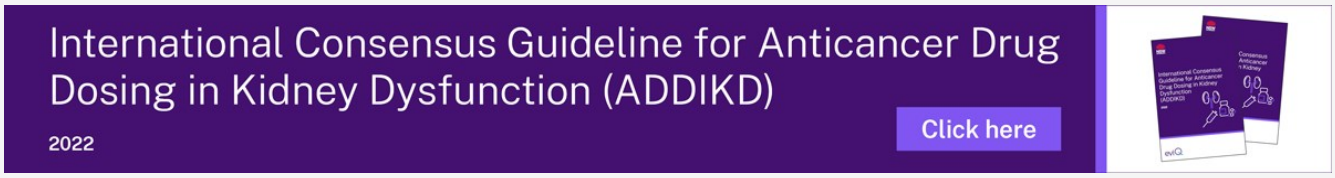
Non-Hodgkin lymphoma R-GDP (rituximab gemcitabine dexamethasone ciSplatin)

ID: 3788 v.2 **Endorsed** Essential Medicine List

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

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



Related pages:

- Lymphoma GDP (gemcitabine dexamethasone ciSplatin)

Treatment schedule - Overview

Cycle 1 and 2

Drug	Dose	Route	Day
Dexamethasone	40 mg ONCE a day	IV/PO	1 to 4
Rituximab	375 mg/m^2	IV infusion	1
Gemcitabine	1,000 mg/m^2	IV infusion	1 and 8
ciSplatin	75 mg/m^2	IV infusion *	1

* Please note the dilution and hydration associated with cisplatin in this protocol has been based on regimens used in the NCIC-CTG LY.12[1] trial and differs from the standard cisplatin hydration used on eviQ.

Frequency: 21 days

Cycles: 2 to 3, responding patients may be considered for high dose chemotherapy and autologous stem cell transplant otherwise, continue up to a total of 6 cycles, unless disease progression or unacceptable toxicity.

Notes:

- It is the consensus of the eviQ Reference Committee that cisplatin may be substituted with carboplatin (5 AUC) in patients with renal impairment (See Dose modifications section). If estimated GFR is greater than 125 mL/min (i.e. 5 AUC dose greater than 750 mg), obtaining direct measurement rather than an estimated renal function and/or dose capping is strongly recommended.

Drug status: All drugs in this protocol are on the PBS general schedule

Dexamethasone is available as **0.5 mg** and **4 mg** tablets

Cost: ~ $650 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
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.*
Rituximab	375 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Gemcitabine	1,000 mg/m^2 (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes
ciSplatin	75 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 60 minutes **

Day 2 to 4		
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.*

Day 8		
Metoclopramide	10 mg (PO)	one tablet when necessary (maximum of 30 mg/24 hours, up to 5 days)
Gemcitabine	1,000 mg/m^2 (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes

* Dose for day 1 should be given 30 to 60 minutes before rituximab infusion.

** Please note the dilution and hydration associated with cisplatin in this protocol has been based on regimens used in the NCIC-CTG LY.12[1] trial and differs from the standard cisplatin hydration used on eviQ.

Frequency: 21 days

Cycles: 2 to 3, responding patients may be considered for high dose chemotherapy and autologous stem cell transplant otherwise, continue up to a total of 6 cycles, unless disease progression or unacceptable toxicity.

Indications and patient population

Indications:

- Relapsed or refractory CD20 positive B-cell non-Hodgkin lymphoma
- Salvage therapy and peripheral chemotherapy followed by high dose chemotherapy and autologous stem cell transplant

Cautions/exclusions:

- Pre existing neuropathies greater than Grade 2
- Moderate/severe renal impairment (creatinine clearance less than 60 mL/min)

- Significant hearing impairment/tinnitus

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with rituximab. Read more about Hypersensitivity reaction
Premedication	The product information states that premedication is required for this treatment. **Note**: a corticosteroid is included as part of this treatment and therefore additional corticosteroid may not be required as premedication. Please refer to the treatment schedule for the suggested premedication regimen. This may be substituted to reflect institutional policy.
Emetogenicity HIGH	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. As a steroid has been included as part of this protocol, additional antiemetic steroids are not required. 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.
Pulmonary toxicity	Dyspnoea developing within hours of the infusion has been reported in about 10% of patients treated with gemcitabine. Read more about pulmonary toxicity associated with anti-cancer drugs.
Hydration	Hydration helps to prevent cisplatin-induced nephrotoxicity. The default regimen is appropriate for patients with normal electrolytes, kidney function, fluid status etc. and should be adjusted according to individual requirements. Read more about cisplatin hydration regimens
Ototoxicity	Ototoxicity may occur with platinum-based therapy; patients should be monitored for signs and symptoms. Platinum compounds should be used with caution in patients with pre-existing conditions or risk factors. Ototoxicity may become more severe in patients being treated with other drugs with nephrotoxic potential e.g. aminoglycosides. An audiometry test should be performed if symptoms develop. Read more about ototoxicity - tinnitus and hearing loss

Peripheral neuropathy	Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Corticosteroids	Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate. Read more about acute short term effects from corticosteroids
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	Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended. Read more about the prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	PJP prophylaxis is recommended e.g. trimethoprim/sulfamethoxazole 160/800 mg PO one tablet twice daily, twice weekly (e.g. on Mondays and Thursdays) OR one tablet three times weekly (e.g. on Mondays, Wednesdays and Fridays). Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Antifungal prophylaxis	Antifungal prophylaxis is recommended. 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, calcium and magnesium at baseline and prior to each cycle. Repeat FBC prior to treatment on day 8 of each cycle.
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.
- Dose modification recommendations in this protocol are based on the 2014 trial by Crump et al.[2]

Haematological toxicity	
Day 1: ANC x 10^9/L (pre-treatment blood test)	
less than 1.0	Delay treatment for 1 week* If after 1 week: • ANC < 1.0 but ≥ 0.5, consider giving treatment and initiate G-CSF** • ANC < 0.5, delay treatment until ANC ≥ 0.5
Day 8: ANC x 10^9/L (pre-treatment blood test)	
Less than 1.0 and greater or equal to 0.5	Consider giving treatment and initiate G-CSF** OR reduce gemcitabine by 25%
Less than 0.5	Omit gemcitabine this cycle and initiate G-CSF**
Day 1: Platelets x 10^9/L (pre-treatment blood test)	
Less than 75	Delay treatment for 1 week.* If after 1 week: • platelets < 75 but ≥ 50, consider giving treatment with platelet transfusions as necessary • platelets <50, delay treatment until platelets ≥ 50
Day 8: Platelets x 10^9/L (pre-treatment blood test)	
Less than 75 and greater or equal to 50	Reduce gemcitabine by 25% from this cycle's day 1 dose
Less than 50	Omit gemcitabine

*If counts presume to be low due to marrow involvement, treat after 1 week delay (i.e. at 4 weeks or day 28) despite counts

** G-CSF should be given prophylactically for all future cycles

Non-haematological toxicity	
Grade 2†	No dose reduction required
Grade 3††	Reduce gemcitabine and cisplatin by 25%
Grade 4	Delay treatment until recovery and consider resuming at a reduced dose at the clinician's discretion.

† Except grade 2 pneumonitis thought to be secondary to gemcitabine, discontinue gemcitabine permanently.

[††] In the event of grade 3 tinnitus, reduce cisplatin dose only

Renal impairment	
Serum Creatinine[#]	
Greater than 1.5 to 3.0 x ULN	Reduce cisplatin by 25%
Greater than 3.0 x ULN	Delay treatment by 1 week until recovery

[#]The renal impairment dose modifications are different from the eviQ standard and are based on the 2014 trial by Crump et al.[2]

Note: It is the consensus of the eviQ reference committee that cisplatin may be substituted with carboplatin (5 AUC) in patients with renal impairment. If estimated GFR is greater than 125 mL/min (i.e. 5 AUC dose greater than 750 mg), obtaining direct measurement rather than an estimated renal function and/or dose capping is strongly recommended.

Hepatic impairment	
Bilirubin	
Greater than 1.5 to 3.0 x ULN	Reduce gemcitabine by 25%
Greater than 3.0 x ULN	Day 1: Delay treatment by 1 week until recovery Day 8: Omit gemcitabine until recovery, and resume at a reduced dose for subsequent cycles

Cease treatment if any one of the following develops:

- Pulmonary toxicity
- Thrombotic microangiopathy (TMA)/haemolytic uraemic syndrome (HUS)
- Grade 4 non-haematologic toxicities
- Elevations of serum creatinine levels greater than 200 mmol/L

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*

Cisplatin		
	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
Neurotoxic drugs (e.g. vincristine, paclitaxel)	Additive neurotoxicity	Monitor closely for neuropathy if combination used
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination
Carbamazepine, phenytoin, valproate	Decreased antiepileptic plasma levels	Monitor antiepileptic serum levels and seizure frequency for efficacy; adjust dosage as appropriate or select alternative antiepileptic (e.g. clonazepam, diazepam, lorazepam)

Dexamethasone		
	Interaction	**Clinical management**
CYP3A4 interactions	Dexamethasone is a substrate of CYP3A4 and a weak to moderate inducer of CYP3A4. The clinical relevance of CYP3A4 induction by dexamethasone is unknown as the mechanism has yet to be established	The effects of the concomitant use of dexamethasone with other CYP3A4 inducers, inhibitors or substrates is variable. If used concomitantly, monitor patients closely for adverse drug reactions
Warfarin	Concurrent use may result in increased risk of bleeding or diminished effects of warfarin	Monitor prothrombin time / INR (especially during initiation or discontinuation) and for signs of drug toxicity during concomitant use; adjust warfarin dose as required
Oral hypoglycaemics	Corticosteroids may cause hyperglycaemia and worsen diabetes control	Monitor blood glucose levels and adjust oral hypoglycaemic dose as required

Gemcitabine		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Warfarin	Increased anticoagulant effect/increased bleeding risk due to decreased hepatic metabolism of warfarin and decreased synthesis of clotting factors	Monitor INR regularly and adjust warfarin dosage as appropriate
Cytidine deaminase (CDA) inhibitors (e.g. cedazuridine)	Increased effect/toxicity of gemcitabine possible due to reduced clearance	Avoid combination or monitor for increased gemcitabine effect/toxicity

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

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	**Clinical management**
Dexamethasone	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of **antiemetic dexamethasone** by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of **antiemetic dexamethasone** has already been taken into account. If **dexamethasone is part of the chemotherapy protocol**, dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
Warfarin	Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant	INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant
Combined oral contraceptive	Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant	Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of NK-1 antagonist possible due to increased clearance	Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of NK-1 antagonist possible due to reduced clearance	Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation)
Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist	Avoid combination or monitor for increased toxicity especially with orally administered drugs

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

Approximate treatment time: 7 hours (initial); 5 hours (subsequent)

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- baseline weight
- dipstick urinalysis prior to treatment

Treatment - Time out

Dexamethasone

- administer orally ONCE a day in the morning with food, on **days 1 to 4 OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%
- patients may receive dexamethasone on day 2, 3 and 4 orally as an outpatient or administered via IV infusion if still an inpatient

Note: if a dose is forgotten or vomited, contact treating team.

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: dexamethasone IV (part of this protocol) or hydrocortisone 100 mg IV

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 ~ 100 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

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

- perform baseline observations and repeat observations prior to each rate increase

- **commence** rituximab 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%

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

Gemcitabine

Administer gemcitabine (irritant):

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

Cisplatin

Commence prehydration for cisplatin:

- administer 10 mmol magnesium sulphate ($MgSO_4$) in 500 mL sodium chloride 0.9% over 60 minutes
- ensure patient has passed urine prior to cisplatin administration as per institutional policy.

Administer cisplatin (irritant):

- via IV infusion over 60 minutes
- flush with 100 mL of sodium chloride 0.9%.

Post hydration:

- 500 mL sodium chloride 0.9% over 60 minutes.

20/11/23 Mannitol information removed to align with updated ID 184 Prevention and management of cisplatin induced nephrotoxicity.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Day 8

Approximate treatment time: 60 minutes

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Gemcitabine

Administer gemcitabine (irritant):

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

Dexamethasone tablets

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

Antiemetics

- Antiemetics as prescribed.

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)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Flu-like symptoms	
Headache	
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
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.
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
Ototoxicity	Tinnitus and hearing loss may occur due to damage in the inner ear. Tinnitus is usually reversible, while hearing loss is generally irreversible. Hearing loss is dose-related, cumulative and may be worse in those with pre-existing hearing problems. Read more about ototoxicity - tinnitus and hearing loss
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
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
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash

Late (onset weeks to months)	
Alopecia - 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
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)
Haemolytic uraemic syndrome (HUS)	A rare but serious acute syndrome characterised by haemolysis of red blood cells and renal failure. Read more about haemolytic uraemic syndrome (HUS)
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 combination of gemcitabine, a pyrimidine antimetabolite, and cisplatin is synergistic in vitro. The GDP regimen, incorporating gemcitabine, cisplatin and high dose dexamethasone, was designed as an alternative outpatient salvage regimen for relapsed aggressive lymphoma, with the aim of reducing toxicity and enhancing stem cell mobilisation compared with pre-existing regimens. Rituximab has subsequently been added to this regimen for patients with relapsed B cell lymphomas.

The most robust evidence supporting this protocol is provided by the phase III NCIC-CTG LY.12 study, a multicentre international randomised trial involving 619 patients comparing GDP and DHAP (dexamethasone, cytarabine, cisplatin) prior to autologous stem cell transplantation in patients with relapsed/refractory aggressive lymphoma.[2] The study group included 524 patients with B cell lymphomas; DLBCL (n=419), transformed indolent (n=87) and primary mediastinal B-cell lymphoma (n=18). From 2005 onwards a protocol amendment allowed for the addition of rituximab to the chemotherapy backbone for CD20+ lymphomas.

Between 2003 and 2011, 310 patients were randomised to receive GDP +/- R (gemcitabine 1000 mg/m^2 days 1 and 8, cisplatin 75 mg/m^2 day 1, dexamethasone 40 mg days 1-4, +/- rituximab 375 mg/m^2 day 1) and 309 patients were randomised to receive DHAP +/- R (dexamethasone 40 mg days 1-4, cytarabine 2 g/m^2 twice daily for two doses on day 2, cisplatin 100 mg/m^2 by 24 hour continuous infusion day 1, +/- rituximab 375 mg/m^2 day 1) for a total of 2-3 cycles, followed by autologous SCT for responding patients. The exact number of patients receiving R-GDP is not reported; of the 414 patients with relapsed B-NHL treated with R-CHOP prior to study entry, n=159 received R-GDP, n = 159 received R-DHAP, n = 48 received GDP and n=48 received DHAP. The median age was 55 (range 18-74) and patients were high-risk, with approximately 70% of patients refractory to or relapsing within one year of previous therapy.

The primary end point was the overall response rate after two cycles of chemotherapy, and secondary end points were event-free and overall survival, successful stem cell-mobilisation, frequency of adverse events, quality of life (QoL) and resource usage. Compared with DHAP, treatment with GDP was associated with a non-inferior response rate and similar rates of transplantation, event free survival (EFS) and overall survival (OS), with less toxicity and hospitalisation and superior quality of life.

Efficacy

In the LY.12 trial, response rates were similar in patients treated with GDP and DHAP (45.1% v 44.1%, p=0.005), meeting the prespecified criteria for non-inferiority. The rates of autologous stem cell transplantation (52% versus 49%) and stem cell mobilisation (88% versus 82%, p=0.14) were similar. After a median follow up of 53 months, there was no difference in 4-year OS (39% in each arm, HR 1.03) or 4-year EFS (26% in each arm, HR 0.99).

Progression-free survival and Overall Survival[2]

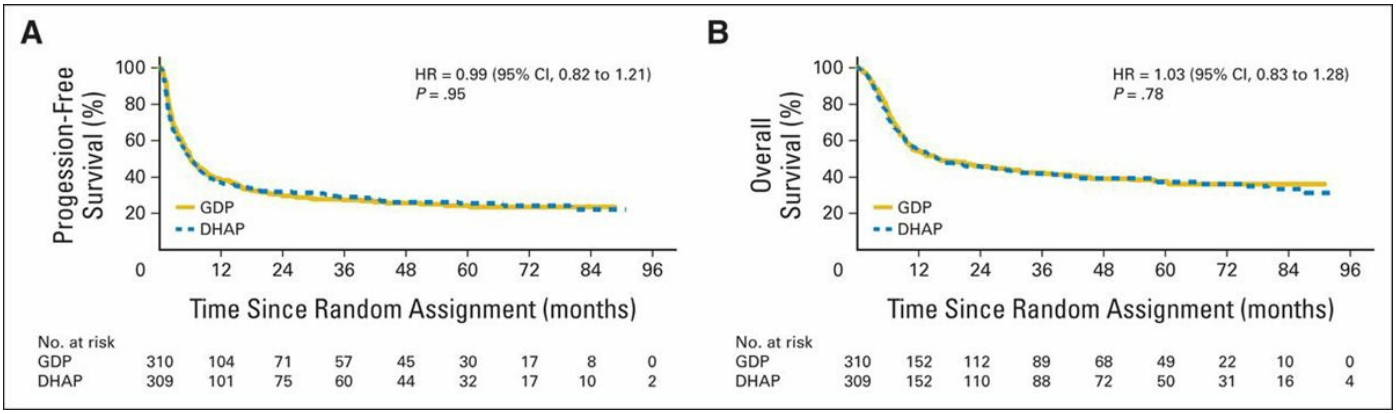


Fig 2. (A) Progression-free survival for patients randomly assigned to gemcitabine, dexamethasone, and cisplatin (GDP; gold line) or dexamethasone, cytarabine, and cisplatin (DHAP; blue dashed line). (B) Overall survival for patients randomly assigned to GDP (gold line) or DHAP (blue dashed line). HR, hazard ratio.

Subgroup analysis of LY.12 demonstrated similar outcomes for patients with transformed follicular lymphoma compared with DLCBL (ORR 47% v 45%, 4y OS 39% v 41%, and 4y EFS 27% v 27%).[3] Outcomes were also similar for patients aged ≤60 and >60 years (4y OS 40% v 36%, 4y EFS 28% v 20%) with comparable toxicity rates.[4]

Quality of life (QoL) assessment by FACT-Total score favoured GDP, with more patients reporting an improved QoL and less patients reporting a worse QoL after 2 cycles of therapy. Fewer patients treated with GDP required hospitalisation for treatment of adverse events or other illnesses (18% v 30%, p<0.001).

Several prospective and retrospective single arm studies have also reported the efficacy of GDP +/- R as follows:

- 51 patients from 9 Canadian centres with relapsed/refractory aggressive B cell lymphoma received GDP in this phase II prospective trial. The ORR was 49% (CR 16%, PR 33%).[1]
- A retrospective review of 152 RR DLBCL patients treated in Canada between 2002 and 2010 with GDP +/-R reported an ORR of 49%, CR 16%, transplantation rate of 52%, 2y OS 28% and 2y progression free survival (PFS) 21%. Only 20% of patients with RR DLBCL received R-GDP (patients with rituximab-refractory disease, i.e. relapse within 6 months of prior therapy, were excluded), of whom 47% had received prior rituximab. The response rate specific to the R-GDP cohort was not reported.[5]
- A retrospective review of 50 RR DLBCL patients treated in China between 2005 and 2010 with R-GDP reported an ORR of 72%, CR 56%, 2y OS 70% and 2y PFS 48%. Responses were higher in relapsed compared with refractory patients (48% v 24%). The response rate in the 18 patients who had received prior rituximab was lower than rituximab-naïve patients, though the difference was not statistically significant (75% v 100%, p=0.3).[6]

Rituximab is routinely incorporated into salvage regimens for aggressive B-cell lymphomas. The addition of rituximab to salvage therapy improves PFS in rituximab-naïve patients,[7] but there is no randomised evidence to support the addition of rituximab to salvage chemotherapy for aggressive B-cell lymphoma refractory to or relapsing after a prior rituximab-containing regimen. However, rituximab was included as a protocol amendment in the phase III LY.12 study and has become a standard addition to salvage regimens. Evidence to support this approach includes:

- A subset analysis of the 414 aggressive B-cell lymphoma patients in the LY.12 study who had received prior R-CHOP revealed a higher response rate in patients receiving R-salvage (n= 318, including both R-GDP or R-DHAP) than salvage alone (n=96, GDP or DHAP alone) of 46% versus 25% (CR 16% v 4%) and higher transplant rates (52% v 31%), with no difference in OS or PFS. Where patients who relapse within 1 year of primary therapy were excluded, the inclusion of rituximab at salvage significantly improved OS with a trend towards improved PFS.[8]
- Of the 396 patients with RR aggressive B-NHL treated on the CORAL study with R-DHAP v R-ICE, prior rituximab exposure did not affect EFS in patients relapsing more than 12 months after a rituximab containing first line regimen. However, in patients with early relapse (<12 months) after first line therapy, previous rituximab exposure predicted a poor outcome compared with rituximab naïve patients.[9]

This data supports the addition of rituximab to GDP for patients with relapsed disease; the role of rituximab in patients with rituximab-refractory disease is less clear, though rituximab is commonly used and is available on the PBS for this indication.

Note that R-GDP has not been formally compared with other salvage regimens (eg R-ICE, R-ESHAP) in a phase III setting and thus there is no clear evidence of superiority of one regimen over another. Outcomes of R-DHAP and R-ICE were essentially equivalent in the large phase III CORAL trial, although patients with germinal centre B-cell (GCB) subtype DLBCL had an improved PFS with R-DHAP versus R-ICE.[9, 10]

Toxicity

In the phase III LY.12 trial, GDP was associated with a favourable toxicity profile compared with DHAP, with reduced rates of grade 3/4 adverse events during the first two cycles (47% v 61%; p<.001), reduced hospitalisation (47% v 99%, p<0.001), fewer episodes

of febrile neutropenia (9% v 23%; p < .001) and less thrombocytopenia requiring platelet transfusions (31% v 47%, p<0.001). Haematological toxicity is universal. Other common adverse events include fatigue, infection and gastrointestinal toxicity (refer to table). There were eight treatment-related deaths, two during treatment with GDP and six after receiving DHAP. Toxicity of R-GDP was similar in the previously mentioned single arm studies.

Table 3. Most Serious Adverse Events

Adverse Event	GDP (n = 306) No.	GDP (n = 306) %	DHAP (n = 304) No.	DHAP (n = 304) %	P
Thrombosis/embolism	18	6	18	6	NS
Fatigue	30	10	28	9	NS
Nausea	13	4	25	8	.04
Vomiting	22	7	21	7	NS
Infection					
With grade 3 to 4 neutropenia	18	6	28	9	NS
Without neutropenia	21	7	22	7	NS
Febrile neutropenia	28	9	70	23	< .001
Syncope	7	2	16	5	
Worst overall	143	47	186	61	< .001

NOTE. Comparison of most frequently occurring serious adverse events, occurring in at least 5% of patients who received at least one dose of protocol therapy, at grade 3 or 4 (National Cancer Institute Common Toxicity Criteria version 2.0).
Abbreviations: DHAP, dexamethasone, cytarabine, cisplatin; GDP, gemcitabine, dexamethasone, cisplatin; NS, not significant.

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History

Version 2

Date	Summary of changes
28/04/2023	Protocol reviewed electronically by the Haematology Reference Committee. Updates include: • subcutaneous rituximab information removed from the following sections - treatment schedule, clinical information, administration, patient information Increased to version 2. Review in 4 years.

Version 1

Date	Summary of changes
27/03/2020	New protocol taken to reference committee meeting.
04/05/2020	Approved and published on eviQ. To be reviewed in 1 year.
01/10/2021	Drug status updated: rituximab SC is TGA registered but no longer PBS listed.
22/10/2021	Electronically reviewed by the Haematology reference committee. Side effects updated. For review in 2 years.
20/01/2022	Interactions updated.

First approved: 4 May 2020
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/3788
26 Nov 2023

Patient information - Non-Hodgkin lymphoma (NHL) - R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin)

Patient's name:

Your treatment

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

R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin)

This treatment cycle is repeated every 21 days. You will have 2 to 3 cycles and may continue up to 6 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 to 4	**Dexamethasone** (*dex-a-METH-a-sone*)	By a drip into a vein **OR** take orally ONCE a day in the morning with food on days 1 to 4 only. If you forget to take your tablets or vomit your tablets, contact your treating team.	About 15 minutes if given by a drip
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
	Gemcitabine (*jem-sie-ta-been*)	By a drip into a vein	About 30 minutes
	Cisplatin (*siss-PLAT-in*)	By a drip into a vein	About 1 hour
8	**Gemcitabine**	By a drip into a vein	About 30 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 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.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you may 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. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.

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)	
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.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • The drug gemcitabine can cause a fever or flu-like illness within the first day or two of having the treatment. • You can take paracetamol to help settle these symptoms. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if the symptoms do not settle or you become unwell.**
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.**
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.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**
Liver problems	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**
Low blood magnesium, potassium and calcium levels (hypomagnesaemia, hypokalaemia, hypocalcaemia)	• This may be found from your routine blood tests and treated by your doctor. • If it is severe you may get: ◦ muscle cramps or twitches ◦ numbness or tingling in your fingers, toes or around your mouth ◦ constipation ◦ an irregular heartbeat ◦ sleepy, drowsy or confused • **Tell your doctor or nurse as soon as possible if you get any of the signs or symptoms listed above.**
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.**
Hearing changes (ototoxicity)	• You may get ringing in your ears or loss of hearing. • You may have your hearing tested before and during your treatment. • **Tell your doctor or nurse as soon as possible if you notice any changes to your hearing.**
Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including: ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.
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.**

Side effects from steroid medication	• Steroid medication may cause:
	  ◦ mood swings and behaviour changes
	  ◦ an increased appetite
	  ◦ weight gain
	  ◦ swelling in your hands and feet
	  ◦ stomach upsets
	  ◦ trouble sleeping
	  ◦ fragile skin and bruising
	  ◦ an increase in your blood sugar level
	  ◦ weak and brittle bones (osteoporosis)
	• Take your steroid medication with food to reduce stomach upset
	• If you have diabetes, your blood sugar levels may be tested more often.
	• 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)	
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)
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.**
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.
Red blood cell and kidney damage (haemolytic uraemic syndrome)	• This side effect is rare, but can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if it has been longer than 12 hours since you have emptied your bladder or if you have any of the following signs or symptoms:** ◦ **black, tarry bowel motions (stools, poo)** ◦ **blood in your urine or are not urinating as often** ◦ **pinpoint red spots on your skin** ◦ **major bruising** ◦ **a fever** ◦ **shortness of breath** ◦ **a severe headache** ◦ **confusion.**
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

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