

## cycloPHOSphamide, DOXOrubicin, vinCRISStine and prednisoLONE (CHOP) Therapy– 21 days

### INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of Non Hodgkins lymphoma (NHL)	C85	00841a	Hospital

### 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 patients individual clinical circumstances.

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

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	DOXOrubicin <sup>1</sup>	50mg/m <sup>2</sup>	IV Bolus	Into the side arm of a fast running 0.9% NaCl infusion	1-6
1	vinCRISStine <sup>2</sup>	1.4mg/m <sup>2</sup> (Max 2mg)	IV infusion	50ml minibag 0.9% NaCl over 15 minutes	1-6
1	cycloPHOSphamide	750mg/m <sup>2</sup>	IV infusion <sup>3</sup>	250 ml 0.9% NaCl over 30 minutes	1-6
1-5	prednisoLONE	100mg*	PO		1-6
<sup>1</sup> Lifetime cumulative dose of DOXOrubicin is 450mg/m <sup>2</sup> . <b>In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors outlined below and to the age of the patient.</b>					
<sup>2</sup> vinCRISStine is a neurotoxic chemotherapeutic agent. Refer to NCCP Guidance on the Safe Use of Neurotoxic drugs (including Vinca Alkaloids) in the treatment of cancer <a href="#">Here</a>					
<sup>3</sup> cycloPHOSphamide may also be administered as an IV bolus over 5-10mins.					
*Alternative steroid regimens may be used at consultant discretion.					

### ELIGIBILITY:

- Indications as above
- Adequate haematological, renal and liver status

NCCP Regimen: CHOP Therapy-21 days	Published: 1/12/2020 Review: 04/10/2026	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00841	IHS Contributor (original regimen 00307): Prof E Vandenberghe ISMO Contributor (original regimen 00307): Prof Maccon Keane	Page 1 of 6
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 <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a> This information is valid only on the day of printing, for any updates please check <a href="http://www.hse.ie/NCCPchemoregimens">www.hse.ie/NCCPchemoregimens</a>		

## EXCLUSIONS:

- Hypersensitivity to DOXOrubicin, cycloPHOSphamide, vinCRISTine sulphate, prednisoLONE, or any of the excipients.
- A cumulative life-long dose of 450mg/m<sup>2</sup> of DOXOrubicin should only be exceeded with extreme caution as there is as risk of irreversible congestive heart failure.
- Pregnancy or lactation.

## 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.

## TESTS:

### Baseline tests:

- FBC, renal and liver profile
  - ECG
  - MUGA or ECHO should be considered prior to the administration of DOXOrubicin
  - LDH, Uric acid
  - Virology screen - Hepatitis B (HBsAg, HBcoreAb) & C, HIV\*
- \*See Adverse Effects/Regimen Specific Complications

### Regular tests:

- FBC, renal and liver profile and LDH prior to each cycle
- Evaluate for peripheral neuropathy prior to each cycle
- MUGA or ECHO as clinically indicated

### Disease monitoring:

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

## DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Consider vinCRISTine dose reduction in elderly patients.

NCCP Regimen: CHOP Therapy-21 days	Published: 1/12/2020 Review: 04/10/2026	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00841	IHS Contributor (original regimen 00307): Prof E Vandenberghe ISMO Contributor (original regimen 00307): Prof Maccon Keane	Page 2 of 6
<p>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 <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a></p> <p><i>This information is valid only on the day of printing, for any updates please check <a href="http://www.hse.ie/NCCPchemoregimens">www.hse.ie/NCCPchemoregimens</a></i></p>		

**Haematological:**

**Table 2: Dose modification in haematological toxicity**

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose
< 1	and/or	< 75	Delay treatment until recovery. Consider treatment delay and/or add G-CSF adding G-CSF.

**Renal and Hepatic Impairment:**

**Table 3: Recommended dose modification in Renal and Hepatic Impairment:**

Drug	Renal impairment		Hepatic impairment				
cycloPHOSphamide	CrCl (ml/min)	Dose	Severe impairment: Clinical decision				
	>20	100%					
	10-20	75%					
	<10	50%					
DOXOrubicin	No dose reduction required. Clinical decision in severe impairment.		Bilirubin (micromole/L)		Dose		
			20-51		50%		
			51-85		25%		
			>85		Omit		
			If AST 2-3 x ULN give 75% dose If AST > 3 x ULN give 50% dose				
vinCRISine	No dose reduction required.		Bilirubin (micromol/L)		AST/ALT	Dose	
			26-51		or	60-180	50%
			>51		and	Normal	50%
			>51		and	>180	Omit

**Management of adverse events:**

**Table 4: Recommended dose modification based on adverse events**

Adverse reactions		Recommended dose modification
<b>vinCRISine</b>		
Neurotoxicity*	Grade 1	100%
	Grade 2	Hold until recovery then reduce dose by 50%
	Grade 3-4	Omit

\*Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

**SUPPORTIVE CARE:**

**EMETOGENIC POTENTIAL:**

**DOXOrubicin/cycloPHOSphamide: High (Refer to local policy)**

**vinCRISine: Minimal (Refer to local policy)**

NCCP Regimen: CHOP Therapy-21 days	Published: 1/12/2020 Review: 04/10/2026	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00841	IHS Contributor (original regimen 00307): Prof E Vandenberghe ISMO Contributor (original regimen 00307): Prof Maccon Keane	Page 3 of 6

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/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

## OTHER SUPPORTIVE CARE:

- Prophylactic regimen against vinCRISTine-induced constipation is recommended (**Refer to local policy**).
- G-CSF prophylaxis may be required.
- Tumour lysis syndrome prophylaxis (**Refer to local policy**).
- Anti-viral prophylaxis (**Refer to local policy**).
- Anti-fungal prophylaxis (Avoid the concurrent use of azoles and vinCRISTine (**Refer to local policy**)).
- Proton-pump inhibitor during steroid treatment (**Refer to local policy**).
- PJP prophylaxis (**Refer to local policy**).
- Patients should have an increased fluid intake of 2-3 litres on day 1 and 2 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.

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy (**Refer to local infectious disease policy**). These patients should be considered for assessment by hepatology.
- **Extravasation:** vinCRISTine and DOXOrubicin causes pain and possible tissue necrosis if extravasated (**Refer to local policy**).

### vinCRISTine

- **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.
- **Constipation:** 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.

### DOXOrubicin

- **Cardiotoxicity:** DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction.

NCCP Regimen: CHOP Therapy-21 days	Published: 1/12/2020 Review: 04/10/2026	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00841	IHS Contributor (original regimen 00307): Prof E Vandenberghe ISMO Contributor (original regimen 00307): Prof Maccon Keane	Page 4 of 6

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/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

## DRUG INTERACTIONS:

- DOXOrubicin cardiotoxicity is enhanced by previous or concurrent use of other anthracyclines, or other potentially cardiotoxic drugs (e.g. 5-Flourouracil, 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 CYP3A4 inhibitors/inducers.

## REFERENCES:

1. McKelvey EM, Gottlieb JA, Wilson HE, Haut A, et al. Hydroxyldaunomycin (Adriamycin) combination therapy in malignant lymphoma. *Cancer* 1976; 38:484-93.
2. Fisher RI, Gaynor ER, Dahlberg S, Oken MM, et al. Comparison of a standard regimen (CHOP) with three intensive chemotherapy regimens for advanced non-Hodgkin's lymphoma. *N Engl J Med* 1993; 328:1002-6.
3. Pfreundschuh M, et al; German High-Grade Non-Hodgkin Lymphoma Study Group (DSHNHL). Six versus eight cycles of bi-weekly CHOP-14 with or without rituximab in elderly patients with aggressive CD20+ B-cell lymphomas: a randomised controlled trial (RICOVER-60). *Lancet Oncol.* 2008 Feb;9(2):105-16.
4. Krens S D, Lassche,Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Onco*/2019; 20: e201-08.
5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: <https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf>
6. Vinca alkaloids + Azoles. Stockley's Drug Interactions 11th Edition
7. cycloPHOSphamide (Endoxana®) Summary of Product Characteristics. Accessed June 2023. Available at: [https://www.hpra.ie/img/uploaded/swedocuments/Licence\\_PA2299-027-001\\_21122018112107.pdf](https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2299-027-001_21122018112107.pdf)
8. vinCRISStine Summary of Product Characteristics. Accessed June 2023. Available at: <https://www.medicines.ie/medicines/vincristine-sulphate-1-mg-ml-solution-for-injection-or-infusion-34195/spc>
9. DOXOrubicin Summary of Product Characteristics. Accessed June 2023. Available at: [https://www.hpra.ie/img/uploaded/swedocuments/Licence\\_PA2315-083-001\\_26022020112618.pdf](https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2315-083-001_26022020112618.pdf)

Version	Date	Amendment	Approved By
1	1/12/2020		Based on NCCP regimen 00307 (*riTUXimab) Cyclophosphamide, DOXOrubicin, vinCRISStine and Prednisolone (*R)-CHOP) Therapy– 21 days V3 12/02/2020
2	04/10/2021	Reviewed. Amended baseline tests and emetogenic potential, added to adverse effects (DOXOrubicin)	Prof Maccon Keane

NCCP Regimen: CHOP Therapy-21 days	Published: 1/12/2020 Review: 04/10/2026	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00841	IHS Contributor (original regimen 00307): Prof E Vandenberghe ISMO Contributor (original regimen 00307): Prof Maccon Keane	Page 5 of 6

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/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

3	01/11/2023	Updated order of administration and number of cycles. Updated emetogenic potential section.	Prof Maccon Keane Prof Elisabeth Vandenberghe
---	------------	--	--

Comments and feedback welcome at [oncologydrugs@cancercontrol.ie](mailto:oncologydrugs@cancercontrol.ie).

<sup>i</sup> 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

NCCP Regimen: CHOP Therapy-21 days	Published: 1/12/2020 Review: 04/10/2026	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00841	IHS Contributor (original regimen 00307): Prof E Vandenberghe ISMO Contributor (original regimen 00307): Prof Maccon Keane	Page 6 of 6
<p>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 <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a></p> <p><i>This information is valid only on the day of printing, for any updates please check <a href="http://www.hse.ie/NCCPchemoregimens">www.hse.ie/NCCPchemoregimens</a></i></p>		