

<b>Patient Name:</b>  <b>Patient Number:</b>  <b>DOB:</b>  <b>Consultant:</b>  <b>Allergies:</b>	<b>Kent and Medway SACT protocol</b>	Date calculated		Protocol No. HAEM-NHL-018
	High Dose Methotrexate High grade NHL CNS prophylaxis NB Caution in patients over 70 years of age, and/or with significant co-morbidities. Disease modification Frequency and number of cycles: 8-15 days Maximum of 3 cycles.	Height (m)		Written/Checked by: M.Archer H.Paddock O.Okuwa
		Weight (kg)		Authorising Consultant: M.Aldouri
		Surface area (m <sup>2</sup> )		Date written:06.08/2021 Finalised: 30.11.2021 Version No: 1
<ul style="list-style-type: none"> <li>• FBC, U&amp;Es and LFTs pre-dose.</li> <li>• <b>Haematological:</b> If WBC &lt; 3.0 x 10<sup>9</sup>/L or platelets &lt; 100 x 10<sup>9</sup>/L delay treatment for 1 week.</li> <li>• Exclude third space fluids (ascites, pleural effusion) before starting methotrexate</li> <li>• Check urine pH &gt; 7 before starting Methotrexate. Dipstick urine every 2 hours to check pH &gt;7. If urine pH &lt;7 give 100mmol Sodium bicarbonate, if urine pH &gt;7 give 50mmol Sodium Bicarbonate. NB Sodium Bicarbonate infusions must be infused via a central line and commence fluid balance chart.</li> <li>• Monitor urine output every 4 hours, aim for 400ml/m<sup>2</sup>/4 hours (approx. 700ml over 4 hours). Consider furosemide 20mg-40mg if necessary to maintain urine output.</li> <li>• <b>Renal Impairment:</b> If GFR &gt; 80ml/min - no dose adjustment required; if GFR 60-80ml/min - give 65% of dose; if GFR 45-59 ml/min - give 50% of dose; if GFR 30-44ml/min discuss with consultant; contraindicated if GFR &lt;30ml/min. Discuss with consultant for all queries with renal function.</li> <li>• <b>Hepatic Impairment:</b> If bilirubin &lt;50 and AST &lt;180 no dose adjustment required, if bilirubin between 51-85 µmol/L or AST &gt;180 give 75% of dose, if bilirubin &gt; 85 µmol/L – Contraindicated. It is expected that patients receiving high dose methotrexate will develop hypertransaminasemia and occasionally hyperbilirubinemia. These elevations can last up to 2 weeks following the methotrexate infusion and are not considered toxicity requiring discontinuation of repeated administration of methotrexate. Persistent hyperbilirubinemia and/or grade 3-4 hypertransaminasemia for longer than 3 weeks should result in discontinuation of the drug.</li> <li>• <b>Monitoring Methotrexate:</b> <ul style="list-style-type: none"> <li>○ Take levels 48 hours after the start of the Methotrexate infusion and every 24 hours thereafter until methotrexate level is below 0.1µmol/L. Continue folinic acid and hydration until methotrexate levels &lt; 0.1 µmol/L.</li> <li>○ Note exact date and time methotrexate level was drawn.</li> <li>○ Check Methotrexate level immediately prior to T48, T72 and T96 dose of Folinic Acid.</li> </ul> </li> <li>• <b>GLUCARPIDASE – reversal agent:</b> NHS England will fund Glucarpidase as a reversal agent for methotrexate (unlicensed in UK) for adults receiving high-dose methotrexate chemotherapy (doses &gt;1g/m<sup>2</sup>)           <ul style="list-style-type: none"> <li>○ Who develop significant deterioration in renal function (&gt;1.5x ULN and rising, or the presence of oliguria) OR</li> <li>○ Have toxic plasma methotrexate level AND</li> <li>○ Have been treated with all standard rescue and supportive measures AND</li> </ul> </li> </ul>				

- At risk of life-threatening methotrexate-induced toxicities
- The recommended dose is one single intravenous injection of 50units/kg
- **Common drug interactions (for comprehensive list refer to BNF/SPC):**  
Patient must not receive NSAID's, salicylates, sulphonamides or high dose penicillin at the same time as Methotrexate. Patients must not receive co-trimoxazole in the week before the methotrexate infusion. Restart co-trimoxazole once methotrexate level is <0.1 µmol/L and neutrophil count recovery.

**References:** <https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16866>

<http://nssg.oxford-haematology.org.uk/lymphoma/documents/lymphoma-chemo-protocols/L-13-high-dose-methotrexate-high-grade-nhl-cns-prophylaxis.pdf>

EKHUFT proforma HAEM-NHL-018 v3

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

Day	Time	Drug	Dose	Route	Infusion Duration	Administration Details	Batch No	Nurses Sign	Start Time	Stop Time
Day -1 Pre hydration .../.../...		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
Day 1	T0	Ondansetron	<75yrs 16mg >=75yrs 8mg	IV	15 min					
	T0	<b>METHOTREXATE</b>	<b>(3g/m<sup>2</sup>)</b>	IV	4 hrs	High dose Methotrexate is infused through one arm of a Y-extension with hydration through the other.				
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
<b>Prescribers signature &amp; date:</b>						<b>Pharmacists clinical screen &amp; date:</b>	<b>Final release signature &amp; date:</b>			

Day	Time	Drug	Dose	Route	Infusion Duration	Administration Details	Batch No	Nurses Sign	Start Time	Stop time
Day 1 cont		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
Day 2 .../.../...	T24	Folinic acid	30mg	IV	bolus					
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
	T30	Folinic acid	30mg	IV	bolus					
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
	T36	Folinic acid	30mg	IV	bolus					
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
	T42	Folinic acid	30mg	IV	bolus					
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
<b>Prescribers signature &amp; date:</b>						<b>Pharmacists clinical screen &amp; date:</b>	<b>Final release signature &amp; date:</b>			

Day	Time	Drug	Dose	Route	Infusion Duration	Administration Details	Batch No	Nurses Sign	Start Time	Stop time
Day 3 .../.../...	T48	Folinic acid	30mg	PO		Check Methotrexate level immediately prior to dose of Folinic Acid.				
		1L 5% glucose +50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
	T54	Folinic acid	30mg	PO						
		1L 5% glucose +50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
	T60	Folinic acid	30mg	PO						
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
	T66	Folinic acid	30mg	PO						
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
<b>Prescribers signature &amp; date:</b>						<b>Pharmacists clinical screen &amp; date:</b>	<b>Final release signature &amp; date:</b>			

Day	Time	Drug	Dose	Route	Infusion Duration	Administration Details	Batch No	Nurses Sign	Start Time	Stop time
Day 4 .../.../...	T72	Folinic acid	30mg	PO		Check Methotrexate level immediately prior to dose of Folinic Acid.				
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
	T78	Folinic acid	30mg	PO						
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
	T84	Folinic acid	30mg	PO						
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8hrs					
	T90	Folinic acid	30mg	PO						
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
		<b>Prescribers signature &amp; date:</b>				<b>Pharmacists clinical screen &amp; date:</b>	<b>Final release signature &amp; date:</b>			

Day	Time	Drug	Dose	Route	Infusion Duration	Administration Details	Batch No	Nurses Sign	Start Time	Stop time
Day 5	T96	Folinic acid	30mg	PO		Check Methotrexate level immediately prior to dose of Folinic Acid.				
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
	T102	Folinic acid	30mg	PO						
		1L 5% glucose + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
	T108	Folinic acid	30mg	PO						
		1L 0.9% NaCl + 50-100mmol Sodium bicarbonate + 20mmol Potassium chloride	125ml/hr	IV	8 hrs					
	T114	Folinic acid	30mg	PO						
<b>Prescribers signature &amp; date:</b>						<b>Pharmacists clinical screen &amp; date:</b>	<b>Final release signature &amp; date:</b>			

TTO Medication	Drug	Dose	Route	Directions	Date	Quantity	Disp	Check
Day 1	Metoclopramide	10mg	PO	TDS orally for 5 days				
	Diffiam 0.9% mouthwash	10ml	TOP	QDS				
	Aciclovir	400mg	PO	BD				
	Fluconazole	50mg	PO	OD				
	Start on admission <b>Sodium Bicarbonate 3000mg</b> PO QDS for 36 hours and then review. Continue until methotrexate level < 0.1 µmol/L.							
<b>Prescribers signature &amp; date:</b>			<b>Pharmacists clinical screen &amp; date:</b>		<b>Final release signature &amp; date:</b>			