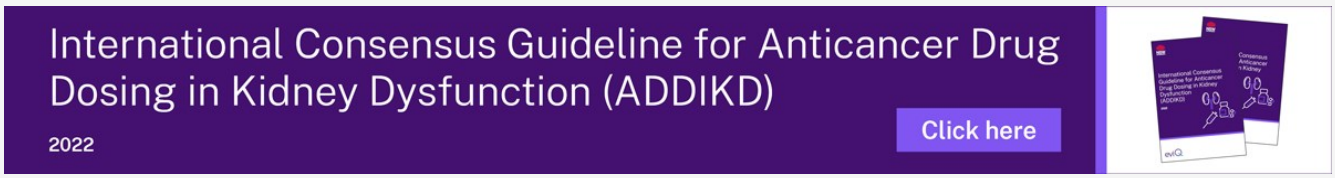
Non-Hodgkin lymphoma chlorambucil and rituximab

ID: 1368 v.7 **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.

This protocol is not exportable and does not have a calculator.

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.



Treatment schedule - Overview

Cycle 1

Drug	Dose	Route	Day
Rituximab	375 mg/m^2	IV infusion	1, 8, 15, 22 (cycle 1 only)
Chlorambucil	6 mg/m^2 ONCE a day	PO	1 to 42 (cycle 1 only)

Duration: 42 days

Cycles: 1

Responding patients or those with stable disease proceed to maintenance therapy (cycles 2 to 5) after a 14 day break post induction (cycle 1).

Cycle 2 to 5

Drug	Dose	Route	Day
RITUximab	375 mg/m^2	IV infusion	1 (every 4 weeks)
Chlorambucil	6 mg/m^2 ONCE a day	PO	1 to 14 (every 4 weeks)

Frequency: 28 days

Cycles: 4

Drug status: **Rituximab and chlorambucil** are available on the PBS general schedule

Chlorambucil is available as **2mg** tablets

Cost: ~ $1,770 (cycle 1 only) and $2,700 per cycle (cycle 2 to 5)

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

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
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Day 2 to 7		
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Day 8		
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
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Day 9 to 14		
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Day 15		
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
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Day 16 to 21		
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Day 22		
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

Day 22		
		administration rate
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Day 23 to 42		
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 42

Duration: 42 days

Cycles: 1

Responding patients or those with stable disease proceed to maintenance therapy (cycles 2 to 5) after a 14 day break post induction (cycle 1).

Cycle 2 to 5

Day 1		
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 14
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

Day 2 to 14		
Chlorambucil	6 mg/m^2 (PO)	ONCE a day on an empty stomach (at least one hour before or three hours after food) on days 1 to 14

Frequency: 28 days

Cycles: 4

Indications and patient population

- Splenic, nodal and marginal zone MALT lymphoma
- Indolent non-Hodgkin B-cell lymphoma (CD20 positive)

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
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 or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk 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.
Seizure risk	Chlorambucil is epileptogenic. Patients with a history of seizures or head trauma, or on other epileptogenic medications may be at increased risk of seizures with chlorambucil. Read more about drugs that may cause seizures
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
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	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	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. Read more about the effect of cancer treatment on fertility

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).

Note: All dose reductions are calculated as a percentage of the starting dose

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
0.5 to less than 1.0	Delay treatment until recovery and consider reducing chlorambucil by 33%
less than 0.5	Discontinue chlorambucil
Platelets x 10^9/L (pre-treatment blood test)	
25 to less than 50	Delay treatment until recovery and consider reducing chlorambucil by 33%
less than 25	Discontinue chlorambucil

Renal impairment	
Creatinine clearance (mL/min)	
Patients with impaired renal function should be closely monitored as they are susceptible to myelosuppression from chlorambucil	
less than 30	Reduce chlorambucil by 50%

Hepatic impairment
Consider dose reduction of chlorambucil in severe hepatic impairment

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*

Chlorambucil
No specific clinically significant drug-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

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 cycle 1

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

product information monographs via the TGA website for further information.

Days 1, 8, 15, and 22 (IV)

Approximate treatment time: 4 to 6 hours (initial); 3 to 4 hours (subsequent)

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each treatment.

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before recommencing treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Note: Rituximab is given on days 1, 8, 15 and 22 of **cycle 1** and on day 1 of **cycles 2 to 5**.

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.

Days 1 to 42 (PO)

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before recommencing treatment.

Chemotherapy - Time out

Note: chlorambucil is given on days 1 to 42 of **cycle 1** and on days 1 to 14 of **cycles 2 to 5.**

Chlorambucil

- administer orally ONCE a day on **days 1 to 42**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken on an empty stomach, one hour before or three hours after food
- may be given in divided doses if nausea is a problem
- chlorambucil tablets should be stored in the fridge (2 to 8 degrees Celsius).

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Continue safe handling precautions until 7 days after completion of drug(s)

Discharge information

Chlorambucil tablets

- Chlorambucil tablets with written instructions on how to take them.

Prophylaxis medication

- Prophylaxis medication (if prescribed) i.e. tumour lysis prophylaxis, antifungals and antivirals.

Patient information

- Ensure patient receives patient information sheet.

Administration cycles 2 to 5

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 product information monographs via the TGA website for further information.

Day 1 (IV)

Approximate treatment time: 4 to 6 hours (initial); 3 to 4 hours (subsequent)

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of treatment.

Any toxicity grade 2 or greater may require delay of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics 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.

Days 1 to 14 (PO)

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Any toxicity grade 2 or greater may require delay of treatment and review by medical officer before commencing treatment.

Chemotherapy - Time out

Chlorambucil

- administer orally ONCE a day on **days 1 to 14**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken on an empty stomach, one hour before or three hours after food

- may be given in divided doses if nausea is a problem
- chlorambucil tablets should be stored in the fridge (2 to 8 degrees C).

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Note: chlorambucil is given on days 1 to 42 of **cycle 1** and on days 1 to 14 of **cycles 2 to 5.**

Continue safe handling precautions until 7 days after completion of drug(s)

Discharge information

Chlorambucil tablets

- Chlorambucil tablets with written instructions on how to take them.

Prophylaxis medication

- Prophylaxis medication (if prescribed) i.e. tumour lysis prophylaxis, antifungals and 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	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes

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
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
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)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. 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
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)
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)

Delayed (onset months to years)	
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

Marginal zone lymphoma (MZL) is a low grade B cell lymphoma that is divided into 3 categories including splenic marginal zone, nodal and extra nodal (MALT) marginal zone lymphoma. There is no accepted first line therapeutic approach except in Helicobacter pylori associated gastric MALT lymphoma where antibiotic eradication therapy is accepted as the initial treatment. Best initial treatment for primary splenic MZL is undefined. Traditionally splenectomy was considered first line; however, recent retrospective studies showed comparable responses with single agent rituximab and rituximab/chemotherapy.[1, 2, 3] Chlorambucil/rituximab has not been studied prospectively in primary splenic MZL thus its use in splenic MZL should be at the discretion of the treating clinician.

Zucca et al. performed the only prospective randomized controlled study in MALT lymphoma. Investigators compared the combination of chlorambucil and rituximab with each agent alone. The interim analysis of this study[4] was referenced in the prior version of this guideline and the recently published final analysis is summarised here.[5]

There are several single institution phase 2 studies evaluating the combination of chlorambucil and rituximab in MALT lymphoma[6, 7, 8] and in low-grade follicular lymphoma.[9] Multiple other phase 2 studies have described different chemotherapy combinations in low-grade lymphomas but have never been compared directly with the rituximab and chlorambucil combination which remains a highly effective first line treatment option.

Zucca et al performed the only multicentre randomized controlled trial in newly diagnosed MALT lymphoma. The study included 454 patients with MALT lymphoma including H. pylori associated gastric MALT lymphoma following failure of antibiotic based eradication therapy. Forty percent of patients had primary gastric involvement while 30% had nodal involvement. The study excluded patients with primary splenic and primary nodal MZL, thus the data should be applied only to patients with MALT lymphoma.[5]

Investigators compared 3 arms: (A) chlorambucil alone (N=151), (B) chlorambucil and rituximab (N=152) and with (C) rituximab alone (N=151). In each arm chlorambucil and rituximab were dosed according to the schedules as outlined below:[5]

'Induction' Cycle 1 (6 weeks)

Drug	Dose	Route	Frequency	Days
Chlorambucil	6 mg/m^2	PO	Once daily	Day 1-42
Rituximab	375 mg/m^2	IV	Once daily	Days 1, 8, 15, 22

'Maintenance' Cycle 2-5 (4 weeks each)

Drug	Dose	Route	Frequency	Days
Chlorambucil	6 mg/m^2	PO	Once daily	Day 1-14
Rituximab	375 mg/m^2	IV	Once daily	Day 1

The three groups were evenly matched. The median age was 61 years (26 to 81 years) and only 2% had ECOG ≥2. Gastric MALT lymphoma was the primary disease site in approximately 40% of patients in each treatment arm. Ann Arbour stage 1 disease was present in 42%.[5]

Efficacy

Table 2. Response to Treatment

	All Patients (N = 401)		Arm A Chlorambucil (n = 131)		Arm B Chlorambucil Plus Rituximab (n = 132)		Arm C Rituximab (n = 138)	
Response	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
Complete remission*	264	65.8 (61.0 to 70.5)	83	63.4 (54.5 to 71.6)	104	78.8 (70.1 to 85.4)	77	55.8 (47.0 to 64.2)
Partial remission	81	20.2 (16.4 to 24.5)	29	22.1 (15.3 to 30.2)	21	15.9 (10.1 to 23.3)	31	22.5 (15.8 to 30.3)
Stable disease	28	7.0 (4.7 to 9.9)	11	8.4 (4.3 to 14.5)	1	0.8 (0.02 to 4.1)	16	11.6 (6.8 to 18.1)
Progressive disease	23	5.7 (3.7 to 8.5)	7	5.3 (2.2 to 10.7)	4	3.0 (0.8 to 7.6)	12	8.7 (3.0 to 12.0)
Not assessed	5	1.3 (0.4 to 2.9)	1	0.8 (0.02 to 4.2)	2	1.5 (0.2 to 5.4)	2	1.5 (0.2 to 5.1)
Overall response rate *	345	86.0 (82.2 to 89.3)	112	85.5 (78.3 to 91.0)	125	94.7 (89.4 to 97.8)	108	78.3 (70.4 to 84.8)

*$P < .001$.

The combination of chlorambucil and rituximab resulted in improved 'remission quality' with more complete remission (CR) and partial remission (PR) events compared to either agent alone (Arm A: 85% vs Arm B: 94% vs Arm C: 78%, respectively). The combination was associated with a longer median progression free survival (PFS) (8.3 years vs not reached vs 6.9 years respectively) but no difference in overall survival (OS).[5]

The International Prognostic Index (IPI) score was associated with longer survival on multivariate analysis, while primary gastric involvement was associated with longer Event Free Survival (EFS), PFS and higher CR rate.[5]

Kaplan-Meier survival curves

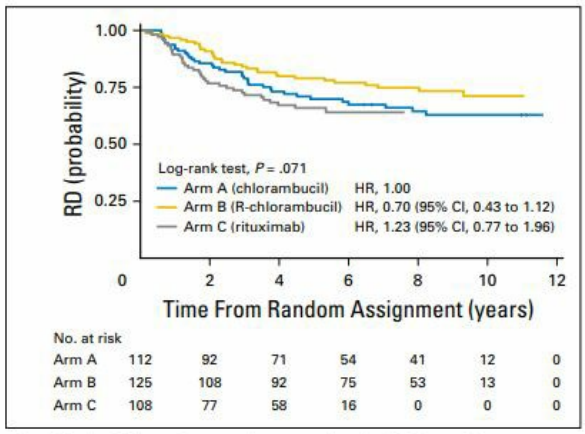


Fig 2. Kaplan-Meier estimates of response duration (RD) according to treatment arm in the 345 patients who achieved a response (partial response, n = 81; complete response, n = 264). HR, hazard ratio.

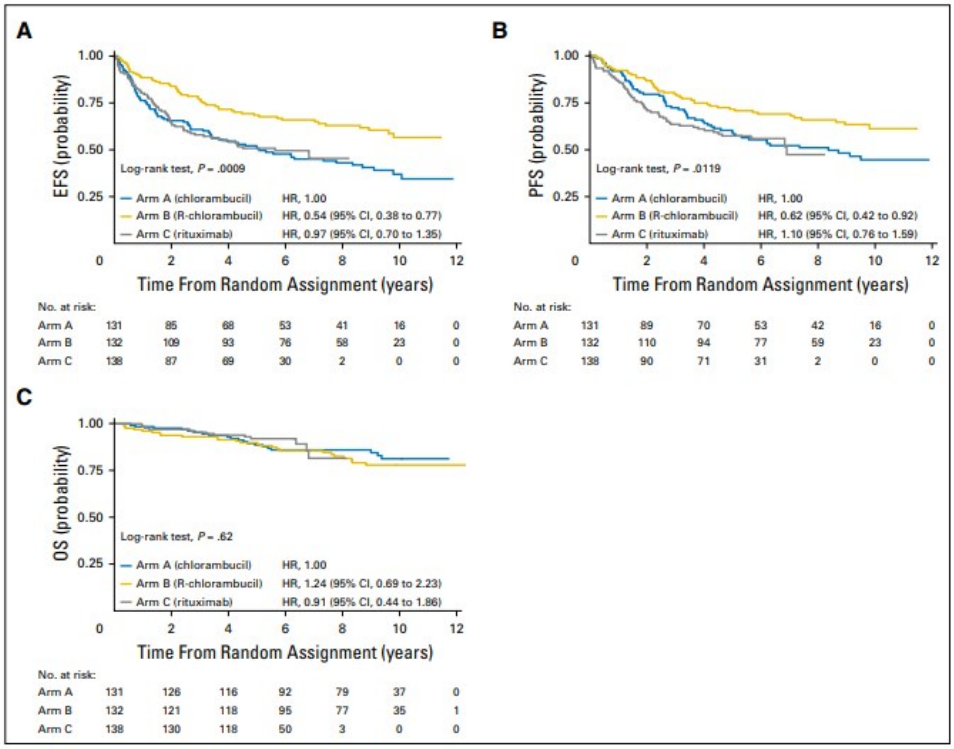


Fig 3. Kaplan-Meier survival curves according to treatment received for (A) event-free survival (EFS), (B) progression-free survival (PFS), and (C) overall survival (OS). HR, hazard ratio.

Six small phase 2 studies have assessed the efficacy and safety of the chlorambucil plus rituximab combination.[6, 10, 7, 11, 12, 13]

Study	Histology	N	Prior therapy	CR %	PR%	PFS	OS%	% patients needed a dose reduction or delay
Martinelli et al 2003[6]	Indolent NHL (SLL, FL, MZL)	29 (6 with MZL)	14/29 (48%)	63	26	Not reported	Not reported	10%
Levy et al 2010[10]	Gastric MALT refractory to HP7	12	Nil	100	0	100% at 24 months	100% at 24 months	Not reported
Rigacci et al 2007[7]	Ocular adnexal MALT	9	0	89	12	92% at 36 months	100% at 25 months	0%
Laszlo et al 2007[11]	Follicular NHL (grade I or II)	25	0	89	9	-	92% at 36	0%

							months	
Bauwens et al 2005[12]	Mantle cell lymphoma	14	12/14 were refractory	36	29	Median 15 months	58% at 24 months	Not reported
Sachanas et al 2011[13]	Non blastoid Mantle cell lymphoma	20	0	90	5	89% at 3 years	95% at 36 months	Not reported

These studies (except Rigacci et al and Sachanas et al) used identical dosing schedules with an induction and consolidation phase as reported by Zucca et al.[5]

In MZL, these smaller phase 2 studies all show similar Overall Response Rate (ORR) (89 to 100%) and median PFS of over 24 months.

The authors felt that treatment was well tolerated with only 10-25% requiring dose reduction.

Grade 3-4 haematologic toxicity occurred in 22-30%. The incidence of febrile neutropenia was very low (0-3%). The need for GCSF and transfusion support was not reported in any of the studies. Non-haematologic toxicity is predominantly gastrointestinal (14 to 18%) and hepatic (3 to 7%).

All studies used identical response assessment protocols with CT scanning following induction and at the completion of consolidation. Importantly, best responses were seen at 6 months.[4]

In summary, the combination of chlorambucil and rituximab compared with chlorambucil or rituximab alone as initial treatment in MALT lymphoma appears to result in improved PFS but not OS. The regimen is well tolerated with few grade 3-4 toxicities. Importantly, 40% of patients in the study by Zucca et al[4] had stage 1 disease and 40% had primary gastric MALT. Radiation therapy can also be considered as a first line treatment option in these patients but has never been compared with chlorambucil and rituximab head to head. Anthracycline containing regimens are not recommended for up-front use as they are toxic and do not appear to result in improved outcomes when compared head to head with lower intensity regimens.[14] The combination of bendamustine and rituximab has been explored in phase 2 studies[15] but never compared to chlorambucil and rituximab.

Toxicity

There were 58 deaths (14.5%) during the study period most were due to secondary cancers (29%) and lymphoma progression (24%). Haematologic toxicity was more prevalent in the combination arm. Grade 3 anaemia (Hb <80g/L) was seen in 1 patient only, grade 3 thrombocytopenia (50-25 x10^9/L) in 3 and febrile neutropenia was only seen in the combination arm (n=3). The most prevalent non-haematologic toxicity was nausea, fatigue and infusion reactions (in the rituximab containing arms). There were no differences in non-haematologic toxicity between the arms. Overall, all three schedules were well tolerated.[5]

Table 4. Hematologic Toxicity and Nonhematologic Adverse Events Experienced by At Least Five Patients

	Arm A Chlorambucil (n = 131)				Arm B Chlorambucil Plus Rituximab (n = 132)				Arm C Rituximab (n = 138)			
Adverse Event	G1	G2	G3	G4	G1	G2	G3	G4	G1	G2	G3	G4
Hematologic toxicity												
Leukopenia	4	5	2	—	2	9	5	—	—	—	1	—
Neutropenia	3	3	—	2	4	3	10	9	—	—	2	—
Lymphocytopenia	—	2	2	—	—	1	1	2	—	—	—	—
Anemia	4	—	1	—	2	1	—	—	1	—	0	—
Thrombocytopenia	2	3	1	—	2	2	2	—	1	—	—	—
Febrile neutropenia	—	—	—	—	—	—	3	—	—	—	—	—
Nonhematologic												
Fatigue	12	4	—	—	11	2	—	—	12	4	—	—
Fever	1	—	—	—	4	2	—	—	5	3	—	1
Diarrhea	1	1	—	—	5	1	—	—	3	—	—	—
Dyspepsia	2	1	—	—	2	—	3	—	1	—	—	—
Nausea	6	1	—	—	17	1	—	—	6	1	—	—
Stomatitis	1	1	—	—	3	—	—	—	1	—	—	—
Skin rash	5	2	—	—	4	2	1	—	3	1	—	—
Infections	3	11	2	1	1	8	4	—	4	6	4	—
Cough	2	—	—	—	—	—	—	—	4	2	—	—
Transaminase increase	—	—	2	1	—	2	—	1	1	—	3	—
Gastric pain	6	2	1	—	6	4	1	—	3	4	—	—
Headaches	2	—	—	—	2	2	—	—	3	2	—	—
IR symptoms	—	—	—	—	15	4	1	1	10	8	2	—

Abbreviations: G, toxicity grade (according to Common Terminology Criteria for Adverse Events version 3); IR, infusion related (including: bronchospasm, chills, fever, rash, arthralgias, pruritus).

Table 3. Cause of Death (n = 26)

Cause of Death	All Patients (N = 227)		Chlorambucil (arm A) (n = 113)		Chlorambucil Plus Rituximab (arm B) (n = 114)	
	No.	%	No.	%	No.	%
Lymphoma progression	8	31	5	42	3	21
Second tumor	7	27	2	17	5	36
Infection	2	8	1	8	1	7
Transformed lymphoma	5	19	1	8	4	29
Other*	3	11	2	17	1	7
Unknown	1	4	1	8	—	—

*Respiratory failure, two patients; stroke, one patient.

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History

Version 7

Date	Summary of changes
28/04/2023	Reviewed electronically by the Haematology Reference Committee. Subcutaneous rituximab information removed from the following sections – treatment schedule, clinical information, administration, patient information. Minor formatting changes. Review in 4 years. Increased to version 7.

Version 6

Date	Summary of changes
09/03/2020	Biosimilar rituximab added to clinical information. Version number changed to V.6
27/03/2020	Reviewed by Haematology Reference Committee with no significant changes, review in 4 years.
01/10/2021	Drug status updated: rituximab SC is TGA registered but no longer PBS listed.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.

Version 5

Date	Summary of changes
11/10/2013	Presented at Haematology reference committee meeting (new Protocol)
12/11/2013	Published on eviQ
13/08/2014	Added link to ALLG, ANZCTR and Lymphoma Australia website with statement 'Patients with NHL should be considered for inclusion into clinical trials'.
11/09/2015	Reviewed at RCM, no changes, review in 2 years, updated drug costs.
20/06/2016	Drug status updated as per PBS: Removed 'NB: Rituximab is not on the PBS for marginal zone lymphoma'.
31/05/2017	Transferred to new eviQ website. Version number change to V.3.
12/03/2018	**Added:** • 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	Protocol reviewed at the Haematology Reference Committee meeting: • Treatment schedule detail: removed 'in 100 mL sodium chloride 0.9%' from hydrocortisone administration details; added to chlorambucil 'on an empty stomach (at least one hour before or three hours after food)' • Clinical information on CNS prophylaxis removed as not applicable. • Administration: removed the monitoring points 'weigh patient on each visit; urinalysis each visit' to reflect clinical practice. • Evidence reviewed and updated. • Version number changed to V.5.

Date	Summary of changes
13/09/2019	Protocol reviewed at the Haematology Reference Committee meeting with no significant changes. For review in 5 years.

First approved: 12 November 2013
Last reviewed: 28 April 2023
Review due: 30 June 2027

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/1368
23 Nov 2023

Patient information - Non-Hodgkin lymphoma (NHL) - Chlorambucil and rituximab

Patient's name:

Your treatment

The treatment schedule below explains how the drugs for this treatment are given.

Chlorambucil and rituximab			
Cycle 1 is given for 42 days. After a 14 day break, cycle 2 to 5 is repeated every 28 days. You will have 5 cycles.			
Day	**Treatment**	**How it is given**	**How long it takes**
1 to 42 **(Cycle 1)** 1 to 14 **(Cycles 2 to 5)**	**Chlorambucil** *(klor-AM-byoo-sil)*	Take orally ONCE a day on an empty stomach, at least one hour before or three hours after food. Do not break, crush or chew the tablets. If you forget to take tablets or vomit tablets, take your normal dose the next time it is due. Do not take an extra dose. Chlorambucil tablets need to be stored in the fridge.	
1, 8, 15 and 22 **(Cycle 1)** 1 **(Cycles 2 to 5)**	**Rituximab** (*ri-TUX-i-mab*)	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.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• 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

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also 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. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or 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

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **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.
- **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.

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	• Allergic reactions are uncommon but can be life threatening.
	• **If you feel unwell during the infusion or shortly after it, or:**
	  ◦ **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**
	
	<u>While you are in hospital:</u> Tell your doctor or nurse immediately.
	<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.

Flu-like symptoms	• You may get:
	  ◦ 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	• 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.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • 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. • 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.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

Early (onset days to weeks)

Infection risk (neutropenia)	• 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:** ◦ **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.**
Low platelets (thrombocytopenia)	• 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.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**

Tiredness and lack of energy (fatigue)	• 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.**
Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin rash	• 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)	
Low red blood cells (anaemia)	• 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.**
Hair thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.
Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]	• 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:** ◦ **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).**

Delayed (onset months to years)	
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

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.

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

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
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- Carer Help - carerhelp.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information - patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

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