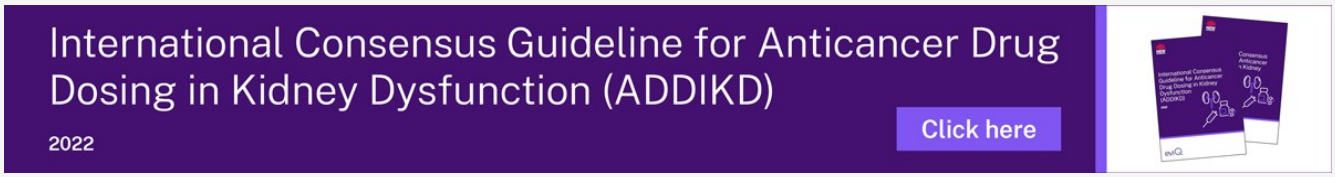
Burkitt lymphoma dose modified R-CODOX-M (rituximab CYCLOPHOSPHamide vinCRISTine DOXOrubicin methotrexate)

ID: 3726 v.3 **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:

- Burkitt lymphoma dose modified R-CODOX-M and R-IVAC overview
- Burkitt lymphoma R-IVAC (rituximab iFOSFamide etoposide cytarabine)

Treatment schedule - Overview

Drug	Dose	Route	Day
Rituximab	375 mg/m^2	IV infusion	1 and 11
DOXOrubicin	40 mg/m^2	IV	1
vinCRISTine	1.5 mg/m^2 (Cap dose at 2 mg)	IV infusion	1 and 8
CYCLOPHOSPHamide	800 mg/m^2	IV infusion	1
Cytarabine (Ara-C)	70 mg	Intrathecal	1 and 3
CYCLOPHOSPHamide	200 mg/m^2	IV infusion	2 to 5
Methotrexate	300 mg/m^2 *	IV infusion	10
Methotrexate	2,700 mg/m^2 *	IV infusion	10
Calcium folinate (Leucovorin)	15 mg/m^2 every 3 hours then see further directions below **	IV infusion	11
Filgrastim	5 micrograms/kg	Subcut	13 and continue daily until neutrophil recovery
Methotrexate	12 mg	Intrathecal	15
Calcium folinate (Leucovorin) ***	15 mg ONCE	PO	16

*See 'Dose modifications' for methotrexate dosing in patients older than 65 years.

**Start 36 hours after commencement of methotrexate infusion and repeat every 3 hours for the next 12 hours (ie between hours 36 to 48). Then continue every 6 hours until methotrexate level less than 0.1 micromol/L.

***Administered 24 hours after intrathecal methotrexate.

Commence next cycle when ANC is greater than 1.0 x 10^9/L and platelets are greater than 75 x 10^9/L. Number of cycles depends on disease risk classification (see below).

Risk stratification

Link to the International Non-Hodgkin Lymphoma International Prognostic Index (IPI)

Low risk disease	THREE cycles of dm R-CODOX-M[1]
High risk disease	Alternating cycles of dm R- CODOX-M / R-IVAC given twice (i.e. dm R-CODOX-M / IVAC / dm R-CODOX-M / IVAC)[1] After the fourth cycle of chemotherapy (second R-IVAC cycle), two further doses of rituximab are administered on day 21 and day 42.[2]
Proven CNS disease	High risk patients with proven CNS disease should receive **additional** CNS-directed therapy (intrathecal cytarabine and methotrexate) as part of dm R-CODOX-M (see below).[3]

Drug	Dose	Route	Day
Cytarabine	70 mg	Intrathecal	5
Methotrexate	12 mg	Intrathecal	17
Calcium folinate (leucovorin)	15 mg	PO	18

Patients are considered **Low Risk** if they have *at least 3* of the following international prognostic index (IPI) factors:

- normal LDH
- Ann Arbor stage I to II
- WHO performance status 0 to 1
- number of extra nodal sites less than or equal to 1.

All other patients are considered **High Risk.**

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

Filgrastim: (PBS authority)

Cost: ~ $750 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.*

Day 1		
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Hydrocortisone	100 mg (IV)	30 minutes before treatment
Rituximab	375 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate

Day 1		
DOXOrubicin	40 mg/m^2 (IV)	over 5 to 15 minutes
vinCRISTine	1.5 mg/m^2 (IV infusion) (Cap dose at 2 mg)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
CYCLOPHOSPHamide	800 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Cytarabine (Ara-C)	70 mg (Intrathecal)	adhere to local institution intrathecal policy
Day 2		
CYCLOPHOSPHamide	200 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Day 3		
CYCLOPHOSPHamide	200 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Cytarabine (Ara-C)	70 mg (Intrathecal)	adhere to local institution intrathecal policy
Day 4 and 5		
CYCLOPHOSPHamide	200 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Day 8		
vinCRISTine	1.5 mg/m^2 (IV infusion) (Cap dose at 2 mg)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Day 10		
Methotrexate	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 60 minutes*
Methotrexate	2,700 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 23 hours*
Day 11		
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Hydrocortisone	100 mg (IV)	30 minutes before treatment
Rituximab	375 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate
Calcium folinate (Leucovorin)	15 mg/m^2 (IV infusion)	start 36 hours after commencement of methotrexate infusion and repeat every 3 hours for the next 12 hours (ie between hours 36 to 48). Then continue every 6 hours until methotrexate level less than 0.1 micromol/L
Day 13		
Filgrastim	5 micrograms/kg (Subcut)	inject subcutaneously ONCE daily starting on day 13 and continue until ANC greater than 1.0 x 10^9/L
Day 15		
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy
Day 16		
Calcium folinate (Leucovorin)	15 mg (PO)	once only 24 hours after intrathecal methotrexate

*See "Dose modifications" for methotrexate dosing in patients older than 65 years.

Commence next cycle when ANC is greater than 1.0 x 10^9/L and platelets are greater than 75 x 10^9/L. Number of cycles depends on disease risk classification (see below).

Link to the International Non-Hodgkin Lymphoma International Prognostic Index (IPI)

Low risk disease	THREE cycles of dm R-CODOX-M[1]
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Drug	Dose	Route	Day
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Calcium folinate (leucovorin)	15 mg	PO	18

Indications and patient population

- Burkitt lymphoma

Caution:

This protocol may not be suitable for immunodeficient patients such as those with advanced HIV disease, as this group of patients was excluded from the trial.[3] 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
Venous access	Central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with 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	Patients being treated with multi-day anticancer protocols should receive antiemetics tailored to the emetogenic risk of the drugs administered each day during treatment and for two days after completion of the anticancer protocol. No standard antiemetic regimen exists for multi-day anticancer protocols. A combination of an NK1 receptor antagonist, 5HT3, and a steroid is available on the PBS for the prevention of nausea and vomiting associated with all moderate to highly emetogenic anti-cancer therapies. 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

Cumulative lifetime dose of anthracyclines	Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone). Criteria for reducing the total anthracycline cumulative lifetime dose include: • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation. Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion. Read more about cardiac toxicity associated with anthracyclines
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.[4] 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. Based on clinical findings, temporary omission, dose reduction or cessation of the vinca alkaloid may be indicated; 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.
Central nervous system (CNS) prophylaxis	Consider CNS relapse assessment in patients with high grade lymphoma. Read more about CNS prophylaxis in diffuse large cell lymphoma
Tumour lysis risk	Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended. Read more about the prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	PJP prophylaxis is recommended. 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. **Note:** Extended spectrum azole antifungals (e.g. posaconazole, voriconazole and itraconazole) should be avoided with vinca alkaloids. Metabolism is inhibited by azoles and neurotoxicity can be potentiated. 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
Commence next cycle when ANC is greater than 1.0 x 10^9/L and platelets are greater than 75 x 10^9/L. Number of cycles depends on risk classification (see above).

Renal impairment
Creatinine clearance must be greater than 50 mL/min prior to administration of high dose methotrexate

Hepatic impairment	
Hepatic dysfunction	
Mild	Reduce doxorubicin and vincristine by 25%
Moderate	Reduce doxorubicin and vincristine by 50%
Severe	Omit doxorubicin and vincristine

Peripheral neuropathy	
Grade 2 which is present at the start of the next cycle	Reduce vincristine by 50%
Grade 3 or Grade 4	Omit vincristine

Age older than 65 years	
Patients older than 65 years of age are to receive a reduced dose of methotrexate on Day 10:[3]	
Day 10	
Methotrexate 100 mg/m^2	in 500 mL sodium chloride 0.9% over 60 minutes
Methotrexate 900 mg/m^2	in 1000 mL sodium chloride 0.9% over 23 hours

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* .

Cyclophosphamide		
	Interaction	**Clinical management**
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Increased toxicity of cyclophosphamide possible due to increased conversion to active (and inactive) metabolites	Avoid combination or monitor for cyclophosphamide toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Reduced efficacy of cyclophosphamide possible due to decreased conversion to active (and inactive) metabolites	Avoid combination or monitor for decreased clinical response to cyclophosphamide
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Amiodarone	Possible additive pulmonary toxicity with high-dose cyclophosphamide (i.e. doses used prior to stem cell transplant; 60 mg/kg daily or 120 to 270 mg/kg over a few days)	Avoid combination or monitor closely for pulmonary toxicity
Allopurinol, hydrochlorothiazide, indapamide	Delayed effect. Increased risk of bone marrow depression; probably due to reduced clearance of active metabolites of cyclophosphamide	Avoid combination, consider alternative antihypertensive therapy or monitor for myelosuppression
Ciclosporin	Reduced efficacy of ciclosporin due to reduced serum concentration	Monitor ciclosporin levels; adjust dosage as appropriate; monitor response to ciclosporin
Suxamethonium	Prolonged apnoea due to marked and persistent inhibition of cholinesterase by cyclophosphamide	Alert the anaesthetist if a patient has been treated with cyclophosphamide within ten days of planned general anaesthesia

Doxorubicin		
	Interaction	**Clinical management**
Cardiotoxic drugs (eg. bevacizumab, calcium channel blockers, propranolol, trastuzumab etc.)	Increased risk of doxorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
Cyclophosphamide	Sensitises the heart to the cardiotoxic effects of doxorubicin; also, doxorubicin may exacerbate cyclophosphamide induced cystitis	Monitor closely for cardiotoxicity and ensure adequate prophylaxis for haemorrhagic cystitis when combination is used
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs etc.)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Glucosamine	Reduced efficacy of doxorubicin (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II *in vitro*)	The clinical effect of glucosamine taken orally is unknown. Avoid combination or monitor for decreased clinical response to doxorubicin
CYP2D6 inhibitors (e.g. SSRIs (esp. paroxetine), perhexiline, cinacalcet, doxepin, flecainide, quinine, terbinafine, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of doxorubicin possible due to increased clearance	Monitor for decreased clinical response to doxorubicin

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

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

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.

Peripheral neuropathy assessment tool

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

Prime IV line(s).

Access CVAD.

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

- baseline weight
- dipstick urinalysis prior to treatment

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Rituximab

Prior to administration:

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

Initial infusion:

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

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

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

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

Subsequent infusions:

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

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

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

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

Read more about rapid infusion rituximab

Chemotherapy - Time out

Doxorubicin

Administer doxorubicin (vesicant):

- over 5 to 15 minutes
  - via a minibag **OR**
  - by IV bolus via a side port of a freely flowing IV infusion
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%
- potential for flare reaction during administration of doxorubicin (facial flushing and red streaking along the vein) stop infusion and exclude extravasation before continuing at a slower rate of infusion.

Although rare, cardiac arrhythmias may occur during or immediately after doxorubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

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%.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 30 to 60 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- rapid infusion can cause dizziness, rhinitis, nausea and perioral numbness. If symptoms develop, slow infusion rate.

Cytarabine intrathecal

⚠ Intrathecal cytarabine is to be administered today. The intrathecal procedure is to be done separately to the IV administration of all other cytotoxic drugs.

Access the clinical procedure for the safe administration of intrathecal cytarabine.

Post intrathecal care:

Local policies and guidelines regarding bed rest post dural puncture should be adhered to. At a minimum:

- the patient should have at least 1 set of observations including:
  - vital signs and GCS
  - any abnormal neurological signs such as nausea, vomiting, chills, fever, confusion, headache or other changes in neurological status
- educate the patient to recognise and immediately report any adverse reactions including blurred vision, dizziness, pain and or headache
- observe the lumbar puncture site for any leakage or bleeding post procedure
- document the procedure including outcomes in the patients notes.

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

Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 30 to 60 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- rapid infusion can cause dizziness, rhinitis, nausea and perioral numbness. If symptoms develop, slow infusion rate.

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

Day 3

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 30 to 60 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- rapid infusion can cause dizziness, rhinitis, nausea and perioral numbness. If symptoms develop, slow infusion rate.

Cytarabine intrathecal

⚠ **Intrathecal cytarabine is to be administered today. The intrathecal procedure is to be done separately to the IV administration of all other cytotoxic drugs.**

Access the clinical procedure for the safe administration of intrathecal cytarabine.

Post intrathecal care:

Local policies and guidelines regarding bed rest post dural puncture should be adhered to. At a minimum:

- the patient should have at least 1 set of observations including:
  - vital signs and GCS
  - any abnormal neurological signs such as nausea, vomiting, chills, fever, confusion, headache or other changes in neurological status
- educate the patient to recognise and immediately report any adverse reactions including blurred vision, dizziness, pain and or headache
- observe the lumbar puncture site for any leakage or bleeding post procedure
- document the procedure including outcomes in the patients notes.

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

Days 4 and 5

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.

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 30 to 60 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- rapid infusion can cause dizziness, rhinitis, nausea and perioral numbness. If symptoms develop, slow infusion rate.

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

Day 8

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.

- daily weight

Hydration if prescribed

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%.

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

Day 10

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.

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

Methotrexate

Prehydration:

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

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

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

First dose of methotrexate:

- administer via IV infusion over 60 minutes
- the starting time of the methotrexate infusion must be documented as the calcium folinate (leucovorin) rescue is to commence exactly 36 hours after commencement of methotrexate

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

- administer via IV infusion over 23 hours
- flush with ~50 mL of sodium chloride 0.9%
- **stop the methotrexate infusion after 23 hours even if the infusion is not completed**

Post methotrexate:

- continue hydration with sodium bicarbonate 8.4% until methotrexate level is less than 0.1 micromol/L
- continue to monitor all urine pH and fluid input and output
- monitor methotrexate concentration every 24 hours until the level is less than 0.1 micromol/L

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

Day 11

Note: Start calcium folinate (leucovorin) rescue 36 hours after commencement of methotrexate infusion and repeat every 3 hours for the next 12 hours (i.e. between hours 36 to 48). Then continue every 6 hours until methotrexate level less than 0.1 micromol/L.

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Prime IV line(s).

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

Treatment - Time out

Rituximab

Prior to administration:

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

Initial infusion:

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

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

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

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

Subsequent infusions:

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

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

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

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

Read more about rapid infusion rituximab

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%.

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

Day 13

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

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%.

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

Filgrastim

- inject subcutaneously ONCE daily starting on day 13 and continue until ANC greater than 1.0 x 10^9/L

Day 15

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.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Intrathecal methotrexate

⚠ Intrathecal methotrexate is to be administered today. The intrathecal procedure is to be done separately to the IV administration of all other cytotoxic drugs

Read more about the procedure for intrathecal methotrexate administration.

Post intrathecal care:

Local policies and guidelines regarding bed rest post dural puncture should be adhered to. At a minimum:

- the patient should have at least 1 set of observations including:
  - vital signs and GCS
  - any abnormal neurological signs such as nausea, vomiting, chills, fever, confusion, headache or other changes in neurological status
- educate the patient to recognise and immediately report any adverse reactions including blurred vision, dizziness, pain and or headache
- observe the lumbar puncture site for any leakage or bleeding post procedure
- document the procedure including outcomes in the patients notes

Deaccess CVAD.

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

Day 16

This is an oral treatment

Calcium Folinate (Leucovorin)

- administer orally ONCE only on day **16**, 24 hours after intrathecal methotrexate administration

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Discharge information

Calcium folinate (leucovorin)

- Calcium folinate (leucovorin) tablets with instructions to take 24 hours after intrathecal methotrexate.

Antiemetics

- Antiemetics as prescribed.

Growth factor support

- Arrangements for administration if prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antifungals, antivirals.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.
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
Flare reaction	Anthracycline flare reaction is caused by a localised allergic reaction. It is characterised by erythematous vein streaking, urticaria and pruritus which may occur during drug administration and is often associated with too rapid an infusion. Extravasation must be ruled out if flare occurs.
Headache	
Haemorrhagic cystitis	An inflammatory process, characterised by diffuse bladder mucosal inflammation resulting in haemorrhage. Patients are at risk following blood and marrow transplant (BMT) or treatment with cyclophosphamide, ifosfamide and/or radiation therapy. Read more about haemorrhagic cystitis
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
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
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

Late (onset weeks to months)	
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
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)
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)

Delayed (onset months to years)	
Cardiotoxicity	Anthracyclines are the most frequently implicated anti-cancer drugs associated with cardiotoxicity, which typically manifests as a reduction in left ventricular ejection fraction (LVEF), cardiomyopathy, or symptomatic CHF. Anthracycline induced cardiotoxicity has been categorised into acute, early-onset chronic progressive and late-onset chronic progressive and is usually not reversible. The risk of clinical cardiotoxicity increases with a number of risk factors including higher total cumulative doses. Read more about cardiac toxicity associated with anthracyclines
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

The dose modified (dm) CODOX-M / IVAC protocol for Burkitt Lymphoma (BL) is an iteration of the original treatment regimen described by Magrath et al. in 1996.[5] The intention was to provide a dose-intensive, compact, non-cross-resistant regimen with effective central nervous system (CNS) targeting. The promising results of this study were confirmed in the LY06 study, a larger, multicentre, international phase 2 trial.[1] This regimen was refined in the LY10 trial, where methotrexate was dose modified to 3 g/m^2 (from 6.7 g/m^2) to reduce toxicity.[3] LY10 forms the basis of the current eviQ protocol.

LY10 was a prospective, international, non-randomised phase 2 study that included 53 patients (median age 37 years; range 17 to 76 years) with newly diagnosed BL. Patients with documented CNS involvement received additional intrathecal therapy. The LY10 trial included 11 low-risk and 42 high-risk patients. Patients were considered 'Low Risk' if they had at least 3 of the 4 following international prognostic index (IPI) factors: normal LDH, Ann Arbor stage I to II, WHO performance status 0 to 1 and number of extranodal sites less than or equal to 1. These patients were treated with three cycles of dm CODOX-M. All other patients were considered 'High Risk' and received alternating cycles of dm CODOX-M / IVAC twice. Two year progression-free survival (PFS) and overall survival (OS) rates were 64% and 67%, respectively.[3]

In recent years, it has been common practice to add rituximab to the dm CODOX-M / IVAC regimen, as its use in combination with standard chemotherapy has demonstrated improved patient outcomes without additional toxicity in several prospective studies.

A French phase 3 multicenter, open-label trial of 260 patients with newly-diagnosed BL, randomised patients to receive dose-dense chemotherapy with or without additional rituximab.[6] After a median follow-up of 38 months, patients receiving rituximab had a superior three year event-free survival (EFS) (hazard ratio [HR], 0.59; 95% CI, 0.38-0.94; P=.025) and OS (HR, 0.51; 95% CI, 0.30-0.86; P=.012) compared with the no-rituximab group.[6] Adverse events and toxicity were comparable across the two groups across each risk category. A phase 2 prospective multicenter trial for adult BL patients examined the efficacy and tolerability of rituximab in addition to dose-dense chemotherapy in 363 patients across 98 European centres.[7] Rituximab was given before each cycle, with two additional maintenance doses, for a total of 8 doses. Five year PFS and OS rates were 71% and 80%, respectively with a complete remission (CR) rate of 88%.

The largest prospective study (n=27) specifically evaluating dm R-CODOX-M / R-IVAC in BL utilised rituximab (375 mg/m^2) on day 1

of each cycle, with additional doses on day 11 of CODOX-M and on days 21 and 42 after the final IVAC cycle.[2] After a median follow-up of 56.9 months (range 2.2-77.5), 2-year PFS was 77.2% and 2-year OS was 80.7%. Six deaths occurred in total, due to progressive lymphoma (n = 3), treatment-effect (n = 2) or salvage chemotherapy (n = 1). Overall, this regimen was associated with acceptable toxicity and outcomes commensurate with historical dm CODOX-M / IVAC patients who were not exposed to rituximab. Comparable results were seen in another prospective study which added rituximab 375 mg/m^2 on day 1 of each dm CODOX-M and IVAC cycle.[8]15 patients with BL were evaluated with four-year PFS of 92% and OS of 82%.

Another prospective study incorporated high-dose rituximab (500 mg/m^2) twice a cycle in addition to the dm CODOX-M / IVAC regimen in 25 newly diagnosed BL patients.[9] Two-year PFS and OS rates of 80% and 84%, respectively across all risk categories, and toxicity profile was comparable to prior reports.

Several other groups have reported retrospective data on CODOX-M / IVAC based regimens combined with rituximab.[10, 11, 12, 13] A recent Canadian study examined survival outcomes of 81 patients with BL treated with dm CODOX-M / IVAC combined with rituximab 375 mg/m^2 (added on day 8 of each dm CODOX-M and day 4 of each IVAC cycle). They obtained a five year PFS and OS of 75% and 77%, respectively, with no treatment-related deaths. Treatment modifications due to toxicity were common in this cohort, however those who completed the regimen per protocol (n = 38) had significantly improved PFS 86% (P = 0.04) and OS 92% (P = 0.012).[13]

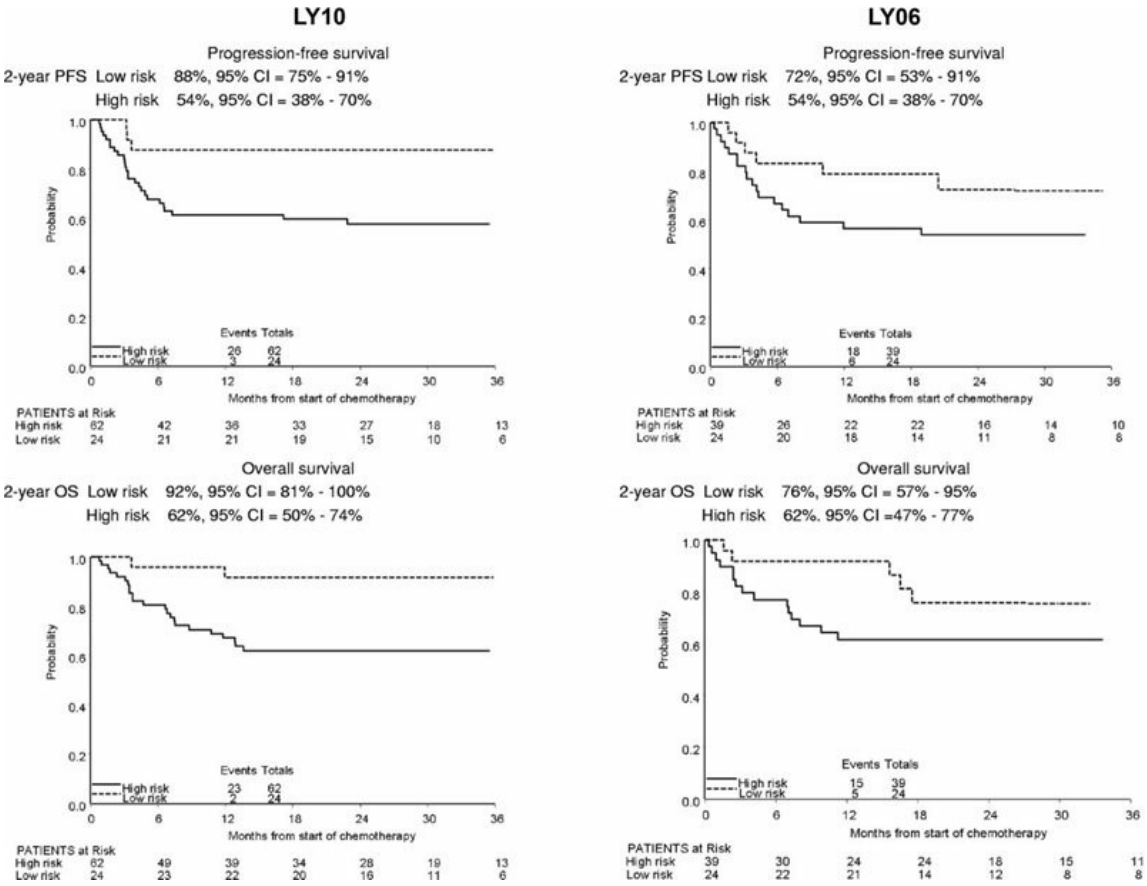
Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase III trials	Ribrag et al.[6]	**Yes**	No	Alternate chemotherapy backbone
	Mead et al. (LY06 trial)[1]	**Yes**	No	Higher methotrexate dose of 6.7 g/m^2
	Mead et al. (LY10 trial)[3]	**Yes**	No	Rituximab not included in the treatment regimen Chemotherapy backbone identical
	Hoelzer et al.[7]	**Yes**	No	Alternate chemotherapy backbone
Phase II trials	McMillan et al.[2]	**Yes**	No	Rituximab 375 mg/m^2 concurrently on day 1 of each cycle, with additional doses on day 11 of CODOX-M and days 21 and 42 after the final IVAC cycle (8 doses of rituximab in total)
	Corazzelli et al.[8]	**Yes**	No	Higher doxorubicin dose of 50 mg/m^2
	Evens et al.[9]	**Yes**	No	Higher rituximab dose of 500 mg/m^2
	Zhu et al.[13]	**Yes**	**Yes**	Rituximab administered on day 8 of dm CODOX-M and day 4 of IVAC, for each cycle

Guidelines	Date published / revised	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
NCCN	v.5 2021	**Yes**	**Yes**	-
BCCA	May 2021	**Yes**	**Yes**	Doses and scheduling of some drugs are different, but overall

Guidelines	Date published / revised	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
				regimen is the same
CCO	August 2020	**Yes**	**Yes**	High-dose methotrexate (day 10) and leucovorin (start day 11) are given as inpatient

Efficacy

Progression-free survival and overall survival in the LY10[3] and LY06[1] and studies, with risk group defined as in LY10:



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Toxicity

In the LY10 study,[3] there were 9 deaths (1 low-risk, 8 high-risk) reported to be treatment-related, of which 5 (all high-risk patients) died within 12 weeks of starting treatment; 2 of the 9 patients were aged over 65 (66 and 67, respectively).

Table 4. Worst toxicity experienced (CTC grade) during the treatment (for 109 patients who received at least 1 cycle of protocol treatment) in dmCODOX-M/IVAC study

	Low risk, N = 33		High risk, N = 76		Total, N = 109	
	n	%	n	%	n	%
WBC						
Grade 3	1	3	0	0	1	1
Grade 4	32	97	75*	99	107	98
Neutropenic fever						
Grade 3	20	61	67	88	87	80
Neutrophil count						
Grade 3	0	0	1	1	1	1
Grade 4	32	97	75	99	107	98
Platelets						
Grade 3	5	15	1	1	6	6
Grade 4	14	42	73	96	87	80
Mucositis						
Grade 3	10	31	29	38	39	36
Grade 4	2	6	8	11	10	9
Unknown	1		0		1	
Neuropath, sensory/motor						
Grade 3	3	10	3	4	6	6
Grade 4	0	0	2	3	2	2
Unknown	3		0		3	

*One patient did not report grade 3/4 leukopenia but received only part of cycle 1 dmCODOX-M prior to disease progression.

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History

Version 3

Date	Summary of changes
05/06/2023	Subcutaneous rituximab information removed from the following sections – treatment schedule, clinical information, administration, patient information. Increased to version 3.

Version 2

Date	Summary of changes
04/05/2023	Methotrexate target level updated. Version number changed to v.2

Version 1

Date	Summary of changes
27/01/2022	New protocol presented at Haematology Reference Committee meeting on 22 October 2021. Further work continued via email. Protocol approved and published on eviQ. Review in 1 year.
08/02/2022	PJP prophylaxis clinical information block updated.
11/11/2022	Protocol electronically reviewed by the Haematology Reference Committee. Rituximab PBS status updated to general schedule.Review in 2 years.

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

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Review due: 31 December 2024

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https://www.eviq.org.au/p/3726
20 Feb 2024

Patient information - Burkitt lymphoma - R-CODOX-M (rituximab, cyclophosphamide, vincristine, doxorubicin, methotrexate)

Patient's name:

Your treatment

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

Dose modified R-CODOX-M (rituximab, cyclophosphamide, vincristine, doxorubicin, methotrexate)

This treatment cycle is repeated, depending on how long it takes for your blood counts to recover. This treatment protocol may be alternated with a different chemotherapy protocol called R-IVAC. Your doctor will decide if this is appropriate for you. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	**Rituximab** (*ri-TUX-i-mab*)	By a drip into a vein	**1st cycle:** About 4 to 6 hours **Cycles thereafter:** About 3 to 4 hours
	Doxorubicin (*dox-oh-roo-bi-sin*)	By a drip into a vein	About 5 to 15 minutes
	Vincristine (*vin-KRIS-teen*)	By a drip into a vein	About 5 to 10 minutes
	Cyclophosphamide (*SYE-kloe-FOS-fa-mide*)	By a drip into a vein	About 1 hour
	Cytarabine (*sye-TARE-a-been*)	By injection into your spine	About 2 hours
2	**Cyclophosphamide**	By a drip into a vein	About 1 hour
3	**Cyclophosphamide**	By a drip into a vein	About 1 hour
	Cytarabine	By injection into your spine	About 2 hours
4 and 5	**Cyclophosphamide**	By a drip into a vein	About 1 hour
8	**Vincristine**	By a drip into a vein	About 5 to 10 minutes
10	**Methotrexate** (*meth-o-TREX-ate*)	By a drip into a vein	For 24 hours
11	**Calcium folinate (Leucovorin)** (loo-koe-VOR-in)	By a drip into a vein	About 5 minutes repeated every THREE hours for 12 hours, then every SIX hours
13	**Granulocyte Colony Stimulating Factor** (*G-CSF*)	By injection under the skin	About 5 minutes
15	**Methotrexate**	By injection into your spine	About 2 hours
16	**Calcium folinate (Leucovorin)**	Take orally for ONE dose only, 24 hours after the methotrexate injection into your spine	

When to get help

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

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

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

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

Other information about your treatment

Changes to your dose or treatment delays

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

Blood tests and monitoring

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

Central venous access devices (CVADs)

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

Treatment with cyclophosphamide

You should drink at least 8 to 10 glasses of fluid (unless you are fluid restricted) for 2 days after treatment with cyclophosphamide. You should also empty your bladder often.

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

- **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.

- **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 will be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Follow this link to read more information on how to give this injection.

Side effects

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

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

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

Immediate (onset hours to days)	
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **While you are in hospital: Tell your doctor or nurse immediately.** **After you leave: Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
Bone pain after G-CSF injection	• You may have discomfort or a dull ache in your pelvis, back, arms or legs. • To reduce the pain, take paracetamol before each injection. • **Tell your doctor or nurse as soon as possible if your pain is not controlled.**

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.**
Redness and itching along vein	• You may get redness and itching along the vein where your chemotherapy is being infused. • This will usually go away within 30 minutes of stopping the injection. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above. Your nurse will check to make sure the drug has not leaked out of the vein.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Bladder irritation (haemorrhagic cystitis)	• You may get: ◦ blood in your urine, sometimes with blood clots ◦ pain or burning when you urinate ◦ the urge to urinate more than normal ◦ stomach or pelvic pain or discomfort. • When you go home, make sure you drink plenty of fluids (unless you are fluid restricted). • Empty your bladder often. • **Tell your doctor or nurse as soon as possible if you notice any blood in your urine.**
Urine turning orange or red	• Your urine will turn an orange or red colour. • This is not harmful and should only last for up to 48 hours after treatment.
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.**
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.

Late (onset weeks to months)	
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
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.

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).**

Delayed (onset months to years)	
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems can occur months to years after treatment. • Tell your doctor if you have a history of heart problems or high blood pressure. • Before or during treatment, you may be asked to have a test to see how well your heart is working. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department 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.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org

- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – https://aci.health.nsw.gov.au/networks/bmtct
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- 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

Additional notes:

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

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