

**Dose Adjusted riTUXimab S/C, Etoposide, prednisoLONE,
DOXOrubicin, cycloPHOSphamide and vinCRISStine
(DA-R(S/C) EPOCH) Therapy**

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of patients with CD20 positive diffuse large B-cell Non Hodgkin’s lymphoma (NHL)	C83	00672a	Hospital

TREATMENT: (Please see treatment table on next page)

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 up to 6 cycles or until disease progression or unacceptable toxicity develops.

Note:

- Patient must have previously received a full dose of intravenous riTUXimab before being switched to subcutaneous (S/C) formulation.
- Patients who have previously received a full dose of intravenous riTUXimab may consider commencing therapy with this regimen using S/C riTUXimab from Cycle 1. Consideration should be given to the length of time since last full dose of intravenous riTUXimab (**Refer to local policy**).

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

ELIGIBILITY:

- Previously untreated high or intermediate risk diffuse large B-cell NHL
- ECOG status 0-2

EXCLUSIONS:

- Hypersensitivity to cycloPHOSphamide, DOXOrubicin, etoposide, vinCRISStine, riTUXimab 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)
- Breast feeding
- Pregnancy

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist or Consultant Haematologist working in the area of haematological malignancies

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 1 of 10

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

Drug	Dose Level								Administration	Day	Cycle
	- 2	- 1	Dose Level 1 Initial dose	2	3	4	5	6			
riTUXimab	375mg/m ²	375mg/m ²	375mg/m ²	375mg/m ²	375mg/m ²	375mg/m ²	375mg/m ²	375mg/m ²	IV infusion in 500ml NaCl 0.9% ^a	1	1 (only)
riTUXimab	1400mg (fixed dose in 11.7ml)	1400mg (fixed dose in 11.7ml)	1400mg (fixed dose in 11.7ml)	1400mg (fixed dose in 11.7ml)	1400mg (fixed dose in 11.7ml)	1400mg (fixed dose in 11.7ml)	1400mg (fixed dose in 11.7ml)	1400mg (fixed dose in 11.7ml)	Subcutaneous injection (SC) over 5 minutes into abdominal wall^{b, c, d}	1	2-6
^e Etoposide	50mg/m ²	50mg/m ²	50mg/m ²	60mg/m ²	72mg/m ²	86.4mg/m ²	103.7mg/m ²	124.4mg/m ²	Dilute in 500ml NaCl 0.9% & infuse over 24 hours	1,2,3,4	1-6
^{e, f} DOXOrubicin	10mg/m ²	10mg/m ²	10mg/m ²	12mg/m ²	14.4mg/m ²	17.3mg/m ²	20.7mg/m ²	24.8mg/m ²	Concomitantly in 1000ml NaCl 0.9% & infuse IV over 24 hours	1,2,3,4	1-6
^{e, g} vinCRiStine	0.4mg/m ²	0.4mg/m ²	0.4mg/m ²	0.4mg/m ²	0.4mg/m ²	0.4mg/m ²	0.4mg/m ²	0.4mg/m ²		1,2,3,4	1-6
cycloPHOSphamide	480mg/m ²	600mg/m ²	750mg/m ²	900mg/m ²	1080mg/m ²	1296mg/m ²	^h 1555mg/m ² (Requires mesna)	ⁱ 1866mg/m ² (Requires mesna)	IV infusion in 250ml NaCl 0.9% over 30 minutes	5	1-6
^l G-CSF (Round to nearest whole syringe)	5mcg/kg	5mcg/kg	5mcg/kg	5mcg/kg	5mcg/kg	5mcg/kg	5mcg/kg	5mcg/kg	SC – No sooner than 24 hrs after the end of cyclophosphamide infusion	^j From day 6, until ANC ≥5 X10 ⁹ /L	1-6
prednisOLONE	120mg/m ²	120mg/m ²	120mg/m ²	120mg/m ²	120mg/m ²	120mg/m ²	120mg/m ²	120mg/m ²	PO in two divided doses (i.e. 6am and 12noon)	1-5	1-6

^a See Table 1: Guidance for administration of riTUXimab.

^b Patient must have previously received a full dose intravenous riTUXimab before being switched to subcutaneous formulation.

^c During treatment with subcutaneous riTUXimab, administer other subcutaneous drugs at alternative injection sites whenever possible.

^d Patients should be observed for at least 15 minutes following riTUXimab subcutaneous administration. A longer period may be appropriate in patients with an increased risk of hypersensitivity reactions.

^e There are various ways of administering **DOXOrubicin, vinCRiStine and etoposide**. See local hospital policy recommendations regarding preferred combinations to be administered concomitantly.

^f Lifetime cumulative dose of **DOXOrubicin** is 450mg/m². In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors outlined belowⁱ and to the age of the patient.

^g **vinCRiStine** is a neurotoxic chemotherapeutic agent. Refer to NCCP Guidance on the Safe Use of Neurotoxic drugs (including Vinca Alkaloids) in the treatment of cancer [here](#).

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 2 of 10
<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 http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

^h At doses of **cycloPHOSphamide** above 1500mg/m² pre-treatment is required with mesna. Give mesna dose equivalent to 20% of cycloPHOSphamide dose IV immediately before cycloPHOSphamide dose (T0) and 40% of the cycloPHOSphamide dose orally 2 and 6 hours (T2, T6) after the end of the cycloPHOSphamide infusion.

Prophylactic Central Nervous System Intrathecal Methotrexate should be administered with this regimen as clinically indicated (Refer to local policy)

ⁱ Pegylated G-CSF should NOT be substituted for standard G-CSF in this regimen.

^j Ensure G-CSF is continued until beyond nadir even if WCC is raised (typically beyond Day 10).

Table 1: Guidance for administration of IV ritUXimab

<p>The recommended initial rate for infusion is 50 mg/hr; after the first 30 minutes, it can be escalated in 50 mg/hr increments every 30 minutes, to a maximum of 400 mg/hr. Subsequent infusions can be infused at an initial rate of 100 mg/hr, and increased by 100 mg/hr increments at 30 minute intervals, to a maximum of 400 mg/hr. Development of an allergic reaction may require a slower infusion rate. See Hypersensitivity/Infusion reactions under Adverse Effects/Regimen Specific Complications below. Any deviation from the advised infusion rate should be noted in local policies.</p>
<p>Recommended Observation period: Patients should be observed for at least six hours after the start of the first infusion and for two hours after the start of the subsequent infusions for symptoms like fever and chills or other infusion-related symptoms. Any deviation should be noted in local policies.</p>
<p>ritUXimab should be diluted to a final concentration of 1-4mg/ml.</p>
<p>Rapid rate infusion schedule ⁱⁱSee NCCP guidance here If patients did not experience a serious infusion related reaction with their first or subsequent infusions of a dose of ritUXimab administered over the standard infusion schedule, a more rapid infusion can be administered for second and subsequent infusions using the same concentration as in previous infusions. Initiate at a rate of 20% of the total dose for the first 30 minutes and then 80% of the dose for the next 60 minutes (total infusion time of 90 minutes). If the more rapid infusion is tolerated, this infusion schedule can be used when administering subsequent infusions. Patients who have clinically significant cardiovascular disease, including arrhythmias, or previous serious infusion reactions to any prior biologic therapy or to ritUXimab, should not be administered the more rapid infusion.</p>

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 3 of 10
<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 http://www.hse.ie/eng/Disclaimer <i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

TESTS:

Baseline tests:

- FBC, renal and liver profile, LDH, Uric acid, SPEP
 - ECG
 - Cardiac function using MUGA or ECHO (LVEF > 50% to administer DOXOrubicin) if >65 years or if clinically indicated (e.g. smoking history, hypertension)
 - Virology screen - Hepatitis B (HBsAg, HBcoreAb) & C, HIV*
- *See Adverse Effects/Regimen Specific Complications

Regular tests:

- FBC (including ANC) twice weekly during treatment, three days apart
- Renal and liver profile prior to each cycle
- Assessment of peripheral neuropathy status prior to each cycle
- Cardiac function if 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.
- Drug doses for subsequent cycles are based on previous cycle ANC nadir (Please see Table 2).
- Measurement of ANC nadir based on twice weekly FBC only which must be taken at least 3 days apart i.e. Low neutrophil count on 3 consecutive days does NOT require decreasing a level.

Haematological:

Table 2: Dose adjustment of R-EPOCH based on previous cycle ANC nadir

FBC result	Action
If nadir ANC $\geq 0.5 \times 10^9/L$ on all measurements	Increase 1 dose level above last cycle
If nadir ANC $< 0.5 \times 10^9/L$ on 1 or 2 measurements	Dose at same level as last cycle
If the nadir ANC $< 0.5 \times 10^9/L$ on three separate measurements <u>OR</u> if the nadir platelet count is $< 25 \times 10^9/L$ on one measurement	Decrease to one level below the last cycle

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 4 of 10
<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 http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

Renal and Hepatic Impairment:

Table 3: Dose modifications based on renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment			
riTUXimab	Probably no dose reduction necessary		Probably no dose reduction necessary			
Etoposide	CrCl(ml/min)	Dose	Bilirubin (micromol/L)		AST (Units)	Dose
	>50	100%	26-51	or	60-180	50%
	15-50	75%				
	<15	50%				
	Subsequent doses should be based on clinical response. Dialysis Start at reduced dose and increase according to clinical response.		>51	or	>180	Clinical decision
DOXOrubicin	No dose reduction required. Clinical decision in severe renal impairment.		Bilirubin (micromol/L)		Dose	
			20-51		50%	
			51-85		25%	
			>85		Omit	
			If AST 2-3 x normal, give 75% dose. If AST >3 x ULN, give 50% dose			
cycloPHOSphamide	CrCl (ml/min)	Dose	Severe impairment: Clinical decision.			
	>20	100%				
	10-20	75%				
	<10	50%				
	Clinical decision – consider whether patient is being treated with high dose treatment. Dialysis Renal Drug Handbook - dose at 50 - 100% dose (CAPD, HD and HDF/High flux). Do not perform dialysis for 12 hours. Dose at 75-100% dose (CAV/VVHD). If anuric, mesna may not be required.					
vinCRISTine	No dose reduction required.		Bilirubin (micromol/L)		AST/ALT (Units)	Dose
			26-51	or	60-180	50%
			>51	and	Normal	50%
			>51	and	>180	Omit

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 5 of 10

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

Neurotoxicity:

Table 4: Dose modification of vinCRISTine based on neurotoxicity (CTCAE v 4.0)

Symptom	Dose of vinCRISTine
Grade 1	100%
Grade 2	Hold until recovery, then reduce dose by 50%
Grade 3,4	Omit

Table 5: Dose modification schedule of riTUXimab based on adverse events

Adverse reactions	Discontinue	Recommended dose modification
Severe infusion related reaction (e.g. dyspnoea, bronchospasm, hypotension or hypoxia) First occurrence		Interrupt infusion immediately. Evaluate for cytokine release/tumour lysis syndrome (appropriate laboratory tests) and pulmonary infiltration (chest x - ray). Infusion may be restarted on resolution of all symptoms, normalisation of laboratory values and chest x-ray findings at no more than one-half the previous rate.
Second occurrence	Consider discontinuing treatment	Consider coverage with steroids for those who are not already receiving steroids.
Mild or moderate infusion-related reaction		Reduce rate of infusion. The infusion rate may be increased upon improvement of symptoms

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

riTUXimab: Minimal (Refer to local policy)

Etoposide: Low (Refer to local policy)

DOXOrubicin: Moderate (Refer to local policy)

vinCRISTine: Minimal (Refer to local policy)

cycloPHOSphamide Dose Level 1-4: Moderate (Refer to local policy)

cycloPHOSphamide Dose Level 5-6 : High (Refer to local policy)

- Consider increased risk of vinca alkaloid-induced adverse effects due to inhibition of CYP3A4 by aprepitant.

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 6 of 10

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

PREMEDICATIONS:

Premedication consisting of an anti-pyretic and an anti-histamine should always be administered before each dose of riTUXimab.

Table 6: Suggested pre-medications prior to IV riTUXimab infusion:

Drugs	Dose	Route
Paracetamol	1g	PO 60 minutes prior to riTUXimab infusion
Chlorphenamine	10mg	IV bolus 60 minutes prior to riTUXimab infusion
Ensure glucocorticoid component of the treatment regimen (prednisolone 120mg/m ²) is given at least 30 minutes prior to riTUXimab infusion		

Table 7: Suggested pre-medications prior to S/C riTUXimab :

Drugs	Dose	Route
Paracetamol	1g	PO 30 minutes prior to riTUXimab administration
Chlorphenamine	4mg	PO 30 minutes prior to riTUXimab administration
Ensure glucocorticoid component of the treatment regimen (prednisolone 120mg/m ²) is given at least 30 minutes prior to riTUXimab infusion.		

OTHER SUPPORTIVE CARE:

- Tumour lysis syndrome prophylaxis (**Refer to local policy**)
- Proton pump Inhibitor(**Refer to local policy**)
- PJP prophylaxis (**Refer to local policy**)
- Anti-viral prophylaxis (**Refer to local policy**)
- Anti-fungal prophylaxis (**Refer to local policy**)
- Prophylactic regimen against vinCRistine induced constipation is recommended (**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.
- Consider mesna if high dose cycloPHOSphamide prescribed on dose escalation (>1.5g/m² at levels 5, 6)

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 7 of 10

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

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Cardiac Toxicity:** Patients with a history of cardiac disease and/or cardiotoxic chemotherapy should be monitored closely while on riTUXimab. DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with cardiac dysfunction.
- **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:** DOXOrubicin and vinCRISTine cause pain and possible tissue necrosis if extravasated (Refer to local policy).

riTUXimab

- Please see NCCP Regimen 00542 riTUXimab 375mg/m² Combination Therapy -21 day for detailed information on the Adverse Effects/Regimen Specific Complications relating to riTUXimab Therapy
- **Hypersensitivity/Infusion Reactions:** Close monitoring is required throughout the first infusion of riTUXimab (Refer to local policy). riTUXimab can cause allergic type reactions during the IV infusion such as hypotension, wheezing, rash, flushing, pruritis, sneezing, cough, fever or faintness. Monitor infusion of etoposide for the first 15 minutes for signs of hypotension.

Before starting riTUXimab subcutaneous injections, all patients must always have received at least one full dose of riTUXimab by intravenous infusion, using riTUXimab intravenous formulation. The highest risk of experiencing an administration related reaction is generally observed at cycle one. Beginning the therapy with riTUXimab intravenous infusion would allow a better handling of the administration reactions by slowing or stopping the intravenous infusion.

If patients were not able to receive one full riTUXimab intravenous infusion dose prior to the switch, they should continue the subsequent cycles with riTUXimab intravenous formulation until a full intravenous dose is successfully administered. Therefore, the switch to riTUXimab subcutaneous formulation can only occur at the second or subsequent cycles of treatment.

Administration related reactions have been observed in up to 50% of patients treated with riTUXimab subcutaneous formulation in clinical trials but the majority of reactions were mild or moderate and resolved without any specific treatment.

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. 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.

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 8 of 10

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

DRUG INTERACTIONS:

- Antihypertensives: Additive effect of hypotension during riTUXimab infusion. Consider withholding antihypertensives 12 hours before and during riTUXimab infusion.
- 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).
- Consider increased risk of vinca alkaloid-induced adverse effects due to inhibition of CYP3A4 by aprepitant.
- Current drug interaction databases should be consulted for more information including potential for interactions with CYP3A4 inhibitors / inducers.

REFERENCES:

1. Wilson WH et al. Dose-adjusted EPOCH chemotherapy for untreated large B-cell lymphomas: a pharmacodynamic approach with high efficacy. *Blood* 2002; 99:2685-93.
2. Wilson WH et al. Phase II Study of Dose-Adjusted EPOCH and Rituximab in Untreated Diffuse Large B-Cell Lymphoma with Analysis of Germinal Center and Post-Germinal Center Biomarkers. *J Clin Oncol.* 2008;26:2717-2724
3. Dunleavy K, Pittaluga S et al. Dose-Adjusted EPOCH-Rituximab Therapy in Primary Mediastinal B-Cell Lymphoma *N Engl J Med* 2013;368:1408-16.
4. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network
5. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009; North London Cancer Network.
6. 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>
7. riTUXimab (MabThera®) Summary of Product Characteristics. Last updated 26/08/2022. Accessed Jan 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/mabthera-epar-product-information_en.pdf
8. cycloPHOSphamide (Endoxana®) Injection 500mg Powder for Solution for Injection. Summary of Product Characteristics. Last updated: 21/12/2018. Accessed Jan 2023. Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2299-027-002_21122018112109.pdf
9. DOXOrubicin Accord 2mg/ml concentrate for solution for infusion. Summary of Product Characteristics. Last updated: 26/02/2020. Accessed Jan 2023 .Available at: https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA0437-026-002_03032016152104.pdf
10. Etoposide 20 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics. Last updated: 17/05/2021. Accessed Jan 2023.Available at: https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1809-020-001_02022016153110.pdf
11. vinCRISTine Summary of Product Characteristics. Last updated: 21/09/2022. Accessed Jan 2023. Available at: <https://www.medicines.ie/medicines/vincristine-sulphate-1-mg-ml-solution-for-injection-or-infusion-34195/spc>

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 9 of 10

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

Version	Date	Amendment	Approved By
1	27/07/2021		NCCP Lymphoid Clinical Advisory Group
2	15/09/2021	Amended footnote in treatment table in relation to pegylated G-CSF.	Dr Cliona Grant
3	06/11/2023	Reviewed. Updated pre medications table for rituximab. Updated emetogenic potential section. Updated adverse events section. Updated drug interactions section.	Dr Cliona Grant, Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

ⁱ 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

ⁱⁱ The rapid infusion is an unlicensed means of administration of riTUXimab for the indications described above, in Ireland. Patient's should be informed of this and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be fully aware of their responsibility in communicating any relevant information to the patient and also ensuring that the unlicensed or "off label" means of administration has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.

NCCP Regimen: Dose Adjusted R (S/C) -EPOCH Therapy	Published: 27/07/2021 Review: 06/11/2028	Version number: 3
Tumour Group: Lymphoma NCCP Regimen Code: 00672	IHS/ISMO Contributor: NCCP Lymphoid Clinical Advisory Group	Page 10 of 10

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