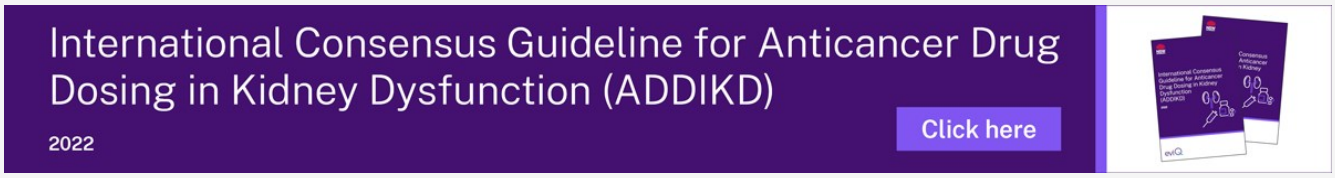
Chronic lymphocytic leukaemia chlorambucil and oBINUTUZumab

ID: 1486 v.3 **Endorsed**

Patients with leukaemia should be considered for inclusion into clinical trials. Link to ALLG website and ANZCTR 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.



Related pages:

- Chronic lymphocytic leukaemia venetoclax and oBINUTUZumab

Treatment schedule - Overview

Cycle 1

Drug	Dose	Route	Day
Chlorambucil	0.5 mg/kg ONCE a day	PO	1 and 15
oBINUTUZumab	100 mg	IV infusion	1
oBINUTUZumab	900 mg	IV infusion	2
oBINUTUZumab	1,000 mg	IV infusion	8 and 15

Cycle 2 to 6

Drug	Dose	Route	Day
Chlorambucil	0.5 mg/kg ONCE a day	PO	1 and 15
oBINUTUZumab	1,000 mg	IV infusion	1

Frequency: 28 days

Cycles: 6

Notes:

- This is a very immunosuppressive therapy; caution required in patients with pre-existing cytopenias, those with a history of opportunistic infections and the elderly.
- For patients with a 17p deletion, consider using an agent other than obinutuzumab.

Drug status: **Obinutuzumab:** (PBS authority)

Chlorambucil is on the PBS general schedule

Chlorambucil is available as **2 mg** tablets

Cost: ~ $4,660 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

Day 1		
Chlorambucil	0.5 mg/kg (PO)	ONCE a day at least one hour before, or 3 hours after food.
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Dexamethasone	20 mg (IV)	60 minutes before treatment
oBINUTUZumab	100 mg (IV infusion)	in 100 mL sodium chloride 0.9% 25 mg/hr over 4 hours (do not increase the infusion rate). If patients can tolerate the first 100 mg infusion at a rate of 25 mg/hr over 4 hours, it is possible to continue to infuse the remaining 900 mg of the dose within 1 day. A total time of at least 8 hours will be required.

Day 2		
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Dexamethasone	20 mg (IV)	60 minutes before treatment
oBINUTUZumab	900 mg (IV infusion)	in 250 mL sodium chloride 0.9%. Start at 50 mg/hr. Rate can be increased by 50 mg/hr every 30 minutes to a maximum rate of 400 mg/hr.

Day 8		
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment. * May be omitted - please see below for criteria.
Dexamethasone	20 mg (IV)	60 minutes before treatment. * May be omitted - please see below for criteria.
oBINUTUZumab	1,000 mg (IV infusion)	in 250 mL sodium chloride 0.9%. Start at 100 mg/hr. Rate can be increased by 100 mg/hr every 30 minutes, to a maximum of 400 mg/hr. **

Day 15		
Chlorambucil	0.5 mg/kg (PO)	ONCE a day at least one hour before, or 3 hours after food.
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment. * May be omitted - please see below for criteria.
Dexamethasone	20 mg (IV)	60 minutes before treatment. * May be omitted - please see below for criteria.
oBINUTUZumab	1,000 mg (IV infusion)	in 250 mL sodium chloride 0.9%. Start at 100 mg/hr.

Day 15		
		Rate can be increased by 100 mg/hr every 30 minutes, to a maximum of 400 mg/hr. **

Cycle 2 to 6

Day 1		
Chlorambucil	0.5 mg/kg (PO)	ONCE a day at least one hour before, or 3 hours after food.
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment. * May be omitted - please see below for criteria.
Dexamethasone	20 mg (IV)	60 minutes before treatment. * May be omitted - please see below for criteria.
oBINUTUZumab	1,000 mg (IV infusion)	in 250 mL sodium chloride 0.9%. Start at 100 mg/hr. Rate can be increased by 100 mg/hr every 30 minutes, to a maximum of 400 mg/hr. **
Day 15		
Chlorambucil	0.5 mg/kg (PO)	ONCE a day at least one hour before, or 3 hours after food.

*** For subsequent infusions (cycle 1, day 8 onwards):**

- **Antihistamine** premedication may be omitted for subsequent infusions if no infusion related reactions (IRR) occurred with the previous infusion.
- **Intravenous corticosteroid** premedication may be omitted for subsequent infusions if no grade 1 or 2 IRR occurred with the previous infusion. If a grade 3 IRR occurred OR lymphocyte count > 25 $x10^9$/L prior to next treatment, intravenous corticosteroid premedication should be continued.

****** If the patient experienced a grade 2 or higher infusion related reaction during the previous administration, commence at 50 mg/hr. The rate of infusion should be titrated up at 50 mg/hr increments every 30 minutes to a maximum of 400 mg/hr.

Frequency: 28 days

Cycles: 6

Indications and patient population

Indications:

- CD20 positive, chronic lymphocytic leukaemia (CLL) in previously untreated patients not suitable for fludarabine-based chemoimmunotherapy

Inclusion:

- must have a creatinine clearance 30 mL/min or greater AND a total cumulative illness rating scale (CIRS) score of greater than 6 (excluding CLL-induced illness or organ damage); OR creatinine clearance less than 70 mL/min.

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 obinutuzumab. Hypotension may occur during obinutuzumab infusion. Evaluate individual patient benefits and risks and consider withholding antihypertensive treatments for 12 hours prior to and during, and for one hour after each infusion. Read more about Hypersensitivity reaction
Premedication	The product information states that the premedication for obinutuzumab should consist of an analgesic/antipyretic, an antihistamine and an intravenous corticosteroid for **cycle 1, day 1 and 2.** **For subsequent infusions (cycle 1, day 8 onwards):** • **Antihistamine** premedication may be omitted for subsequent infusions if no infusion related reactions (IRR) occurred with the previous infusion. • **Intravenous corticosteroid** premedication may be omitted for subsequent infusions if no grade 1 or 2 infusion related reactions (IRR) occurred with the previous infusion. If a grade 3 IRR occurred OR lymphocyte counts > 25 x10^9/L prior to next treatment, intravenous corticosteroid premedication should be continued. • **Analgesic/antipyretic** premedication is given before all infusions. A suggested default premedication has been added to the treatment schedule, and may be substituted to reflect institutional policy. **Note:** hydrocortisone is not recommended as it has not been effective in reducing the rate of infusion reactions.
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
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.
Thrombocytopenia	Severe and life-threatening thrombocytopenia, including acute thrombocytopenia (occurring within 24 hours after the infusion), has been observed during treatment with obinutuzumab. Fatal haemorrhagic events have also been reported in cycle one of treatment. Patients should be closely monitored for thrombocytopenia throughout treatment, especially during the first cycle, and use of concomitant medications that may worsen haemorrhagic risk (e.g. antiplatelets, anticoagulants) should be taken into consideration. Correlating the timing of thrombocytopenia after obinutuzumab can assist in differentiating from other causes. In clinical trials, thrombocytopenia was reported in 10.4% of patients treated with obinutuzumab.
Cardiac toxicity	Arrhythmias (such as atrial fibrillation and tachyarrhythmia), angina pectoris, acute coronary syndrome, myocardial infarction and heart failure may occur with obinutuzumab, particularly in patients with underlying cardiac disease. These cardiac events may occur as part of an infusion-related reaction and can be fatal. Monitor patients for signs and symptoms of cardiac toxicity or fluid overload and refer to cardiologist if suspected. Read more about cardiac toxicity associated with anti-cancer drugs
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
Blood tests	FBC, EUC, eGFR and LFTs at baseline then FBC within 24 hours of the first dose of obinutuzumab during cycle 1 at physician's discretion. Then repeat FBC, EUC, eGFR and LFTs prior to each treatment and regularly throughout treatment 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[1, 2, 3]	
ANC x 10^9/L and Platelets x 10^9/L (pre-treatment blood test)	
ANC less than 1 OR platelets between 20 and 50 with concurrent bleeding complications	Delay treatment for one week and consider supportive measures (e.g. G-CSF, transfusions) if clinically indicated. Consider reducing chlorambucil by 25% when resuming treatment.

Haematological toxicity[1, 2, 3]	
	If thrombocytopaenia occurs within 24 hours of obinutuzumab administration, consider omitting obinutuzumab, or alternatively, resume same dose and monitor with supportive management (i.e. transfusions, intravenous immunoglobulins).
ANC less than 0.5 OR platelets less than 20	Initiate supportive measures (e.g. G-CSF, transfusions) and consider delaying the next cycle AND reducing chlorambucil by 50%. If thrombocytopaenia occurs within 24 hours of obinutuzumab administration, consider omitting obinutuzumab, or alternatively, resume same dose and monitor with supportive management (i.e. transfusions, intravenous immunoglobulins).

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%. No data available for obinutuzumab.

Hepatic impairment
No data available for obinutuzumab. Consider dose reduction of chlorambucil in severe hepatic impairment.

Infusion-related reactions (IRR)	
Grade 1 or 2	Reduce infusion rate of obinutuzumab and manage symptoms. Once resolved, continue infusion. **For obinutuzumab dose on Cycle 1, Day 1:** infusion rate may be increased back to 25 mg/hr after 60 minutes but not increased further. **For all doses of obinutuzumab (excluding split dose on Cycle 1 Day 1):** infusion rate escalation may resume at the increments and intervals as appropriate for the treatment dose if no further IRR symptoms occur.
Grade 3	**For obinutuzumab dose on Cycle 1, Day 1** First occurrence: interrupt obinutuzumab infusion and manage symptoms. Once resolved, infusion may be resumed at a maximum rate of 25 mg/hr after 60 minutes. Second occurrence: immediately interrupt obinutuzumab infusion and manage symptoms. Discontinue obinutuzumab and continue chlorambucil or consider switching to another protocol if appropriate. **For all doses of obinutuzumab (excluding split dose on Cycle 1 Day 1)** First occurrence: interrupt obinutuzumab infusion and manage symptoms. Once resolved, restart infusion at no more than half the rate of the infusion rate when IRR occurred. Second occurrence: immediately interrupt obinutuzumab infusion and manage symptoms. Discontinue obinutuzumab and continue chlorambucil or consider switching to another protocol if appropriate.
Grade 4	Immediately interrupt the obinutuzumab infusion and discontinue treatment. Continue chlorambucil or consider switching to another protocol if appropriate.

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

Obinutuzumab		
	Interaction	**Clinical management**
Antihypertensives	Additive hypotensive effect	Consider withholding antihypertensive medications 12 hours prior to, throughout and 1 hour after the obinutuzumab infusion

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.

Day 1 and 2

Approximate treatment time: 7 to 8 hours

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.

- weigh patient on each visit

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Chlorambucil

- administer orally ONCE a day on **days 1 and 15**
- 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.

Obinutuzumab infusion

Prior to administration:

- check baseline observations
- check for previous adverse events with drug infusions
- verify premedication has been taken. If not, administer 60 minutes prior to obinutuzumab administration:
- paracetamol 1000 mg orally AND
- loratadine 10 mg orally (or similar antihistamine)
- dexamethasone 20 mg IV

Note: The incidence of infusion related reactions was 65% with the first 1000 mg, subsequent infusions was 3% with the second 1000 mg dose and 1% thereafter.

Initial infusion:

- administer obinutuzumab at 25 mg/hr over 4 hours (do not increase the infusion rate)
- perform baseline observations and repeat every 30 minutes
- flush with ~ 100 mL of sodium chloride 0.9%

Hypotension may occur during obinutuzumab infusion. Consider withholding antihypertensive medication for 12 hours before, during, and for one hour after each infusion (if appropriate).

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer, on resolution of symptoms, (after 60 minutes) recommence the infusion at half the previous rate. If the patient dose not experience any further IRR symptoms the dose may be increased to 25 mg/hr. DO NOT INCREASE FURTHER.

Note: If patients can tolerate the first 100 mg infusion at a rate of 25 mg/hr over 4 hours, it is possible to continue to infuse the remaining 900 mg of the dose on day 1. A total time of at least 8 hours will be required.

Day 2 (or day 1 continued)

Note: If an adverse event was experienced with initial infusion (cycle 1, day 1 or 2) recommence infusion at the same rate as initial infusion.

If **no** adverse event experienced with initial infusion:

- administer obinutuzumab at 50 mg/hr
- increase rate by 50 mg/hr increments every 30 minutes to a maximum rate of 400 mg/hr if observations are stable
- perform baseline observations and repeat at each rate increase
- flush with ~ 100 mL of sodium chloride 0.9%

If a patient experiences any grade infusion related reaction during infusion, adjust the infusion as outlined below:

Grade 4 (life threatening)

- stop infusion and permanently discontinue therapy

Grade 3 (severe)

- temporarily interrupt infusion and treat symptoms
- upon resolution of symptoms, restart the infusion at no more than half the previous rate (the rate being used at the time that the IRR occurred)
- if patient does not experience any further IRR symptoms, infusion rate escalation may resume at the increments and intervals as appropriate for the treatment dose. (if not tolerated, use a rate of 25 mg/hr.
- the day 1 infusion rate may be recommenced to 25 mg/hr after 60 minutes, but not increased further
- stop infusion and permanently discontinue therapy if patients experience a second occurrence of a grade 3 IRR

Grade 1-2 (mild to moderate)

- reduce infusion rate and treat symptoms
- upon resolution of symptoms, continue infusion
- if patient dose not experience any IRR symptoms, infusion rate escalation may resume at the increments and intervals as appropriate for the treatment dose.
- the day 1 infusion rate may be increased back to 25 mg/hr after 60 minutes, but not increased further

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

Day 8

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).

- weigh patient on each visit

Treatment - Time out

Obinutuzumab infusion

Prior to administration:

- check baseline observations
- check for previous adverse events with drug infusions
- verify premedication has been taken. If not, administer 60 minutes prior to obinutuzumab administration:
- paracetamol 1000 mg orally AND
- loratadine 10 mg orally (or similar **antihistamine** premedication may be omitted for subsequent infusions if no infusion related reactions (IRR) occurred with the previous infusion)
- dexamethasone 20 mg IV (**corticosteroid** premedication may be omitted for subsequent infusions if no grade 1 or 2 infusion related reactions (IRR) occurred with the previous infusion. If a grade 3 IRR occurred OR lymphocyte counts > 25 x10^9/L prior to next treatment, intravenous corticosteroid premedication should be continued.)

Note: The incidence of infusion related reactions was 65% with the first 1000 mg, subsequent infusions was 3% with the second 1000 mg dose and 1% thereafter.

NOTE: If an adverse event was experienced with initial infusion (cycle 1, day 1 or 2) recommence infusion at the same rate as initial infusion

If **no** adverse event experienced with initial infusion:

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

Hypotension may occur during obinutuzumab infusion. Consider withholding antihypertensive medication for 12 hours before, during, and for one hour after each infusion (if appropriate).

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Day 15

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.

Prime IV line(s).

- weigh patient on each visit

Chemotherapy - Time out

Chlorambucil

- administer orally ONCE a day on **days 1 and 15**
- 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.

Obinutuzumab infusion

Prior to administration:

- check baseline observations
- check for previous adverse events with drug infusions
- verify premedication has been taken. If not, administer 60 minutes prior to obinutuzumab administration:
- paracetamol 1000 mg orally AND
- loratadine 10 mg orally (or similar **antihistamine** premedication may be omitted for subsequent infusions if no infusion related reactions (IRR) occurred with the previous infusion)
- dexamethasone 20 mg IV (**corticosteroid** premedication may be omitted for subsequent infusions if no grade 1 or 2 infusion related reactions (IRR) occurred with the previous infusion. If a grade 3 IRR occurred OR lymphocyte counts > 25 $x10^9$/L prior to next treatment, intravenous corticosteroid premedication should be continued.)

Note: The incidence of infusion related reactions was 65% with the first 1000 mg, subsequent infusions was 3% with the second 1000 mg dose and 1% thereafter.

NOTE: If an adverse event was experienced with initial infusion (cycle 1, day 1 or 2) recommence infusion at the same rate as initial infusion

If **no** adverse event experienced with initial infusion:

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

Hypotension may occur during obinutuzumab infusion. Consider withholding antihypertensive medication for 12 hours before, during, and for one hour after each infusion (if appropriate).

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

Antiemetics

- Antiemetics as prescribed.

Chlorambucil tablets

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

Patient information

- Ensure patient receives patient information sheet.

Administration cycles 2 to 6

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

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.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- weigh patient on each visit

Chemotherapy - Time out

Chlorambucil

- administer orally ONCE a day on **days 1 and 15**
- 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.

Obinutuzumab infusion

Prior to administration:

- check baseline observations
- check for previous adverse events with drug infusions
- verify premedication has been taken. If not, administer 60 minutes prior to obinutuzumab administration:
- paracetamol 1000 mg orally AND
- loratadine 10 mg orally (or similar **antihistamine** premedication may be omitted for subsequent infusions if no infusion related reactions (IRR) occurred with the previous infusion)
- dexamethasone 20 mg IV (**corticosteroid** premedication may be omitted for subsequent infusions if no grade 1 or 2 infusion related reactions (IRR) occurred with the previous infusion. If a grade 3 IRR occurred OR lymphocyte counts > 25 $x10^9$/L prior to next treatment, intravenous corticosteroid premedication should be continued.)

Note: The incidence of infusion related reactions was 65% with the first 1000 mg, subsequent infusions was 3% with the second 1000 mg dose and 1% thereafter.

NOTE: If an adverse event was experienced with initial infusion (cycle 1, day 1 or 2) recommence infusion at the same rate as initial infusion

If **no** adverse event experienced with initial infusion:

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

Hypotension may occur during obinutuzumab infusion. Consider withholding antihypertensive medication for 12 hours before, during, and for one hour after each infusion (if appropriate).

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Day 15

This is an oral treatment

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.

- weigh patient on each visit

Chemotherapy - Time out

Chlorambucil

- administer orally ONCE a day on **days 1 and 15**
- 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.

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

Discharge information

Antiemetics

- Antiemetics as prescribed.

Chlorambucil tablets

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

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

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
Atrial fibrillation	
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Insomnia	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
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
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
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

This regimen has a limited role in chronic lymphocytic leukaemia (CLL) due to the superior progression-free survival (PFS) associated with venetoclax-obinutuzumab (ID 3798 CLL venetoclax and obinutuzumab).[4] However, it may still be used on a case-per-case basis e.g. where access to venetoclax is difficult.

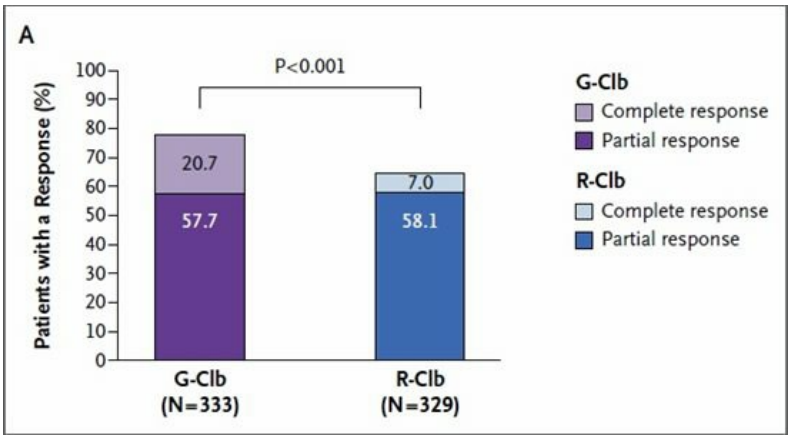
The evidence supporting the combination of obinutuzumab and chlorambucil for treatment of CLL comes from a phase 3 randomised control trial published in 2014.[5] 781 participants who were considered unsuitable for standard fludarabine-based chemotherapy (based on age and/or co-morbidities) were randomised to either chlorambucil alone, rituximab plus chlorambucil, or obinutuzumab plus chlorambucil. Treatment was administered for six 28-day cycles, and the dose of chlorambucil was chosen based on a previous study that showed chlorambucil was non-inferior to fludarabine in patients over 70 years of age.[1]

The median age of the patients was 73 years, creatinine clearance 62 mL/min and, Cumulative Illness Rating Scale (CIRS) score 8. The primary endpoint was progression-free survival (PFS).

Efficacy

The combination of obinutuzumab and chlorambucil resulted in a superior overall response rate (78.4%) when compared with rituximab plus chlorambucil (65.1%; see Figure 1). The response rate for chlorambucil alone was 31.4% (with no complete responses seen). Molecular responses were also higher in the obinutuzumab treated patients, with 37.7% negative for minimal residual disease (MRD) in blood, compared with 3.3% of those treated with the rituximab-chlorambucil combination.

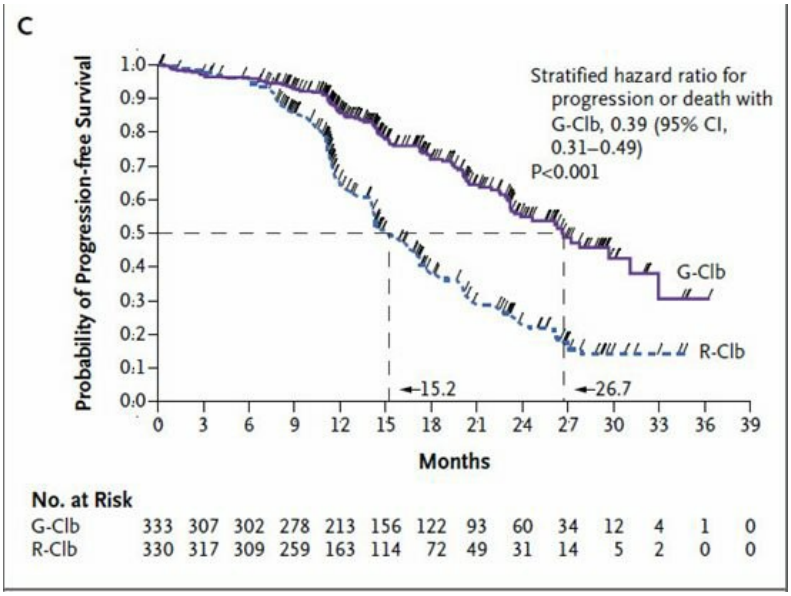
Figure 1. Response rates at 3 months after completion of therapy in the obinutuzumab-chlorambucil and rituximab-chlorambucil treated groups.[5]



G-Clb: obinutuzumab and chlorambucil; R-Clb: rituximab and chlorambucil

Treatment with obinutuzumab-chlorambucil also resulted in a superior PFS of 26.7 months compared with 15.2 months for rituximab-chlorambucil (see Figure 2).

Figure 2. Progression free survival in the obinutuzumab-chlorambucil and rituximab-chlorambucil treated groups.[5]



G-Clb: obinutuzumab and chlorambucil; R-Clb: rituximab and chlorambucil

Overall survival (OS) was superior in those receiving obinutuzumab-chlorambucil compared with chlorambucil alone (rate of death 9% vs 20% at a follow up of less than 3 years). No benefit in OS was seen with obinutuzumab-chlorambucil compared with rituximab-chlorambucil.

Toxicity

Grade 3 or 4 neutropenia occurred more commonly in the obinutuzumab-chlorambucil group than in the other two treatment groups.[5] Despite this, grade 3 to 5 infection rates were not significantly different (11-14% across all groups). Infusion reactions were also more common with obinutuzumab (20% grade 3-4 reactions), all of which were seen with the first infusion and resulted in treatment discontinuation in 7% of patients. Of note, death due to adverse events was not higher in the obinutuzumab-chlorambucil group (4%, compared with 6% for rituximab-chlorambucil and 9% for chlorambucil alone).

Table 2. Adverse Events of Grade 3 or Higher, Safety Population.*

Event	Obinutuzumab–Chlorambucil vs. Chlorambucil Alone		Rituximab–Chlorambucil vs. Chlorambucil Alone		Obinutuzumab–Chlorambucil vs. Rituximab–Chlorambucil	
	Obinutuzumab–Chlorambucil (N=241)	Chlorambucil Alone (N=116)	Rituximab–Chlorambucil (N=225)	Chlorambucil Alone (N=116)	Obinutuzumab–Chlorambucil (N=336)	Rituximab–Chlorambucil (N=321)
	number of patients (percent)					
Any event	175 (73)	58 (50)	125 (56)	58 (50)	235 (70)	177 (55)
Infusion-related reactions	51 (21)	—	9 (4)	—	67 (20)	12 (4)
Neutropenia	84 (35)	18 (16)	60 (27)	18 (16)	111 (33)	91 (28)
Anemia	11 (5)	5 (4)	10 (4)	5 (4)	14 (4)	12 (4)
Thrombocytopenia	27 (11)	5 (4)	8 (4)	5 (4)	35 (10)	10 (3)
Leukopenia	13 (5)	0	3 (1)	0	15 (4)	3 (1)
Infections	27 (11)	16 (14)	30 (13)	16 (14)	40 (12)	44 (14)
Pneumonia	8 (3)	4 (3)	11 (5)	4 (3)	13 (4)	17 (5)
Febrile neutropenia	4 (2)	5 (4)	4 (2)	5 (4)	8 (2)	4 (1)

* The safety population included all patients who received at least one dose of study medication. Shown are adverse events of grade 3, 4, or 5 with an incidence of 3% or higher in any treatment group, irrespective of whether the event was considered related or unrelated to treatment by the investigators.

In summary, the combination of obinutuzumab plus chlorambucil for treatment of older, unfit patients with CLL, has improved outcomes but higher toxicity compared with the other options of rituximab plus chlorambucil or chlorambucil alone.

References

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3 Fujiwara, Y., T. Urata, D. Niiya, et al. 2022. "Higher incidence of thrombocytopenia during obinutuzumab plus bendamustine therapy for untreated follicular lymphoma: a retrospective analysis by the Okayama Hematology Study Group." Int J Hematol 115(6):811-815.

4 Fischer, K., O. Al-Sawaf, J. Bahlo, et al. 2019. “Venetoclax and obinutuzumab in patients with CLL and coexisting conditions.” N Engl J Med 380(23):2225-2236

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History

Version 3

Date	Summary of changes
28/04/2023	Protocol reviewed by the Haematology Reference Committee; review continued out of session.
10/10/2023	Updates include: • Indication - note from treatment schedule now listed as 'inclusion' • Clinical information - cardiac toxicity added, information about obinutuzumab-related thrombocytopenia updated • Dose modifications - updated management for haematological toxicity where obinutuzumab is suspected to be the cause of thrombocytopenia, renal impairment updated, management of infusion-related reactions added • Evidence - limited use note added Version increased to V.3, review in 1 year.

Version 2

Date	Summary of changes
11/09/2015	New protocol discussed at Haematology Reference Committee meeting.
02/12/2015	Approved and published on eviQ. Review in 1 year.
31/05/2017	Transferred to new eviQ website. Version number change to v.2
05/12/2017	Premedication details aligned with the product information in the following sections: • Treatment schedule detail. • Clinical information. • Administration.
25/05/2018	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years.
27/03/2020	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years.
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.
11/03/2022	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years.
19/05/2022	Protocol title updated to reflect eviQ naming convention.

First approved: 2 December 2015
Last reviewed: 12 September 2023
Review due: 31 December 2024

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/1486
19 Oct 2023

Patient information - Chronic lymphocytic leukaemia (CLL) - Chlorambucil and obinutuzumab

Patient's name:

Your treatment

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

Chlorambucil and obinutuzumab			
This treatment cycle is repeated every 28 days. You will have up to 6 cycles. Your doctor will advise you of the number of treatments you will have.			
Cycle 1			
Day	**Treatment**	**How it is given**	**How long it takes**
1 and 15	**Chlorambucil** (*klor-AM-byoo-sil*)	Take orally ONCE a day on days 1 and 15 only. Take 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, 2, 8 and 15	**Obinutuzumab** (*OH-bi-nue-TOOZ-ue-mab*)	By a drip into a vein	(Day 1) About 4 to 8 hours; (Day 2) About 4 hours; (Days 8 and 15) About 3 hours
Cycles 2 to 6			
Day	**Treatment**	**How it is given**	**How long it takes**
1 and 15	**Chlorambucil**	Take orally ONCE a day on days 1 and 15 only. Take 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	**Obinutuzumab**	By a drip into a vein	About 3 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.

Tumour lysis syndrome

Some people having treatment for cancer can develop Tumour Lysis Syndrome (TLS), which results from the fast breakdown of cancer cells especially during the first couple of weeks of treatment. As the cancer cells are destroyed, they break open and the content of the cancer cell (uric acid, potassium, phosphorus) gets into the blood. This can lead to changes in kidney function, sudden kidney failure or even death.

If you do not have any heart or kidney problems, keep your fluids up by drinking at least 8 to 10 glasses of fluid daily. It is also important for you to keep your scheduled appointments for blood tests.

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

Obinutuzumab 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 obinutuzumab infusions.

Other medications given during this treatment

- **Obinutuzumab premedication:** before your treatment with obinutuzumab you will need to take some tablets called a premedication to help prevent you from having a reaction to the obinutuzumab.
- **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.

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)	
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.**
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.**
Low blood pressure (hypotension)	• You may get low blood pressure from this treatment. • You may feel dizzy or light-headed. • Tell your doctor if you are taking blood pressure medication. • Your doctor will monitor your blood pressure regularly while you are on this treatment. • Drink plenty of fluids (unless you are fluid restricted). • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Do not drive or operate machinery if you feel dizzy or light-headed. • Tell your doctor or nurse if you get any of the signs or symptoms listed above.

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.**
Heart palpitations	• You may get: ◦ chest pain ◦ a pounding or fluttering heart (palpitations) ◦ shortness of breath ◦ dizzy or light-headed ◦ confused ◦ more tired than usual. • Tell your doctor if you have any heart problems or are on any heart medications. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**
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.**
Difficulty sleeping (insomnia)	• You may have trouble falling or staying asleep. • Try some gentle exercise daily. • Avoid coffee, tea and other caffeinated drinks around bedtime. • Try something to relax before bed, like a bath or meditation. • If you can't sleep get up and do something quietly, such as reading, until you feel tired. • Tell your doctor or nurse if you have difficulty sleeping.
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.**

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 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)
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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