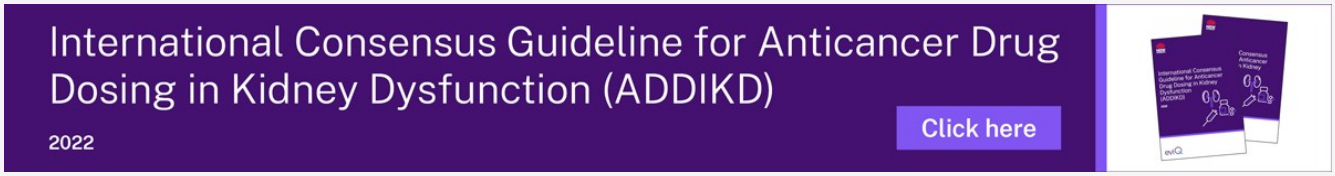
Non-Hodgkin lymphoma hyper CVAD Part B

ID: 225 v.6 **Endorsed** Essential Medicine List

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

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

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 hyper CVAD Part A and B overview
- Non-Hodgkin lymphoma hyper CVAD Part A

Treatment schedule - Overview

Cycle 2, 4, 6

Drug	Dose	Route	Day
Methotrexate	200 mg/m^2	IV infusion	1
Methotrexate	800 mg/m^2	IV infusion	1
Calcium folinate (Leucovorin)	15 mg/m^2 every 6 hours *	IV infusion	2
Cytarabine (Ara-C)	3,000 mg/m^2 TWICE a day **	IV infusion	2 and 3
Pegfilgrastim	6 mg	Subcut	4

* Every 6 hours until methotrexate level less than 0.1 micromol/L. Start 36 hours after commencement of methotrexate infusion.

** Cytarabine to be reduced to 1000 mg/m^2 in patients older than 60 years[1] (refer to 'dose modifications' below).

This hyper CVAD protocol consists of 3-4 cycles of Part A (cycles 1, 3, 5, 7) alternating with 3-4 cycles of Part B (cycles 2, 4, 6, 8) for a total of 6-8 cycles.

Frequency: 21 days
Commence next cycle (i.e. Part A) on day 21 or when WCC is greater than or equal to 2.0 x 10^9/L and platelets are greater than 60 x 10^9/L, whichever is earlier.

Cycles: 3 to 4 depending on response.
For mantle cell lymphoma (MCL)
If complete response (CR) achieved after 1 cycle of Part A and 1 cycle of Part B, give a further 2 cycles of Part A (cycles 3, 5) alternating with 2 more cycles of Part B (cycles 4, 6)
If partial response (PR) achieved after 1 cycle of Part A and 1 cycle of Part B, give a further 3 cycles of Part A (cycles 3, 5, 7) alternating with 3 more cycles of Part B (cycles 4, 6, 8)

Notes:

- Calcium folinate (Leucovorin®) must be administered at the precise timings as prescribed; the first dose must be given 36 hours after the commencement of the methotrexate infusion. See ID 3535 Management of high-dose methotrexate toxicity for more information.
- Methotrexate levels should be monitored at 24 hours after the completion of the methotrexate infusion and daily until the level is less than 0.1 micromol/L.
- Cease PJP prophylaxis with sulfamethoxazole/trimethoprim at least one day prior to methotrexate infusion and recommence once neutrophils have recovered to greater than 1.0 x 10^9/L.
- Addition of rituximab to chemotherapy has been shown to be beneficial in the treatment of MCL; for more information see ID 4296 Lymphoma R-hyper CVAD Part A and B overview

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

All other drugs in this protocol are on the PBS general schedule

Cost: ~ $2,880 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 2, 4, 6

Day 1		
Palonosetron	0.25 mg (IV bolus)	30 minutes before chemotherapy *
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy *
Methotrexate	200 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 2 hours
Methotrexate	800 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 22 hours
Day 2		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food *
Calcium folinate (Leucovorin)	15 mg/m^2 (IV infusion)	every 6 hours until methotrexate level less than 0.1 micromol/L. Start 36 hours after commencement of methotrexate infusion.
Cytarabine (Ara-C)	3,000 mg/m^2 (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours) **
Day 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food *
Cytarabine (Ara-C)	3,000 mg/m^2 (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours) **
Day 4		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 4 and 5 may not be required and may be reduced or omitted at the clinician's discretion. *
Pegfilgrastim	6 mg (Subcut)	inject subcutaneously at least 24 hours after chemotherapy
Day 5		

Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 4 and 5 may not be required and may be reduced or omitted at the clinician's discretion. *

* Link to ID 7 Prevention of chemotherapy induced nausea and vomiting

** Cytarabine to be reduced to 1000 mg/m^2 in patients older than 60 years[1] (refer to 'dose modifications' below).

Notes:

- Calcium folinate (Leucovorin®) must be administered at the precise timings as prescribed; the first dose must be given 36 hours after the commencement of the methotrexate infusion. See ID 3535 Management of high-dose methotrexate toxicity for more information.
- Methotrexate levels should be monitored at 24 hours after the completion of the methotrexate infusion and daily until the level is less than 0.1 micromol/L.
- Cease PJP prophylaxis with sulfamethoxazole/trimethoprim at least one day prior to methotrexate infusion and recommence once neutrophils have recovered to greater than 1.0 x 10^9/L.
- Addition of rituximab to chemotherapy has been shown to be beneficial in the treatment of MCL; for more information see ID 4296 Lymphoma R-hyper CVAD Part A and B overview

Frequency: 21 days
Commence next cycle (i.e. Part A) on day 21 or when WCC is greater than or equal to 2.0 x 10^9/L and platelets are greater than 60 x 10^9/L, whichever is earlier.

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Indications and patient population

Indications:

- Mantle cell lymphoma (MCL)
- Aggressive non-Hodgkin lymphoma (NHL)

Caution:

- This is an aggressive regimen; caution is advised in patients older than 60 years of age.

The eviQ reference committee suggests that when treating patients with lymphoblastic lymphoma refer to the Ph- hyper CVAD part A and B/POMP protocol.

Clinical information

Venous access	Central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection

Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist is available on the PBS in combination with a $5HT_3$ antagonist and steroid. 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
Pre-hydration	Pre-hydration with sodium bicarbonate 8.4% infusion. Urinary pH must be greater than 7 prior to commencing methotrexate infusion. Consider prescribing sodium bicarbonate oral capsules for administration prior to methotrexate infusion. Sodium bicarbonate 8.4% should continue until the methotrexate level is equal to or less than 0.1 micromol/L. Read more about high dose methotrexate-induced toxicity.
Methotrexate interactions	Avoid administering the following drugs in combination with high dose methotrexate: ciprofloxacin, NSAIDs, probenecid, proton pump inhibitors (PPIs) (e.g. esomeprazole, omeprazole, pantoprazole), sulphonamides (e.g. sulfamethoxazole (in Bactrim®, Septrin®)), penicillins (e.g. piperacillin (in Tazocin®)) and trimethoprim. Severe mucositis may occur if administered together.
High dose methotrexate	Monitoring of methotrexate levels is essential as delayed methotrexate excretion is potentially an emergency situation. Methotrexate levels to be monitored every 24 hours until level is less than 0.1 micromol/L. Methotrexate is renally eliminated. Kidney function must be evaluated prior to treatment. Methotrexate exits slowly from third space compartments (e.g. pleural effusions or ascites), resulting in a prolonged terminal plasma half-life and unexpected toxicity. In patients with significant third space accumulations, it is advisable to evacuate the fluid before treatment and to monitor plasma methotrexate levels. Glucarpidase is recommended in patients with high dose methotrexate (HDMTX)-induced acute kidney injury and delayed methotrexate clearance. It can rapidly lower methotrexate levels and early administration within 48 to 60 hours from the start of the HDMTX infusion is critical, as life-threatening toxicities may not be preventable beyond this time point.[2] Read more about high dose methotrexate-induced toxicity.
Cytarabine-induced neurotoxicity	This may occur in patients treated with high-dose cytarabine. Assess cerebellar function prior to each cytarabine dose. Note: an increased risk of cytarabine-induced neurotoxicity has been associated with kidney dysfunction. Read more about neurotoxicity associated with high-dose cytarabine and access the cytarabine cerebellar neurotoxicity assessment chart
Ocular toxicities	Administer corticosteroid eye drops to minimise corneal toxicity from high dose cytarabine. Commence on the day of first dose of cytarabine and continue for at least 72 hours after completion of final cytarabine dose. Read more about ocular toxicities associated with high dose cytarabine
Cytarabine syndrome	Treatment with cytarabine may cause a "cytarabine syndrome" characterised by flu-like symptoms, skin rash and occasionally chest pain.
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	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.
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
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
Blood tests	FBC, EUC, eGFR, LFTs, LDH at baseline, prior to each treatment and regularly throughout treatment. Methotrexate levels to be monitored every 24 hours until level is less than 0.1 micromol/L.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

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

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

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

Haematological toxicity
Commence next cycle on day 21 or when WCC is greater than or equal to 2 x 10^9/L and platelets are greater than 60 x 10^9/L, whichever is earlier.

Renal impairment	
Creatinine clearance (mL/min)	
10 to 50	Reduce methotrexate by 50%
less than 10	Contraindicated

Note: *an increased risk of neurotoxicity has been associated with high dose cytarabine when creatinine clearance is less than 60 mL/min*

Hepatic impairment	
Mild	No dose modifications necessary
Moderate	No dose modifications necessary
Severe	Reduce methotrexate by 25%

Age older than 60 years
For patients aged older than 60 years, reduce cytarabine dose to 1000 mg/m^2.[3]

Mucositis, stomatitis and diarrhoea	
Grade 3 or Grade 4	Diarrhoea and ulcerative stomatitis require interruption of therapy otherwise, haemorrhagic enteritis and death from intestinal perforation may occur; reduce methotrexate by 25%

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*

Cytarabine		
	Interaction	**Clinical management**
Cytidine deaminase (CDA) inhibitors (e.g. cedazuridine)	Potential increased effect/toxicity of cytarabine due to reduced clearance	Avoid combination or monitor for increased cytarabine effect/toxicity

Methotrexate		
	Interaction	**Clinical management**
Ciprofloxacin **NSAIDS** **Probenecid** **Proton pump inhibitors (e.g. esomeprazole, omeprazole, pantoprazole)**	Increased toxicity of methotrexate possible due to reduced clearance	Avoid combination or monitor for methotrexate toxicity Important note: with high-dose methotrexate therapy, many of these drug combinations are *contraindicated*
Sulphonamides and penicillins (e.g. sulfamethoxazole (in Bactrim®, Septrin®), piperacillin (in Tazocin®) etc.)	Increased toxicity of methotrexate possible due to displacement from serum protein binding	Avoid combination or monitor for methotrexate toxicity
Trimethoprim	Increased toxicity of methotrexate possible due to additive antifolate activity	Avoid combination or monitor for methotrexate toxicity
Mercaptopurine	Increased toxicity of mercaptopurine possible due to reduced clearance	Avoid combination or monitor for mercaptopurine toxicity
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Hepatotoxic drugs (e.g. azathioprine, leflunomide, retinoids, sulfasalazine)	Additive hepatotoxicity	Avoid combination or monitor liver function closely
Folic acid (e.g. as in multivitamins) **Asparaginase (administered immediately prior or concurrently)**	Reduced efficacy of methotrexate possible due antagonism of its action	Avoid combination or monitor for decreased clinical response to methotrexate Note: asparaginase administered shortly after methotrexate can enhance its efficacy and reduce its toxicity
Infliximab	Altered methotrexate concentration	Monitor for signs of methotrexate toxicity or reduced efficacy

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 treatment.

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

Prime IV line(s).

Access CVAD.

- daily weight
- strict fluid balance
- dipstick urinalysis to monitor pH:
  - prior to treatment
  - on all urine output

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Commence corticosteroid eye drops 24 hours before starting cytarabine. Continue for 72 hours after completion of the last dose of cytarabine.

Chemotherapy - Time out

Methotrexate

Prehydration:

- administer 100 mL sodium bicarbonate 8.4% in 1000 mL glucose **OR** sodium chloride 0.9% over 4 hours
- continue hydration with sodium bicarbonate 8.4% as prescribed
- when urine pH is greater than 7 commence methotrexate

If the urine pH drops below 7 during the methotrexate infusion:

- administer stat dose of 100 mL sodium bicarbonate 8.4% over 15 minutes
- continue to test all urine for pH, if the pH continues to drop below 7 seek medical review as further doses of sodium bicarbonate may be required.

Note: A large volume of intravenous fluid is 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 is present review by medical officer (diuretics may be required).

First dose of methotrexate

- administer via IV infusion over 2 hours
- the starting time of the methotrexate infusion **must** be documented as the calcium folinate (leucovorin) rescue is to commence exactly 36 hours after the commencement of the methotrexate and continue until the methotrexate level is less than 0.1 micromol/L

Second dose of methotrexate (to commence immediately after the first dose):

- administer via IV infusion over 22 hours
- flush with ~50 mL of sodium chloride 0.9%
- **Stop the methotrexate infusion after 22 hours even if the infusion is not completed**

Post methotrexate:

- continue hydration with sodium bicarbonate 8.4% until methotrexate level is less than 0.1 micromol/L
- continue to monitor all urine pH and fluid input and output

- monitor methotrexate concentration every 24 hours until the level is less than 0.1 micromol/L

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 treatment.

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

- daily weight
- strict fluid balance
- dipstick urinalysis to monitor pH:
  - prior to treatment
  - on all urine output

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Continue corticosteroid eye drops until 72 hours after completion of the last dose of cytarabine.

Chemotherapy - Time out

Cytarabine

Prior to administration:

Ensure corticosteroid eye drops have been administered before starting cytarabine. Please see ocular toxicities associated with high dose cytarabine for more information.

Verify that cytarabine neurological assessment has been performed prior to administration of cytarabine:

- if the patient scores 0 then administer cytarabine as charted
- if the patient scores 1 or above, do not administer the cytarabine and immediately notify medical officer.

Administer cytarabine:

- via IV infusion over 3 hours
- flush with ~50 mL of sodium chloride 0.9%.

Administer second dose of cytarabine 12 hours after first dose.

Calcium Folinate (Leucovorin)

Commence 36 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L.

- administer via IV bolus via the side port of the IV line over 1 to 2 minutes
- flush with ~ 50 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 treatment.

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

- daily weight

- strict fluid balance
- dipstick urinalysis to monitor pH:
  - prior to treatment
  - on all urine output

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Continue corticosteroid eye drops until 72 hours after completion of the last dose of cytarabine.

Note: Continue to administer calcium folinate (leucovorin) every 6 hours until methotrexate level is less than 0.1 micromol/L.

Chemotherapy - Time out

Cytarabine

Prior to administration:

Verify that cytarabine neurological assessment has been performed prior to administration of cytarabine:

- if the patient scores 0 then administer cytarabine as charted
- if the patient scores 1 or above, do not administer the cytarabine and immediately notify medical officer.

Administer cytarabine:

- via IV infusion over 3 hours
- flush with ~50 mL of sodium chloride 0.9%.

Administer second dose of cytarabine 12 hours after first dose.

Deaccess CVAD.

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

Day 4

Subcutaneous injection

General patient assessment prior to each day of treatment.

Continue corticosteroid eye drops until 72 hours after completion of the last dose of cytarabine.

Pegfilgrastim

- administer subcutaneously at least 24 hours post chemotherapy.

Discharge information

Antiemetics

- Antiemetics as prescribed.

Corticosteroid eye drops

- Continue corticosteroid eye drops for at least 72 hours after completion of final cytarabine dose.

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.
Cytarabine (Ara-C) syndrome	Flu-like symptoms including fever, myalgia and malaise can occur 6 to 12 hours after cytarabine administration. Symptoms generally resolve within 24 hours of completing therapy.
Headache	
Neurotoxicity	High dose cytarabine has been associated with acute cerebellar syndrome and diffuse cerebral dysfunction. Read more about neurotoxicity associated with high dose cytarabine
Ocular toxicities	Reversible corneal toxicity (keratitis), haemorrhagic conjunctivitis, vision loss and other ocular side effects can occur with high dose cytarabine. Corticosteroid eye drops must be administered concurrently with treatment. Read more about ocular toxicities associated with cytarabine
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
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
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
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
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)

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

Evidence

The following evidence pertains to the use of hyper CVAD in mantle cell lymphoma (MCL). Specific evidence is not cited for use in other aggressive lymphomas, and use of hyper CVAD will be at the physician's discretion in most cases.

Hyper CVAD alternating with methotrexate and cytarabine is an aggressive chemotherapy regimen that has proven effective in treating patients with aggressive histopathological variants of MCL. The evidence for this regimen in the treatment of MCL comes from three prospective trials:

1. Khouri et al.[4] reported a prospective phase II trial that included 45 patients aged 65 years or younger, with newly diagnosed or previously treated MCL evaluating hyper CVAD followed by autologous or allogeneic stem cell transplant (SCT). Complete response (CR) after four cycles of hyper CVAD was reported at 38%, while partial response (PR) was reported at 55.5%.
2. Romaguera et al.[1, 5] reported a prospective open-label phase II trial of six cycles of hyper CVAD plus rituximab in newly diagnosed MCL. Of the 97 assessable patients (aged 41-80 years; median age 61 years), 87% achieved CR or unconfirmed CR. No patients went on to receive SCT. At a median follow-up of 40 months, three-year failure-free survival was 64%, and overall survival (OS) was 82%. In a subsequently published Short Report in 2010, at 10 years of follow-up (median of 8 years), the median OS for all patients had not been reached, and the time to treatment failure was 4.6 years. On subset analysis, patients 65 years or younger had significantly higher OS rates at eight years (68 versus 33%) than older patients.
3. Merli et al. [6] reported a prospective, multicentre trial of 8 cycles of hyper CVAD plus rituximab in 63 patients with newly diagnosed MCL. The overall response and complete response rates were 83% and 72%, respectively. After a median follow-up of 46 months, the estimated 5 years OS and progression-free survival (PFS) rates were 73% and 61%, respectively. However, this study reported significant toxicity; only 37% of patients completed the full 8 cycles and 3 died during therapy.

Source	Study & Year Published	Supports Use Yes/No/NA	Is the dose and regimen consistent with the protocol? Yes/No	Comments	
Phase II trials	Khouri et al.1998[4]	**Yes**	No	Doxorubicin dose in Part A is given over 2 days.	
				Cycles 1, 3, 5, 7 Cyclophosphamide 300 mg/m^2 IV every 12 hrs for six doses D1-3 Doxorubicin 50 mg/m^2 IVI over 48 hrs D4-5 Vincristine 2 mg/m^2 IV (maximum 2 mg) D4 & D11 Dexamethasone 40 mg IV or PO D1-5 and D11-14	**Cycles 2, 4, 6, 8** Methotrexate 200 mg/m^2 IV bolus D1 Methotrexate 800 mg/m^2 continuous IVI over 24 hrs D1 Cytarabine 3,000 mg/m^2 IV over 2 hrs every 12 hrs for four doses D2-3
	Romaguera et	**Yes**	No	Continuous doxorubicin infusion in Part A, rituximab on day 1 of	

Source	Study & Year Published	Supports Use Yes/No/NA	Is the dose and regimen consistent with the protocol? Yes/No	Comments	
	al.2005[1]			each cycle of Part A and B.	
				Cycles 1, 3, 5, 7 Rituximab 375 mg/m^2 D1 Cyclophosphamide 300 mg/m^2 IV over 3 hrs every 12 hrs for six doses D2-4 Doxorubicin 16.6 mg/m^2/day continuous IVI over 72 hrs D5-7 Vincristine 1.4 mg/m^2 IV (maximum 2 mg) D5 & D12 Dexamethasone 40 mg IV or PO D2-5 and D12-15	**Cycles 2, 4, 6, 8** Rituximab 375 mg/m^2 D1 Methotrexate 200 mg/m^2 IV over 2 hrs D2 Methotrexate 800 mg/m^2 continuous IVI over 22 hrs D2 Cytarabine 3,000 mg/m^2 IV over 2 hrs every 12 hrs for four doses D3-4
	Merli et al. 2012[6]	**Yes**	No	Rituximab 375 mg/m^2 on day 1 of each cycle. Additional dose of doxorubicin 50 mg/m^2 on day 5 of part A.	
				Cycles 1, 3, 5, 7 Rituximab 375 mg/m^2 D1 Cyclophosphamide 300 mg/m^2 IV every 12 hrs for six doses D1-3 Doxorubicin 50 mg/m^2 IV D4-5 Vincristine 1.4 mg/m^2 IV (maximum 2 mg) D4 & D11 Dexamethasone 40 mg IV or PO D1-5 and D11-14	**Cycles 2, 4, 6, 8** Rituximab 375 mg/m^2 D1 Methotrexate 200 mg/m^2 IV bolus D1 Methotrexate 800 mg/m^2 continuous IVI over 24 hrs D1 Cytarabine 3,000 mg/m^2 IV D2-3

Guidelines	Date published/revised	Supports Use Yes/No/NA	Is the dose and regimen consistent with the protocol? Yes/No	Comments
NCCN	June 2022	**Yes**	No	Includes rituximab 375 mg/m^2 on day 1 of each cycle
CCO	April 2022	**Yes**	No	Vincristine 1.4 mg/m^2 IV (maximum 2 mg) D4 & D11
BCCA	N/A	**N/A**	N/A	-

Abbreviations: IV - intravenous; hrs - hours; D - day(s); IVI - intravenous continuous infusion; PO - per oral

The addition of rituximab to chemotherapy has shown to be beneficial, with a 2007 meta-analysis[7] of rituximab plus chemotherapy for patients with indolent non-Hodgkin lymphoma (NHL) or MCL finding those treated with rituximab plus chemotherapy had superior OS, response and disease control than those that were treated with chemotherapy alone. However, only three small studies for MCL were available for inclusion in the meta-analysis. Consideration should be given to the addition of rituximab to each cycle of hyper CVAD.

Efficacy

Figure 1: Failure-free and overall survival[1]

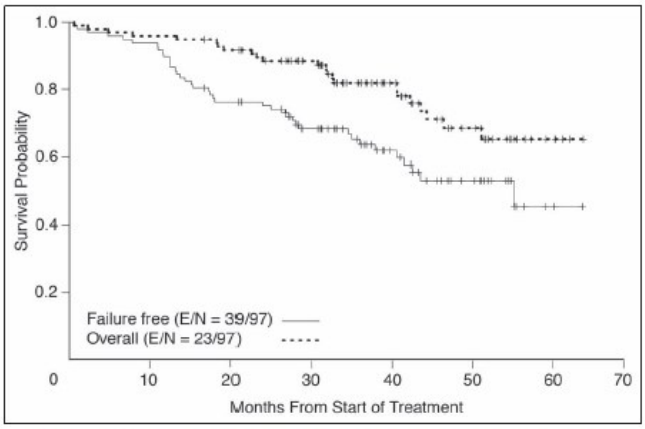

Fig 1. Failure-free and overall survival rates in 97 patients with newly diagnosed aggressive mantle-cell lymphoma treated with rituximab plus fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyper-CVAD) alternating with rituximab plus methotrexate-cytarabine. With a median follow-up of 40 months, the 3-year failure-free and overall survival rates were 64% and 82%, respectively. E, events; N, total patients.

Toxicity

Figure 2: Haematological toxicity[1]

	Neutropenia (%)		Thrombocytopenia (%)	
Course No.	Grade 3	Grade 4	Grade 3	Grade 4
1	10	51	12.5	2
2	7	64	9	28
3	7	28	23	14
4	5	64	9	42
5	7	31	17	12
6	3	68	5	46
7	14	37	15	17
8	4	55	7	50

NOTE. Course Nos. 1, 3, 5, and 7 = rituximab plus fractionated cyclophosphamide; vincristine, doxorubicin, and dexamethasone; course Nos. 2, 4, 6, and 8 = rituximab plus methotrexate-cytarabine.

Figure 3: Non-haematological toxicity[1]

Grade 3 to 4 Toxic Effect	No. of Events	%
Neutropenic fever*	80	13
R-HCVAD	20†	
R-Mtx/AraC	60†	
Infection*	35	6
Bacteremia	20	3
Pneumonia	6	1
Other	9	1.5
Fatigue	18	3
Stomatitis	6	1
Bleeding	3	0.5
Pancreatitis	1	0.1
Kidney failure	1	0.1
CNS	1	0.1

NOTE. Lethal acute toxicity occurred in five patients: sepsis (*Staphylococcus aureus, Escherichia coli, Proteus mirabilis*) = three patients; pulmonary hemorrhage = one patient; unknown cause = one patient.
Abbreviations: R-HCVAD, rituximab plus fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; R-Mtx/Ara-C, rituximab plus methotrexate and cytarabine.
*No difference for patients ≤ 65 years and patients > 65 years.
†P = .00001.

References

1 Romaguera, J. E., L. Fayad, M. A. Rodriguez, et al. 2005. "High rate of durable remissions after treatment of newly diagnosed aggressive mantle-cell lymphoma with rituximab plus hyper-CVAD alternating with rituximab plus high-dose methotrexate and cytarabine." J Clin Oncol 23(28):7013-7023

2 Ramsey, L. B., F. M. Balis, M. M. O'Brien, et al. 2018. "Consensus Guideline for Use of Glucarpidase in Patients with High-Dose Methotrexate Induced Acute Kidney Injury and Delayed Methotrexate Clearance." Oncologist 23(1):52-61.

3 Romaguera JE, Fayad L, Rodriguez MA et al. 2005 " High rate of durable remissions after treatment of newly diagnosed aggressive mantle-cell lymphoma with rituximab plus hyper-CVAD alternating with rituximab plus high-dose methotrexate and cytarabine". J Clin Oncol. Oct 1;23(28):7013-23.

4 Khouri, I. F., J. Romaguera, et al. (1998). "Hyper-CVAD and high-dose methotrexate/cytarabine followed by stem-cell transplantation: an active regimen for aggressive mantle-cell lymphoma." J.Clin Oncol. 16(12): 3803-3809

5 Romaguera JE, Fayad LE, Feng L et al. 2010 " Ten-year follow-up after intense chemoimmunotherapy with Rituximab-HyperCVAD alternating with Rituximab-high dose methotrexate/cytarabine (R-MA) and without stem cell transplantation in patients with untreated aggressive mantle cell lymphoma". Br J Haematol. Jul;150(2):200-8.

6 Merli, F., S. Luminari, F. Ilariucci, et al. 2012. "Rituximab plus HyperCVAD alternating with high dose cytarabine and methotrexate for the initial treatment of patients with mantle cell lymphoma, a multicentre trial from Gruppo Italiano Studio Linfomi." Br J Haematol 156(3):346-353.

7 Schulz, H., J. F. Bohlius, S. Trelle, et al. 2007. "Immunochemotherapy with rituximab and overall survival in patients with indolent or mantle cell lymphoma: a systematic review and meta-analysis." J Natl Cancer Inst 99(9):706-714.

History

Version 6

Date	Summary of changes
28/06/2023	Methotrexate target level updated.
27/11/2023	Protocol reviewed by the Haematology Reference Committee at 2022 Lymphoma Reference Committee Meeting. • Evidence reformatted • Headings and reference added to figures in evidence section Review in 1 year.

Version 5

Date	Summary of changes
22/09/2020	Biosimilar drug added to clinical information. Version number changed to v.5
24/01/2022	Pulmonary toxicity added to side effects.

Version 4

Date	Summary of changes
20/04/2007	Reformatting and minor editing
28/05/2008	Renaming cycles 1, 3, 5 and 7 as part A and cycles 2, 4, 6 and 8 as part B as requested in feedback
06/11/2008	Revision and reformatting of patient sheet
08/09/2009	Reviewed and transferred to eviQ
21/03/2011	New format to allow for export of protocol information. Protocol version number changed to *V.2.*

Date	Summary of changes
	Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
19/08/2011	Review at Reference Committee meeting (RCM)
23/11/2011	Removal of methylprednisolone from treatment schedule as was not included in original published papers for NHL (Khouri et al 1998 and Thomas et al 2004).
16/11/2012	Addition of further administration instructions for calcium leucovorin to the treatment schedule summary
21/11/2012	Protocol updates included and protocol republished: • frequency and cycle numbers for LBL and MCL amended as per RCM • CNS prophylaxis link added as per RCM • addition of statement regarding use of rituximab • inclusion of CNS prophylaxis link per RCM • evidence section rewritten with addition updated references - Romaguera et al 2010 and Merli et al 2012 • addition of links to POMP and Part A protocols
11/09/2015	Protocol updates included and protocol republished: • frequency and cycle numbers for LBL deleted as per RCM • added link to Hyper CVAD overview for Lymphoblastic Leukaemia as per RCM • added note under drug schedule suggesting that patients being treatment for Lymphoblatic Lymphoma should use the Hyper CVAD Lymphoblastic Leukaemia protocol • removed Lymphoblastic Lymphoma from the indications • removed link to POMP maintenance as per RCM • removed the paragraph on Lymphoblastic Lymphoma from the evidence and efficacy section (added to the protocol Lymphoblastic Leukaemia ID:788) • removed Cortelazzo et al 2011 and Thomas et al 2004 from the reference list
10/11/2016	Peripheral neuropathy dose modification removed.
31/05/2017	Transferred to new eviQ website. Version number change to V.4.
25/05/2018	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years
25/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
25/10/2018	Link added to high dose methotrexate-induced toxicity document in clinical information.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.
27/03/2020	Reviewed by Haematology Reference Committee with no changes, review in 2 years

First approved: 16 March 2006
Last reviewed: 11 November 2022
Review due: 31 December 2024

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/225
04 Dec 2023

Patient information - Non-Hodgkin lymphoma (NHL) - Hyper CVAD Part B

Patient's name:

Your treatment

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

Hyper CVAD part B

This treatment cycle alternates with hyper CVAD Part A and usually continues for a total of 6 to 8 cycles. Your doctor will advise you of the number of treatments you will have. The timing of each treatment cycle depends on how long it takes for your blood counts to recover from the previous cycle.

Day	Treatment	How it is given	How long it takes
1	**Methotrexate** (*Meth-o-TREX-ate*)	By a drip into a vein	About 24 hours
2	**Calcium folinate (Leucovorin)** (*loo-koe-VOR-in*)	By a drip into a vein	About 5 minutes every SIX hours
2 and 3	**Cytarabine** (*sye-TARE-a-been*)	By a drip into a vein	About 3 hours TWICE a day
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 38ºC 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.

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.
- **Eye drops:** you will be given eye drops to help prevent sore eyes. You will start using the eye drops before you have your first dose of cytarabine and continue to use the eye drops until 72 hours after your last dose of cytarabine.
- **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.

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.**
Flu-like symptoms from cytarabine	• You may get a fever, skin rash, aches and pains or increased sweating. • These symptoms are caused by the drug cytarabine. • Symptoms usually happen 6 to 12 hours after your dose, and may last until 24 hours after your treatment has finished. • To reduce any pain or fever, take paracetamol, if needed. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if these symptoms do not get better after 24 hours.
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.**
Nervous system changes from cytarabine	• High doses of cytarabine can affect the nervous system. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms during or soon after your treatment:** ◦ **dizziness, drowsiness or double vision** ◦ **agitation** ◦ **difficulty walking in a straight line** ◦ **difficulty writing with a pen or pencil** ◦ **jerky movements** ◦ **slow, slurred speech.**
Eye problems from cytarabine	• You may get: ◦ eye pain or irritation ◦ blurred vision ◦ watery or gritty eyes ◦ sensitivity to light. • You will be given eye drops to help prevent and control these symptoms. It is important to use these eye drops as directed. • Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes. • Tell your doctor or nurse if you get any of the symptoms listed above.
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.**
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Mouth pain and soreness (mucositis)	• You may have:
	  ◦ bleeding gums
	  ◦ mouth ulcers
	  ◦ a white coating on your tongue
	  ◦ pain in the mouth or throat
	  ◦ difficulty eating or swallowing.
	• Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.
	• Try bland and soft foods.
	• Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.
	• Rinse your mouth after you eat and brush your teeth, using either:
	  ◦ 1/4 teaspoon of salt in 1 cup of warm water, or
	  ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water
	• Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment.
	• **Tell your doctor or nurse if you get any of the symptoms listed above.**

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.

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
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.

Delayed (onset months to years)	

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

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking

aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

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

Diet and food safety

- While you are receiving this treatment, it is important that you try to maintain a healthy diet.
- 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.

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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