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Non Hodgkins Lymphoma – primary treatment

R-CHOP 21

Indication: Primary chemotherapy for diffuse large B cell NHL.

Treatment option for:
* low-grade NHL with high-grade transformation or high risk features.
* Mantle cell lymphoma.
* Lymphocyte predominant nodular HL

Refer to Network NHL guidelines

Drugs:

Drug	Dose	Route of administration	Day 1	Day 2	Day 3	Day 4	Day 5
Cyclosphosphamide	**750 mg/m^2**	IV	X				
Doxorubicin	**50mg/m^2**	IV	X				
Vincristine*	**1.4mg/m^2**	IV	X				
Prednisolone	**100mg**	PO	X	X	X	X	X
Rituximab	**375mg/m^2**	IV	X				

Repeat every 21 days to a maximum of 8 cycles.

R-CHOP 14

Indication: Primary chemotherapy for diffuse large B cell NHL, except Stage 1A non-bulky.

As part of NCRI trial.

Refer to Network NHL guidelines

Drugs:

Drug	Dose	Route of administration	Day 1	Day 2	Day 3	Day 4	Day 5
Cyclosphosphamide	**750 mg/m^2**	IV	X				
Doxorubicin	**50mg/m^2**	IV	X				
Vincristine	**2mg**	IV	X				
Prednisolone	**100mg**	PO	X	X	X	X	X
Rituximab	**375mg/m^2**	IV	X				

Repeat every 14 days to a maximum of 6 cycles, with further 2 doses of Rituximab.
GCSF support required Day 4-12.

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Non Hodgkins Lymphoma – primary treatment

CHOP

Indication: Primary treatment of T-cell NHL and anaplastic large cell lymphomas.

Refer to Network NHL guidelines

Drugs:

Drug	Dose	Route of administration	Day 1	Day 2	Day 3	Day 4	Day 5
Cyclosphosphamide	**750 mg/m^2**	IV	X				
Doxorubicin	**50mg/m^2**	IV	X				
Vincristine	**2mg**	IV	X				
Prednisolone	**100mg**	PO	X	X	X	X	X

Repeat every 21 days to a maximum of 8 cycles.

R-CVP

Indication: Primary treatment of follicular NHL, except stage 1A disease.

Treatment option for low-grade B-cell NHL: nodal and extranodal marginal zone lymphoma.

Drugs:

Drug	Dose	Route of administration	Day 1	Day 2	Day 3	Day 4	Day 5
Cyclosphosphamide	**750 mg/m^2**	IV	X				
Vincristine*	**1.4mg/m^2**	IV	X				
Prednisolone	**40mg/m^2**	PO	X	X	X	X	X
Rituximab	**375mg/m^2**	IV	X				

Repeat every 21-28 days to a maximum of 8 cycles.

CVP

Indication: Primary treatment for indolent lymphoma and CLL.

Drugs:

Drug	Dose	Route of administration	Day 1	Day 2	Day 3	Day 4	Day 5
Cyclosphosphamide	**750 mg/m^2**	IV	X				
Vincristine*	**1.4mg/m^2**	IV	X				
Prednisolone	**40mg/m^2**	PO	X	X	X	X	X

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Non Hodgkins Lymphoma – primary treatment

REGIMEN	Indication	Drugs
Chlorambucil	Primary and relapse treatment of follicular NHL, except stage 1A disease. Treatment option for low-grade B-cell NHL: marginal zone lymphoma and mantle cell NHL	Chlorambucil orally 10mg daily for 14 days. Repeat every 28 days, depending on blood counts and tolerability
FC (iv protocol)	Primary treatment of mantle cell lymphoma.	Cyclophosphamide 250mg/m² IV Day 1-3 inclusive Fludarabine 25mg/m² IV Day 1-3 inclusive Repeat every 28 days, to a maximum of 6 cycles Irradiated blood products and cotrimoxazole prophylaxis required.
FC (oral protocol)	Primary treatment of mantle cell lymphoma.	Cyclophosphamide 150mg/m² po Day 1-5 inclusive Fludarabine 24mg/m² po Day 1-5 inclusive Repeat every 28 days, to a maximum of 6 cycles Irradiated blood products and cotrimoxazole prophylaxis required.
FCR	Primary treatment of mantle cell lymphoma.	Cyclophosphamide 150mg/m² po Day 1-5 inclusive Fludarabine 24mg/m² po Day 1-5 inclusive Rituximab 375mg/m2 iv Day 1 Repeat every 28 days, to a maximum of 6 cycles Irradiated blood products and cotrimoxazole prophylaxis required.

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Non Hodgkins Lymphoma – primary treatment

<table>
<tr><th>REGIMEN</th><th>Indication</th><th>Drugs</th></tr>
<tr><td>HyperCVAD</td><td>Primary therapy for young patients with mantle cell lymphoma.

Alternates CVAD/ MA – 4 cycles if proceeding to stem cell transplant.
Up to 8 cycles in total</td><td>
Course 1: Hyper-CVAD (Cycles 1, 3, 5, & 7)
<table>
<tr><th>Days</th><th>Drug</th><th>Dose</th><th>Route</th><th>Comments</th></tr>
<tr><td>1-3</td><td>Cyclophosphamide</td><td>300mg/m²</td><td>IV over 2hrs, 12hrly total of 6 doses.</td><td>Mesna see below</td></tr>
<tr><td>4-5</td><td>Doxorubicin</td><td>50mg/m²</td><td>IV continuously over 48hrs</td><td></td></tr>
<tr><td>4 & 11</td><td>Vincristine</td><td>1.4mg/m²</td><td>Intravenous infusion in 50ml sodium chloride 0.9% over 10 minutes, as per national guidance. Nurse to remain with patient throughout infusion</td><td>Maximum 2mg</td></tr>
<tr><td>1-4
11-14</td><td>Dexamethasone</td><td>40mg</td><td>Oral, daily</td><td></td></tr>
</table>
Course 2: MTX/ARA-C (Cycles 2, 4, 6, & 8)
<table>
<tr><th>Days</th><th>Drug</th><th>Dose</th><th>Route</th><th>Comments</th></tr>
<tr><td>1-2</td><td>Methotrexate</td><td>1g/m²</td><td>IV for 24hrs continuously</td><td>200mg/m² for 2hrs then 800mg/m² for 22hrs</td></tr>
<tr><td>2-3</td><td>Cytarabine</td><td>3g/m²</td><td>IV over 2hrs, 12hrly total of 4 doses</td><td></td></tr>
</table>
</td></tr>
<tr><td>IDARAM</td><td>Treatment of primary and secondary CNS diffuse large B-cell NHL.

Alternative regimen is high dose Methotrexate as a single agent (see</td><td>
Cytarabine 70mg intrathecal Day 1, then weekly if CSF disease.
Methotrexate 12.5mg intrathecal Day 1, then weekly if CSF disease.

Idarubicin 10mg/m2 IV Day 2 and Day 3
Cytarabine 1000mg/m2 IV Day 2 and Day 3
Methotrexate 2000mg/m2 IV Day 4 **
Dexamethasone 100mg IV Days 2, 3 and 4
</td></tr>
</table>

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	below)	**** Starting 24 hours from end of methotrexate (MTX) infusion:** **Folinic acid** 15mg/m2 (adjusted if MTX levels indicate) IV every 6 hours Refer to local Trust protocol for folinic acid rescue. **G-CSF** (Lenograstim 263mcg **or** Filgrastim 300mcg) from Day 7
High dose Methotrexate	Treatment of primary and secondary CNS diffuse large B-cell NHL.	Methotrexate 300mg/m² IV IV infusion in 200mLs Sodium Chloride 0.9% over 1hr as a loading dose, immediately followed by the 23hr infusion. Methotrexate 2700mg/m² IV IV infusion in 1000mLs Sodium Chloride 0.9% over 23hrs, immediately following the 1hrloading dose. Follow local Trust policy for high dose Methotrexate and fluid support, urinary alkalinisation and folinic acid rescue. Repeat every 14-21 days, up to 4 treatments in total. Monitor renal function with GFR, on alternate cycles.
CODOX-M / IVAC	These are complex protocols for highly aggressive B-NHL, most commonly Burkitts or Burkitts-like NHL. Rituximab should be given with each cycle for CD20+ B-cell lymphoma. There is a dose modified protocol for patients aged >65 years and those with	These are complex protocols, please note also there are dose modifications for older patients (>65 years old). Please refer to local Trust protocols for details of regimens. Perform GFR/creatinine clearance before each course of high-dose Methotrexate. Low risk patients receive 3 cycles of CODOX-M (refer to protocol for risk factors). High risk patients received 4 cycles in total CODOX-M/ IVAC/ CODOX-M/ IVAC. CNS intensification with the first two cycles of treatment should be considered, for patients with known CNS involvement.

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	comorbidities.	
NORDIC PROTOCOL	For mantle cell lymphoma	Maxi-CHOP21 x3 alternating with High dose Cytarabine x2 MAXI-CHOP21: cyclophosphamide 1200 mg/m^2 intravenously, doxorubicin 75 mg/m^2 intravenously, vincristine 2 mg total intravenously day 1; prednisone 100 mg days 1-5 orally Cytarabine: 3 g/m^2 (3-hour infusion intravenously) every 12 hours for a total of 4 doses; patients older than 60 years, cytarabine 2 g/m^2 Rituximab 375 mg/m^2 intravenously on day 1 of each cycle from cycle 4 Mobilisation with High-dose Cytarabine (Day 1+9: Rituximab as in vivo purging)

Non Hodgkins Lymphoma – relapse treatment

REGIMEN	Indication	Drugs
ICE +/- Rituximab	For patients with relapsed NHL, considered fit for intensive treatment and a candidate for autologous stem cell transplant. ICE is an alternative salvage regimen (Rituximab omitted) for patients with relapsed T cell or anaplastic NHL.	

Chemotherapy regimen	Dose	D –2*	D1	D2	D3	D4	D5	D6 to D13
Rituximab	375 mg/m^2	X	X					
Etoposide	100 mg/m^2		X	X	X			
Carboplatine	AUC (5) max 800			X				
Ifosfamide continous infusion + mesna*	5 g/m²/24h			X	→			
G-CSF (SC)	Recommended							X

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<table>
<tr><td>DHAP +/- Rituximab</td><td>For patients with relapsed NHL, considered fit for intensive treatment and a candidate for autologous stem cell transplant.

DHAP is an alternative salvage regimen (Rituximab omitted) for patients with relapsed T cell or anaplastic NHL.</td><td>
<table>
<tr><th>Days</th><th>Drug</th><th>Dose</th><th>Route</th><th>Comments</th></tr>
<tr><td>1-4</td><td>Dexamethasone</td><td>40mg od</td><td>PO</td><td>Take in morning with food</td></tr>
<tr><td>1</td><td>Cisplatin</td><td>100mg/m²</td><td>IV</td><td>Infusion in 500mls-1litre 0.9% NaCl over 24hrs</td></tr>
<tr><td>2</td><td>Cytarabine †</td><td>2gm/m² 12hourly for 2 doses</td><td>IV</td><td>Infusion in 1litre 0.9% NaCl over 3hrs Start time of each infusion is 12hrs apart</td></tr>
</table>
</td></tr>
</table>

Non Hodgkins Lymphoma – relapse treatment

<table>
<tr><th>REGIMEN</th><th>Indication</th><th>Drugs</th></tr>
<tr><td>ESHAP +/- Rituximab</td><td>For patients with relapsed NHL, considered fit for intensive treatment and a candidate for autologous stem cell transplant.

ESHAP is an alternative salvage regimen (Rituximab omitted) for patients with relapsed T cell or anaplastic NHL.</td><td>
<table>
<tr><th>Days</th><th>Drug</th><th>Dose</th><th>Route</th><th>Comments</th></tr>
<tr><td>1 OR 5</td><td>Cytarabine</td><td>2g/m²</td><td>IV</td><td>Infusion in 500mls-1litre 0.9% NaCl over 2hrs</td></tr>
<tr><td>1-4</td><td>Etoposide</td><td>40mg/m² od</td><td>IV</td><td>Infusion in 250-1000mls 0.9% NaCl infusion over 1hr</td></tr>
<tr><td>1-4</td><td>Cisplatin</td><td>25mg/m² od</td><td>IV</td><td>Infusion in 500mls-1litre 0.9% NaCl over 24hrs</td></tr>
<tr><td>1-5</td><td>Methylprednisolone</td><td>500mg od</td><td>IV</td><td>Infusion in 100mls 0.9% NaCl over 15-30 mins</td></tr>
</table>
Please note significant risk of nephrotoxicity and GFR should be monitored
</td></tr>
</table>

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<table>
<tr><td></td><td></td><td></td></tr>
<tr><td>IVE +/- Rituximab</td><td>For patients with relapsed NHL, considered fit for intensive treatment and a candidate for autologous stem cell transplant.

IVE is an alternative salvage regimen (Rituximab omitted) for patients with relapsed T cell or anaplastic NHL.</td><td>
<table>
<tr><th>Days</th><th>Drug</th><th>Dose</th><th>Route</th><th>Comments</th></tr>
<tr><td>1</td><td>Epirubicin</td><td>50mg/m²</td><td>IV</td><td>Bolus injection via fast running drip of 0.9% NaCl</td></tr>
<tr><td>1-3</td><td>Etoposide</td><td>200mg/m²</td><td>IV</td><td>Infusion in 1litre 0.9% NaCl over 2hrs</td></tr>
<tr><td>1-3</td><td>Mesna †</td><td>600mg/m² od</td><td>IV</td><td>Bolus</td></tr>
<tr><td>1-3</td><td>Ifosfamide + Mesna</td><td>3g/m² + 3g/m²</td><td>Combined IV</td><td>Infusion in 1litre 0.9% NaCl over 22hrs</td></tr>
<tr><td>4</td><td>Mesna</td><td>1.8g/m²</td><td>IV</td><td>Infusion in 1litre 0.9% NaCl over 12hrs</td></tr>
</table>
</td></tr>
<tr><td>Rituximab (single agent)</td><td>Relapsed follicular NHL.</td><td>Rituximab 375mg/m^2 iv

Given weekly x 4. Maximum of 4 infusions</td></tr>
<tr><td>Rituximab (maintenance)</td><td>Relapsed follicular NHL.</td><td>Rituximab 375mg/m^2 iv

Given every 3 months for a maximum total of 8 doses (2 years). Stop if evidence of disease progression on treatment.</td></tr>
<tr><td>Fludarabine (single agent)</td><td>Relapsed low grade NHL and mantle cell lymphoma.</td><td>Fludarabine 40mg/m^2 po once daily for 5 days

Repeat every 28 days as tolerated. Up to 6 cycles of treatment.</td></tr>
</table>

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<table>
<tr>
<td>Mini-BEAM +/-</td>
<td>For patients with relapsed NHL, considered fit for intensive treatment and a candidate for autologous stem cell transplant.

Mini-BEAM is an alternative salvage regimen (Rituximab omitted) for patients with relapsed T cell or anaplastic NHL.</td>
<td>
<table>
<tr><th>Days</th><th>Drug</th><th>Dose</th><th>Route</th><th>Comments</th></tr>
<tr><td>1</td><td>Carmustine</td><td>60mg/m²</td><td>IV</td><td>Infusion in 250-500mls 0.9% NaCl (use PVC free infusion bag) over 1hr</td></tr>
<tr><td>2-5</td><td>Cytarabine</td><td>100mg/m² twice daily</td><td>IV</td><td>Infusion in 100mls 0.9% NaCl over 30mins</td></tr>
<tr><td>2-5</td><td>Etoposide</td><td>75mg/m² od</td><td>IV</td><td>Infusion in 500mls 0.9% NaCl over 1hr</td></tr>
<tr><td>6</td><td>Melphalan †‡</td><td>30mg/m²</td><td>IV</td><td>Bolus injection; give within 30mins of preparation OR infusion in 0.9% NaCl over 30mins (use within 3 hours after reconstitution).</td></tr>
</table>
</td>
</tr>
<tr>
<td>GEM-P</td>
<td>Relapsed high-grade NHL and Hodgkins lymphoma.

This is often applied as a third line protocol, for patients receiving previous salvage chemotherapy.</td>
<td>Gemcitabine (1000 mg m^{-2}) days 1, 8 and 15.
Cisplatin (100 mg m^{-2}) day 15 only, with pre & post hydration
Methylprednisolone 1000 mg either orally or intravenously on days 1–5.

The cycle is repeated every 28 days</td>
</tr>
</table>

Lymphoma – conditioning schedules for high dose chemotherapy and stem cell transplantation *Relevant only for Level 3 & 4 units as appropriate to deliver transplantation.*		
REGIMEN	**Indication**	**Drugs**

Please note the protocols within this list are highly complex and local policies for prescribing and supportive care should be referred to. The list below is advisory and not to be used as a prescribing template.

BEAM

High dose chemotherapy for relapsed, chemo-sensitive Non-Hodgkins Lymphoma and relapsed/refractory Hodgkins Lymphoma

Days	Drug	Dose	Route	Comments
1	Carmustine	300mg/m²	IV	Infusion in 500mls 0.9% NaCl (use PVC free infusion bag) over 2hrs
2-5	Cytarabine	200mg/m² **twice daily**	IV	Infusion in 100mls 0.9% NaCl over 30mins
2-5	Etoposide	200mg/m²	IV	Infusion in 1litre 0.9% NaCl over 2hrs
6	Melphalan ‡	140mg/m²	IV	Infusion in 250mls 0.9% NaCl over 30mins within 3hrs of reconstitution
8	**Thaw and reinfuse haemopoietic stem cells §**			

LACE

High dose chemotherapy for relapsed, chemo-sensitive Non-Hodgkins Lymphoma and relapsed/refractory Hodgkins Lymphoma

Days	Drug	Dose	Route	Comments
1	Lomustine	200mg/m²	PO	Single dose; round dose to nearest 40mg
1-3	Etoposide *	330mg/m² od	IV	Infusion in 500ml-1litre 0.9% NaCl over 2hrs
2-3	Cytarabine	2g/m² od	IV	Infusion in 1litre 0.9% NaCl over 2hrs.
4-6	Mesna †	1.8g/m²	IV	Bolus or IV infusion in 100mls 0.9% NaCl over 15mins immediately before each dose of Cyclophosphamide.
4-6	Cyclophosphamide	1.8g/m² od	IV	Infusion in 500mls 0.9% NaCl over 60mins
4-6	Mesna †	800mg/m² x 6/day †	IV	Bolus or IV infusion in 100mls 0.9% NaCl over 15mins every 3hrs
8	**Thaw and reinfuse haemopoietic stem cells §**			