

Non-Hodgkin lymphoma rituximab maintenance

ID: 1385 v.8 **Endorsed** Essential Medicine List

Patients with lymphoma should be considered for inclusion into clinical trials. Link to [ALLG website](#), [ANZCTR website](#) and [Lymphoma Australia website](#).

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the [eviQ Estimated Glomerular Filtration Rate \(eGFR\) calculator](#).

International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADIKD)

2022

[Click here](#)



Related pages:

- [Non-Hodgkin lymphoma R-CHOP21 \(rituximab CYCLOPHOSPHamide DOXOrubicin vinCRISTine prednisolone\)](#)
- [Non-Hodgkin lymphoma R-CHOP14 \(rituximab CYCLOPHOSPHamide DOXOrubicin vinCRISTine prednisolone\)](#)

Treatment schedule - Overview

Cycle 1 to 8

Drug	Dose	Route	Day
Rituximab	375 mg/m ²	IV infusion	1

Frequency: 84 days (3 monthly) or 56 days (2 monthly) depending on the indication

Cycles: 8 (3 monthly) or 12 (2 monthly)*

Notes:

*Previously untreated patients who responded to induction treatment: every 2 months until disease progression or for a maximum period of two years. Relapsed/refractory patients who responded to induction treatment: every 3 months until disease progression or for a maximum period of two years.

Drug status: Rituximab is on the [PBS general schedule](#)

Cost: ~ \$360 per cycle

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. [Select here for recommended doses of alternative antiemetics.](#)*

Cycle 1 to 8

Day 1		
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Hydrocortisone	100 mg (IV)	30 minutes before treatment
Rituximab	375 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate

Frequency: 84 days (3 monthly) or 56 days (2 monthly) depending on the indication

Cycles: 8 (3 monthly) or 12 (2 monthly)*

Indications and patient population

- CD20 positive, previously untreated, Stage III/IV follicular, B-cell non-Hodgkin's lymphoma; following induction treatment
- CD20 positive, relapsed or refractory low grade or follicular, B-cell non-Hodgkin's lymphoma

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with rituximab. Read more about Hypersensitivity reaction
Premedication	The product information states that premedication is required for this treatment. Please refer to the treatment schedule for suggested premedication regimen. This may be substituted to reflect institutional policy.
Emetogenicity MINIMAL	No antiemetics should be routinely administered before treatment in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Rituximab rapid infusion	This regimen is not in line with the product monograph, however published literature indicates that it can be completed safely. Read more about the rapid infusion of rituximab
Progressive multifocal leukoencephalopathy	Use of monoclonal antibodies may be associated with an increased risk of progressive multifocal leukoencephalopathy (PML), a rare but potentially fatal opportunistic viral infection of the brain. Patients must be monitored for any new or worsening neurological symptoms. Read more about progressive multifocal leukoencephalopathy and the Therapeutic Goods Administration Medicines Safety update on progressive multifocal leukoencephalopathy from the Australian Government, Department of Health.
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
Blood tests	FBC, EUC, eGFR, LFTs and LDH at baseline, and prior to each cycle and as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy

Vaccinations	<p>Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.</p> <p>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.</p> <p>Read more about COVID-19 vaccines and cancer.</p>
Fertility, pregnancy and lactation	<p>Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients.</p> <p>Read more about the effect of cancer treatment on fertility</p>

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences. Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus. The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on [Common Terminology Criteria for Adverse Events \(CTCAE\)](#) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see [dosing considerations & disclaimer](#).

The dose recommendations in kidney dysfunction (i.e renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.

[International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction \(ADDIKD\)](#).

No dose modifications required

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. [References & Disclaimer](#)

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- [MIMS - interactions tab](#) (includes link to a CYP-450 table) (login required)
- [Australian Medicines Handbook \(AMH\) – interactions tab](#) (login required)
- [Micromedex Drug Interactions](#) (login required)
- [Cancer Drug Interactions](#)
- [Cytochrome P450 Drug Interactions](#)

Rituximab		
	Interaction	Clinical management
Antihypertensives	Additive hypotensive effect	Consider withholding antihypertensive medications 12 hours prior to the rituximab infusion
Immunosuppressants (eg. abatacept and baricitinib etc.)	Increased risk of infection	Concurrent use not recommended. If an immunosuppressant must be used, monitor closely for signs of infection

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General		
	Interaction	Clinical management
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

Day 1

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of treatment.

Prime IV line(s).

Insert IV cannula or access [TIVAD](#) or [CVAD](#).

Pre treatment medication

Verify premedication taken or administer as prescribed.

🕒 Treatment - Time out

Rituximab

Prior to administration:

- check baseline observations
- check for previous adverse events during previous infusions
- verify premedication has been taken. If not, administer 30 to 60 minutes prior to rituximab administration:
 - paracetamol 1000 mg orally AND
 - loratadine 10 mg orally (or similar antihistamine)
 - a steroid may also be included as a premed according to local guidelines

Initial infusion:

- **commence rituximab** infusion at 50 mg/hr for 30 minutes
- repeat observations prior to each rate increase
- **increase rate** by 50 mg/hr every 30 minutes, up to a maximum of 400 mg/hr if observations are stable
- flush with ~ 50 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have completely resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Transient hypotension may occur. Consider withholding antihypertensive medication for 12 hours before and during infusion.

Subsequent infusions:

If an adverse event was experienced with initial infusion recommence infusion at the same rate as initial infusion

- **commence** rituximab infusion at 100 mg/hr
- repeat observations prior to each rate increase
- increase rate by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr if observations are stable
- flush with ~ 50 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about rapid infusion rituximab

Remove IV cannula and/or deaccess [TIVAD](#) or [CVAD](#).

Discharge information

Prophylaxis medication

- Prophylaxis medication (if prescribed) i.e. antivirals.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)

Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Flu-like symptoms	
Headache	

Early (onset days to weeks)

Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Fatigue	Read more about fatigue
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash

Late (onset weeks to months)

Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Progressive multifocal leukoencephalopathy (PML)	A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose. Read more about progressive multifocal leukoencephalopathy (PML)

Evidence

Follicular B cell lymphoma

In 2006 the EORTC 20981 intergroup study¹ randomised 474 patients with relapsed or resistant follicular B cell lymphoma (grade 1 to 3A), maximum of two prior non-anthracycline or immunotherapy containing regimens, to R-CHOP or CHOP for six cycles following randomisation to maintenance (375 mg/m² every 3 months for two years) or observation.

R-CHOP significantly increased overall response rate compared to CHOP (85.1% versus 72.3%, $p < 0.01$). Rituximab maintenance was associated with a median PFS of 51.5 months versus 14.9 months ($P < 0.01$). In addition, overall survival was superior with rituximab maintenance over observation only (OS at 3 years of 85% versus 77%, $P=0.011$, HR 0.52). In 2010, these results were

updated,² and remained highly significant. Comparing maintenance with no maintenance, PFS was 3.7 versus 1.3 years.

The PRIMA (Primary Rituximab and MAintenance) study randomised 1,217 patients with previously untreated follicular lymphoma, following immunochemotherapy (R-CHOP, R-CVP or R-FCM) to observation or maintenance rituximab (375 mg/m²) every 8 weeks for two years.³

At 36 months median follow up, the progression free survival (PFS) in the maintenance arm was 74.9% versus 57.6% in the observation only arm (P<0.0001). Overall survival was not significantly different and there was an increase in grade 3 or 4 adverse events (24% versus 17%, P=0.0026) in the maintenance arm and grade 2-4 infective episodes (39% versus 24%, P < 0.0001). The ECOG1496⁴ study (included de novo small lymphocytic as well as follicular grade 1 and 2) showed a significant PFS advantage to rituximab maintenance (given as weekly X 4 repeated every six months for two years) of 68% versus 33% at 3 years.

There was no significant difference in OS. Modelling of the PRIMA data yielded an increased mean PFS of 1.5 years, OS by 1.21 years, and QALYs gained by 1.11 years.⁵

In a study of 280 patients with relapsed rituximab-naïve follicular NHL, which also involved rituximab "purging" pre autograft, patients randomised to post transplant rituximab demonstrated improved PFS (10 years 54% v 37%) but not OS. Maintenance was administered 4 times at 2 monthly interval.⁶

The SAKK 35/03 trial randomised 165 patients with untreated, relapsed, stable or chemotherapy-resistant follicular lymphoma to receive short-term (n=82) or long-term (n=83) rituximab maintenance therapy. Rituximab 375 mg/m² was administered intravenously every 2 months as four doses for short-term therapy and for a maximum of 5 years or until relapse, progression or unacceptable toxicity occurred for long term therapy. The primary end point was EFS and secondary end points PFS, OS and toxicity.⁷

At a median follow-up period of 6.4 years, in the short-term arm the median EFS was 3.4 years (95% CI, 2.1 to 5.3) and in the longer-term arm it was 5.3 years (95% CI, 3.5 to not available) (P = .14). More adverse effects were experienced in patients who received long term rituximab treatment compared to those who received four doses, with 76% v 50% of patients with at least one adverse event (P, .001), five versus one patient with grade 3 and 4 infections, and three versus zero patients discontinuing treatment because of unacceptable toxicity, respectively. There was no difference in OS between the two groups.⁷

A retrospective analysis found maintenance rituximab to improve PFS in patients who were treated with bendamustine and rituximab induction therapy on the BRIGHT study. Randomised controlled studies may be required to further test maintenance rituximab after BR therapy.⁸

A meta-analysis of seven trials including 2315 patients treated with rituximab maintenance (n=1145) for follicular lymphoma had improved overall survival compared with observation (n=1170). Median overall survival in the rituximab maintenance group was 12 years (95% CI 11.5 to not yet reached) compared to 11.5 years in the observation group. PFS was improved by rituximab maintenance compared to observation for patients with follicular lymphoma (HR 0.57, 95% CI 0.51-0.64).⁹

Rituximab was associated with a higher risk of adverse events, with infection being the major toxicity. Infection occurred in 33.6% (7.1% grade 3-4) of patients on maintenance rituximab and 23.6% (4.9% grade 3-4) of the observation group.⁹

Mantle cell lymphoma

Rituximab has been used as maintenance therapy following initial chemotherapy for mantle cell lymphoma and may be a reasonable alternative in transplant ineligible patients.¹⁰

It has also been used in transplant eligible patients in a phase 3 trial involving 299 patients was conducted by Le Gouill et al. between September 2008 through August 2012. The role of rituximab maintenance therapy given after autologous stem-cell transplantation (AuSCT) in patients with untreated mantle cell lymphoma (MCL) was investigated.¹¹

Four courses of induction R-DHAP (rituximab, dexamethasone, cytarabine, and a platinum derivative) immunochemotherapy given every 21 days, was followed by the R-BEAM (rituximab, carmustine, etoposide, cytarabine, and melphalan) conditioning regimen prior to AuSCT. Patients who had a partial response received a rescue induction therapy with four courses of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) every 14 days. Only patients who had a response (confirmed or unconfirmed complete remission (CR) or a partial response (PR)) were eligible to undergo transplantation. The overall response rate was 89%, and the complete response rate 77% and transplantation was performed in 257 patients. After AuSCT, 240 patients were randomised to receive maintenance therapy (n=120) with intravenous rituximab 375 mg/m² every 2 months for 3 years, or to undergo observation (n=120). The primary end point was event-free survival (EFS).¹¹

The rate of EFS at 4 years from start of randomisation was 79% (95% confidence interval [CI], 70 to 86) in the rituximab group versus 61% (95% CI, 51 to 70) in the observation group (P=0.001).

PFS at 4 years was 83% (95% CI, 73 to 88) in the rituximab group versus 64% (95% CI, 55 to 73) in the observation group (P<0.001). OS rate was 89% (95% CI, 81 to 94) in the rituximab group versus 80% (95% CI, 72 to 88) in the observation group (P=0.04). The

rate of overall survival at 4 years was higher in the rituximab group than in the observation group (hazard ratio for death, 0.50; 95% CI, 0.26 to 0.99; P=0.04) according to a Cox regression unadjusted analysis.¹¹

Conclusions

Maintenance rituximab significantly improves OS and PFS in patients re-treated with chemotherapy for relapsed or resistant follicular B cell lymphoma (375 mg/m² every 12 weeks for 2 years in the EORTC study).²

In patients with untreated follicular B cell lymphoma, maintenance therapy every eight weeks significantly improves PFS although the benefits in overall survival are less certain.³

In patients with mantle-cell lymphoma who were younger than 66 years of age at diagnosis, rituximab maintenance therapy after transplantation prolonged event-free survival, progression-free survival, and overall survival.¹¹

Eight weekly versus 12 weekly delivery schedules have not been cross compared in the two patient populations. The duration of maintenance in the EORTC and PRIMA studies was 2 years. Ongoing studies are examining the optimal duration of maintenance.¹²

The role of maintenance rituximab in other indolent lymphomas is less clear.

References

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- 2 van Oers, M. H., M. Van Glabbeke, L. Giurgea, et al. 2010. "Rituximab maintenance treatment of relapsed/resistant follicular non-Hodgkin's lymphoma: long-term outcome of the EORTC 20981 phase III randomized intergroup study." *J Clin Oncol* 28(17):2853-2858.
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- 5 Hornberger, J., C. Reyes, A. Shewade, et al. 2012. "Cost-effectiveness of adding rituximab to fludarabine and cyclophosphamide for the treatment of previously untreated chronic lymphocytic leukemia." *Leuk Lymphoma* 53(2):225-234.
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- 7 Taverna, C., G. Martinelli, F. Hitz, et al. 2016. "Rituximab Maintenance for a Maximum of 5 Years After Single-Agent Rituximab Induction in Follicular Lymphoma: Results of the Randomized Controlled Phase III Trial SAKK 35/03." *J Clin Oncol* 34(5):495-500.
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- 9 Vidal, L., A. Gafter-Gvili, G. Salles, et al. 2017. "Rituximab maintenance improves overall survival of patients with follicular lymphoma-Individual patient data meta-analysis." *Eur J Cancer* 76:216-225.
- 10 Chaudhary, L., M. A. Kharfan-Dabaja, P. Hari, et al. 2013. "Is hematopoietic cell transplantation still a valid option for mantle cell lymphoma in first remission in the chemoimmunotherapy-era?" *Bone Marrow Transplant*.
- 11 Le Gouill, S., C. Thieblemont, L. Oberic, et al. 2017. "Rituximab after Autologous Stem-Cell Transplantation in Mantle-Cell Lymphoma." *N Engl J Med* 377(13):1250-1260.

History

Version 8

Date	Summary of changes
05/06/2023	Subcutaneous rituximab information removed from the following sections – treatment schedule, clinical information, administration, patient information. Increased to version 8.

Version 7

Date	Summary of changes
22/10/2021	Protocol reviewed at Haematology Reference Committee meeting. Indications and drug status updated. Version number changed to v.7. Review in 1 year.
11/11/2022	Protocol reviewed electronically by the Haematology Reference Committee, Rituximab PBS status changed to general schedule. Review in 2 years

Version 6

Date	Summary of changes
9/03/2020	Biosimilar rituximab added to clinical information. Version number changed to v.6
25/02/2021	ID 3909 added as a related page and note in treatment schedule updated to include link.
01/10/2021	Drug status updated: rituximab SC is TGA registered but no longer PBS listed.

Version 5

Date	Summary of changes
11/10/2013	Presented at Haematology Reference Committee meeting.
15/11/2013	Published on eviQ. Review in 2 years.
17/11/2014	Added link to ALLG, ANZCTR and Lymphoma Australia website with statement 'Patients with lymphoma should be considered for inclusion into clinical trials'. Safe handling precautions (waste) removed.
11/09/2015	Reviewed at HRCM. Added studies by Pettengell et al., Taverna et al. and Fowler et al. to the evidence and reference list.
31/05/2017	Transferred to new eviQ website. Version number change to v.3.
7/03/2018	<p>Added:</p> <ul style="list-style-type: none"> • Link to subcutaneous rituximab document underneath the treatment schedule. • Clinical information block on subcutaneous rituximab. • Link to the subcutaneous rituximab document into administration section. • Injection-site reaction side effect. • Note about subcutaneous rituximab to the patient information. • Version number changed to v.4.
25/05/2018	<p>Protocol reviewed at Haematology Reference Committee meeting:</p> <ul style="list-style-type: none"> • Treatment schedule: Frequency updated. Added 'Note: the PBS restriction for rituximab maintenance is limited to follicular lymphoma, in the front-line and relapsed setting.' to the drug status. • Indications updated per the PBS and TGA updates. • Evidence updated. • Version number changed to v.5.
13/09/2019	Reviewed by Haematology Reference Committee, no changes made. Review in 2 years.

The information contained in this protocol is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to treatment. Any clinician (medical oncologist, haematologist, radiation oncologist, medical physicist, radiation therapist, pharmacist or nurse) seeking to apply or consult this protocol is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at www.eviQ.org.au

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<https://www.eviq.org.au/p/1385>

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Patient information - Non-Hodgkin lymphoma (NHL) - Rituximab maintenance

Patient's name:

Your treatment

The treatment schedule below explains how the drug for this treatment is given.

Rituximab maintenance

This treatment cycle is repeated every 3 months for two years. You will have 8 treatments in total. Alternatively, this treatment cycle can be given every 2 months for two years, for a total of 12 treatments.

Day	Treatment	How it is given	How long it takes
1	Rituximab (<i>ri-TUX-i-mab</i>)	By a drip into a vein	1st cycle: About 4 to 6 hours Cycles thereafter: About 3 to 4 hours

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

 <p>IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:</p>	Emergency contact details Ask your doctor or nurse from your treating team who to contact if you have a problem
<ul style="list-style-type: none">• a temperature of 38°C or higher• chills, sweats, shivers or shakes• shortness of breath• uncontrolled vomiting or diarrhoea• pain, tingling or discomfort in your chest or arms• you become unwell.	Daytime:..... Night/weekend:..... Other instructions:.....

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Treatment delays

There may be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope

with the treatment. Your doctor will explain if you need any delays to your treatment and the reason why.

Blood tests and monitoring

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the [eviQ patient information sheets](#) on CVADs.

Medications for blood pressure

Rituximab may lower your blood pressure. Tell your doctor if you are taking any blood pressure medications. Your doctor may advise you to temporarily stop your blood pressure medications before your rituximab infusions.

Other medications given during this treatment

- **Rituximab premedication:** before your treatment with rituximab you will need to take some tablets called a premedication to help prevent you from having a reaction to the rituximab.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Allergic reaction	<ul style="list-style-type: none"> • Allergic reactions are uncommon but can be life threatening. • If you feel unwell during the infusion or shortly after it, or: <ul style="list-style-type: none"> ◦ get a fever, shivers or shakes ◦ feel dizzy, faint, confused or anxious ◦ start wheezing or have difficulty breathing ◦ have a rash, itch or redness of the face <p><u>While you are in hospital:</u> Tell your doctor or nurse immediately.</p> <p><u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.</p>
Flu-like symptoms	<ul style="list-style-type: none"> • You may get: <ul style="list-style-type: none"> ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • Tell your doctor or nurse if you get any of the symptoms listed above. • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.
Headache	<ul style="list-style-type: none"> • You can take paracetamol if you have a headache. • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.

Early (onset days to weeks)	
Infection risk (neutropenia)	<ul style="list-style-type: none"> • This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms: <ul style="list-style-type: none"> ◦ a temperature of 38°C or higher ◦ chills, shivers, sweats or shakes ◦ a sore throat or cough ◦ uncontrolled diarrhoea ◦ shortness of breath ◦ a fast heartbeat ◦ become unwell even without a temperature.

<p>Low platelets (thrombocytopenia)</p>	<ul style="list-style-type: none"> • This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.
<p>Tiredness and lack of energy (fatigue)</p>	<ul style="list-style-type: none"> • You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • Tell your doctor or nurse if you get any of the symptoms listed above.
<p>Nausea and vomiting</p>	<ul style="list-style-type: none"> • You may feel sick (nausea) or be sick (vomit). • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Anti-sickness medication is usually not needed but may help in some people. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.
<p>Skin rash</p>	<ul style="list-style-type: none"> • You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • Talk to your doctor or nurse about other ways to manage your skin rash.

Late (onset weeks to months)

Hair loss (alopecia)	<ul style="list-style-type: none">• Your hair may start to fall out from your head and body.• Hair loss usually starts 2 to 3 weeks after your first treatment.• You may become completely bald and your scalp might feel tender.• Use a gentle shampoo and a soft brush.• Take care with hair products like hairspray, hair dye, bleaches and perms.• Protect your scalp from the cold with a hat, scarf or wig.• Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher.• Moisturise your scalp to prevent itching.• Ask your doctor or nurse about the Look Good Feel Better program
Low red blood cells (anaemia)	<ul style="list-style-type: none">• You may feel dizzy, light-headed, tired and appear more pale than usual.• Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion.• Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.
Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]	<ul style="list-style-type: none">• This treatment can affect your central nervous system. This can be very serious.• Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:<ul style="list-style-type: none">◦ trouble with your speech or vision◦ confusion or memory loss◦ changes in your personality◦ weakness in your arms and legs◦ poor balance or coordination◦ fits (seizures).

General advice for people having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - [Chemotherapy safety at home](#).

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet and food safety

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For more information on foods to avoid and food hygiene please ask for a copy of the [Listeria and food brochure](#).

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our [Patient and carers section](#).

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – <https://aci.health.nsw.gov.au/networks/bmtct>

This document is a guide only and cannot cover every possible situation. The health professionals caring for you should always consider your individual situation when making decisions about your care. Contact your cancer clinic staff or doctor if you have any questions or concerns about your treatment, or you are having problems coping with side effects. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use of this document is subject to eviQ's disclaimer available at www.eviq.org.au

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