Non-Hodgkin lymphoma RICE (rituximab infusional iFOSFamide cARBOplatin etoposide)

ID: 1559 v.7 **Endorsed** Essential Medicine List

⚠ ADDIKD Carboplatin dosing:

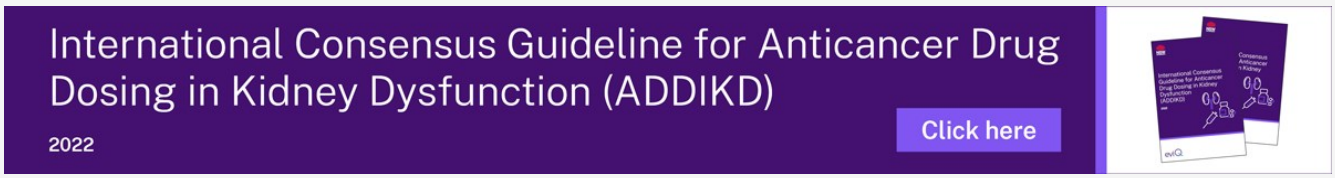
For dosing carboplatin, ADDIKD recommends that:

- Directly measured glomerular filtration rate (mGFR) is the preferred kidney function value in the Calvert formula, especially where estimated kidney function may be unreliable for accurate therapeutic dosing.
- Where mGFR is unavailable, eGFR adjusted to an individual's body surface area (BSA-adjusted eGFR) is a suitable alternative for use in the Calvert formula.
- Kidney function should not be capped at 125 mL/min for use in the Calvert formula.
- Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by > 20% or when there is a change in the clinical status of the patient.

For further information refer the eviQ Factsheet around carboplatin dosing and the carboplatin drug monograph within the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) and carboplatin dose calculators.

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

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



Related pages:

- Non-Hodgkin lymphoma RICE (rituximab fractionated iFOSFamide cARBOplatin etoposide)
- Haemorrhagic cystitis

Treatment schedule - Overview

Cycle 1 and 2

Drug	Dose	Route	Day
Rituximab	375 mg/m^2	IV infusion	1
Etoposide *	100 mg/m^2	IV infusion	1 to 3
cARBOplatin	5 AUC (Cap dose at 800 mg)	IV infusion	2
iFOSFamide	5,000 mg/m^2	IV infusion	2
Mesna	5,000 mg/m^2	IV infusion	2
Mesna **	2,000 mg at 2 and 6 hours post completion of ifosfamide	PO	3

Drug	Dose	Route	Day
Filgrastim	5 micrograms/kg	Subcut	4 and continue daily until neutrophil recovery

* Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.

** at 2 and 6 hours after completion of ifosfamide infusion

Frequency: 21 days

Cycles: 2 to 3

Notes:

- Rituximab should be included in second line therapy if there is relapse after a reasonable remission (longer than 6 months); however rituximab should often be omitted in patients with primary refractory disease.[1]
- This is an intense chemotherapy regimen and patients with poor ECOG performance status and significant co-morbidities may not be appropriate for this regimen.
- This protocol may be used for mobilisation of peripheral blood haematopoietic stem cells. The dose of filgrastim for mobilisation is 10 micrograms/kg/day in divided doses and should be commenced from day +4 after the last cycle of chemotherapy.

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

All other drugs are on the PBS general schedule (with the exception of oral mesna)

Cost: ~ $1,520 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 and 2

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
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes *
Day 2		
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes *
cARBOplatin	5 AUC (IV infusion) (Cap dose at 800 mg)	in 500 mL glucose 5% over 30 to 60 minutes
iFOSFamide	5,000 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 24 hours (loaded with mesna)
Mesna	5,000 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 24 hours (loaded with ifosfamide)

Day 3		
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes *
Mesna	2,000 mg (PO)	at 2 hours and 6 hours after completion of ifosfamide infusion

Day 4		
Filgrastim	5 micrograms/kg (Subcut)	inject subcutaneously once daily at least 24 hours post chemotherapy and continue until neutrophil recovery

* Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.

Frequency: 21 days

Cycles: 2 to 3

Indications and patient population

- Relapsed or refractory CD20 positive B-cell non-Hodgkin lymphoma
- Transplant eligible patients for both salvage and peripheral blood stem cell (PBSC) mobilisation

Clinical information

Venous access	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 etoposide and rituximab. High risk with carboplatin. Hypersensitivity risk increases with number of cycles of carboplatin. Rechallenge with carboplatin after hypersensitivity carries a high risk of anaphylaxis, and where clinically indicated, should be undertaken with a desensitisation protocol with appropriate supports in place. Refer to local institutional policy. 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.
Antiemetics for multi-day protocols	Antiemetic therapy should be administered throughout the duration of the chemotherapy protocol and to cover delayed nausea. The acute and delayed emetic risk of multi-day chemotherapy protocols will overlap depending on the individual drugs and their sequence of administration. More or less antiemetic cover may be required. A NK1 receptor antagonist and a 5HT$_3$ receptor antagonist in combination with dexamethasone are available on the PBS for primary prophylaxis of carboplatin induced nausea and vomiting. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. 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.
Ifosfamide-induced encephalopathy	May occur in patients treated with high dose ifosfamide (~ 5 to 8 g/m^2). Assess neurological function prior to each ifosfamide dose. Read more about ifosfamide-induced encephalopathy Link to ifosfamide-induced encephalopathy assessment chart
Haemorrhagic cystitis associated with high dose chemotherapy	Hydration regimen pre high dose cyclophosphamide or ifosfamide (as per local guidelines). There is limited evidence and no consensus regarding hydration regimens and mesna dose, route or timing of administration. Read more about haemorrhagic cystitis
Etoposide conversion factor	Note: Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.
Central nervous system (CNS) prophylaxis	Consider CNS relapse assessment in patients with high grade lymphoma. Read more about CNS prophylaxis in diffuse large cell lymphoma
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Mesna dosing and administration	There is evidence supporting variations in mesna doses and administration timings, with no clear evidence that one particular regimen is superior to another. The eviQ mesna recommendations may be based upon the individual trial/study or reference committee consensus and provide guidance on one safe way to administer the protocol. Individual institutional policy may vary and should be evidence-based. Read more about haemorrhagic cystitis
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Antifungal prophylaxis	Read more about antifungal prophylaxis drugs and doses.
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
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).

For dosing carboplatin, ADDIKD recommends that:

- Directly measured glomerular filtration rate (mGFR) is the preferred kidney function value in the Calvert formula, especially where estimated kidney function may be unreliable for accurate therapeutic dosing.
- Where mGFR is unavailable, eGFR adjusted to an individual's body surface area (BSA-adjusted eGFR) is a suitable alternative for use in the Calvert formula.
- Kidney function should not be capped at 125 mL/min for use in the Calvert formula.
- Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by > 20% or when there is a change in the clinical status of the patient.

*For further information refer the **eviQ Factsheet** around carboplatin dosing and the carboplatin drug monograph within the ADDIKD guideline. To assist with calculations, use the eviQ **Estimated Glomerular Filtration Rate (eGFR)** and **carboplatin** dose calculators.*

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

Haematological toxicity
Delay treatment until ANC is greater than 1.0 x 10^9/L and platelets greater than 50 x 10^9/L

Renal impairment	
Creatinine clearance (mL/min)	
10 to 50	Reduce ifosfamide and etoposide by 25%
less than 10	Reduce ifosfamide and etoposide by 50%. Recalculate carboplatin dose using Calvert formula

Hepatic impairment
No dose modifications required

Interactions

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

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

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

Carboplatin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination

Etoposide and Etoposide Phosphate		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin etc.)	Increased toxicity of etoposide possible due to reduced clearance	Avoid combination or monitor for etoposide toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of etoposide possible due to increased clearance	Avoid combination or monitor for decreased clinical response to etoposide
Glucosamine	Reduced efficacy of etoposide (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II)	Avoid combination or monitor for decreased clinical response to etoposide
Grapefruit juice	Reduced efficacy of oral etoposide possible due to possible alteration of P-gp mediated intestinal transport of etoposide	Avoid combination or monitor for decreased clinical response to etoposide

Ifosfamide		
	Interaction	**Clinical management**
Aprepitant	Increased risk of ifosfamide-induced neurotoxicity due to increased levels of active metabolites	Avoid combination or monitor closely for neurotoxicity; consider alternate antiemetic regimens
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
CYP3A4 inducers (e.g. carbamazepine,	Increased toxicity of ifosfamide possible	Avoid combination or monitor for

Ifosfamide		
phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	due to increased conversion to active and toxic metabolites	ifosfamide toxicity
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Reduced efficacy of ifosfamide possible due to decreased conversion to active metabolites	Avoid combination or monitor for decreased clinical response to ifosfamide
Suxamethonium	Potentiation of muscle relaxant effect possible	Alert the anaesthetist if a patient has been treated with ifosfamide within ten days of planned general anaesthesia
CNS depressants (including opiates, opioids, phenothiazines)	Increased risk of ifosfamide-induced neurotoxicity due to additive CNS effects	Avoid combination or monitor for excessive CNS depression/encephalopathy

Mesna
No specific or clinically significant 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

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).

Access CVAD.

Note: A large volume of intravenous fluid may be given with this protocol. If weight increases by more than 1 kg from baseline or fluid balance becomes positive by one litre or any other signs of fluid overload are present, review by medical officer (diuretics may be required).

- daily weight
- daily dipstick urinalysis to assess for haematuria
- strict fluid balance

Hydration if 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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Etoposide

Administer etoposide (irritant):

- via IV infusion over 30 to 60 minutes
- rapid infusion may cause hypotension
- observe for hypersensitivity
- flush with ~ 100 mL sodium chloride 0.9%
- if using etoposide phosphate administer in ~ 50 mL sodium chloride 0.9% or glucose 5% over ~15 minutes.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate.
- for severe reactions seek medical assistance immediately and do not restart infusion.

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

Day 2

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.

Note: A large volume of intravenous fluid may be given with this protocol. If weight increases by more than 1 kg from baseline or fluid balance becomes positive by one litre or any other signs of fluid overload are present, review by medical officer (diuretics may be required).

- daily weight
- strict fluid balance
- dipstick urinalysis to assess for haematuria prior to treatment

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Etoposide

Administer etoposide (irritant):

- via IV infusion over 30 to 60 minutes
- rapid infusion may cause hypotension
- observe for hypersensitivity
- flush with ~ 100 mL sodium chloride 0.9%
- if using etoposide phosphate administer in ~ 50 mL sodium chloride 0.9% or glucose 5% over ~15 minutes.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate.
- for severe reactions seek medical assistance immediately and do not restart infusion.

Carboplatin

Administer carboplatin (irritant):

- via IV infusion over 30 to 60 minutes
- observe for hypersensitivity reactions
- flush with ~100 mL of sodium chloride 0.9%
- hypersensitivity risk increases with number of cycles administered.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate
- for severe reactions seek medical assistance immediately and do not restart infusion.

Ifosfamide infusion

Prior to administration:

- assess neurological function at baseline and prior to each ifosfamide dose
  - inpatients: 4 hourly assessments until 24 hours after ifosfamide infusion is completed
    - neurological assessment tool
- perform baseline urinalysis and monitor for haematuria prior to each ifosfamide dose
  - note the administration of mesna will cause a false positive for ketonuria
- ensure patient receives at least 3 L of IV or oral fluids per day

Administer ifosfamide (irritant) with mesna:

- via IV infusion over 24 hours
- encourage patient to void every couple of hours to reduce the time urine remains in the bladder
- infusion must stop after 24 hours regardless of the volume left in the bag
- flush with ~100 mL of sodium chloride 0.9%

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

Day 3

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.

- daily weight
- strict fluid balance
- dipstick urinalysis to assess for haematuria prior to treatment

Continue neurological assessment for 24 hours after ifosfamide treatment is completed.

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Etoposide

Administer etoposide (irritant):

- via IV infusion over 30 to 60 minutes
- rapid infusion may cause hypotension
- observe for hypersensitivity
- flush with ~ 100 mL sodium chloride 0.9%

- if using etoposide phosphate administer in ~ 50 mL sodium chloride 0.9% or glucose 5% over ~15 minutes.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate.
- for severe reactions seek medical assistance immediately and do not restart infusion.

Mesna

- administer orally 2 hours and 6 hours post completion of ifosfamide infusion
- if vomiting occurs within 2 hours of taking oral mesna, repeat the dose or give IV mesna
- if patient cannot tolerate oral mesna, it may be given by IV bolus
- the oral mesna dose is equivalent to twice the IV dose

Note: the administration of mesna causes a false positive ketonuria.

Deaccess CVAD.

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

Day 4

Filgrastim

- administer filgrastim by subcutaneous injection once daily at least 24 hours after last dose of chemotherapy and continue until neutrophil recovery

---

Discharge information

Antiemetics

- Antiemetics as prescribed.

Mesna tablets

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

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antifungals, 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
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.
Encephalopathy	Ifosfamide induced encephalopathy has been reported in 10 to 30% of patients receiving high dose ifosfamide. Common symptoms include confusion, ataxia, weakness, seizures, somnolence and hallucinations. Onset may be 2 to 48 hours after commencing treatment. When reversible, symptoms usually resolve within 1 to 3 days. Read more about ifosfamide-induced encephalopathy
Flu-like symptoms	
Headache	
Haemorrhagic cystitis	An inflammatory process, characterised by diffuse bladder mucosal inflammation resulting in haemorrhage. Patients are at risk following blood and marrow transplant (BMT) or treatment with cyclophosphamide, ifosfamide and/or radiation therapy. Read more about haemorrhagic cystitis
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
Injection-site reaction	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
Nephrotoxicity	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.
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	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Progressive multifocal leukoencephalopathy (PML)	A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose. Read more about progressive multifocal leukoencephalopathy (PML)

Evidence

The major evidence supporting this protocol is provided by a phase III multicentre international randomised trial (CORAL) involving 396 patients that compared R-ICE (rituximab, ifosfamide, carboplatin and etoposide) with R-DHAP (rituximab, dexamethasone, high-dose cytarabine and cisplatin) in patients with relapsed or refractory CD20+ diffuse large B-cell lymphoma (DLBCL).[2] Between July 2003 and September 2007, 202 patients were randomised to receive R-ICE and 194 patients were randomised to receive R-DHAP. Both arms were given every 3 weeks for 3 cycles followed by autologous stem cell transplant (ASCT) and an additional rituximab dose was given on day -1 in the first course of each arm. The primary end point was the mobilization-adjusted response rate after three cycles of chemotherapy. Overall efficacy measurements were similar between R-DHAP and R-ICE with different toxicity profiles. Prior to CORAL, Kewalramani et al. were the first to investigate whether the addition of rituximab to the ICE regimen improved the complete remission rates in patients with relapsed or refractory DLBCL under consideration for ASCT.[3] Thirty-six patients who had not received rituximab previously were treated with R-ICE every 2 weeks for 3 cycles. R-ICE appeared to improve CR rates when compared with historical controls treated with ICE. It should be noted that the CORAL study compared two rituximab combination chemotherapy regimens head to head and that there have been no randomised studies to confirm the efficacy of adding rituximab to ICE in this patient population.

Efficacy

In the CORAL study, the 3-year EFS rate was 31% (95% CI, 26% to 36%) and was not significantly different between the R-ICE and R-DHAP arms (26% and 35%, respectively; P=0.6). Three-year PFS was 37% (95% CI, 31% to 42%), and the R-ICE and R-DHAP arms were not significantly different (31% and 42%, respectively; P=0 .4). Three-year OS was 49% (95% CI, 43% to 55%), with no difference between the R-ICE and R-DHAP arms (47% and 51%, respectively; P=0.4). For patients who underwent ASCT, 3-year PFS was 53%. There was no difference between the numbers of patients who achieved CR (38%) and PR prior to ASCT. Response rates, PFS and OS were all significantly affected by prior use of rituximab, early relapse (<12 months) and the secondary IPI (prognostic index) (see Table 3 below).[2] In the earlier, non-randomised study the CR rate with R-ICE was 53% compared with 27% in historical controls treated with ICE (see Table 4 below). The PFS in this group was 54% at 2 years.[3]

Table 3. Response Rate and Survival According to Prognostic Factors

Factor	Total No. of Patients	Response CR/CRu/PR			3-Year Event-Free Survival		3-Year Overall Survival	
		No. of Patients	%	*P*	%	*P*	%	*P*
All patients	398	246	63		31		50	
CR/CRu		148	38		51		70	
Prior rituximab								
No	147	122	83	< .001	47	< .001	66	< .01
Yes	244	124	51		21		40	
Relapse, > 12 months	160	140	88	< .001	45	< .001	64	
Refractory, < 12 months	228	106	46		20		39	< .001
saaIPI								
< 2	224	160	71	< .001	40		62	
> 1	146	76	52		18	< .001	32	< .001

Abbreviations: CR, complete response; CRu, unconfirmed complete response; PR, partial response; saaIPI, secondary age-adjusted International Prognostic Index.

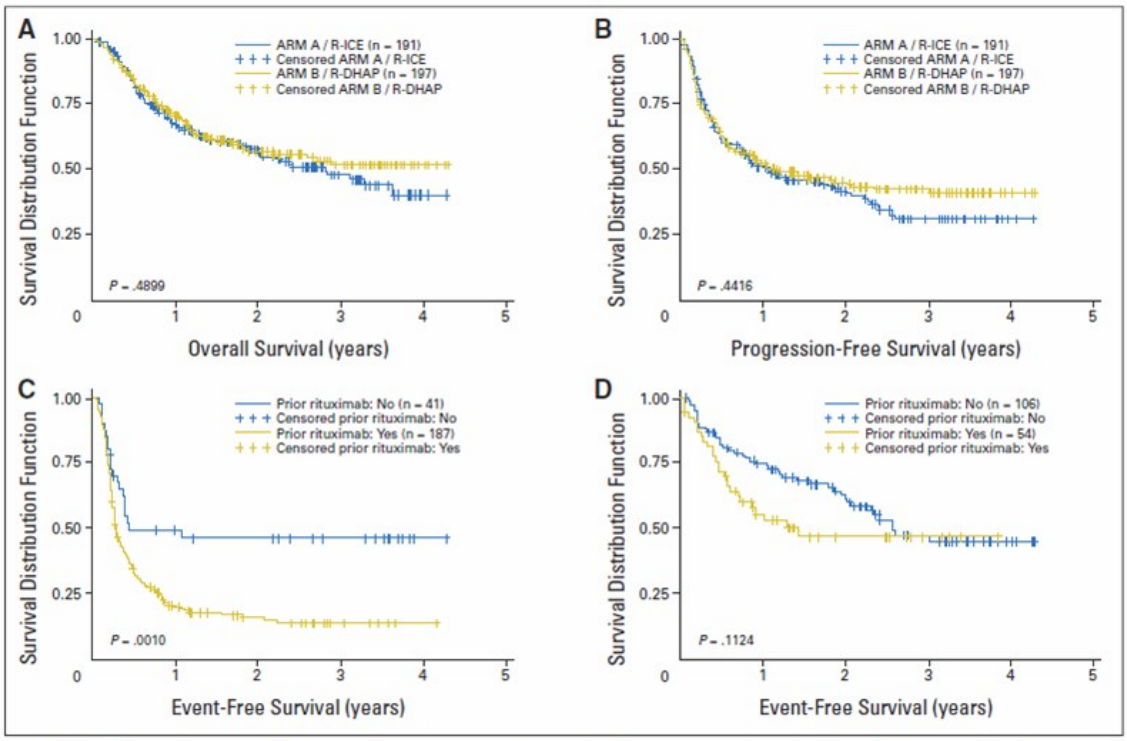


Fig 3. (A) Overall survival according to the first random assignment (intent to treat). (B) Progression-free survival according to treatment arm. (C) Event-free survival (EFS) according to prior rituximab treatment and relapse less than 12 months after diagnosis. (D) EFS according to prior rituximab treatment and relapse more than 12 months after diagnosis. R-ICE, rituximab, ifosfamide, carboplatin, etoposide; R-DHAP, rituximab, dexamethasone, high-dose cytarabine, cisplatin.

© Journal of Clinical Oncology 2010

Table 4. Response rates to RICE compared with ICE historical controls

Patient subgroup	Overall response rate, %			Complete response rate, %		
	RICE	ICE historical controls	*P*	RICE	ICE historical controls	*P*
All patients	78	71	.53	53	27	.01
Relapsed	96	79	.07	65	34	.01
Refractory	46	63	.36	31	19	.46
sAAIPI L/LI	79	86	.47	53	39	.42
sAAIPI HI/H	76	61	.28	53	19	.01

© Blood 2004

Toxicity

In the CORAL study, grade 3 to 4 haematologic toxicities were more severe in the R-DHAP arm than the R-ICE arm and included grade 4 renal toxicity in 11 patients.[2]

In the R-ICE arm 90 serious adverse events occurred in 58 patients, and in the R-DHAP arm 120 serious events occurred in 68 patients. In both arms, the most common serious adverse events were infections, with a similar rate of infection as a result of neutropenia (16%) in both arms.[2]

Table 3. Grade 3 or 4 nonhematologic toxicity

Toxicity	No. incidents
Grade 3	
Neutropenic fever	8
Infection	4
Cardiac ischemia	2
Deep venous thrombosis/pulmonary embolus	2
Hemorrhagic cystitis	2
Nausea/vomiting	2
Syncope	1
Grade 4	
Fever of unknown origin	1

© Blood 2004

References

1 NCCN Clinical Practice Guidelines in Oncology - Non-Hodgkin Lymphomas - Version 2.2012 www.nccn.org

2 Gisselbrecht, C., B. Glass, N. Mounier, et al. 2010. "Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era." J Clin Oncol 28(27):4184-4190.

3 Kewalramani, T., A. D. Zelenetz, S. D. Nimer, et al. 2004. "Rituximab and ICE as second-line therapy before autologous stem cell transplantation for relapsed or primary refractory diffuse large B-cell lymphoma." Blood 103(10):3684-3688.

History

Version 7

Date	Summary of changes
28/04/2023	Protocol electronically reviewed by Haematology reference committee. Subcutaneous rituximab information removed from treatment schedule, clinical information, administration and patient information. Increase to v.7, review in 4 years

Version 6

Date	Summary of changes
16/04/2020	'Mesna dosing and administration' block 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.

Version 5

Date	Summary of changes
09/03/2020	Biosimilar rituximab added to clinical information. Version number changed to V.5

Version 4

Date	Summary of changes
07/03/2014	New protocol presented at Haematology reference committee meeting.
15/05/2014	Approved and published on eviQ review in 2 years.
17/11/2014	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. Updated drug costs.
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	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years
13/09/2019	Reviewed by Haematology Reference Committee, no changes made. Review in 5 years.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.

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

First approved: 15 May 2014
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/1559
22 Nov 2023

Patient information - Non-Hodgkin lymphoma (NHL) - RICE (rituximab, infusional ifosfamide, carboplatin, etoposide)

Patient's name:

Your treatment

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

RICE (rituximab, infusional ifosfamide, carboplatin, etoposide)			
This treatment cycle is repeated every 21 days. You will have 2 to 3 cycles. Your doctor will advise you of the number of treatments you will have.			
Day	**Treatment**	**How it is given**	**How long it takes**
1	**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
1, 2 and 3	**Etoposide** (*e-TOE-poe-side*)	By a drip into a vein	About 1 hour
2	**Carboplatin** (*carb-o-PLAT-in*)	By a drip into a vein	About 30 minutes to 1 hour
	Ifosfamide (*eye-FOS-fa-mide*)	By a drip into a vein	About 24 hours
	Mesna (*MES-na*)	By a drip into a vein	
3	**Mesna**	Take orally at 2 hours and 6 hours after ifosfamide is completed. If vomiting occurs within 2 hours of taking oral mesna, repeat the dose.	
4	**Granulocyte Colony Stimulating Factor** (*G-CSF*)	By injection under the skin	About 5 minutes

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 involves 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.
- **Mesna**: you will be given a drug called mesna with this treatment. Mesna helps to protect your bladder from the chemotherapy. It can be given by mouth as a tablet or by injection through your drip. Your doctor or nurse will tell you how and when to take the mesna tablets.
- **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.
- **G-CSF:** you will be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Follow this link to read more information on how to give this injection.
- **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.

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.**
Bone pain after G-CSF injection	• You may have discomfort or a dull ache in your pelvis, back, arms or legs. • To reduce the pain, take paracetamol before each injection. • **Tell your doctor or nurse as soon as possible if your pain is not controlled.**

Brain swelling (encephalopathy)	• You may feel:
	  ◦ dizzy
	  ◦ sleepy
	  ◦ confused or agitated.
	• You may also get:
	  ◦ headaches
	  ◦ loss of balance
	  ◦ hallucinations
	  ◦ seizure (fits).
	• These symptoms are caused by the drug ifosfamide.
	• If you are being treated as an outpatient, try to have someone stay at home with you during the days that you are having this medicine.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

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.**

Bladder irritation (haemorrhagic cystitis)	• You may get: ◦ blood in your urine, sometimes with blood clots ◦ pain or burning when you urinate ◦ the urge to urinate more than normal ◦ stomach or pelvic pain or discomfort. • When you go home, make sure you drink plenty of fluids (unless you are fluid restricted). • Empty your bladder often. • **Tell your doctor or nurse as soon as possible if you notice any blood in your urine.**
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.**
Injection-site reaction	• At the injection site you may get pain, redness, swelling, bruising or rash. • Reactions can occur more than 24 hours after the injection. • These symptoms are usually not serious. • **Tell your doctor or nurse immediately if you notice any redness or pain during or after treatment.**
Kidney damage	• This treatment can cause changes to how your kidneys work. • You will have blood tests to make sure your kidneys are working properly. • You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this. • **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.**

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 loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
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).**

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.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- 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 further 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

Additional notes:

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

First approved: 15 May 2014
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/pi/1559
23 Nov 2023