Primary CNS lymphoma (PCNSL) high dose methotrexate SUPERSEDED

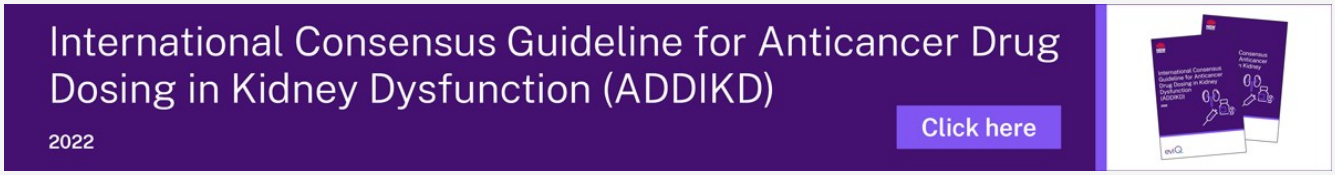
ID: 1565 v.7 **Superseded** Essential Medicine List

This protocol has been superseded as it is the consensus of the haematology reference committee that this dose of methotrexate is not commonly used in clinical practice.

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:

- Primary CNS lymphoma (PCNSL) whole brain consolidation EBRT

Treatment schedule - Overview

Cycle 1 to 8

Drug	Dose	Route	Day
Methotrexate	8,000 mg/m^2	IV infusion	1
Calcium folinate (Leucovorin)	50 mg every 6 hours (for 4 doses) *	IV bolus	2
Filgrastim	5 micrograms/kg	Subcut	4 and continue daily until ANC> 1 x 10^9/L

* Commence 24 hours after the start of methotrexate infusion. Calcium folinate 50 mg IV is given every 6 hours for the first 4 doses, then 30 mg IV/PO is given every 6 hours until methotrexate level is less than 0.1 micromol/L.

Frequency: 14 days

Cycles: 6 to 8 (4 cycles of induction. 2 further cycles if complete response achieved and 4 further cycles if partial response achieved)

Notes:

Intrathecal (IT) Treatment

IT treatment is not recommended upfront in the diagnostic setting, as there is low level evidence on the efficacy of IT prophylaxis.[1] Up to 20% of patients with PCNSL will have leptomeningeal disease (positive cerebrospinal fluid (CSF) cytology) at diagnosis, most of whom will clear the CSF following induction of high dose methotrexate.

CSF testing is recommended in all patients at diagnosis and if the CSF cytology/flowcytometry is positive a repeat CSF test is recommended half way through induction. If the CSF has cleared, then no further action is required. However if the CSF cytology/flowcytometry continues to be positive despite intravenous treatment, then the addition of IT chemotherapy is recommended.[2]

Intrathecal methotrexate

When given as prophylaxis in addition to systemic intravenous methotrexate in primary treatment, IT methotrexate confers no clinical advantage and is not recommended but it may be useful where CSF cytology/flowcytometry yields positive findings.[3]

Rituximab

There is some literature to indicate the addition of rituximab in this setting may be beneficial, although further study is required to verify whether this results in significant improvement to patient outcome.[4]

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

Cost: ~ $580 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 to 8

Day 1		
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)
Dexamethasone	12 mg (PO)	ONCE a day 60 minutes before chemotherapy
Methotrexate	8,000 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 4 hours
Day 2		
Dexamethasone	8 mg (PO)	ONCE a day with or after food (or in divided doses).
Calcium folinate (Leucovorin)	50 mg (IV bolus)	over 1 to 2 minutes. Commence 24 hours after the start of methotrexate infusion. Calcium folinate 50 mg IV is given every 6 hours for the first 4 doses, then 30 mg IV/PO every 6 hours until methotrexate level is less than 0.1 micromol/L.
Day 3		
Dexamethasone	8 mg (PO)	ONCE a day with or after food (or in divided doses).
Day 4		
Dexamethasone	8 mg (PO)	ONCE a day with or after food (or in divided doses).
Filgrastim	5 micrograms/kg (Subcut)	Inject subcutaneously once daily starting day 4 and continue until ANC> 1 x 10^9/L

Frequency: 14 days

Cycles: 6 to 8 (4 cycles of induction. 2 further cycles if complete response achieved and 4 further cycles if partial response achieved)

Indications and patient population

Indications:

- Newly diagnosed primary CNS lymphoma (PCNSL)
- Patients who cannot tolerate methotrexate in combination with cytarabine due to toxicities

Caution:

- This protocol may not be suitable for immunodeficient patients such as those with advanced HIV disease. Seek further specialist advice.

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 HIGH	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. 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.
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.[5] 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.
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. Myelosuppression may be exacerbated if trimethoprim/sulfamethoxazole is used in combination with methotrexate. Read about prophylaxis of pneumocystis jirovecii (carinii) in cancer patients
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

Age older than 60 years

Age older than 60 years
The incidence of neurotoxicity related to the combination of WBRT and high dose methotrexate is significantly higher in patients aged older than 60 years; withholding WBRT in the primary setting in these patients may be considered.[6]

Renal impairment
Creatinine clearance must be greater than 80 mL/min prior to administration of full dose high dose methotrexate. It is advised to reduce the methotrexate dose in proportion to the calculated creatinine clearance when this is less than 80 mL/min e.g. if creatinine clearance is 75 mL/min, then 75% of the calculated methotrexate dose is given.[7] Methotrexate is contraindicated if CrCl is less than 30 mL/min.

Hepatic impairment	
Hepatic dysfunction[8]	
Mild	No dose modifications necessary
Moderate	No dose modifications necessary
Severe	Withhold treatment, consider alternative therapy.

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

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*

For more information see References & Disclaimer .

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

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

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.

Chemotherapy - Time out

Methotrexate infusion

Prehydration:

- administer 100 mL sodium bicarbonate 8.4% in 1000 mL glucose 5% 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 are present, review by medical officer (diuretics may be required)

Methotrexate:

- administer via IV infusion over 4 hours
- the starting time of the methotrexate infusion must be documented as the calcium folinate (leucovorin) rescue is to commence exactly 24 hours after the start of the methotrexate and continue until the methotrexate level is less than 0.1 micromol/L
- flush with ~50 mL of sodium chloride 0.9%

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)

Days 2 and 3

- daily weight
- strict fluid balance
- dipstick urinalysis to monitor pH:

- prior to treatment
- on all urine output

Hydration if prescribed

Calcium Folinate (Leucovorin)

Commence 24 hours after the start of the 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%

Deaccess CVAD.

Day 4

Filgrastim

- administer filgrastim by subcutaneous injection on day 4 and continue until neutrophil recovery

Discharge information

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.

Headache	
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
Taste and smell alteration	Read more about taste and smell changes

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
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.
Fatigue	Read more about fatigue
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
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	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)
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

This protocol has been superseded as it is the consensus of the haematology reference committee that this dose of methotrexate is not commonly used in clinical practice.

A search of the literature did not find strong evidence to support the use of high dose methotrexate (HD-MTX) alone in the treatment of PCNSL. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by the phase II study by Batchelor et. al.[9]

The study conducted by Batchelor et. al assessed HD-MTX alone in patients with newly diagnosed PCNSL. Between June 1998 and December 1999, 25 patients were accrued to receive HD-MTX 8 g/m^2 every 2 weeks for a maximum of 8 cycles initially. Patients who achieved CR were given an extra two cycles of consolidation which was followed by maintenance treatment of 8 g/m^2 every 28 days for 11 cycles.[9]

The primary end point was radiographic response (complete response (CR) or partial response (PR)) and secondary end points were survival and progression-free survival. This study indicates that methotrexate monotherapy results in radiographic response

proportions comparable to potentially more toxic combination regimens. However the median progression-free survival is inferior to that achieved with other more toxic combination chemotherapy plus radiation regimens.[9]

Ferreri et. al conducted a randomized phase II study, in which monotherapy with HD-MTX was compared with HD-MTX combined with high dose cytarabine (HDAC). Between March 2004 and December 2007, 79 patients were either treated with 4 courses of MTX 3.5 g/m^2 every 21 days or with the same MTX dose combined with cytarabine 2 doses of 2 g/m^2/day on days 2 to 3.[10]

Primary endpoint was complete remission rate after chemotherapy. Secondary endpoints were overall response rate, response duration for responder patients, overall and failure-free survival, meningeal relapse rate, and neurotoxicity. This study concluded that the addition of HDAC to HD-MTX provides improved outcome compared with HD-MTX alone.

More recently, Thiel et al[7] conducted a phase III randomised, non-inferiority trial involving 551 patients with newly diagnosed PCNSL. The trial investigated whether first-line chemotherapy based on high-dose methotrexate was non-inferior to the same chemotherapy regimen followed by whole brain radiation therapy for overall survival. Between May 2000 and May 2009, patients were randomised to receive 6 cycles of high-dose methotrexate (HD-MTX) 4 g/m^2 every 14 days or HD-MTX plus ifosfamide 1.5 g/m^2 on days 3 to 5 of a 14 day cycle.

The primary end point was overall survival. Several secondary endpoints were assessed: rate of complete response with first-line chemotherapy, whole brain radiation therapy, or high-dose cytarabine; progression-free survival; toxic effects according to WHO's 1996 classification; and delayed neurotoxicity assessed by clinical examination, and by white matter changes or brain atrophy on MRI or CT. No significant difference in overall survival was recorded when whole brain radiation therapy was omitted from first-line chemotherapy in patients with newly diagnosed PCNSL.

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Batchelor et al 2003	**Yes**	Yes	-
	Ferreri et al 2009	**Yes**	No	MTX 3.5 g/m^2 or MTX 3.5 g/m^2 on day 1 + cytarabine 2 g/m^2 bd on day 2 to 3 every 3 weeks for 4 cycles
Case series	N/A	**N/A**	N/A	-
Observational studies	N/A	**N/A**	N/A	-
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	Sep 2013	**Yes**	N/A	-
BCCA	Feb 2013	**Yes**	No	8 g/m^2 (cycle 1 to 4) and 3.5 g/m^2 (cycle 5 to 8) every 2 weeks
CCO	Aug 2012	**Yes**	N/A	-

Efficacy

There was a total response of 74% (CR: 52%, 12 of 23 patients; PR: 22%, 5 of 23 patients) whereas 5 patients progressed during methotrexate treatment. The median number of cycles to CR was 6.[9]

Median progression-free survival for all patients was 12.8 months and median overall survival had not been reached at 22.8+ months of follow up.[9]

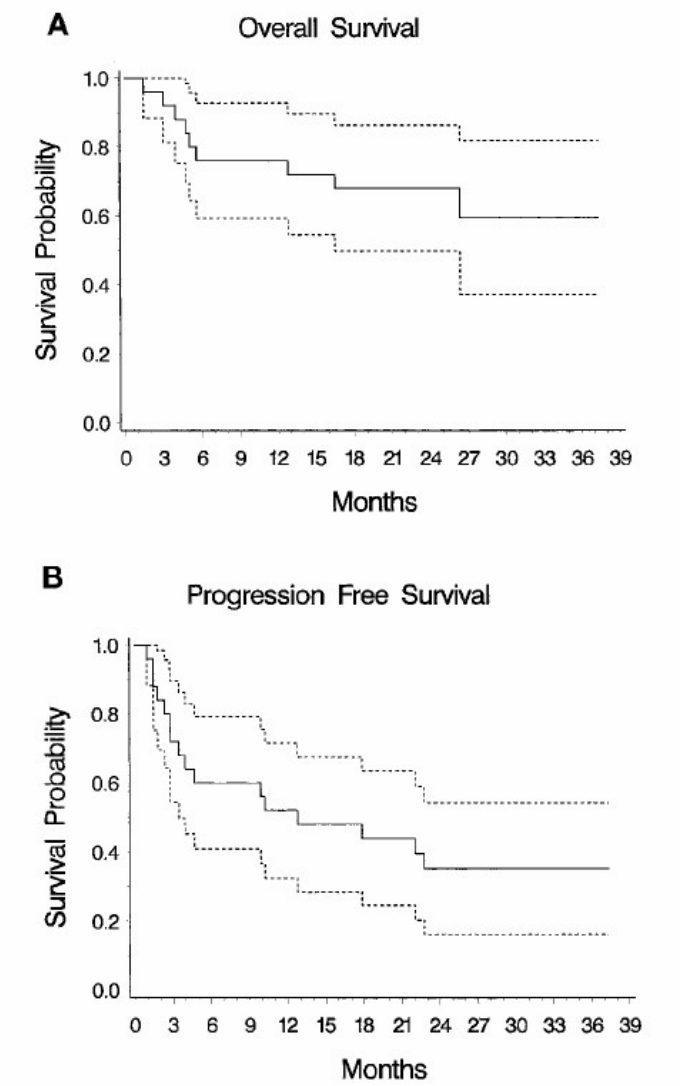


Fig 2. (A) Overall survival and 95% confidence intervals (Kaplan-Meier curves). (B) Progression-free survival and 95% confidence intervals (Kaplan-Meier curves).

Table 2. Mean (SD) or No. (%) of Baseline Clinical Characteristics by Radiographic Response

Characteristic	No Response	Partial or Compete Response
No.	6	17
Age, years	65.8 (8.2)	58.2 (13.2)
KPS	70.0 (11.0)	80.0 (12.7)
KPS ≥ 80	1 (16.7%)	11 (64.7%)
Mini-Mental State Examination	24.7 (4.8)	24.5 (6.5)
Females	3 (50.0%)	5 (29.4%)
Multiple brain lesions	2 (33.3%)	11 (64.7%)
Leptomeningeal lymphoma	2 of 3 (67%)	0 (0.0%)
Ocular involvement	0 (0.0%)	5 (29.4%)
Median peak MTX level	22.4 (37.5)	8.4 (16.7)

Abbreviations: KPS, Karnofsky Performance Score; MTX, methotrexate.

An improved response (46% vs 18% CR rate) and survival (35% vs 24% 3 year EFS) was found in the combination arm.[10]

	Methotrexate (n=40)	Methotrexate+cytarabine (n=39)	p value
Complete remission	7 (18%)	18 (46%)	0·006
Partial response	9 (23%)	9 (23%)	..
Overall response	16 (40%)	27 (69%)	0·009
Stable disease	1 (3%)	2 (5%)	..
Progressive disease	22 (55%)	7 (18%)	..
Toxic deaths	1 (3%)	3 (8%)	0·35
CRR/IELSG score*			
Low risk	5/12 (42%)	5/10 (50%)	..
Intermediate risk	2/24 (8%)	11/24 (46%)	..
High risk	0/4 (0%)	2/5 (40%)	..
ORR/IELSG score*			
Low risk	8/12 (67%)	10/10 (100%)	..
Intermediate risk	7/24 (29%)	15/24 (63%)	..
High risk	1/4 (25%)	2/5 (40%)	..
3-year FFS (SE)†			
Low risk	33% (13)	70% (14)	..
Intermediate risk	14% (8)	32% (11)	..
High risk	11% (10)	20% (17)	..

Data are n (%) or n/N (%), unless otherwise stated. *Complete remission rate (CRR) and overall response rate (ORR) for both groups according to the International Extranodal Lymphoma Study Group (IELSG) risk score.[24] Relation between complete responders and number of patients in the risk subgroup. No interaction between treatment group and IELSG risk score was detected (p=0·82). †For 3-year failure-free survival (FFS), no interaction between treatment group and IELSG risk score was detected (p=0·33). Webappendix p 1 summarises activity of both therapeutic groups according to the MSKCC (Memorial Sloan-Kettering Cancer Center) score. Webappendix p 3 summarises activity of both therapeutic groups according to patients' age.

Table 3: Activity of both treatment groups

	First-line chemotherapy with whole brain radiotherapy			First-line chemotherapy without whole brain radiotherapy		
	Patients	Events	Median time (months; 95% CI)	Patients	Events	Median time (months; 95% CI)
All patients						
Progression-free survival	154	113	18·3 (11·6–25·0)	164	124	11·9 (7·3–16·5)
Overall survival	154	97	32·4 (25·8–39·0)	164	96	37·1 (27·5–46·7)
Patients with complete response						
Progression-free survival	56	33	36·3 (19·3–53·3)	96	62	21·5 (12·5–30·5)
Overall survival	56	32	38·8 (23·2–54·4)	96	46	39·4 (20·7–58·0)
Patients without complete response						
Progression-free survival	98	80	5·6 (1·6–9·5)	68	62	3·0 (2·7–3·3)
Overall survival	98	65	24·3 (12·2–36·3)	68	50	18·6 (8·3–29·0)

Table 3: Progression-free and overall survival (per-protocol population)

Toxicity

The toxicity was modest after 287 cycles of high-dose methotrexate. 12 patients experienced 18 episodes of grade 3 or 4 toxicity. However 4 of these 18 episodes were unlikely to be methotrexate related. 13 patients experienced no grade 3 or 4 toxicity.[9]

However in the study by Ferreri et al, toxicity was considerably increased in the combination arm with 90% vs 15% grade 3 or 4 neutropenia and 23% vs 3% infections. Moreover, in the combination arm in 18% of patients interruption of treatment due to toxicity was necessary, and dose reduction was necessary in 40% of patients. Treatment-related mortality was 8% in the HD-MTX + HDAC arm, compared with 3% in the monotherapy arm.[10]

	Methotrexate (n=40)	Methotrexate+cytarabine (n=39)	pvalue
Toxic deaths	1 (3%)	3 (8%)	0·35
Neutropenia	6 (15%)	35 (90%)	0·00001
Thrombocytopenia	3 (8%)	36 (92%)	0·00001
Anaemia	4 (10%)	18 (46%)	0·00001
Infective complications	1 (3%)	9 (23%)	0·0002
Hepatotoxicity	1 (3%)	4 (10%)	0·05
Nephrotoxicity	2 (5%)	1 (3%)	0·31
GI/mucositis	2 (5%)	1 (3%)	0·31
Cardiotoxicity	1 (3%)	1 (3%)	0·87
Neurotoxicity	0	1 (3%)	0·29
Coagulation/DVT	4 (10%)	1 (3%)	0·002

The worst toxicity per organ, per patient was considered for analyses. GI=gastrointestinal. DVT=deep venous thrombosis.

Table 2: **Grade 3–4 toxic effects per treatment group**

	All patients (n=526)	Patients younger than 60 years (n=189)	Patients aged 60 years or older (n=337)
Response			
Complete response	182 (35%)	72 (38%)	110 (33%)
Partial response	101 (19%)	48 (25%)	53 (16%)
Stable disease	24 (5%)	6 (3%)	18 (5%)
Progressive disease	123 (23%)	48 (25%)	75 (22%)
Died on therapy	66 (13%)	10 (5%)	56 (17%)
Unknown	30 (6%)	5 (3%)	25 (7%)
Haematological toxic effects			
Leucopenia	112/470 (24%)	23/166 (14%)	89/304 (29%)
Infections	128/475 (27%)	29/164 (18%)	99/311 (32%)
Anaemia	65/469 (14%)	14/166 (8%)	51/303 (17%)
Thrombocytopenia	54/470 (11%)	8/166 (5%)	46/304 (15%)
Non-haematological toxic effects			
Elevation of aminotransferases*	85/458 (19%)	35/162 (22%)	50/296 (17%)
Lung toxicity	45/460 (10%)	10/163 (6%)	35/297 (12%)
Stomatitis	22/459 (5%)	3/163 (2%)	19/296 (6%)
Elevation of urea or creatinine*	17/470 (4%)	4/165 (2%)	13/305 (4%)
Impaired consciousness	36/457 (8%)	9/161 (6%)	27/296 (9%)
Peripheral neuropathy	18/451 (4%)	3/161 (2%)	15/290 (5%)
Vomiting	10/461 (2%)	4/163 (2%)	6/298 (2%)

Data are number (%); denominators are provided for toxic effects for which data were not available for all patients.
*Defined as 1·25 times the upper limit of the normal range.

Table 2: **Response to first-line chemotherapy and associated grade 3–4 toxic effects, by age-group**

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History

Version 7

Date	Summary of changes
04/05/2023	Methotrexate target level updated. Version number changed to v.7
28/04/2023	Reviewed electronically by Haematology reference committee with no changes. For review in 4 years.
19/12/2023	Minor changes to monitoring in administration section.

Version 6

Date	Summary of changes
22/09/2020	Biosimilar drug added to clinical information. Version number changed to v.6
17/11/2021	Dose modifications section amended.
08/02/2022	PJP prophylaxis clinical information block updated.

Version 5

Date	Summary of changes
6/08/2020	Dose modifications updated to be inline across PCNSL protocols. Version number increased to v.5.

Version 4

Date	Summary of changes
27/03/2020	Reviewed at Haematology Reference Committee meeting. Protocol superseded as it is the consensus of the committee that this higher dose of methotrexate is not commonly used in clinical practice.

Version 3

Date	Summary of changes
11/10/2013	New protocol taken to Haematology Reference Committee meeting.
04/12/2013	Approved and published on eviQ. Review in 2 years.
16/12/2013	Calcium folinate dosing schedule changed from 25 mg every 6 hours to "Calcium folinate 50 mg IV is given every 6 hours for the first 4 doses, then 30 mg IV/PO is given every 6 hours until methotrexate level is less than 0.05 micromol/L" per as Haematology Reference Committee consensus.
24/09/2014	Added link to ALLG, ANZCTR and Lymphoma Australia website with statement 'Patients with lymphoma should be considered for inclusion into clinical trials'.
11/09/2015	Reviewed at Haematology Reference Committee meeting, no changes. Review in 2 years. Updated drug costs.

Date	Summary of changes
03/06/2016	Changed the leucvorin rescue post-MTX from 36 hours post to 24 hours post.
31/05/2017	Transferred to new eviQ website. Version number changed to v.3. Antiemetic change: Netupitant/palonosetron combination has replaced aprepitant and a $5HT_3$ receptor antagonist in combination with dexamethasone for all highly emetogenic regimens.
25/05/2018	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years
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.

First approved: 4 December 2013
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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/1565
20 Feb 2024

Patient information - Primary CNS lymphoma - High dose methotrexate

Patient's name:

Your treatment

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

High dose methotrexate

This treatment cycle is repeated every 14 days. Your doctor will advise you of the number of treatments you will have. Once you have finished your chemotherapy, you may be given radiation therapy; your doctor will advise you if this is necessary.

Day	Treatment	How it is given	How long it takes
1	**Methotrexate** (*Meth-o-TREX-ate*)	By a drip into a vein	About 4 hours
2	**Calcium folinate (Leucovorin)** (*loo-koe-VOR-in*)	By a drip into a vein	About 5 minutes every SIX hours
4	**Granulocyte Colony Stimulating Factor** (*G-CSF*)	By injection under the skin	About 5 minutes

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime: Night/weekend: Other instructions:

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Central venous access devices (CVADs)

This treatment involves having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information see the eviQ patient information sheets on CVADs.

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 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.

Superseded treatments

This treatment is superseded meaning that better treatments have taken its place. Uncommonly superseded treatments are still used. Your doctor will explain why this treatment has been selected for you.

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.

Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

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.
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.**
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.**
Kidney damage	• This treatment can cause changes to how your kidneys work. • You will have blood tests to make sure your kidneys are working properly. • You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this. • **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.**

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

Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair 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.
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.

- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

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

Diet and food safety

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For more information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

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/
- Beyond Blue – 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 – https://www.foodstandards.gov.au/publications/listeriabrochuretext
- 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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