

ID: 1286 v.7    **Superseded**    Essential Medicine List

This protocol has been superseded as native form L-asparaginase is no longer available in Australia. [Acute lymphoblastic leukaemia ALL06](#) is the recommended treatment.

Patients with leukaemia should be considered for inclusion into clinical trials. Link to [ALLG website](#) and [ANZCTR website](#).

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

## International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD)

2022

[Click here](#)



### Related pages:

- [Acute lymphoblastic leukaemia BFM 2000 overview SUPERSEDED](#)
- [Management of asparaginase therapy](#)

- [Overall BFM 2000 treatment schema](#)
- [Overall BFM 2000 protocol flow diagram](#)

## Treatment schedule - Overview

### Cycle 1 and 2

Drug	Dose	Route	Day
Dexamethasone	20 mg/m <sup>2</sup> ONCE a day	PO	1 to 5
vinCRISTine	1.5 mg/m <sup>2</sup> (Cap dose at 2 mg)	IV infusion	1 and 6
Methotrexate	500 mg/m <sup>2</sup>	IV infusion	1
Methotrexate	4,500 mg/m <sup>2</sup>	IV infusion	1
Methotrexate *	12 mg	Intrathecal	1
Cytarabine (Ara-C)	30 mg	Intrathecal	1
Hydrocortisone	50 mg	Intrathecal	1
Calcium folinate (Leucovorin)	15 mg/m <sup>2</sup> every 6 hours**	IV bolus	2
Mesna	300 mg/m <sup>2</sup>	IV infusion	2 to 4
iFOSFamide	800 mg/m <sup>2</sup> TWICE a day every 12 hours for total of 5 doses	IV infusion	2 to 4

Drug	Dose	Route	Day
Mesna	300 mg/m <sup>2</sup> at 4 and 8 hours post each ifosfamide dose	IV infusion ***	2 to 4
DAUNOrubicin	30 mg/m <sup>2</sup>	IV	5
Asparaginase (colaspase)	25,000 International Units/m <sup>2</sup> ****	IV infusion	6 and 11
Filgrastim	5 micrograms/kg	Subcut	7 and continue daily until neutrophil recovery

\* Patients with CNS involvement receive an additional intrathecal treatment on day 5 i.e. total of 2 intrathecal doses

\*\* Commence 36 hours after the start of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L

The commencement of calcium folinate (leucovorin) rescue has been modified from a more complex algorithm to start at 36 hours after the start of the methotrexate infusion in all patients to reduce the risk of error or treatment delay. Similarly the number of calcium folinate doses has been modified, in line with other eviQ protocols, to continue until methotrexate level is less than 0.1 micromol/L,

\*\*\* Oral mesna may be given as an alternative at 4 and 8 hours post each ifosfamide dose. Note: the oral mesna dose is double that of the intravenous dose.

\*\*\*\* The manufacturers of Leunase® brand of asparaginase (colaspase) have confirmed that one Kyowa Unit (KU) is equivalent to one International Unit (IU). Colaspase has been included in the treatment schedule as per the BFM 2000 study, but peg-asparaginase may be used as an alternative (not registered in Australia, but is available on the Special Access Scheme (SAS)). **It is important to note that there are three commercially available formulations of asparaginase and the dosing of all three formulations is different. Clinicians should therefore ensure that the dose prescribed is appropriate for the asparaginase product being administered.**

#### Criteria for starting High Risk Block 2:

- regenerating (increasing) haematological values
- neutrophil count greater than  $0.2 \times 10^9/L$
- platelets greater than  $50 \times 10^9/L$
- creatinine/creatinine clearance within normal limits
- ALT/ALT less than 5 x upper normal limit
- bilirubin less than 2 x upper normal limit with direct bilirubin
- normal ejection fraction confirmed by gated heart pool scan or echocardiogram

A bone marrow aspirate is required for MRD testing prior to each High Risk block.

**Frequency:** 11 days

Commence High Risk Block 2 as soon as possible after haematological recovery after the preceding High Risk Block 1. Filgrastim should be discontinued at least 2 days before the start of HR2.

**Cycles:** 2 in sequence with other High Risk Blocks.

Patients receive the sequence of HR1, HR2, HR3, HR1, HR2, HR3, except in patients who proceed to allogeneic stem cell transplantation after the first HR2 or HR3. Patients who are not transplanted complete all of the High Risk Blocks and then commence Reinduction Protocol II followed by cranial irradiation.

#### Notes:

- This treatment should only be carried out in a major centre as intense monitoring and support is required

**Drug status:** **Asparaginase (colaspase):** TGA registered but not PBS listed

**Filgrastim:** (PBS authority)

## Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. [Select here for recommended doses of alternative antiemetics.](#)

### Cycle 1 and 2

Day 1		
Dexamethasone	20 mg/m <sup>2</sup> (PO)	ONCE a day on days 1 to 5. Take in the morning with food.
vinCRISTine	1.5 mg/m <sup>2</sup> (IV infusion) (Cap dose at 2 mg)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Methotrexate	500 mg/m <sup>2</sup> (IV infusion)	in 250 mL sodium chloride 0.9% over 30 minutes
Methotrexate	4,500 mg/m <sup>2</sup> (IV infusion)	in 1000 mL sodium chloride 0.9% over 23.5 hours
Methotrexate	12 mg (Intrathecal)	Administer 2 hours after the start of the methotrexate infusion.*
Cytarabine (Ara-C)	30 mg (Intrathecal)	adhere to local institution intrathecal policy
Hydrocortisone	50 mg (Intrathecal)	adhere to local institution intrathecal policy
Day 2		
Dexamethasone	20 mg/m <sup>2</sup> (PO)	ONCE a day on days 1 to 5. Take in the morning with food.
Calcium folinate (Leucovorin)	15 mg/m <sup>2</sup> (IV bolus)	Commence 36 hours after the start of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L
Mesna	300 mg/m <sup>2</sup> (IV infusion)	administer 15 minutes prior to each ifosfamide dose (loading dose)
iFOSFamide	800 mg/m <sup>2</sup> (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 2 hours TWICE a day every 12 hours (total of 5 doses)
Mesna	300 mg/m <sup>2</sup> (IV infusion)	at 4 and 8 hours after initiation of each ifosfamide dose. Oral mesna may be given as an alternative at 4 and 8 hours post ifosfamide. Note: the oral mesna dose is double that of the intravenous dose.
Day 3 and 4		
Dexamethasone	20 mg/m <sup>2</sup> (PO)	ONCE a day on days 1 to 5. Take in the morning with food.
Mesna	300 mg/m <sup>2</sup> (IV infusion)	administer 15 minutes prior to each ifosfamide dose (loading dose)
iFOSFamide	800 mg/m <sup>2</sup> (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 2 hours TWICE a day every 12 hours (total of 5 doses)
Mesna	300 mg/m <sup>2</sup> (IV infusion)	at 4 and 8 hours after initiation of each ifosfamide dose. Oral mesna may be given as an alternative at 4 and 8 hours post ifosfamide. Note: the oral mesna dose is double that of the intravenous dose.
Day 5		
Dexamethasone	20 mg/m <sup>2</sup> (PO)	ONCE a day on days 1 to 5. Take in the morning with

Day 5		
		food.
DAUNOrubicin	30 mg/m <sup>2</sup> (IV)	over 5 to 15 minutes
Day 6		
vinCRISTine	1.5 mg/m <sup>2</sup> (IV infusion) (Cap dose at 2 mg)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Asparaginase (colaspase)	25,000 International Units/m <sup>2</sup> (IV infusion)	in 250 mL to 500 mL sodium chloride 0.9% over 2 to 4 hours **
Day 7		
Filgrastim	5 micrograms/kg (Subcut)	inject subcutaneously ONCE daily starting day 7 until neutrophil recovery
Day 11		
Asparaginase (colaspase)	25,000 International Units/m <sup>2</sup> (IV infusion)	in 250 mL to 500 mL sodium chloride 0.9% over 2 to 4 hours **

\* Patients with CNS involvement receive an additional intrathecal treatment on day 5 i.e. total of 2 intrathecal doses

\*\* The manufacturers of Leunase® brand of asparaginase (colaspase) have confirmed that one Kyowa Unit (KU) is equivalent to one International Unit (IU). Colaspase has been included in the treatment schedule as per the BFM 2000 study, but peg-asparaginase may be used as an alternative (not registered in Australia, but is available on the Special Access Scheme (SAS)). **It is important to note that there are three commercially available formulations of asparaginase and the dosing of all three formulations is different. Clinicians should therefore ensure that the dose prescribed is appropriate for the asparaginase product being administered.**

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- normal ejection fraction confirmed by gated heart pool scan or echocardiogram

A bone marrow aspirate is required for MRD testing prior to each High Risk block.

**Frequency:** 11 days

Commence High Risk Block 2 as soon as possible after haematological recovery after the preceding High Risk Block 1. Filgrastim should be discontinued at least 2 days before the start of HR2.

**Cycles:** 2 in sequence with other High Risk Blocks.

Patients receive the sequence of HR1, HR2, HR3, HR1, HR2, HR3, except in patients who proceed to allogeneic stem cell transplantation after the first HR2 or HR3. Patients who are not transplanted complete all of the High Risk Blocks and then commence Reinduction Protocol II followed by cranial irradiation.

## Indications and patient population

- For the treatment of adolescent and young adult (AYA) patients with acute lymphoblastic leukaemia (precursor B-ALL, T-ALL but not mature B-ALL/Burkitt lymphoma).
- This regimen could be reasonably be considered for patients < 30, although published data are not available for patients older than 18 years of age.
- High Risk Blocks are for high risk and very high risk patients only. Link to [definition of risk groups](#).

## Clinical information

<b>Safety alert vincristine administration</b>	For safe administration of vincristine refer to the safety alert issued by the <a href="#">Australian Commission on Safety and Quality in Health Care</a>
<b>Venous access</b>	Central venous access device (CVAD) is required to administer this treatment. Read more about <a href="#">central venous access device line selection</a>
<b>Hypersensitivity/infusion related reaction</b>	<p>High risk with asparaginase.</p> <p>Acute anaphylactoid reactions are the most common dose-limiting toxicity, particularly with IV administration. Patients that develop hypersensitivity to the E. coli derived formulation may be able to switch to Erwinia asparaginase.</p> <p>The Leunase brand of asparaginase (colaspase) is the only formulation for which the manufacturer advises an intradermal test dose prior to the initial dose or when a week or more has elapsed between doses. A negative skin reaction does not preclude the development of an allergic reaction and therefore the practice of a test dose is controversial.</p> <p>Read more about <a href="#">Management of asparaginase therapy</a></p> <p>Read more about <a href="#">Hypersensitivity reaction</a></p>
<b>Antiemetics for multi-day protocols</b>	<p>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.</p> <p>Ensure that patients also have sufficient antiemetics for breakthrough emesis:</p> <p>Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR</p> <p>Prochlorperazine 10 mg PO every 6 hours when necessary.</p> <p>Read more about <a href="#">preventing anti-cancer therapy induced nausea and vomiting</a></p>
<b>Cumulative lifetime dose of anthracyclines</b>	<p>Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone).</p> <p>Criteria for reducing the total anthracycline cumulative lifetime dose include:</p> <ul style="list-style-type: none"> <li>• patient is elderly</li> <li>• prior mediastinal radiation</li> <li>• hypertensive cardiomegaly</li> <li>• concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine).</li> </ul> <p>Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation.</p> <p>Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) &gt; 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.</p> <p>Read more about <a href="#">cardiac toxicity associated with anthracyclines</a></p>
<b>Asparaginase</b>	<p>Asparaginase is associated with numerous toxicities including hypersensitivity, hepatotoxicity, coagulation abnormalities, pancreatitis, hyperlipidaemia, hyperglycaemia and CNS effects. Therefore routine monitoring and assessment of several parameters are required throughout treatment.</p> <p>There are several different formulations of asparaginase available, each with different dosing and administration recommendations.</p> <p>For comprehensive information on formulations, dosing, interactions, adverse reactions and specific monitoring parameters for asparaginase, see <a href="#">Management of asparaginase therapy</a> document.</p>

<b>Pancreatitis</b>	<p>Pancreatitis can occur despite normal serum amylase, and can be fatal. In cases of clinical pancreatitis (unequivocal diagnosis based on lipase/amylase elevation, ultrasound and clinical findings) asparaginase treatment should be ceased and must not be resumed. Mild asymptomatic biochemical pancreatitis does not warrant discontinuing asparaginase therapy.</p>
<b>Corticosteroids</b>	<p>Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate.</p> <p>Read more about <a href="#">acute short term effects from corticosteroids</a></p>
<b>Peripheral neuropathy</b>	<p>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.</p> <p>Read more about <a href="#">peripheral neuropathy</a></p> <p>Link to <a href="#">chemotherapy-induced peripheral neuropathy screening tool</a></p>
<b>Constipation</b>	<p>Prescribe prophylactic laxatives to prevent constipation related to the use of vinca alkaloids.</p>
<b>Haemorrhagic cystitis associated with high dose chemotherapy</b>	<p>Hydration regimen pre high dose cyclophosphamide or ifosfamide (as per local guidelines). There is limited evidence and no consensus regarding hydration regimens and mesna dose, route or timing of administration.</p> <p>Read more about <a href="#">haemorrhagic cystitis</a></p>
<b>Methotrexate interactions</b>	<p>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<sup>®</sup>, Septrin<sup>®</sup>)), penicillins (e.g. piperacillin (in Tazocin<sup>®</sup>)) and trimethoprim. Severe mucositis may occur if administered together.</p>
<b>High dose methotrexate</b>	<p>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.</p> <p>Methotrexate is renally eliminated. Kidney function must be evaluated prior to treatment.</p> <p>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.</p> <p>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.<sup>1</sup></p> <p>Read more about <a href="#">high dose methotrexate-induced toxicity</a>.</p>
<b>Pre-hydration</b>	<p>Pre-hydration with sodium bicarbonate 8.4% infusion. Urinary pH must be greater than 7 prior to commencing methotrexate infusion.</p> <p>Consider prescribing sodium bicarbonate oral capsules for administration prior to methotrexate infusion.</p> <p>Sodium bicarbonate 8.4% should continue until the methotrexate level is equal to or less than 0.1 micromol/L.</p> <p>Read more about <a href="#">high dose methotrexate-induced toxicity</a>.</p>
<b>Ifosfamide-induced encephalopathy</b>	<p>May occur in patients treated with high dose ifosfamide (~ 5 to 8 g/m<sup>2</sup>). Assess neurological function prior to each ifosfamide dose.</p> <p>Read more about <a href="#">ifosfamide-induced encephalopathy</a></p> <p>Link to <a href="#">ifosfamide-induced encephalopathy assessment chart</a></p>
<b>Mesna dosing and administration</b>	<p>There is evidence supporting variations in mesna doses and administration timings, with no clear evidence that one particular regimen is superior to another. The eviQ mesna recommendations may be based upon the individual trial/study or reference committee consensus and provide guidance on one safe way to administer the protocol. Individual institutional policy may vary and should be evidence-based.</p> <p>Read more about <a href="#">haemorrhagic cystitis</a></p>

<b>Pneumocystis jirovecii pneumonia (PJP) prophylaxis</b>	<p>PJP prophylaxis is recommended.</p> <p>Myelosuppression may be exacerbated if trimethoprim/sulfamethoxazole is used in combination with methotrexate.</p> <p>Read about <a href="#">prophylaxis of pneumocystis jirovecii (carinii) in cancer patients</a></p>
<b>Antiviral prophylaxis</b>	<p>Antiviral prophylaxis is recommended.</p> <p>Read more about <a href="#">antiviral prophylaxis</a> drugs and doses</p>
<b>Antifungal prophylaxis</b>	<p>Antifungal prophylaxis is recommended e.g. AmBisome 50 mg IV ONCE daily three times weekly (e.g. on Mondays, Wednesdays and Fridays) or fluconazole 200 mg to 400 mg PO daily.</p> <p><b>Note:</b> 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.</p> <p>Read more about <a href="#">antifungal prophylaxis</a> drugs and doses.</p>
<b>Biosimilar drug</b>	<p>Read more about biosimilar drugs on the <a href="#">Biosimilar Awareness Initiative</a> page</p>
<b>Growth factor support</b>	<p>G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk.</p> <p>Access the <a href="#">PBS website</a></p>
<b>Blood product support</b>	<p>The use of FFP and cryoprecipitate may be required to maintain fibrinogen levels to a normal range.</p> <p>Read more about <a href="#">Management of asparaginase therapy</a></p>
<b>Blood tests</b>	<p>FBC, EUC, LFTs, BSL, at baseline and prior to each treatment. Monitor pancreatic lipase and serum amylase, lipids and uric acid prior to and regularly during asparaginase therapy.</p> <p>Monitor fibrinogen levels, INR, APTT and PT at least once or twice weekly and consider monitoring antithrombin levels.</p>
<b>Hepatitis B screening and prophylaxis</b>	<p>Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy.</p> <p>Read more about <a href="#">hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy</a></p>
<b>Vaccinations</b>	<p>Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.</p> <p>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the <a href="#">Australian Immunisation Handbook</a>.</p> <p>Read more about <a href="#">COVID-19 vaccines and cancer</a>.</p>
<b>Fertility, pregnancy and lactation</b>	<p>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.</p> <p>Read more about the <a href="#">effect of cancer treatment on fertility</a></p>

## 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 \(ADDIKD\)](#).

Doses are rarely modified in acute lymphoblastic leukaemia chemotherapy protocols, except in instances of severe hepatic or renal impairment or toxicity. Consult with treating team and pharmacist.

## 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](#)

### Asparaginase

	Interaction	Clinical management
<b>Methotrexate</b>	Reduced efficacy of methotrexate if asparaginase is given immediately prior to or with methotrexate. Enhanced efficacy and reduced toxicity of methotrexate if asparaginase is given shortly after methotrexate	Administer asparaginase 9 to 10 days before or, preferably, shortly after methotrexate to enhance its efficacy and reduce its toxicity (unless otherwise scheduled per protocol)
<b>Vincristine</b>	Increased vincristine neurotoxicity if given after or concurrently with asparaginase	Administer vincristine 12 to 24 hours before asparaginase
<b>Prednisolone</b>	Increased risk of asparaginase toxicity (including decreased production of clotting factors and hyperglycaemia) if given after or concurrently with asparaginase	Administer prednisolone before asparaginase to avoid increased toxicity; monitor fibrinogen, ATIII and blood glucose levels

### Daunorubicin

	Interaction	Clinical management
<b>Cardiotoxic drugs (eg. calcium channel blockers, propranolol)</b>	Increased risk of daunorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity



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

<b>Ifosfamide</b>		
	<b>Interaction</b>	<b>Clinical management</b>
<b>Aprepitant</b>	Increased risk of ifosfamide-induced neurotoxicity due to increased levels of active metabolites	Avoid combination or monitor closely for neurotoxicity; consider alternate antiemetic regimens
<b>CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)</b>	Increased toxicity of ifosfamide possible due to increased conversion to active and toxic metabolites	Avoid combination or monitor for ifosfamide toxicity
<b>CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)</b>	Reduced efficacy of ifosfamide possible due to decreased conversion to active metabolites	Avoid combination or monitor for decreased clinical response to ifosfamide
<b>Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)</b>	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
<b>Suxamethonium</b>	Potential of muscle relaxant effect possible	Alert the anaesthetist if a patient has been treated with ifosfamide within ten days of planned general anaesthesia
<b>CNS depressants (including opiates, opioids, phenothiazines)</b>	Increased risk of ifosfamide-induced neurotoxicity due to additive CNS effects	Avoid combination or monitor for excessive CNS depression/encephalopathy

<b>Mesna</b>		
No specific or clinically significant drug interactions		

Methotrexate		
	Interaction	Clinical management
<b>Ciprofloxacin</b>  <b>NSAIDs</b>  <b>Probenecid</b>  <b>Proton pump inhibitors (e.g. esomeprazole, omeprazole, pantoprazole)</b>	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 <i>contraindicated</i>
<b>Sulphonamides and penicillins (e.g. sulfamethoxazole (in Bactrim<sup>®</sup>, Septrin<sup>®</sup>), piperacillin (in Tazocin<sup>®</sup>) etc.)</b>	Increased toxicity of methotrexate possible due to displacement from serum protein binding	Avoid combination or monitor for methotrexate toxicity
<b>Trimethoprim</b>	Increased toxicity of methotrexate possible due to additive antifolate activity	Avoid combination or monitor for methotrexate toxicity
<b>Mercaptopurine</b>	Increased toxicity of mercaptopurine possible due to reduced clearance	Avoid combination or monitor for mercaptopurine toxicity
<b>Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)</b>	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
<b>Hepatotoxic drugs (e.g. azathioprine, leflunomide, retinoids, sulfasalazine)</b>	Additive hepatotoxicity	Avoid combination or monitor liver function closely
<b>Folic acid (e.g. as in multivitamins)</b>  <b>Asparaginase (administered immediately prior or concurrently)</b>	Reduced efficacy of methotrexate possible due to 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

Vincristine		
	Interaction	Clinical management
<b>CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)</b>	Increased toxicity of vincristine possible due to reduced clearance	Monitor for vincristine toxicity (esp. neurotoxicity, paralytic ileus)
<b>CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)</b>	Reduced efficacy of vincristine possible due to increased clearance	Monitor for decreased clinical response to vincristine
<b>Mitomycin</b>	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
<b>Ototoxic drugs (e.g. cisplatin, aminoglycosides, frusemide, NSAIDs)</b>	Additive ototoxicity	Avoid combination or perform regular audiometric testing

General		
	Interaction	Clinical management
<b>Warfarin</b>	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
<b>Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran</b>	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.
<b>Digoxin</b>	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
<b>Antiepileptics</b>	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.
<b>Antiplatelet agents and NSAIDs</b>	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.
<b>Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)</b>	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 <a href="#">TGA Medicines Safety Update</a>
<b>Vaccines</b>	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 <a href="#">Australian Immunisation Handbook</a>

## 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*

## 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).

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### Dexamethasone

- administer orally ONCE a day in the morning on **days 1 to 5**
- to be taken with or immediately after food.

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

## 🕒 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
- continuous 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 30 minutes
- the starting time of the methotrexate infusion **must** be documented as the calcium folinate (leucovorin) rescue is to commence exactly 36 hours after the commencement of the methotrexate and continue until the methotrexate level is less than 0.1 micromol/L

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

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

### Post methotrexate:

- continue hydration over 8 hours with sodium bicarbonate 8.4% until methotrexate level is less than 0.1 micromol/L
- a minimum of 3 litres of fluid should be administered daily
- 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 36 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L.

### Methotrexate, cytarabine and hydrocortisone

**▲ Intrathecal methotrexate, cytarabine and hydrocortisone are to be administered today. Give two (2) hours after the start of the methotrexate infusion.**

Read more about the [procedure for intrathecal methotrexate and cytarabine 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

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

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## Days 2 to 4

### 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).

- continue daily weight
- monitor pH on all urine output
- dip stick all urine for haematuria
- strict fluid balance input and output

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### Dexamethasone

- administer orally ONCE a day in the morning on **days 1 to 5**
- to be taken with or immediately after food.

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

## 🕒 Chemotherapy - Time out

### Prehydration

Administer 1000 mL sodium chloride 0.9% over 2 hours.

- A minimum of 3 litres of fluid should be administered daily.

### Mesna (loading dose)

- administer via IV infusion over 15 minutes
- the administration of mesna causes a false positive ketonuria.

### Ifosfamide infusion

#### Prior to administration:

- assess neurological function at baseline and prior to each ifosfamide dose
  - inpatients: 4 hourly assessments until 24 hours after ifosfamide infusion is completed
  - outpatients: advise patient/carer of the potential for neurotoxicity
    - [neurological assessment tool](#)
- perform baseline urinalysis and monitor for haematuria prior to each ifosfamide dose
  - note the administration of mesna will cause a false positive for ketonuria
- ensure patient receives at least 3 L of IV or oral fluids per day

#### Administer ifosfamide (irritant):

- via IV infusion over 2 hours
- flush with ~100 mL of sodium chloride 0.9%

### Mesna

- administer via IV infusion over 15 minutes
- at 4 and 8 hours post completion of each ifosfamide dose.

Administer second dose of ifosfamide 12 hours after first dose.

### Calcium Folate (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:** Start calcium folinate (leucovorin) rescue 36 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L.

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

Continue hydration as prescribed.

**Continue [safe handling](#) precautions until 7 days after completion of drug(s)**

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## Day 5

[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).

- continue daily weight
- monitor pH on all urine output
- dip stick all urine for haematuria
- strict fluid balance input and output

Hydration if prescribed

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### Dexamethasone

- administer orally ONCE a day in the morning on **days 1 to 5**
- to be taken with or immediately after food.

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

## ⌚ Chemotherapy - Time out

### Daunorubicin

#### Administer daunorubicin (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 daunorubicin (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 daunorubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

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

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## Day 6

### 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
- daily urinalysis
- strict fluid balance input and output

Hydration if prescribed

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

## ⌚ Chemotherapy - Time out

**Note:** Asparaginase (colaspase) should be administered AFTER vincristine as there may be increased neuropathy if asparaginase (colaspase) is given first.

## 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%.

## Asparaginase (colaspase)

### Prior to administration:

Test dose

- Administer asparaginase (colaspase) 1 to 10 KU (= 1 international unit) in 0.1 mL of water for injection by intradermal injection:
- observe the injection site for at least 60 minutes for any evidence of hypersensitivity.

**Note:** Leunase<sup>®</sup> product information advises an intradermal test dose to be administered prior to initial dose or when a week or more has elapsed between doses. A negative skin reaction does not preclude the development of an allergic reaction and thus the practice of an intradermal test dose is controversial.

Read more on [detailed dosing information](#) regarding asparaginase (colaspase) and the formulations available.

### Administer asparaginase (colaspase)

- via IV infusion over 2 to 4 hours
- monitor for hypersensitivity reaction
- flush with 100 mL sodium chloride 0.9%.

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

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## Day 7

### Filgrastim

- inject subcutaneously ONCE daily, starting on day 7 and continuing until neutrophil recovery
- 

## Day 11

### 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
- daily urinalysis
- strict fluid balance input and output

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

## 🕒 Chemotherapy - Time out

### Asparaginase (colaspase)

#### Administer asparaginase (colaspase)

- administer via IV infusion over 2 to 4 hours
- monitor for hypersensitivity reaction



- flush with 100 mL sodium chloride 0.9%.

Deaccess [CVAD](#).

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

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## Discharge information

### Antiemetics

- Antiemetics as prescribed.

### Laxatives

- Ensure patient has prophylactic laxatives.

### Growth factor support

- Arrangements for administration if prescribed.

### Prophylaxis medications

- Prophylaxis medications (if prescribed) e.g. 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)	
<b>Cardiotoxicity</b>	<p>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.</p> <p>Read more about <a href="#">cardiac toxicity associated with anthracyclines</a></p>
<b>Encephalopathy</b>	<p>Ifosfamide induced encephalopathy has been reported in 10 to 30% of patients receiving high dose ifosfamide. Common symptoms include confusion, ataxia, weakness, seizures, somnolence and hallucinations. Onset may be 2 to 48 hours after commencing treatment. When reversible, symptoms usually resolve within 1 to 3 days.</p> <p>Read more about <a href="#">ifosfamide-induced encephalopathy</a></p>
<b>Extravasation, tissue or vein injury</b>	<p>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.</p> <p>Read more about <a href="#">extravasation management</a></p>
<b>Haemorrhagic cystitis</b>	<p>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.</p> <p>Read more about <a href="#">haemorrhagic cystitis</a></p>
<b>Hypersensitivity reaction</b>	<p>Anaphylaxis and infusion related reactions can occur with this treatment.</p> <p>Read more about <a href="#">hypersensitivity reaction</a></p>
<b>Nausea and vomiting</b>	<p>Read more about <a href="#">prevention of treatment induced nausea and vomiting</a></p>
<b>Red-orange discolouration of urine</b>	<p>Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.</p>
<b>Taste and smell alteration</b>	<p>Read more about <a href="#">taste and smell changes</a></p>

Early (onset days to weeks)	
<b>Neutropenia</b>	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 <a href="#">immediate management of neutropenic fever</a>
<b>Thrombocytopenia</b>	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding.  Read more about <a href="#">thrombocytopenia</a>
<b>Oral mucositis</b>	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 <a href="#">oral mucositis</a>
<b>Anorexia</b>	Loss of appetite accompanied by decreased food intake. Read more about <a href="#">anorexia</a>
<b>Arthralgia and myalgia</b>	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about <a href="#">arthralgia and myalgia</a>
<b>Pancreatitis</b>	Inflammation of the pancreas with impairment of function is associated with asparaginase formulations.
<b>Fatigue</b>	Read more about <a href="#">fatigue</a>
<b>Fluid retention and oedema</b>	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
<b>Hepatotoxicity</b>	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.
<b>Hyperglycaemia</b>	High blood sugar, an excess of glucose in the blood stream.
<b>Nephrotoxicity</b>	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.
<b>Peripheral neuropathy</b>	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 <a href="#">peripheral neuropathy</a>
<b>Photosensitivity</b>	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
<b>Side effects of corticosteroids</b>	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.
<b>Skin rash</b>	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 <a href="#">skin rash</a>

Late (onset weeks to months)	
<b>Anaemia</b>	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about <a href="#">anaemia</a>
<b>Alopecia</b>	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 <a href="#">alopecia</a> and <a href="#">scalp cooling</a>
<b>Cognitive changes (chemo fog)</b>	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 <a href="#">cognitive changes (chemo fog)</a>
<b>Pulmonary toxicity</b>	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about <a href="#">pulmonary toxicity associated with anti-cancer drugs</a>

## Evidence

This protocol has been superseded as native form L-asparaginase is no longer available in Australia. [Acute lymphoblastic leukaemia ALL06](#) is the recommended treatment.

In most published studies, adolescent patients with ALL achieve better results when treated with paediatric rather than adult protocols.<sup>2, 3, 4</sup> It is unclear as to the relative contributions of the composition of paediatric protocols, disease differences between children and older patients, the hospital settings in which they are delivered or the effects of selection bias.

A collaborative French study<sup>5</sup> retrospectively analysed patients aged between 15 and 20 who had been treated with either an adult ALL protocol (LALA94) or a paediatric protocol (FRALLE-93) showing a 5 year event free survival (EFS) advantage in favour of FRALLE-93 (67% versus 41% 5 year EFS, P<0.001) as well as an advantage for the paediatric protocol in overall survival (78% versus 45% at 5 years, P<0.001). Pui et al 2011 reported an event free survival at 5 years of 86.4% for adolescent patients aged 15 to 18 treated with a paediatric protocol (total therapy study XV, st Jude).

Moricke et al 2008<sup>6</sup> reported the results of 2169 paediatric and adolescent patients up to age 18 treated for ALL with the ALL-BFM95 protocol. Overall event free survival was estimated to be 79.6% at 6 years. Patients were stratified and treated according to risk (standard, medium and high risk). The 6 year EFS in the MR patients was 79.7% and 49.2% in the HR patients, and 58.3% for all patients aged 15 and older. Minimal residual disease criteria were not used for risk stratification in the ALL-BFM95 regimen. The published results of the ALL-BFM95 study did not demonstrate a benefit from the two randomisations (cytarabine in the intensification phase and pulse during maintenance).<sup>7</sup>

One retrospective Finnish study<sup>8</sup> did not show any improvement in the survival for patients aged 10 to 25 treated on a paediatric rather than an adult protocol, with a 5 year event free survival of 67% for the paediatric and 60% for the adult.

The ALL-BFM95 regimen was used as the standard arm of ALL-BFM 2000 with the incorporation of the minimal residual disease testing in patients with precursor B ALL. With this ALL- BFM 2000 regimen, the 5 year event free survival in this pre-B ALL subpopulation were 92.3%, 77.6% and 50.1% for the standard (42% of patients), intermediate (52% of patients) and high risk patients (6% of patients).<sup>9</sup>

The ALL- BFM 2000 standard arm has been used as the treatment regimen in this protocol, since it is common to both ALL-BFM95 and ALL- BFM 2000 regimens. If minimal residual disease (MRD) testing is available, then the incorporation of these results appears justified on the published data, at least for the pre-B ALL group.<sup>9</sup>

The selection of asparaginase preparations is reviewed in the [Asparaginase](#) document. Leunase<sup>®</sup> (colaspase, E. coli preparation) is the most commonly used preparation and the default option as presented in these protocols. Pegasparaginase is given as an alternative preparation and has the advantage of longer half life, lower immunogenicity and more efficient asparaginase depletion than standard preparations.<sup>10, 11</sup> All patients on the ongoing MRC UKALL 14 protocol receive pegylated asparaginase. The doses employed in the current treatment protocol are in line with those employed in the ongoing ANZCHOG, ALLG ALL6 and MRC UKALL 14 studies.

MRD testing has become a standard part of managing children with acute lymphoblastic leukaemia, but is not generally available outside clinical trials. Since many centres are performing MRD testing in AYA patients, the ALL-BFM 2000 risk groups defined on MRD are included. With no standard care approach to ALL in the younger population of patients defined, which risk criteria to utilize is not yet defined. To avoid confusion between groups of patients on studies such as ALLG ALL6 and ANZCHOG, the risk group definitions from these protocols have been adopted.

## Toxicity

ALL BFM 2000 is a high intensity regimen with the published results for patients up to the age of 18 years. It is unknown what is the safe upper age limit in tolerability for this regimen.

## References

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## History

### Version 7

Date	Summary of changes
04/05/2023	Methotrexate target level updated. Version number changed to v.7

### Version 6

Date	Summary of changes
30/03/2021	Protocol reviewed electronically by Haematology Reference Committee in September 2020 with consensus to supersede once the ALL06 protocol is published given L-asparaginase is no longer available. Version number increased to v.6. Review in 2 years.

Date	Summary of changes
20/01/2022	Interactions updated.
08/02/2022	PJP prophylaxis clinical information block updated.

### Version 5

Date	Summary of changes
22/09/2020	Biosimilar drug added to clinical information. Version number changed to v.5

### Version 4

Date	Summary of changes
16/04/2020	'Mesna dosing and administration' block added to clinical information. Version number changed to v.4

### Version 3

Date	Summary of changes
04/05/2012	New protocol taken to Haematology Reference Committee meeting.
18/12/2012	Approved and published on eviQ.
27/06/2014	Protocol reviewed by email survey. Added link to ALLG with statement Patients with ALL should be considered for inclusion into clinical trials. Added asparaginase monitoring. Next review in 2 years.
20/05/2016	Protocol reviewed at Haematology Reference Committee meeting. Replaced vindesine (not available in Australia) with vincristine as per Reference Committee consensus. No other changes, review in 2 years.
31/05/2017	Transferred to new eviQ website. Version number change to v.3. Other changes include: <ul style="list-style-type: none"> <li>diluent volume of vincristine changed from '50 to 100 mL' to '50 mL' as per Australian Injectable Handbook Sixth Edition.</li> <li>L- asparaginase (colaspase) changed to asparaginase (colaspase) per TGA update, to align with names used internationally <a href="https://www.tga.gov.au/updating-medicine-ingredient-names-list-affected-ingredients#active">https://www.tga.gov.au/updating-medicine-ingredient-names-list-affected-ingredients#active</a></li> </ul>
25/10/2018	Link added to <a href="#">high dose methotrexate-induced toxicity</a> document in clinical information.
12/04/2019	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.

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](http://www.eviQ.org.au)

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<https://www.eviq.org.au/p/1286>

26 Jun 2023

## Patient information - BFM 2000 high risk block 2

Patient's name:

### Your treatment


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

BFM 2000 High Risk block 2			
This treatment cycle is usually given twice in sequence with the other High Risk block protocols.			
Day	Treatment	How it is given	How long it takes
1 to 5	<b>Dexamethasone</b> ( <i>dex-a-METH-a-son</i> e)	Take orally ONCE a day in the morning on days 1 to 5. To be taken with or immediately after food.  If you forget to take your tablets or vomit your tablets, contact your treating team.	
1	<b>Vincristine</b> ( <i>vin-KRIS-teen</i> )	By a drip into a vein	About 5 to 10 minutes
1	<b>Methotrexate (IV)</b> ( <i>meth-o-TREX-ate</i> )	By a drip into a vein	For 24 hours
1	<b>Methotrexate (intrathecal)</b>	By injection into your spine	About 4 hours
	<b>Cytarabine (intrathecal)</b> ( <i>sy</i> e-TARE-a-been)	By injection into your spine	
	<b>Hydrocortisone (intrathecal)</b> ( <i>hydro-cort-is-own</i> )	By injection into your spine	
2	<b>Calcium folinate (Leucovorin)</b> ( <i>loo-koe-VOR-in</i> )	By a drip into a vein every 6 hours after methotrexate infusion	About 5 minutes
2 to 4	<b>Ifosfamide</b> ( <i>eye-FOS-fa-mide</i> )	By a drip into a vein for total of 5 doses	About 2 hours TWICE a day
	<b>Mesna</b> ( <i>MES-na</i> )	By a drip into a vein	About 15 minutes before and at 4 and 8 hours after ifosfamide
5	<b>Daunorubicin</b> ( <i>daw-noe-ROO-bi-sin</i> )	By a drip into a vein	About 15 minutes
6	<b>Vincristine</b>	By a drip into a vein	About 5 to 10 minutes
	<b>Asparaginase</b> ( <i>as-PAR-a-jin-ase</i> )	By a drip into a vein	About 2 to 4 hours
7	<b>Granulocyte Colony Stimulating Factor</b> ( <i>G-CSF</i> )	By injection under the skin daily until white cell count increases	About 5 minutes
11	<b>Asparaginase</b>	By a drip into a vein	About 2 to 4 hours

- You may have additional intrathecal (injections into your spine) methotrexate, cytarabine and hydrocortisone doses. Your doctor will advise if you require these.

## 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.

 <p><b>IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:</b></p>	<b>Emergency contact details</b> Ask your doctor or nurse from your treating team who to contact if you have a problem
<ul style="list-style-type: none"><li>• a temperature of 38°C or higher</li><li>• chills, sweats, shivers or shakes</li><li>• shortness of breath</li><li>• uncontrolled vomiting or diarrhoea</li><li>• pain, tingling or discomfort in your chest or arms</li><li>• you become unwell.</li></ul>	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

You will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

### Central venous access devices (CVADs)

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

### Other medications given during this treatment

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

### Superseded treatments



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

## Side effects

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

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

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

Immediate (onset hours to days)	
<b>Heart problems</b>	<ul style="list-style-type: none"> <li>• You may get:               <ul style="list-style-type: none"> <li>◦ chest pain or tightness</li> <li>◦ shortness of breath</li> <li>◦ swelling of your ankles</li> <li>◦ an abnormal heartbeat.</li> </ul> </li> <li>• Heart problems can occur months to years after treatment.</li> <li>• Tell your doctor if you have a history of heart problems or high blood pressure.</li> <li>• Before or during treatment, you may be asked to have a test to see how well your heart is working.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.</b></li> </ul>
<b>Brain swelling (encephalopathy)</b>	<ul style="list-style-type: none"> <li>• You may feel:               <ul style="list-style-type: none"> <li>◦ dizzy</li> <li>◦ sleepy</li> <li>◦ confused or agitated.</li> </ul> </li> <li>• You may also get:               <ul style="list-style-type: none"> <li>◦ headaches</li> <li>◦ loss of balance</li> <li>◦ hallucinations</li> <li>◦ seizure (fits).</li> </ul> </li> <li>• These symptoms are caused by the drug ifosfamide.</li> <li>• If you are being treated as an outpatient, try to have someone stay at home with you during the days that you are having this medicine.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.</b></li> </ul>
<b>Pain or swelling at injection site (extravasation)</b>	<ul style="list-style-type: none"> <li>• This treatment can cause serious injury if it leaks from the area where it is going into the vein.</li> <li>• This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein.</li> <li>• If not treated correctly, you may get blistering and ulceration.</li> <li>• <b>Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.</b></li> </ul>

<b>Bladder irritation (haemorrhagic cystitis)</b>	<ul style="list-style-type: none"> <li>• You may get: <ul style="list-style-type: none"> <li>◦ blood in your urine, sometimes with blood clots</li> <li>◦ pain or burning when you urinate</li> <li>◦ the urge to urinate more than normal</li> <li>◦ stomach or pelvic pain or discomfort.</li> </ul> </li> <li>• When you go home, make sure you drink plenty of fluids (unless you are fluid restricted).</li> <li>• Empty your bladder often.</li> <li>• <b>Tell your doctor or nurse as soon as possible if you notice any blood in your urine.</b></li> </ul>
<b>Allergic reaction</b>	<ul style="list-style-type: none"> <li>• Allergic reactions are uncommon but can be life threatening.</li> <li>• <b>If you feel unwell during the infusion or shortly after it, or:</b> <ul style="list-style-type: none"> <li>◦ <b>get a fever, shivers or shakes</b></li> <li>◦ <b>feel dizzy, faint, confused or anxious</b></li> <li>◦ <b>start wheezing or have difficulty breathing</b></li> <li>◦ <b>have a rash, itch or redness of the face</b></li> </ul> </li> </ul> <p><b><u>While you are in hospital:</u> Tell your doctor or nurse immediately.</b></p> <p><b><u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.</b></p>
<b>Nausea and vomiting</b>	<ul style="list-style-type: none"> <li>• You may feel sick (nausea) or be sick (vomit).</li> <li>• Take your anti-sickness medication as directed even if you don't feel sick.</li> <li>• Drink plenty of fluids (unless you are fluid restricted).</li> <li>• Eat small meals more frequently.</li> <li>• Try food that does not require much preparation.</li> <li>• Try bland foods like dry biscuits or toast.</li> <li>• Gentle exercise may help with nausea.</li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Nausea and vomiting during cancer treatment</a>.</li> <li>• <b>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.</b></li> </ul>
<b>Urine turning orange or red</b>	<ul style="list-style-type: none"> <li>• Your urine will turn an orange or red colour.</li> <li>• This is not harmful and should only last for up to 48 hours after treatment.</li> </ul>
<b>Taste and smell changes</b>	<ul style="list-style-type: none"> <li>• You may find that food loses its taste or tastes different.</li> <li>• These changes are likely to go away with time.</li> <li>• Do your mouth care regularly.</li> <li>• Chew on sugar-free gum or eat sugar-free mints.</li> <li>• Add flavour to your food with sauces and herbs.</li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Taste and smell changes during cancer treatment</a>.</li> </ul>

**Early (onset days to weeks)**

<b>Infection risk (neutropenia)</b>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Wash your hands often.</li> <li>• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.</li> <li>• Do your mouth care regularly.</li> <li>• Inspect your central line site (if you have one) daily for any redness, pus or swelling.</li> <li>• Limit contact with people who are sick.</li> <li>• Learn how to recognise the signs of infection.</li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Infection during cancer treatment</a>.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:</b> <ul style="list-style-type: none"> <li>◦ <b>a temperature of 38°C or higher</b></li> <li>◦ <b>chills, shivers, sweats or shakes</b></li> <li>◦ <b>a sore throat or cough</b></li> <li>◦ <b>uncontrolled diarrhoea</b></li> <li>◦ <b>shortness of breath</b></li> <li>◦ <b>a fast heartbeat</b></li> <li>◦ <b>become unwell even without a temperature.</b></li> </ul> </li> </ul>
<b>Low platelets (thrombocytopenia)</b>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Try not to bruise or cut yourself.</li> <li>• Avoid contact sport or vigorous exercise.</li> <li>• Clear your nose by blowing gently.</li> <li>• Avoid constipation.</li> <li>• Brush your teeth with a soft toothbrush.</li> <li>• Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to.</li> <li>• Tell your doctor or nurse if you have any bruising or bleeding.</li> <li>• <b>Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.</b></li> </ul>
<b>Mouth pain and soreness (mucositis)</b>	<ul style="list-style-type: none"> <li>• You may have: <ul style="list-style-type: none"> <li>◦ bleeding gums</li> <li>◦ mouth ulcers</li> <li>◦ a white coating on your tongue</li> <li>◦ pain in the mouth or throat</li> <li>◦ difficulty eating or swallowing.</li> </ul> </li> <li>• Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.</li> <li>• Try bland and soft foods.</li> <li>• Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.</li> <li>• Rinse your mouth after you eat and brush your teeth, using either: <ul style="list-style-type: none"> <li>◦ 1/4 teaspoon of salt in 1 cup of warm water, or</li> <li>◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water</li> </ul> </li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Mouth problems during cancer treatment</a>.</li> <li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</b></li> </ul>
<b>Appetite loss (anorexia)</b>	<ul style="list-style-type: none"> <li>• You may not feel like eating.</li> <li>• Try to avoid drinking fluids at meal times.</li> <li>• Try to eat small meals or snacks regularly throughout the day.</li> <li>• Try to eat food that is high in protein and calories.</li> <li>• If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.</li> </ul>

<b>Joint and muscle pain and stiffness</b>	<ul style="list-style-type: none"> <li>• You may get muscle, joint or general body pain and stiffness.</li> <li>• Applying a heat pack to affected areas may help.</li> <li>• Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.</li> </ul>
<b>Inflamed pancreas (pancreatitis)</b>	<ul style="list-style-type: none"> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get:</b> <ul style="list-style-type: none"> <li>◦ abdominal (stomach) pain</li> <li>◦ a swollen stomach</li> <li>◦ nausea or vomiting</li> <li>◦ fever or chills</li> <li>◦ a fast heartbeat.</li> </ul> </li> </ul>
<b>Tiredness and lack of energy (fatigue)</b>	<ul style="list-style-type: none"> <li>• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy.</li> <li>• Do not drive or operate machinery if you are feeling tired.</li> <li>• Nap for short periods (only 1 hour at a time)</li> <li>• Prioritise your tasks to ensure the best use of your energy.</li> <li>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).</li> <li>• Try some gentle exercise daily.</li> <li>• Allow your friends and family to help.</li> <li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</b></li> </ul>
<b>Extra fluid in the body (fluid retention)</b>	<ul style="list-style-type: none"> <li>• You may gain weight over a short amount of time.</li> <li>• Your hands and feet may become swollen, appear red or feel hot and uncomfortable.</li> <li>• Wear loose clothing and shoes that are not too tight.</li> <li>• Try not to stand up or walk around too much at one time.</li> <li>• If your ankles or legs get swollen, try raising them.</li> <li>• Make sure that any cuts or areas of broken skin are treated as soon as possible.</li> <li>• <b>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.</b></li> <li>• <b>Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.</b></li> </ul>
<b>Liver problems</b>	<ul style="list-style-type: none"> <li>• You may get: <ul style="list-style-type: none"> <li>◦ yellowing of your skin or eyes</li> <li>◦ itchy skin</li> <li>◦ pain or tenderness in your stomach</li> <li>◦ nausea and vomiting</li> <li>◦ loss of appetite</li> </ul> </li> <li>• You will have regular blood tests to check how well your liver is working.</li> <li>• <b>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.</b></li> </ul>
<b>High blood sugar level (hyperglycaemia)</b>	<ul style="list-style-type: none"> <li>• You may feel thirsty and need to urinate more often than normal.</li> <li>• You may get repeated infections, especially thrush.</li> <li>• If you are a diabetic you will need to have your blood sugar levels checked more often. You may also need to have your diabetes medication increased.</li> <li>• <b>Tell your doctor or nurse if you get any of the signs or symptoms listed above.</b></li> </ul>
<b>Kidney damage</b>	<ul style="list-style-type: none"> <li>• This treatment can cause changes to how your kidneys work.</li> <li>• You will have blood tests to make sure your kidneys are working properly.</li> <li>• 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.</li> <li>• <b>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.</b></li> </ul>

<b>Nerve damage (peripheral neuropathy)</b>	<ul style="list-style-type: none"> <li>• You may notice a change in the sensations in your hands and feet, including: <ul style="list-style-type: none"> <li>◦ tingling or pins and needles</li> <li>◦ numbness or loss of feeling</li> <li>◦ pain.</li> </ul> </li> <li>• You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects.</li> <li>• Test water temperature with your elbow when bathing to avoid burns.</li> <li>• Use rubber gloves, pot holders and oven mitts in the kitchen.</li> <li>• Wear rubber shoes or boots when working in the garden or garage.</li> <li>• Keep rooms well lit and uncluttered.</li> <li>• Ask your doctor or nurse for eviQ patient information – <a href="#">Nerve problems during cancer treatment</a>.</li> <li>• Tell your doctor or nurse if you get any of the symptoms listed above.</li> </ul>
<b>Skin that is more sensitive to the sun (photosensitivity)</b>	<ul style="list-style-type: none"> <li>• After being out in the sun you may develop a rash like a bad sunburn.</li> <li>• Your skin may become red, swollen and blistered.</li> <li>• Avoid direct sunlight.</li> <li>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.</li> <li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</b></li> </ul>
<b>Side effects from steroid medication</b>	<ul style="list-style-type: none"> <li>• Steroid medication may cause: <ul style="list-style-type: none"> <li>◦ mood swings and behaviour changes</li> <li>◦ an increased appetite</li> <li>◦ weight gain</li> <li>◦ swelling in your hands and feet</li> <li>◦ stomach upsets</li> <li>◦ trouble sleeping</li> <li>◦ fragile skin and bruising</li> <li>◦ an increase in your blood sugar level</li> <li>◦ weak and brittle bones (osteoporosis)</li> </ul> </li> <li>• Take your steroid medication with food to reduce stomach upset</li> <li>• If you have diabetes, your blood sugar levels may be tested more often.</li> <li>• Tell your doctor or nurse if you get any of the symptoms listed above.</li> </ul>
<b>Skin rash</b>	<ul style="list-style-type: none"> <li>• You may get a red, bumpy rash and dry, itchy skin.</li> <li>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.</li> <li>• Do not scratch your skin.</li> <li>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.</li> <li>• <b>Talk to your doctor or nurse about other ways to manage your skin rash.</b></li> </ul>

Late (onset weeks to months)	
<b>Low red blood cells (anaemia)</b>	<ul style="list-style-type: none"> <li>You may feel dizzy, light-headed, tired and appear more pale than usual.</li> <li>Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion.</li> <li><b>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.</b></li> </ul>
<b>Hair loss (alopecia)</b>	<ul style="list-style-type: none"> <li>Your hair may start to fall out from your head and body.</li> <li>Hair loss usually starts 2 to 3 weeks after your first treatment.</li> <li>You may become completely bald and your scalp might feel tender.</li> <li>Use a gentle shampoo and a soft brush.</li> <li>Take care with hair products like hairspray, hair dye, bleaches and perms.</li> <li>Protect your scalp from the cold with a hat, scarf or wig.</li> <li>Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher.</li> <li>Moisturise your scalp to prevent itching.</li> <li>Ask your doctor or nurse about the <a href="#">Look Good Feel Better</a> program</li> </ul>
<b>Chemo brain (chemotherapy-related cognitive impairment)</b>	<ul style="list-style-type: none"> <li>You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory.</li> <li>These symptoms usually improve once treatment is completed.</li> <li>Ask your doctor or nurse for eviQ patient information – <a href="#">Memory changes and chemotherapy (chemo brain)</a>.</li> <li>Tell your doctor or nurse if you get any of the symptoms listed above.</li> </ul>
<b>Lung problems</b>	<ul style="list-style-type: none"> <li>Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.</li> <li>You may get: <ul style="list-style-type: none"> <li>shortness of breath</li> <li>fever</li> <li>dry cough</li> <li>wheezing</li> <li>fast heartbeat</li> <li>chest pain.</li> </ul> </li> <li>Your doctor will monitor how well your lungs are working during your treatment.</li> <li><b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.</b></li> </ul>

## General advice for people having cancer treatment

### Chemotherapy safety

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

### Blood clot risk

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

### Medications and vaccinations

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

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

### Other medical and dental treatment

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

### Diet and food safety

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

### Fertility

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

### Pregnancy and breastfeeding

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

### Sex life and sexuality

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

### Quitting smoking

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

### Staying active

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

**For more information about cancer treatment, side effects and side effect management see our [Patient and carers](#) section.**

## Where to get more information

### Telephone support

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

## Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – [arrow.org.au](http://arrow.org.au)
- Australasian Menopause Society – [menopause.org.au](http://menopause.org.au)
- Chris O'Brien Lifehouse - Total Body Irradiation - [mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/](http://mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/)
- Healthy Male Andrology Australia – [healthymale.org.au/](http://healthymale.org.au/)
- International Myeloma Foundation – [myeloma.org](http://myeloma.org)
- Leukaemia Foundation – [leukaemia.org.au](http://leukaemia.org.au)
- Lymphoma Australia – [lymphoma.org.au](http://lymphoma.org.au)
- Myeloma Australia – [myeloma.org.au](http://myeloma.org.au)
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – [aci.health.nsw.gov.au/resources/blood-and-marrow-transplant](http://aci.health.nsw.gov.au/resources/blood-and-marrow-transplant)
- NSW Agency for Clinical Innovation - [aci.health.nsw.gov.au/projects/immune-effector-cell-service](http://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](http://nccn.org/patientresources/patient-resources/guidelines-for-patients)
- Talk Blood Cancer – [cmlsupport.org.uk/organisation-type/social-media-groups](http://cmlsupport.org.uk/organisation-type/social-media-groups)

## General cancer information and support

- Australian Rare Cancer (ARC) Portal – [arcportal.org.au/](http://arcportal.org.au/)
- Beyondblue – [beyondblue.org.au](http://beyondblue.org.au)
- Cancer Australia – [canceraustralia.gov.au](http://canceraustralia.gov.au)
- Cancer Council Australia – [cancer.org.au](http://cancer.org.au)
- Cancer Voices Australia – [cancervoicesaustralia.org](http://cancervoicesaustralia.org)
- CanTeen – [canteen.org.au](http://canteen.org.au)
- Carers Australia – [carersaustralia.com.au](http://carersaustralia.com.au)
- eviQ Cancer Treatments Online – [eviQ.org.au](http://eviQ.org.au)
- Food Standards Australia New Zealand: Listeria & Food Safety – [foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx](http://foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx)
- LGBTQI+ People and Cancer - [cancercouncil.com.au/cancer-information/lgbtqi](http://cancercouncil.com.au/cancer-information/lgbtqi)
- Look Good Feel Better – [lgfb.org.au](http://lgfb.org.au)
- Patient Information - [patients.cancer.nsw.gov.au](http://patients.cancer.nsw.gov.au)
- Radiation Oncology Targeting Cancer - [targetingcancer.com.au](http://targetingcancer.com.au)
- Redkite – [redkite.org.au](http://redkite.org.au)
- Return Unwanted Medicines – [returnmed.com.au](http://returnmed.com.au)
- Staying active during cancer treatment – [patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active](http://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](http://iCanQuit.com.au)
- Patient Information - [patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking](http://patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking)
- Quitnow – [quitnow.gov.au](http://quitnow.gov.au)

### Additional notes:

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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](http://www.eviq.org.au)

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