (more frequently if patient is reacting). Following infusion: Observe for delayed side effects, for 1 hour following 1st infusion. If patient has reacted, observe following subsequent infusion also.	

	Time	Rate	Comments
Baseline			

Note: •Monitor patients with high tumour burden for infusion related reactions and tumour lysis syndrome.
•Ensure adequate hydration and consider addition of allopurinol for 1 – 3 courses.
DO NOT SHAKE during preparation, rotate gently. Aggregation & precipitation of antibody can occur.

PRN medications for Hypersensitivity reactions

Date	Time	Medication	Dose	Route	Doctor	Nurse	Check
		Hydrocortisone	100 mg	Slow IV bolus			
		Paracetamol	1000 mg	PO			
		Chlorphenamine	10 mg	Slow IV bolus			

PRN antiemetics				DR	NURSE SIGN				
	Domperidone	10 mg	PO QID						
	Cyclizine	50 mg	PO/IV Q8H						
	Lorazepam	0.5-1 mg	PO BD						

Rituximab 375 mg/m ² giving instructions		
	<i>Patient label</i>	
Date		
Standard infusion:	Commence infusion at 50 mg/hr for the first hour, if no side effects; increase the infusion rate in 50 mg increments every 30 minutes to a maximum rate of 400 mg/hr. Remember that the IV line will have been primed with saline therefore rituximab will not be infused immediately. To calculate 50mg in ____mL	
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		Chlorphenamine	10 mg	Slow IV bolus			

PRN antiemetics				DR	NURSE SIGN					
	Domperidone	10 mg	PO QID							
	Cyclizine	50 mg	PO/IV Q8H							
	Lorazepam	0.5-1 mg	PO BD							