CHOEP Therapy– 21 days

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Protocol Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of T-cell Non-Hodgkins Lymphoma</td>
<td>C85</td>
<td>00396a</td>
</tr>
</tbody>
</table>

ELIGIBILITY:
- Indication as above
- Age < 60 years
- Adequate haematological, renal and liver status

EXCLUSIONS:
- Hypersensitivity to DOXOrubicin, cyclophosphamide, etoposide, vinCRISTine sulphate or any of the excipients.
- A cumulative life-long dose of 450mg/m² of DOXOrubicin should only be exceeded with extreme caution as there is as risk of irreversible congestive heart failure
- Severe liver impairment (etoposide)
- Pregnancy.
- Lactation.

TESTS:
**Baseline tests:**
- FBC, U&Es, LFTs, LDH, blood glucose.
- ECG
- MUGA or ECHO should be considered prior to the administration of DOXOrubicin in high-risk patients.
- Virology screen -Hepatitis B (HBsAg, HBcoreAb) & C, HIV.

**Hepatitis B Reactivation:** All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with Lamivudine 100 mg/day orally, for the entire duration of chemotherapy.
Regular tests:
- FBC, U&Es, LFTs, LDH prior to each cycle.
- Evaluate for peripheral neuropathy prior to each cycle.
- Cardiac function if clinically indicated

Disease monitoring/assessment:
Disease monitoring/assessment should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant

TREATMENT:
The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient’s individual clinical circumstances.

Treatment is administered every 21 days for a maximum of 6 cycles or until disease progression or unacceptable toxicity develops.

Treatment can then be followed by BEAM (Ref NCCP Protocol 00408) and autologous transplant in suitable patients.

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cyclophosphamide</td>
<td>750mg/m²</td>
<td>IV infusion a</td>
<td>100 to 250mL 0.9% NaCl over 20 min to 1 hour</td>
</tr>
<tr>
<td>1</td>
<td>DOXOubicin b</td>
<td>50mg/m²</td>
<td>IV Bolus over 2-15 mins</td>
<td>Into the side arm of a fast running 0.9% NaCl infusion</td>
</tr>
<tr>
<td>1</td>
<td>VinCRIStine c</td>
<td>1.4mg/m² (Max 2mg)</td>
<td>IV infusion</td>
<td>50ml minibag 0.9% NaCl over 5-15 minutes</td>
</tr>
<tr>
<td>1-5</td>
<td>Prednisolone d</td>
<td>100mg(9)</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>IV infusion</td>
<td>1000mls 0.9% NaCl or Dextrose 5% over 30-60minutes</td>
</tr>
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a Cyclophosphamide may also be administered as an IV bolus over 5-10 mins
b Lifetime cumulative dose of doxorubicin is 450mg/m²

c VinCRIStine is a neurotoxic chemotherapeutic agent.

In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors below and to the age of the patient

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d Alternative steroid regimens may be used at consultant discretion

NCCP Protocol: CHOEP Therapy- 21 days

Published: 08/03/2017
Review: 08/03/2019

Tumour Group: Lymphoma and Myeloma
NCCP Protocol Code: 00396

IHS Contributor: Prof. Elizabeth Vandenberghe
ISMO Contributor : Prof Maccon Keane

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE’s terms of use available at http://www.hse.ie/eng/Disclosure

This information is valid only on the day of printing; for any updates please check www.hse.ie/NCCPchemoprotocols
DOSE MODIFICATIONS:
- Any dose modification should be discussed/ approved by with a Consultant
- Consider vinCRIStine dose reduction in elderly patients

Haematological:

<table>
<thead>
<tr>
<th>ANC x 10^9/L</th>
<th>Platelets x 10^9/L</th>
<th>Dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 and/or &lt; 75</td>
<td></td>
<td>Dose modification not generally indicated. Consider treatment delay and/or add G-CSF.</td>
</tr>
</tbody>
</table>

Renal and Hepatic Impairment:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>GFR (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td></td>
<td>&gt;20 100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10-20 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;10 50%</td>
<td></td>
</tr>
<tr>
<td>DOXOrubicin</td>
<td>No dose reduction required. Clinical decision in severe impairment</td>
<td>Total Bilirubin (micromol/L)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20-51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51-85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;85</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VinCRIStine</td>
<td>No dose modification required</td>
<td>Total Bilirubin (micromol/L)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26-51 or 60-180</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;51 and Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;51 and &gt;180</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Cr Cl (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td></td>
<td>&gt;50 100%</td>
<td>26-51 or 60-180</td>
</tr>
<tr>
<td></td>
<td>15-50 75%</td>
<td>&gt;51 or &gt;180</td>
</tr>
<tr>
<td></td>
<td>&lt;15 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subsequent doses should be based on clinical response</td>
<td></td>
</tr>
</tbody>
</table>
Neurotoxicity:
Table 1: Dose modification of vinCRISTine based on neurotoxicity (CTCAE v4.0)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dose of VinCRISTine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>100%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Hold until recovery then reduce dose by 50%</td>
</tr>
<tr>
<td>Grade 3.4</td>
<td>Omit</td>
</tr>
</tbody>
</table>

SUPPORTIVE CARE:
EMETOGENIC POTENTIAL: High (Refer to local policy).

PREMEDICATIONS:
Not usually required unless the patient has had a previous hypersensitivity.

TAKE HOME MEDICATION:
Prednisolone tablets.
See supportive care below.

OTHER SUPPORTIVE CARE:
G-CSF prophylaxis may be required, please discuss with consultant
Tumour lysis syndrome prophylaxis – consider use of allopurinol 300mg daily for the first cycle (Refer to local policy)
PJP prophylaxis (Refer to local policy)
Anti-viral prophylaxis (Refer to local policy)
Anti-fungal prophylaxis (Avoid the concurrent use of azoles and vinCRISTine (6) (Refer to local policy)
Prophylactic regimen against vinCRISTine induced constipation is recommended (Refer to local policy).
Proton Pump Inhibitor while on prednisolone (Refer to local policy)
Patients should have an increased fluid intake of 2-3 litres on day 5 to prevent haemorrhagic cystitis associated with cyclophosphamide.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- Neuropathy: VinCRISTine may cause peripheral neuropathy which is dose related and cumulative, requiring monitoring before each dose is administered. The presence of pre-existing neuropathies or previous treatment with other neurotoxic drugs may increase risk of peripheral neuropathy. Patients with mild peripheral neuropathy can usually continue to receive full doses of vinCRISTine, but when
symptoms increase in severity and interfere with neurologic function, dose reduction or discontinuation of the drug may be necessary. The natural history following discontinuation of treatment is gradual improvement, which may take up to several months. A routine prophylactic regimen against constipation is recommended for all patients receiving vinCRIStine sulphate. Paralytic ileus may occur. The ileus will reverse itself upon temporary discontinuance of vinCRIStine and with symptomatic care.

- **Cardiac Toxicity**: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with cardiac dysfunction.
- **Extravasation**: DOXOrubicin and vinCRIStine cause pain and possible tissue necrosis if extravasated (refer to local policy).

### DRUG INTERACTIONS:
- DOXOrubicin cardiotoxicity is enhanced by previous or concurrent use of other anthracyclines, or other potentially cardiotoxic drugs (e.g. 5-FU, cyclophosphamide or paclitaxel) or with products affecting cardiac function (e.g. calcium antagonists).
- Current drug interaction databases should be consulted for more information including potential for interactions with CYP3AR inhibitors/inducers.

### ATC CODE:
- Cyclophosphamide - L01AA01
- DOXOrubicin - L01DB01
- Etoposide - L01CB01
- VinCRIStine - L01CA02

### REIMBURSEMENT CATEGORY:
All of these drugs are funded through local hospital budgets (Jan. 2017).

### PRESCRIPTIVE AUTHORITY:
The treatment plan must be initiated by a Consultant Medical Oncologist or by a Consultant Haematologist working in the area of haematological malignancies.
REFERENCES:


NCCP Chemotherapy Protocol

Version | Date | Amendment | Approved By
--- | --- | --- | ---
1 | 08/03/2017 | | Prof Elizabeth Vandenberghe
| | | Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie

Cardiotoxicity is a risk associated with anthracycline therapy that may be manifested by early (acute) or late (delayed) effects.

Risk factors for developing anthracycline-induced cardiotoxicity include:
• high cumulative dose, previous therapy with other anthracyclines or anthracenediones
• prior or concomitant radiotherapy to the mediastinal/pericardial area
• pre-existing heart disease
• concomitant use of other potentially cardiotoxic drugs

In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors above and to the age of the patient.