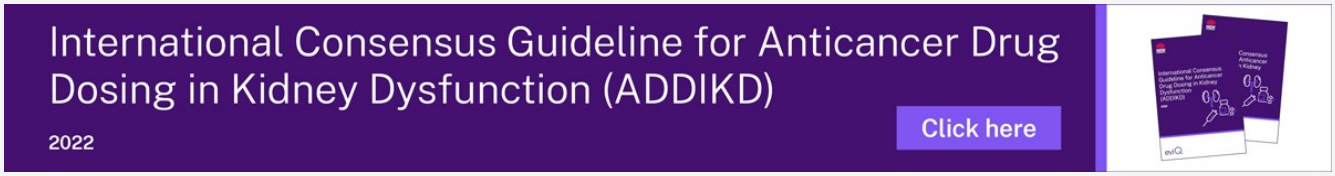
Primary CNS lymphoma (PCNSL) R-MPV (rituximab methotrexate procarbazine vinCRISTine) - part 1

ID: 1881 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:

- Primary CNS lymphoma (PCNSL) R-MPV/high dose cytarabine overview
- Primary CNS lymphoma (PCNSL) consolidation high dose cytarabine - part 2
- Primary CNS lymphoma (PCNSL) whole brain consolidation EBRT

Treatment schedule - Overview

Cycle 1, 3, 5

Drug	Dose	Route	Day
Procarbazine	100 mg/m^2 ONCE a day	PO	1 to 7
Rituximab	500 mg/m^2	IV infusion	1
vinCRISTine	1.4 mg/m^2 ** (Cap dose at 2.8 mg)	IV infusion	2
Methotrexate	3,500 mg/m^2	IV infusion	2
Calcium folinate (Leucovorin)	25 mg every 6 hours *	IV bolus	3
Filgrastim	5 micrograms/kg	Subcut	8

Cycle 2 and 4

Drug	Dose	Route	Day
Rituximab	500 mg/m^2	IV infusion	1
vinCRISTine	1.4 mg/m^2 ** (Cap dose at 2.8 mg)	IV infusion	2
Methotrexate	3,500 mg/m^2	IV infusion	2
Calcium folinate (Leucovorin)	25 mg every 6 hours *	IV bolus	3
Filgrastim	5 micrograms/kg	Subcut	6

* Commence 24 hours after the start of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L

** Cap of 2.8 mg is as per Shah et al. 2007[1]

Frequency: 14 days

Cycles: 5 if in complete remission; if in partial remission after 5 cycles, administer 2 additional cycles of R-MPV. ie. cycle 6: R-MV (no procarbazine) and cycle 7: R-MPV

Notes:

- In the study by Morris et al., WBRT commenced 3 to 5 weeks after the completion of R-MPV.[2]
- Patients with ocular involvement were irradiated without orbital shielding to the full dose of 23.4 Gy (patients in CR) or to a dose of 36 Gy (patients with less than a CR).[1]
- The incidence of neurotoxicity related to the combination of WBRT and high dose methotrexate is significantly higher in patients aged greater than 60 years old, withholding WBRT in the primary setting in these patients should be strongly considered.[3]

Intrathecal (IT) Treatment

CSF testing is recommended in all patients at diagnosis and if the CSF cytology/flow cytometry is positive a repeat CSF test is recommended half way through induction (after cycle 2). If the CSF has cleared, then no further action is required. However if the CSF cytology/flow cytometry continues to be positive despite intravenous treatment, then the addition of IT chemotherapy is recommended.[4]

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/flow cytometry yields positive findings.[5] In the trial by Shah et al, Intra-Ommaya methotrexate was administered between days 5 and 12 of each cycle to patients with positive cytology.[1]

It is the consensus of the eviQ Haematology Reference Committee based on clinical practice that IT methotrexate 12 mg may be given twice weekly until CSF clears and then tapered down. IT cytarabine may be added if the CSF continues to be positive.[6]

Drug status: **Methotrexate**, **vincristine, rituximab** and **calcium folinate** are on the PBS general schedule

Procarbazine: TGA registered for this indication but not PBS reimbursed

Procarbazine is available as **50 mg** capsules

Cost: ~ $3560 (Cycles 1, 3 and 5); ~ $3320 (Cycles 2 and 4)

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, 3, 5

Day 1		
Procarbazine	100 mg/m^2 (PO)	ONCE a day on days 1 to 7 of odd cycles only. Swallowed whole. (Round dose to nearest 50mg)
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Hydrocortisone	100 mg (IV)	30 minutes before treatment
Rituximab	500 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% as per graded

Day 1		
		administration rate

Day 2		
Procarbazine	100 mg/m^2 (PO)	ONCE a day on days 1 to 7 of odd cycles only. Swallowed whole. (Round dose to nearest 50mg)
vinCRISTine	1.4 mg/m^2 (IV infusion) (Cap dose at 2.8 mg)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes *
Methotrexate	3,500 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 2 hours

Day 3		
Procarbazine	100 mg/m^2 (PO)	ONCE a day on days 1 to 7 of odd cycles only. Swallowed whole. (Round dose to nearest 50mg)
Calcium folinate (Leucovorin)	25 mg (IV bolus)	over 1 to 2 minutes. Commence 24 hours after the start of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L

Day 4 to 7		
Procarbazine	100 mg/m^2 (PO)	ONCE a day on days 1 to 7 of odd cycles only. Swallowed whole. (Round dose to nearest 50mg)

Day 8		
Filgrastim	5 micrograms/kg (Subcut)	inject subcutaneously ONCE a day starting 24 hours after the last dose of procarbazine.

Cycle 2 and 4

Day 1		
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Hydrocortisone	100 mg (IV)	30 minutes before treatment
Rituximab	500 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate

Day 2		
vinCRISTine	1.4 mg/m^2 (IV infusion) (Cap dose at 2.8 mg)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes *
Methotrexate	3,500 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 2 hours

Day 3		
Calcium folinate (Leucovorin)	25 mg (IV bolus)	over 1 to 2 minutes. Commence 24 hours after the start of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L

Day 6		
Filgrastim	5 micrograms/kg (Subcut)	inject subcutaneously ONCE a day starting 96 hours after the methotrexate infusion

* Cap of 2.8 mg is as per Shah et al. 2007[1]

Frequency: 14 days

Cycles: 5 if in complete remission; if in partial remission after 5 cycles, administer 2 additional cycles of R-MPV. ie. cycle 6: R-MV (no procarbazine) and cycle 7: R-MPV

Indications and patient population

Indication:

- Newly diagnosed primary CNS lymphoma (PCNSL)

Caution:

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

Clinical information

Safety alert vincristine administration	For safe administration of vincristine refer to the safety alert issued by the Australian Commission on Safety and Quality in Health Care
Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Procarbazine oral administration	Procarbazine is a weak monoamine oxidase inhibitor (MAOI) and has the potential to interact with certain medications, alcohol and food. For further information see *Interactions* section of the protocol.
Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with rituximab. Read more about Hypersensitivity reaction
Premedication	The product information states that premedication is required for this treatment. Please refer to the treatment schedule for suggested premedication regimen. This may be substituted to reflect institutional policy.
Antiemetics for multi-day protocols	Antiemetic therapy should be administered throughout the duration of the chemotherapy protocol and to cover delayed nausea. The acute and delayed emetic risk of multi-day chemotherapy protocols will overlap depending on the individual drugs and their sequence of administration. More or less antiemetic cover may be required. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Rituximab rapid infusion	This regimen is not in line with the product monograph, however published literature indicates that it can be completed safely. Read more about the rapid infusion of rituximab
Progressive multifocal leukoencephalopathy	Use of monoclonal antibodies may be associated with an increased risk of progressive multifocal leukoencephalopathy (PML), a rare but potentially fatal opportunistic viral infection of the brain. Patients must be monitored for any new or worsening neurological symptoms. Read more about progressive multifocal leukoencephalopathy and the Therapeutic Goods Administration Medicines Safety update on progressive multifocal leukoencephalopathy from the Australian Government, Department of Health.

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.[7] 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.
Peripheral neuropathy	Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Constipation	Prescribe prophylactic laxatives to prevent constipation related to the use of vinca alkaloids.
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
Antiviral prophylaxis	Antiviral prophylaxis is recommended. Read more about antiviral prophylaxis drugs and doses
Antifungal prophylaxis	Antifungal prophylaxis is recommended. Read more about antifungal prophylaxis drugs and doses.
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
Blood tests	FBC, EUC, eGFR, LFTs, LDH and BSL 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

Consider adding G-CSF at physician's discretion if neutrophils less than 1 x 10^9/L ANC. Treatment delay is not recommended.

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.[8] Methotrexate is contraindicated if CrCl is less than 30 mL/min.

Hepatic impairment

Hepatic dysfunction

Hepatic impairment	
Mild	Omit procarbazine and reduce vincristine by 25%
Moderate	Omit procarbazine and reduce vincristine and cytarabine by 50%
Severe	Omit procarbazine and vincristine. Consider omitting cytarabine and reduce methotrexate by 25%

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.[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*

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

Procarbazine		
	Interaction	**Clinical management**
CNS depressants (including opiates, opioids, phenothiazines)	Additive CNS depressant effects (e.g. drowsiness, ataxia)	Avoid combination or monitor for excessive CNS depression
Alcohol	Disulfiram-like reaction (can include copious vomiting, dyspnoea, syncope) and increased sedation	Patients should abstain from alcohol during and for one week after completing treatment with procarbazine
Anti-depressants (including SSRIs, tricyclics, monoamine oxidase inhibitors (MAO-Is)), other MAO-Is (e.g. linezolid, selegiline), serotonergic agents (e.g. 'triptans', tramadol, pethidine, St John's wort)	Serotonin syndrome (hypertension, hyperthermia, agitation, hallucinations, rigidity, hyperreflexia, diaphoresis, tremor etc.) may be precipitated due to weak monoamine oxidase inhibition by procarbazine	Avoid combination
Sympathomimetic agents (e.g. pseudoephedrine and other cold and flu medications, stimulants such as guarana, some appetite suppressants)	Hypertensive crisis (headache, hyperpyrexia, hypertension) may be precipitated due to weak monoamine oxidase inhibition by procarbazine	Avoid combination
Tyramine-rich foods (e.g. aged cheeses, yoghurt, cured meats, liver, pickled herrings, over-ripe bananas, avocados and yeast extracts such as Vegemite® and Marmite®)	Hypertensive crisis (headache, hyperpyrexia, hypertension) may be precipitated due to weak monoamine oxidase inhibition by procarbazine	Patients should be advised to avoid excessive consumption of tyramine-rich foods while taking procarbazine; total abstinence is not considered necessary
Oral hypoglycaemics	Hypoglycaemia (MAO-Is can stimulate insulin secretion; procarbazine is a weak MAO-I)	Monitor blood glucose levels. Adjustment of the dose of antidiabetic medication may be required
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John’s wort etc.)	Increased risk of hypersensitivity reactions due to increased production of the reactive metabolite of procarbazine thought to be responsible	Avoid combination; select alternative antiepileptic (e.g. clonazepam, diazepam, lorazepam) or monitor for hypersensitivity reaction

Rituximab		
	Interaction	**Clinical management**
Antihypertensives	Additive hypotensive effect	Consider withholding antihypertensive medications 12 hours prior to the rituximab infusion
Immunosuppressants (eg. abatacept and baricitinib etc.)	Increased risk of infection	Concurrent use not recommended. If an immunosuppressant must be used, monitor closely for signs of infection

Vincristine		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of vincristine possible due to reduced clearance	Monitor for vincristine toxicity (esp. neurotoxicity, paralytic ileus)
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of vincristine possible due to increased clearance	Monitor for decreased clinical response to vincristine
Mitomycin	Acute shortness of breath and severe bronchospasm has occurred following use of vincristine in patients who had received mitomycin simultaneously or within 2 weeks	Use combination with caution
Ototoxic drugs (e.g. cisplatin, aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing

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 cycles 1, 3 and 5

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

product information monographs via the TGA website for further information.

Day 1

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- baseline weight

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Procarbazine

- administer orally ONCE a day on **days 1 to 7 (odd cycles only)**
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken with food or on an empty stomach.

Note: missed doses should not be replaced, if a tablet is forgotten or vomited, consult treating team. If treating team unavailable, advise patient that normal dosing should be resumed at the next scheduled dose.

Patients should be advised to avoid alcohol and large amounts of tyramine-rich foods (e.g. aged cheeses, cured meats, yeast extracts such as Vegemite® etc) while taking procarbazine.

Rituximab

Prior to administration:

- check baseline observations
- check for previous adverse events during previous infusions
- verify premedication has been taken. If not, administer 30 to 60 minutes prior to rituximab administration:
  - paracetamol 1000 mg orally AND
  - loratadine 10 mg orally (or similar antihistamine)
  - a steroid may also be included as a premed according to local guidelines

Initial infusion:

- **commence rituximab** infusion at 50 mg/hr for 30 minutes
- repeat observations prior to each rate increase
- **increase rate** by 50 mg/hr every 30 minutes, up to a maximum of 400 mg/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have completely resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Transient hypotension may occur. Consider withholding antihypertensive medication for 12 hours before and during infusion.

Subsequent infusions:

If an adverse event was experienced with initial infusion recommence infusion at the same rate as initial infusion

- **commence** rituximab infusion at 100 mg/hr
- repeat observations prior to each rate increase

- increase rate by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about rapid infusion rituximab

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

Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Procarbazine

- administer orally ONCE a day on **days 1 to 7 (odd cycles only)**
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken with food or on an empty stomach.

Note: missed doses should not be replaced, if a tablet is forgotten or vomited, consult treating team. If treating team unavailable, advise patient that normal dosing should be resumed at the next scheduled dose.

Patients should be advised to avoid alcohol and large amounts of tyramine-rich foods (e.g. aged cheeses, cured meats, yeast extracts such as Vegemite® etc) while taking procarbazine.

Vincristine

Administer vincristine (vesicant)

- via a minibag over 5 to 10 minutes
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%.

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 2 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

Note: Start calcium folinate (leucovorin) rescue 24 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L.

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

Day 3

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Hydration if prescribed

Calcium Folinate (Leucovorin)

- administer by IV bolus via a side port of the IV line over 1 to 2 minutes
- flush with ~ 50mL of sodium chloride 0.9%.

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Procarbazine

- administer orally ONCE a day on **days 1 to 7 (odd cycles only)**
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken with food or on an empty stomach.

Note: missed doses should not be replaced, if a tablet is forgotten or vomited, consult treating team. If treating team unavailable, advise patient that normal dosing should be resumed at the next scheduled dose.

Patients should be advised to avoid alcohol and large amounts of tyramine-rich foods (e.g. aged cheeses, cured meats, yeast

extracts such as Vegemite® etc) while taking procarbazine.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Days 4 to 7

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Procarbazine

- administer orally ONCE a day on **days 1 to 7 (odd cycles only)**
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken with food or on an empty stomach.

Note: missed doses should not be replaced, if a tablet is forgotten or vomited, consult treating team. If treating team unavailable, advise patient that normal dosing should be resumed at the next scheduled dose.

Patients should be advised to avoid alcohol and large amounts of tyramine-rich foods (e.g. aged cheeses, cured meats, yeast extracts such as Vegemite® etc) while taking procarbazine.

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

Discharge information

Procarbazine capsules

- Procarbazine capsules with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

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.

Administration cycles 2 and 4

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

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- baseline weight

Treatment - Time out

Rituximab

Prior to administration:

- check baseline observations
- check for previous adverse events during previous infusions
- verify premedication has been taken. If not, administer 30 to 60 minutes prior to rituximab administration:
  - paracetamol 1000 mg orally AND
  - loratadine 10 mg orally (or similar antihistamine)
  - a steroid may also be included as a premed according to local guidelines

Initial infusion:

- **commence rituximab** infusion at 50 mg/hr for 30 minutes
- repeat observations prior to each rate increase
- **increase rate** by 50 mg/hr every 30 minutes, up to a maximum of 400 mg/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have completely resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Transient hypotension may occur. Consider withholding antihypertensive medication for 12 hours before and during infusion.

Subsequent infusions:

If an adverse event was experienced with initial infusion recommence infusion at the same rate as initial infusion

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

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about rapid infusion rituximab

Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Vincristine

Administer vincristine (vesicant)

- via a minibag over 5 to 10 minutes
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%.

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 2 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

Note: Start calcium folinate (leucovorin) rescue 24 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L.

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

Day 3

General patient assessment prior to each day of treatment.

- 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%

Remove IV cannula and/or deaccess TIVAD or CVAD.

Discharge information

Procarbazine capsules

- Procarbazine capsules with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

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)	
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Flu-like symptoms	
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

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
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
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
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash

Late (onset weeks to months)	
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)
Progressive multifocal leukoencephalopathy (PML)	A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose. Read more about progressive multifocal leukoencephalopathy (PML)
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

Primary central nervous system lymphoma (PCNSL) represents an aggressive subset of lymphoma exclusively affecting the CNS (brain parenchyma, spinal cord, eyes, cranial nerves and/or meninges).[9] Diffuse large B-cell lymphoma (DLBCL) comprises the majority (90%) of PCNSL.[10] Landmark prospective randomised clinical trials have led to the accepted standard of high-dose methotrexate chemotherapy, and later the addition of high-dose cytarabine chemotherapy for the management of PCNSL.[11, 8, 12]

Rituximab has been shown to reduce CNS relapse from systemic DLBCL,[13] and evidence is now accumulating for a benefit with the addition of rituximab to standard methotrexate-containing treatment regimens.[1, 14, 2, 15, 16] The evidence supporting this protocol is provided by a phase II multicentre international trial involving 52 patients with primary CNS B-cell lymphoma receiving rituximab, methotrexate, procarbazine and vincristine, followed by consolidation reduced-dose whole-brain radiation therapy (rdWBRT) and cytarabine.[2]

Between October 2002 and February 2009, 52 patients received five 14-day cycles of induction chemotherapy with rituximab, methotrexate, procarbazine, and vincristine (R-MPV)[2] as follows:

- day 1, rituximab 500 mg/m^2; day 2, methotrexate 3.5 g/m^2 (over 2 hours), vincristine 1.4 mg/m^2 (max 2.8 mg);[1] days 1 - 7, procarbazine 100 mg/m^2/d (odd cycles only).
- patients who achieved a complete response (CR) after five cycles received rdWBRT (23.40 Gy in 1.8-Gy fractions x 13) 3 - 5 weeks after chemotherapy completion.
- patients who achieved a partial response (PR) after 5 cycles received another 2 cycles of R-MPV. If CR achieved after 2 further cycles, patients received rdWBRT (23.40 Gy in 1.8-Gy fractions x 13) 3 - 5 weeks after chemotherapy completion. If PR, stable disease (SD) or progression, then patients offered WBRT (45 Gy in 25 fractions)
- following radiation therapy, all patients received two-consolidation high-dose cytarabine cycles (each cycle 28 days) comprising of cytarabine 3 g/m^2/d on days 1 and 2 of each cycle.

The primary endpoint was 2-year progression-free survival (PFS) in patients who received rdWBRT, and secondary endpoints were objective response rate to R-MPV, overall response rate (ORR), overall survival (OS), and neurocognitive outcome.

The R-MPV protocol has a high response rate and acceptable safety profile for the treatment of PCNSL. Similar results have been observed in two retrospective analyses of rituximab in addition with MPV or other combination chemotherapy protocols[14, 17], whilst a single centre phase II study has demonstrated autologous stem cell transplantation as a viable alternative to WBRT. [15]

R-MPV can be safely delivered to older patients (i.e. > 60 years), including those over 80 years, and it appears to be superior to other therapies (i.e. methotrexate-temozolomide) in this age group.[18, 19] Outcomes in older patients have generally been poor (median PFS: 6.5 - 10 months, median OS: 7.9 - 31 months), but this may be reflective of a reduction in the total methotrexate dose in these studies as a recent large multicentre retrospective analysis has demonstrated that older patients (≥ 65 years) who complete methotrexate-based therapy (with minimal dose reductions) can achieve clinical outcomes similar to younger patients.[20, 21, 19]

Source	Study & Year published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Shah et al. 2007[1]	**Yes**	Yes	-
	Morris et al. 2013[2]	**Yes**	Yes	-
	Omuro et al. 2015[15]	**Yes**	Yes	Followed by autologous stem cell transplantation
Retrospective studies	Hattori et al. 2017[17]	**Yes**	No	Rituximab dose in R-MPV reduced from 500 mg/m^2 to 375 mg/m
	Houillier et al. 2017[20]	**Yes**	No	Total number of methotrexate doses = 6
Guidelines	**Date published / revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	December 2022	**Yes**	Yes	-
BCCA	-	**N/A**	N/A	-
CCO	-	**N/A**	N/A	-

Efficacy

Thirty-one patients (60%) achieved CR following 5 - 7 cycles of R-MPV and proceeded to rdWBRT. Of these, 2-year PFS was 77%, and median PFS was 7.7 years. Median OS was not reached (with median follow-up 5.9 years for survivors); 3 year OS was 87%. Overall median PFS was 3.3 years, and median OS was 6.6 years. Following chemotherapy, cognitive assessment showed improvement in executive function ($p < 0.01$) and verbal memory ($p < 0.05$).[2]

Figure 1. CONSORT diagram showing treatment and outcome for all enrolled patients.[2]

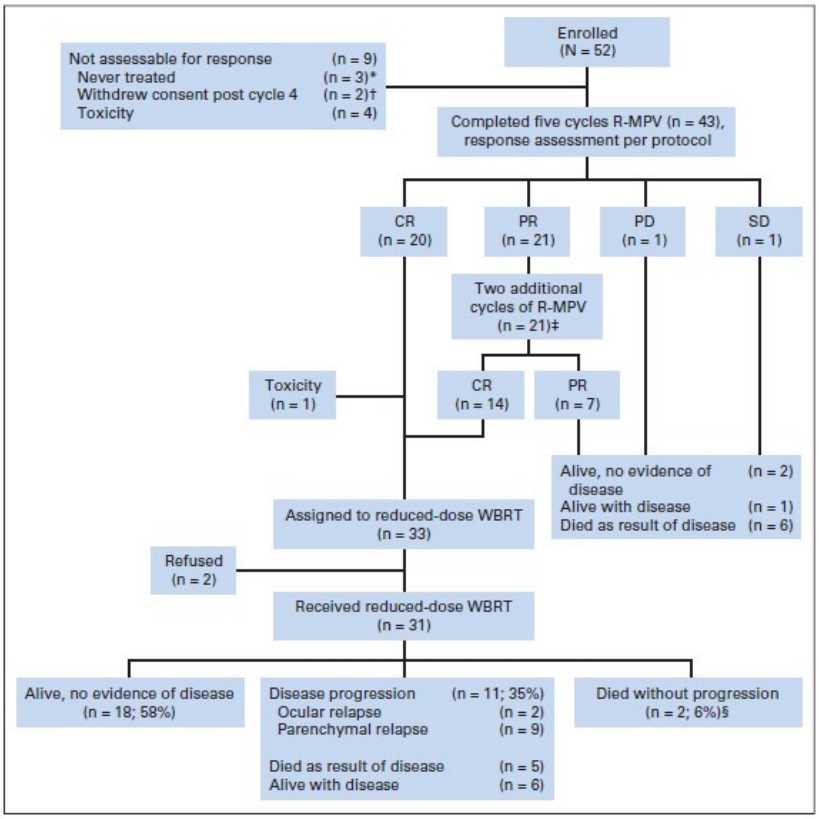
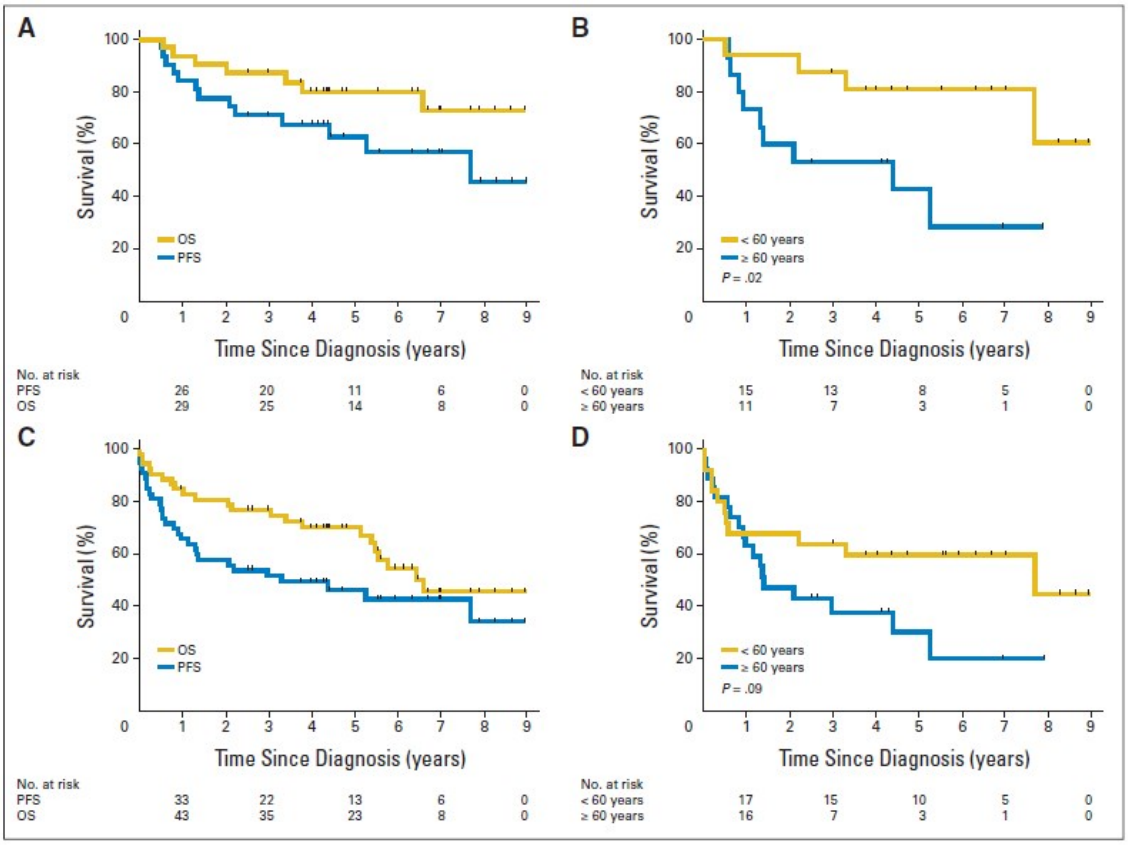


Figure 2. Kaplan-Meier survival curves[2]



Kaplan-Meier survival curves showing (A) OS and PFS for patients that received rdWBRT after achieving CR with 5 - 7 cycles of R-MPV; (B) PFS according to age for patients that received rdWBRT after achieving CR with 5 - 7 cycles of R-MPV; (C) Intent-to-treat OS and PFS for entire cohort; (D) Intent-to-treat PFS by age for entire cohort.

Of 31 patients who received rdWBRT, 12 patients were progression-free and completed neuropsychological evaluations up to 48 months (median age 58 years). Baseline cognitive impairment was evident across several categories. Following induction chemotherapy (R-MPV), significant improvement in executive function ($p < 0.01$) and verbal memory ($p < 0.05$) were observed. No significant cognitive decline occurred during follow-up except for motor speed ($p < 0.05$), and memory performances fluctuated only mildly throughout the follow-up period. Importantly, self-reported quality of life remained stable, and there was no significant depressed mood observed.[2]

Toxicity

Figure 3. Observed toxicities[2]

Toxicity (n = 52)	Grade 3	Grade 4	Grade 5
Renal	1	-	-
Febrile neutropenia	NR	NR	3* (6%)
Pneumonitis	-	-	1*
Gastrointestinal • **ileus** • **perforated diverticulum**	1	1	-

*NR not reported, *denotes same patient experienced grade 5 febrile neutropenia with pneumonitis. Regarding febrile neutropenia and other toxicities, an earlier interim report of the same study (n = 30) previously reported by the same group revealed the following toxicities in figure 4.*

Figure 4. Haematological toxicity[1]

Toxicity (n = 30)	Grade 4	Grade 5
Febrile neutropenia, pre G-CSF	2 (40%)	1 (20%)

Toxicity (n = 30)	Grade 4	Grade 5
amendment (n = 5)**		
Post G-CSF amendment**	1 (4%)	1 (3%)
All (n = 30)	3 (10%)	

***Due to complications of febrile neutropenia in 2 of the first 5 treated patients, a protocol amendment was made to include GCSF 5 µg/kg/d subcutaneously for 3-5 days with each cycle, starting 24 hours after last dose of procarbazine (odd cycles) and 96 hours after methotrexate or when methotrexate levels reached below $1x10^{-8}$mg/dL (even cycles).*

Figure 5. Observed toxicities[1]

Toxicity (n = 30)	Grade 3	Grade 4	Grade 5
Renal	1 (3%)	-	-
Anaemia	3 (10%)	-	-
Thrombocytopenia	8 (27%)	-	-
Lymphocytopenia	12 (40%)	-	-

It should be noted that in another independent retrospective analysis of rituximab in combination with differing chemotherapy regimens (n = 121), 2 patients (2%) experienced grade 5 toxicity due to perforated viscera.[14] This appears to be a specific and recurrent complication affecting a small number of patients despite compliance with recommendations for pharmacologic gastric acid suppression within the protocol.[2]

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History

Version 6

Date	Summary of changes
18/09/2023	Treatment schedule updated and evidence section reformatted. Version number changed to V.6

Version 5

Date	Summary of changes
04/05/2023	Methotrexate target level updated. Version number changed to v.5
28/04/2023	Protocol reviewed at Haematology Reference Committee meeting. Notes under treatment schedule updated, review in 1 year.

Version 4

Date	Summary of changes
14/11/2022	Filgrastim added to treatment schedule and patient information as per Morris et al. Version number changed

Date	Summary of changes
	to v.4

Version 3

Date	Summary of changes
09/03/2020	Biosimilar rituximab added to clinical information. Version number changed to v.3
27/03/2020	Reviewed by Haematology Reference Committee: • Dose modifications updated • Evidence updated. • Review in 4 years.
08/02/2022	PJP prophylaxis clinical information block updated.

Version 2

Date	Summary of changes
11/05/2016	Approved and published on eviQ.
03/06/2016	Changed the leucovorin rescue from 36 hours post-MTX to 24 hours post.
31/05/2017	Transferred to new eviQ website. Version number changed to v.2. Other changes include: • diluent volume of vincristine changed from '50 to 100 mL' to '50 mL' as per Australian Injectable Handbook Sixth Edition.
09/06/2017	Updated wording in throughout protocol regarding procarbazine from (cycles 1, 3 and 5 only) to (odd cycles only) and added 'ie. cycle 6: R-MV (no procarbazine) and cycle 7: R-MPV' to sentences about partial response.
25/05/2018	Protocol reviewed at Haematology Reference Committee meeting: • Treatment schedule: note about intrathecal treatment added under notes section as per reference committee consensus. • Clinical information: added information about glucarpidase to the 'High dose methotrexate'.
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: 11 May 2016
Last reviewed: 28 April 2023
Review due: 30 June 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/1881
26 Nov 2023

Patient information - Primary CNS lymphoma - R-MPV (rituximab, methotrexate, procarbazine, vincristine) - part 1

Patient's name:

Your treatment

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

R-MPV (rituximab, methotrexate, procarbazine, vincristine) - part 1

This treatment cycle is repeated every 14 days. You will usually have 5 - 7 cycles. 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. After radiation therapy, you will have two cycles of 'Primary CNS lymphoma - Consolidation high dose cytarabine - part 2'.

Day	Treatment	How it is given	How long it takes
1 to 7 **(cycles 1, 3 and 5)**	**Procarbazine** (*pro-KAR-ba-zeen*)	Take orally ONCE a day on days 1 to 7, with or without food. Swallow whole with a glass of water, do not break, crush or chew the tablets. if you forget to take a dose or vomit a dose, call your treating team for further instructions. If you cannot reach your doctor or nurse, take your normal dose the next time it is due. Do not take an extra dose.	
1	**Rituximab** (*ri-TUX-i-mab*)	By a drip into a vein	**1st cycle:** About 4 to 6 hours **Cycles thereafter:** About 3 to 4 hours
2	**Vincristine** (*vin-KRIS-teen*)	By a drip into a vein	About 10 minutes
2	**Methotrexate** (*Meth-o-TREX-ate*)	By a drip into a vein	About 2 hours
3	**Calcium folinate (Leucovorin)** (*loo-koe-VOR-in*)	By a drip into a vein	About 5 minutes repeated every 6 hours
6 **(cycles 2 and 4)**	**Granulocyte Colony Stimulating Factor** (*G-CSF*)	By injection under the skin	About 5 minutes
8 **(cycles 1, 3 and 5)**	**Granulocyte Colony Stimulating Factor** (*G-CSF*)	By injection under the skin	About 5 minutes

Missed doses

Procarbazine: if you forget to take a dose or vomit a dose, call your treating team for further instructions. If you cannot reach your doctor or nurse, take your normal dose the next time it is due. Do not take an extra dose.

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

Medications for blood pressure

Rituximab may lower your blood pressure. Tell your doctor if you are taking any blood pressure medications. Your doctor may advise you to temporarily stop your blood pressure medications before your rituximab infusions.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Laxatives:** you may be given some medication to prevent or treat constipation. Your doctor or nurse will tell you how and when to take the laxatives.

- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.
- **Rituximab premedication:** before your treatment with rituximab you will need to take some tablets called a premedication to help prevent you from having a reaction to the rituximab.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.**
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • Tell your doctor or nurse if you get any of the symptoms listed above. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
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.
Early (onset days to weeks)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**
Liver problems	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**
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.**

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 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.**

Side effects from steroid medication	• Steroid medication may cause:
	  ◦ mood swings and behaviour changes
	  ◦ an increased appetite
	  ◦ weight gain
	  ◦ swelling in your hands and feet
	  ◦ stomach upsets
	  ◦ trouble sleeping
	  ◦ fragile skin and bruising
	  ◦ an increase in your blood sugar level
	  ◦ weak and brittle bones (osteoporosis)
	• Take your steroid medication with food to reduce stomach upset
	• If you have diabetes, your blood sugar levels may be tested more often.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Late (onset weeks to months)	
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.
Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]	• This treatment can affect your central nervous system. This can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:** ◦ **trouble with your speech or vision** ◦ **confusion or memory loss** ◦ **changes in your personality** ◦ **weakness in your arms and legs** ◦ **poor balance or coordination** ◦ **fits (seizures).**
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.
- Certain foods may cause an unpleasant reaction (e.g. nausea/vomiting, headache, sweating) while taking procarbazine. The reaction is due to a substance called tyramine. Tyramine containing foods include mature cheeses (including processed cheeses), yeast or meat extracts (such as Vegemite®, Marmite®, Bovril®), broad bean pods, pickled herring, salami and pepperoni sausage, overripe fruit, and other foods that are not fresh, particularly if they have been fermented, pickled, smoked or aged. These reactions are very rare and if you want to eat any of these types of food, you could try a little at a time, until you are sure that you do not react.
- Alcohol can also cause a reaction with this treatment, and should be avoided while taking procarbazine and for a week after your last dose.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, please 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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