

# Acute lymphoblastic leukaemia ALL06 Protocol II

ID: 3900 v.2 Endorsed

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

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

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

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

2022

[Click here](#)



### Related pages:

- [Acute lymphoblastic leukaemia ALL06 overview](#)
- [Management of asparaginase therapy](#)
- [Acute lymphoblastic leukaemia ALL06 - Treatment schema](#)
- [Acute lymphoblastic leukaemia ALL06 - Protocol flow diagram](#)

## Treatment schedule - Overview

Drug	Dose	Route	Day
Dexamethasone *	5 mg/m <sup>2</sup> TWICE a day	PO	1 to 21 then taper and cease
Pegaspargase **	1,000 Units/m <sup>2</sup>	IM	1
DOXOrubicin	30 mg/m <sup>2</sup>	IV	8, 15, 22, 29
vinCRISTine	1.5 mg/m <sup>2</sup> (Cap dose at 2 mg)	IV infusion	8, 15, 22, 29
Tioguanine	60 mg/m <sup>2</sup> ONCE a day	PO	36 to 49
Cytarabine (Ara-C) ***	75 mg/m <sup>2</sup>	Subcut	36 to 39 and 43 to 46
CYCLOPHOSPHamide	1,000 mg/m <sup>2</sup>	IV infusion	36
Mesna	400 mg/m <sup>2</sup> at 0, 4 and 8 hours after the start of each cyclophosphamide dose****	IV infusion	36
Methotrexate *****	12 mg	Intrathecal	36 and 43

\* Taper dexamethasone from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29.

\*\* Intramuscular (IM) injection of pegaspargase may result in lower incidence of hepatotoxicity, coagulopathy, and gastrointestinal and renal disorders, as compared with the intravenous route.<sup>1</sup> Pegaspargase can be administered intravenously over 1 - 2 hours.

\*\*\* Start cytarabine blocks if WCC  $\geq 0.5 \times 10^9/L$  and platelets  $\geq 30 \times 10^9/L$ ; if a cytarabine block is delayed, then tioguanine is suspended. Omitted tioguanine doses should be made up until the total of 14 doses (total of 840 mg/m<sup>2</sup>) is reached.

\*\*\*\* The mesna doses scheduled at 4 and 8 hours after the start of cyclophosphamide may be administered orally if appropriate. The oral dose of mesna is twice that of the IV dose.

\*\*\*\*\* Patients with CNS involvement receive additional intrathecal therapy on day 1 and 18 i.e. a total of 4 intrathecal doses.

#### Criteria for starting Protocol II - Day 1 to 35:

- complete remission
- good general condition with no active infections
- haematological recovery: WCC  $\geq 2.5 \times 10^9/L$ , neutrophils  $\geq 1.0 \times 10^9/L$ , platelets  $\geq 100 \times 10^9/L$
- normal ejection fraction confirmed by gated heart pool scan or echocardiogram

#### Criteria for starting Protocol II - Day 36 to 50:

- good general condition with no active infections
- haematological recovery: WCC  $\geq 2.0 \times 10^9/L$ , neutrophils  $\geq 0.5 \times 10^9/L$ , platelets  $\geq 50 \times 10^9/L$

A bone marrow aspirate is required for MRD testing prior to Protocol II.

**Duration:** 50 days

**Cycles:** 1

For standard-risk and medium-risk patients, Protocol II begins 2 weeks after the end of Protocol M i.e. on day 70 after the start of Protocol M. For high-risk patients (and very high-risk patients not proceeding to allogeneic stem cell transplantation [ASCT]), Protocol II begins 3 weeks after the end of the 6th High Risk block i.e. on Day 57 after the start of HR block 6.

#### Notes:

- This treatment should only be carried out in a major centre as intensive monitoring and support is required.
- **Cranial irradiation** should be considered in patients with initial CNS involvement; as prophylaxis treatment for all HR and VHR patients not undergoing allogeneic stem cell transplant; and in T-ALL patients (other than low-risk patients), especially those with initial WCC  $> 100 \times 10^9/L$ . Cranial irradiation is usually administered on day 38 of Protocol II depending on the patient's clinical condition.

**Drug status:** **Pegaspargase:** TGA registered but not PBS listed

All other drugs in this protocol are on the [PBS general schedule](#)

Tioguanine is available as **40 mg** tablets

## Treatment schedule - Detail

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

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

Day 1		
Dexamethasone	5 mg/m <sup>2</sup> (PO)	TWICE a day on days 1 to 21. Take with food. Taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29.
Pegaspargase	1,000 Units/m <sup>2</sup> (IM)	inject intramuscularly. Rotate site of administration.*
Day 2 to 7		
Dexamethasone	5 mg/m <sup>2</sup> (PO)	TWICE a day on days 1 to 21. Take with food. Taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29.
Day 8		

Day 8		
Dexamethasone	5 mg/m <sup>2</sup> (PO)	TWICE a day on days 1 to 21. Take with food. Taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29.
DOXOrubicin	30 mg/m <sup>2</sup> (IV)	over 5 to 15 minutes.**
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

Day 9 to 14		
Dexamethasone	5 mg/m <sup>2</sup> (PO)	TWICE a day on days 1 to 21. Take with food. Taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29.

Day 15		
Dexamethasone	5 mg/m <sup>2</sup> (PO)	TWICE a day on days 1 to 21. Take with food. Taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29.
DOXOrubicin	30 mg/m <sup>2</sup> (IV)	over 5 to 15 minutes.**
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

Day 16 to 21		
Dexamethasone	5 mg/m <sup>2</sup> (PO)	TWICE a day on days 1 to 21. Take with food. Taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29.

Day 22 and 29		
DOXOrubicin	30 mg/m <sup>2</sup> (IV)	over 5 to 15 minutes.**
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

Day 36		
Tioguanine	60 mg/m <sup>2</sup> (PO)	ONCE a day. Best taken on an empty stomach, but may be taken with food if necessary.
Cytarabine (Ara-C)	75 mg/m <sup>2</sup> (Subcut)	via subcutaneous injection ***
CYCLOPHOSPHamide	1,000 mg/m <sup>2</sup> (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Mesna	400 mg/m <sup>2</sup> (IV infusion)	in 100 mL sodium chloride 0.9% over 15 to 30 minutes at 0, 4 and 8 hours after the start of cyclophosphamide dose (first dose may be loaded in the same bag as cyclophosphamide). The mesna doses scheduled at 4 and 8 hours after the start of cyclophosphamide may be administered orally if appropriate. The oral dose of mesna is twice that of the IV dose.
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy****

Day 37 to 39		
Tioguanine	60 mg/m <sup>2</sup> (PO)	ONCE a day. Best taken on an empty stomach, but may be taken with food if necessary.
Cytarabine (Ara-C)	75 mg/m <sup>2</sup> (Subcut)	via subcutaneous injection ***

Day 40 to 42		
Tioguanine	60 mg/m <sup>2</sup> (PO)	ONCE a day. Best taken on an empty stomach, but may

Day 40 to 42		
		be taken with food if necessary.
Day 43		
Tioguanine	60 mg/m <sup>2</sup> (PO)	ONCE a day. Best taken on an empty stomach, but may be taken with food if necessary.
Cytarabine (Ara-C)	75 mg/m <sup>2</sup> (Subcut)	via subcutaneous injection ***
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy****
Day 44 to 46		
Tioguanine	60 mg/m <sup>2</sup> (PO)	ONCE a day. Best taken on an empty stomach, but may be taken with food if necessary.
Cytarabine (Ara-C)	75 mg/m <sup>2</sup> (Subcut)	via subcutaneous injection ***
Day 47 to 49		
Tioguanine	60 mg/m <sup>2</sup> (PO)	ONCE a day. Best taken on an empty stomach, but may be taken with food if necessary.

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\*\* In the trial doxorubicin was administered over 1 hour; RCM consensus to change to 5 to 15 mins.

\*\*\* Start cytarabine blocks if WCC  $\geq 0.5 \times 10^9/L$  and platelets  $\geq 30 \times 10^9/L$ ; if a cytarabine block is delayed, then tioguanine is suspended. Omitted tioguanine doses should be made up until the total of 14 doses (total of 840 mg/m<sup>2</sup>) is reached.

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#### Criteria for starting Protocol II - Day 36 to 50:

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**Cycles:** 1

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## Indications and patient population

#### Indications:

- 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 is for the treatment of adolescents aged 15 years and above, and young adults aged up to 40 years.
- For information on which protocol is used for each risk group, refer to the [definition of risk groups](#).

## Contraindications<sup>2</sup>

Pegaspargase should not be used in patients who have:

- previous anaphylaxis or severe hypersensitivity to asparaginase formulations
- severe hepatic impairment
- existing or a history of pancreatitis
- previous haemorrhagic or severe thrombotic events.

## Cautions/exclusions<sup>3</sup>

- Pegaspargase should be used with caution in patients over 40 years of age and those with a body mass index (BMI) greater than 30 due to an increased risk of side effects.

See [ID 918 Management of asparaginase therapy](#) for more information.

## 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>Caution with oral anti-cancer drugs</b>	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the <a href="#">COSA guidelines</a> and <a href="#">oral anti-cancer therapy</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>	High risk with pegaspargase. Hypersensitivity reactions may occur, e.g. life-threatening anaphylaxis, particularly in patients with known hypersensitivity to the other forms of asparaginase. Adequate medical treatment and provisions should be available for immediate use in the event of an anaphylactic reaction. Patients that develop hypersensitivity to the E. coli derived formulation may be able to switch to Erwinia asparaginase. Read more about <a href="#">Management of asparaginase therapy</a> Read more about <a href="#">Hypersensitivity reaction</a>
<b>Antiemetics for multi-day protocols</b>	Antiemetic therapy should be administered throughout the duration of the chemotherapy protocol and to cover delayed nausea. The acute and delayed emetic risk of multi-day chemotherapy protocols will overlap depending on the individual drugs and their sequence of administration. More or less antiemetic cover may be required. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about <a href="#">preventing anti-cancer therapy induced nausea and vomiting</a>

<p><b>Cumulative lifetime dose of anthracyclines</b></p>	<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>
<p><b>Thiopurine-S-methyltransferase (TPMT) enzyme deficiency</b></p>	<p>Patients with an inherited deficiency of the TPMT enzyme are at an increased risk of, and prone to developing, rapid bone marrow depression which may lead to severe, life-threatening myelosuppression when undergoing treatment with thiopurines (azathioprine, mercaptopurine, tioguanine). This may be exacerbated by coadministration with drugs that inhibit TPMT, such as olsalazine, mesalazine or sulfasalazine.</p> <p>Consider assessing thiopurine-S-methyltransferase (TPMT) activity prior to administration of thiopurines.</p>
<p><b>Pegaspargase</b></p>	<p>Pegaspargase 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>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>
<p><b>Pancreatitis</b></p>	<p>Pancreatitis (both haemorrhagic or necrotising) has been reported in patients receiving pegaspargase with fatal outcomes. If pancreatitis is suspected pegaspargase should be discontinued and not restarted if confirmed. Serum amylase and/or lipase measurements should be performed frequently to identify early signs of pancreatic inflammation. If treatment is discontinued due to pancreatitis, appropriate investigations (e.g. ultrasound) should be performed at least four months following termination of therapy.</p>
<p><b>Hepatotoxicity</b></p>	<p>Caution is required when pegaspargase is given in combination with other hepatotoxic substances. If pegaspargase is given in combination with hepatotoxic substances, the patient should be closely monitored for liver impairment, especially if there is pre-existing hepatic impairment.</p>
<p><b>Thrombotic events</b></p>	<p>Serious thrombotic events may occur in patients receiving pegaspargase and should be discontinued if they occur. Increased prothrombin time (PT), increased activated partial thromboplastin time (APTT), and hypofibrinogenaemia may occur in patients receiving pegaspargase. A baseline coagulation profile (including antithrombin III) should be established and periodically monitored during and after treatment.</p> <p>Patients should be on thromboprophylaxis with enoxaparin to prevent thrombotic events unless contraindicated.</p> <p>Read more about <a href="#">Management of asparaginase therapy</a></p>
<p><b>Peripheral neuropathy</b></p>	<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>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>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>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 e.g. trimethoprim/sulfamethoxazole 160/800 mg PO one tablet twice daily, twice weekly (e.g. on Mondays and Thursdays) OR one tablet three times weekly (e.g. on Mondays, Wednesdays and Fridays).</p> <p>Read more 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>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, LDH, bilirubin, albumin, uric acid, lipase, amylase, APTT, INR, fibrinogen, ATIII at baseline and twice a week or more frequent as clinically indicated.</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 \(ADDIKD\)](#).

### Note:

- All dose reductions are calculated as a percentage of the starting dose.
- Dose modifications are based on the ALL06 trial.

### Haematological toxicity

Dose modifications are generally not recommended

### Renal impairment

#### Creatinine clearance (mL/min)

less than 10	Reduce cyclophosphamide dose by 50%
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### Hepatic impairment

#### Direct bilirubin (micromol/L)

21 - 51	Reduce doxorubicin by 50%
52 - 85	Reduce doxorubicin by 75% and vincristine by 50%
85 - 102	Withhold doxorubicin and reduce vincristine by 75%
> 102	Withhold doxorubicin and vincristine and administer next dose once toxicity has resolved. Do not make up missed doses.

Pegaspargase contraindicated if bilirubin > 3 x ULN or transaminases > 10 x ULN

### Peripheral neuropathy

Grade 2	Consider a reduced dose of vincristine.
Grade 3 or greater	Withhold vincristine until symptoms resolve, resume at 50% dose reduction. Escalate dose to full dose as tolerated.

### Pegaspargase-related reactions

Grade 1 local allergic reactions not requiring intervention	Continue pegaspargase
Grade 2 or greater systemic reactions	Consider discontinuation of pegaspargase and substitute with erwinia asparaginase if available
Grade 3 or 4 allergic	Discontinue pegaspargase, if discontinued due to allergy/hypersensitivity, consider



reaction/hypersensitivity (such as anaphylaxis), pancreatitis or thrombotic events	changing to erwinia asparaginase.
Pegaspargase should not be withheld for asymptomatic coagulation laboratory abnormalities. Cryoprecipitate and anti-thrombin III infusions may be required.	

## 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](#)

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

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

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

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

Pegaspargase		
There are no documented interactions for pegaspargase. However, a range of clinical effects can occur due to the mechanism of action of pegaspargase.		
Clinical effect	Action	Clinical management
<b>Effect on use with other chemotherapy agents</b>	Pegaspargase may affect the action of other cytotoxic drugs requiring cell division for their effect (i.e. methotrexate, cytarabine). This effect can be either synergistic or antagonistic, depending on the timing of administration of the agents.	Adherence to the treatment schedule is recommended to minimise these potential interactions.
	Immediately preceding or concomitant treatment with vincristine can increase the toxicity of pegaspargase and increases the risk of anaphylactic reactions.	Administer vincristine 12 hours prior to pegaspargase to minimise toxicity.
<b>Effects on protein-bound drugs</b>	Due to its effects on protein synthesis and hepatic function, pegaspargase can potentially interfere with metabolism and clearance of other drugs including chemotherapy drugs known to interact with CYP enzymes.	Monitor for hepatotoxicity if used concomitantly.
<b>Coagulation effects</b>	Use of pegaspargase can lead to fluctuating levels of coagulation factors. This may increase the risk of bleeding and/or thrombosis.	Caution is needed when anticoagulants are given concomitantly.
	Alterations in coagulation parameters can be more pronounced when glucocorticoids (e.g. prednisolone) and pegaspargase are given concomitantly.	Monitor levels of coagulation parameters such as fibrinogen and ATIII
<b>Oral contraceptive effects</b>	Pegaspargase hepatotoxicity may impair the hepatic clearance of oral contraceptives.	Concomitant use of pegaspargase and oral contraceptives is not recommended. A method other than oral contraception should be used in women of childbearing potential
<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>

Tioguanine		
	Interaction	Clinical management
<b>Aminosalicylate derivatives (e.g. balsalazide, olsalazine, mesalazine, sulfasalazine)</b>	Increased toxicity of tioguanine possible due to inhibition of its metabolism (aminosalicylates inhibit the enzyme TPMT) resulting in increased exposure	Avoid combination or monitor for increased tioguanine toxicity

<b>Vincristine</b>		
	<b>Interaction</b>	<b>Clinical management</b>
<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.

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

- baseline weight
- baseline urinalysis

Hydration if prescribed

### Pre treatment medication

Administer antiemetics if required

### Dexamethasone

- administer orally TWICE a day on **days 1 to 21**
- taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29
- to be taken with or immediately after food.

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

## 🕒 Chemotherapy - Time out

### Pegaspargase

- administer via intramuscular (IM) injection (alternatively may be administered intravenously over 1 to 2 hours)
- when administered IM, the volume at the injection site should be less than or equal to 2 mL; if volume to administer is larger than 2 mL, use multiple injection sites and ensure site rotation

**Note:** monitor patient during and for one hour after drug administration, as anaphylaxis may occur. Ensure immediate access to emergency / adverse-reaction kit is available.

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

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## Day 8 and 15

### 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](#).

Hydration if prescribed

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### Dexamethasone

- administer orally TWICE a day on **days 1 to 21**
- taper from day 22, reducing the dose by half every 3 days. Cease dexamethasone on day 29
- to be taken with or immediately after food.

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

## ⊖ Chemotherapy - Time out

### Doxorubicin

#### Administer doxorubicin (vesicant):

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

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

### Vincristine

#### Administer vincristine (vesicant)

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

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

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## Days 22 and 29

### 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.

Hydration if prescribed

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

## ⊖ Chemotherapy - Time out

### Doxorubicin

#### Administer doxorubicin (vesicant):

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

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

### Vincristine

### Administer vincristine (vesicant)

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

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

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## Day 36

### 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.

Hydration if prescribed

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

## 🕒 Chemotherapy - Time out

### Tioguanine

- administer orally ONCE daily from **day 36 to 49**
- swallow whole with a glass of water; do not break, crush or chew

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

### Cytarabine

- administer via subcutaneous injection on **days 36 to 39 and 43 to 46**
- localised reactions at the injection site can occur
  - treat with warm compress
- rotate the injection site each time.

### Prehydration

Administer 1000 mL sodium chloride 0.9% over 2 hours.

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

### Cyclophosphamide

#### Administer cyclophosphamide:

- via IV infusion over 60 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- cyclophosphamide should be administered as early as possible in the day to decrease the amount of drug remaining in the bladder overnight
- rapid infusion can cause dizziness, rhinitis, nausea and perioral numbness. If symptoms develop, slow infusion rate.

### Mesna

- administer via IV infusion over 15 minutes at 0, 4 and 8 hours after the start of each cyclophosphamide dose
- the administration of mesna causes a false positive ketonuria.

Continue hydration as prescribed.

### Intrathecal methotrexate

#### Note:

- intrathecal methotrexate may not be administered with every cycle
- the number of IT treatments is dependent on patient risk category



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

Read more about the [procedure for intrathecal methotrexate administration](#).

#### Post intrathecal care:

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

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

Deaccess [CVAD](#).

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

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### Days 37 to 39

[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.

Hydration if prescribed

#### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

#### 🕒 Chemotherapy - Time out

##### Tioguanine

- administer orally ONCE daily from **day 36 to 49**
- swallow whole with a glass of water; do not break, crush or chew

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

##### Cytarabine

- administer via subcutaneous injection on **days 36 to 39 and 43 to 46**
- localised reactions at the injection site can occur
  - treat with warm compress
- rotate the injection site each time.

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

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### Day 43

[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.

Hydration if prescribed

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

## 🕒 Chemotherapy - Time out

### Tioguanine

- administer orally ONCE daily from **day 36 to 49**
- swallow whole with a glass of water; do not break, crush or chew

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

### Cytarabine

- administer via subcutaneous injection on **days 36 to 39 and 43 to 46**
- localised reactions at the injection site can occur
  - treat with warm compress
- rotate the injection site each time.

### Intrathecal methotrexate

#### Note:

- intrathecal methotrexate may not be administered with every cycle
- the number of IT treatments is dependent on patient risk category

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

Read more about the [procedure for intrathecal methotrexate administration](#).

#### Post intrathecal care:

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

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

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

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## Days 44 to 46

### Safe handling and waste management

### Safe administration

General patient assessment prior to each treatment.

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

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

## 🕒 Chemotherapy - Time out

### Tioguanine

- administer orally ONCE daily from **day 36 to 49**

- swallow whole with a glass of water; do not break, crush or chew

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

### Cytarabine

- administer via subcutaneous injection on **days 36 to 39 and 43 to 46**
- localised reactions at the injection site can occur
  - treat with warm compress
- rotate the injection site each time.

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

## Discharge information

### Dexamethasone tablets

- Dexamethasone tablets with written instructions on how to take them.

### Tioguanine tablets

- Tioguanine tablets with written instructions on how to take them.

### Antiemetics

- Antiemetics as prescribed.

### Laxatives

- Ensure patient has prophylactic laxatives.

### 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>Headache</b>	
<b>Hypersensitivity reaction</b>	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about <a href="#">hypersensitivity reaction</a>
<b>Injection-site reactions</b>	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
<b>Nausea and vomiting</b>	Read more about <a href="#">prevention of treatment induced nausea and vomiting</a>
<b>Red-orange discolouration of urine</b>	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
<b>Taste and smell alteration</b>	Read more about <a href="#">taste and smell changes</a>

### 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>
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<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>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>Cardiotoxicity</b>	Anthracyclines (e.g. daunorubicin, doxorubicin, epirubicin, idarubicin etc.) may cause acute cardiotoxicities such as arrhythmias, pericarditis-myocarditis syndrome and cardiac failure.
<b>Constipation</b>	
<b>Fatigue</b>	Read more about <a href="#">fatigue</a>
<b>Haemorrhagic cystitis</b>	An inflammatory process, characterised by diffuse bladder mucosal inflammation resulting in haemorrhage. Patients are at risk following blood and marrow transplant (BMT) or treatment with cyclophosphamide, ifosfamide and/or radiation therapy.  Read more about <a href="#">haemorrhagic cystitis</a>
<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>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>Pancreatitis</b>	Inflammation of the pancreas with impairment of function is associated with asparaginase formulations.
<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>
<b>Thromboembolism</b>	Serious thromboembolic events can occur in patients receiving pegaspargase. The majority of thromboses occur in the CNS. Patients should be carefully assessed for risk factors with baseline and regular monitoring of coagulation profile (including PT, APTT, fibrinogen, antithrombin III) during and after treatment. Antithrombotic prophylaxis is recommended.  Read more about <a href="#">Management of asparaginase therapy</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>Hyperpigmentation</b>	Darkening of an area of skin caused by the overproduction of melanin.

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

A search of the literature found limited evidence to support the use of intensive paediatric-inspired regimens in the treatment of acute lymphoblastic leukaemia (ALL) in older adolescents and young adults. The expert reference committee supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by data from the ALL06 phase II trial.<sup>4</sup>

Intensive paediatric regimens have been extensively used for the treatment of ALL in children and young adolescents. A French retrospective study<sup>5</sup> of 177 adolescent patients (15-20 years) compared outcomes of patients treated with either a paediatric regimen (FRALLE-93) or an adult regimen (LALA-94). Patients who received the paediatric regimen were more likely to reach complete remission (CR; 94% vs 83%, p=0.04) and had improved 5-year event-free survival (EFS; 67% vs 41%, p < 0.0001).

When compared to children and adolescents, adults with ALL tend to have poorer outcomes. This may be in part due to differences in the biology of ALL in adults, the increased prevalence of poor risk cytogenetic changes such as presence of the Philadelphia chromosome (9;22 translocation) and reduced prevalence of good risk cytogenetic changes such as hyperdiploidy.<sup>6</sup>

The use of paediatric protocols in adults with ALL is promising. A retrospective study by the PETHEMA group<sup>7</sup> compared the outcomes of adolescents (age 15-18) and young adults (age 19-30) treated with a paediatric regimen (ALL-96). There was no significant difference in overall survival (OS; 77% vs 63%, p=0.44) or 6-year EFS (60% vs 63%, p=0.97) between the two groups.

The GRAALL 2003 study<sup>8</sup> treated 225 Philadelphia negative ALL patients aged 15–60 with a paediatric-inspired regimen. The CR rate was 93.5%, with an EFS rate of 55% and OS rate of 60%. Results were compared with the LALA-94 study of 712 patients treated with an adult regimen: the CR rate, EFS and OS rate were more favourable in patients treated with the GRAALL 2003 protocol.

The current ALL06 protocol is a BFM 2000-derived protocol developed for the ALL06 study of adults with ALL. The efficacy data from ALL06 is presented below.<sup>4</sup>

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	ALL06 (2021) <sup>4</sup>	Yes	Yes	
	PETHEMA (2008) <sup>7</sup>	Yes	No	

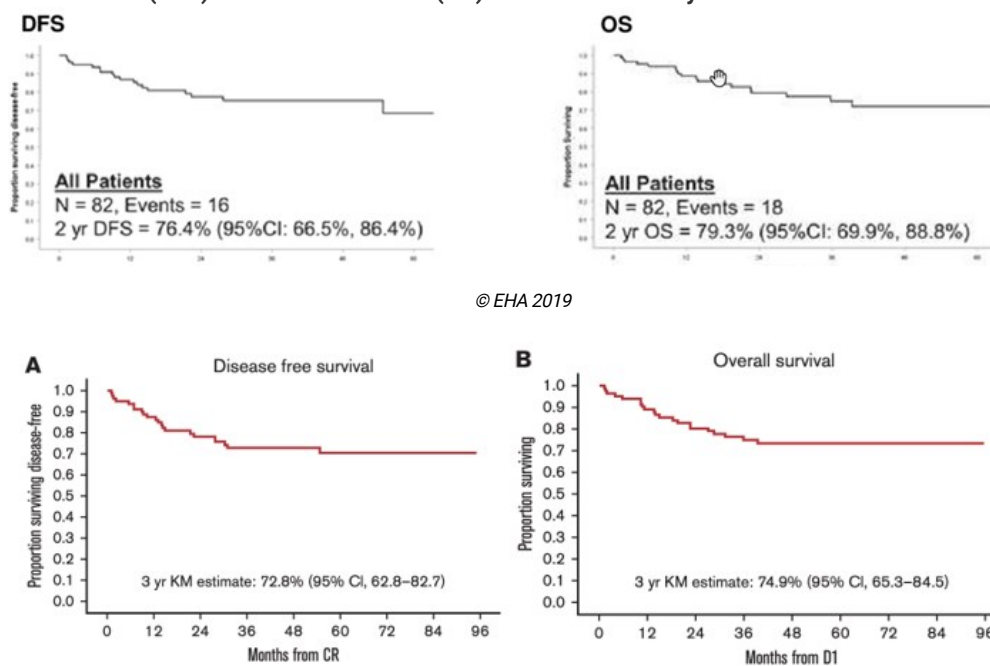
Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
	GRAALL (2009) <sup>8</sup>	Yes	No	

## Efficacy

The ALL06 regimen, a BFM 2000-derived protocol, was used by Greenwood et al.<sup>4,9</sup> in a phase II trial of 82 patients between 15-40 years with newly diagnosed Philadelphia-negative ALL. The primary outcome was the proportion of patients that commenced protocol M or High Risk (HR) Block 1 by day 94. The results were as follows:

Outcome <sup>4</sup>	ALL06
Total patients	82
Proportion receiving protocol M by day 94	34 (41.5%, p=0.77)
Median time to commencement of protocol M	97 days (IQR 87.5 - 103)
Induction mortality	3.6%
Complete response (CR)	79 (96.3%)
3-year overall survival (OS)	74.9% (95% CI: 65.3 - 84.5%)
3-year disease-free survival (DFS)	72.8% (95% CI: 62.8 - 82.7%)

Figure 1: Disease-free survival (DFS) and overall survival (OS) in the ALL06 Study<sup>4,9</sup>



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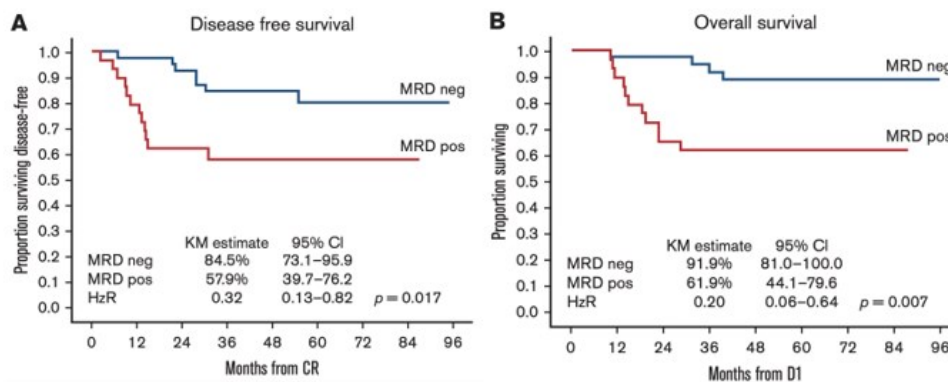
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## Role of Minimal Residual Disease Testing

Minimal residual disease (MRD) testing has commonly been used in a research setting in order to stratify risk, and is increasingly used in clinical practice for this purpose.

In the ALL06 study<sup>4,9</sup>, those who achieved a negative MRD at day 79 had improved 3-year DFS (HR 0.35, p=0.034) and OS (HR 0.19, p=0.006) when compared to those whose day 79 MRD was positive.

Figure 2: Role of MRD testing<sup>4</sup>



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## Toxicity

In the ALL06 study,<sup>4</sup> the most frequent grade 3 and grade 4 toxicities in the 34 patients who achieved protocol M / HR by day 94 were neutropenia (100%), anaemia (94%) and thrombocytopenia (91%).

The most common non-haematological toxicities were hepatic of which the most common were mild elevation of transaminases, cholestatic enzymes and bilirubin. 6% of patients experienced grade 4 non-haematological toxicities.

Neutropenic fevers and related infections were the most commonly seen infectious toxicities.

## References

- 1 Wilkes, G.M., M. Barton-Burke. 2020 -2021 Oncology Nursing Drug Handbook.
- 2 Shire Australia Pty Limited. Oncaspar® (Pegaspargase) Product Information. Last revision date: 23 April 2018
- 3 Patel, B., A. Kirkwood, A. Dey, et al. 2017. "Pegylated-asparaginase during induction therapy for adult acute lymphoblastic leukaemia: toxicity data for the UKALL14 trial". *Leukemia*. 2017. Jan;31(1):58-64
- 4 Greenwood, M., T. Trahair, R. Sutton, et al. 2021. "An MRD-stratified pediatric protocol is as deliverable in adolescents and young adults as in children with ALL." *Blood Adv* 5(24): 5574-5583.
- 5 Boissel, N., M. F. Auclerc, V. Lheritier, et al. 2003. "Should adolescents with acute lymphoblastic leukemia be treated as old children or young adults? Comparison of the French FRALLE-93 and LALA-94 trials." *J.Clin Oncol*. 21(5):774-780.
- 6 Moorman, Anthony V., Lucy Chilton, Jennifer Wilkinson, et al. 2010. "A population-based cytogenetic study of adults with acute lymphoblastic leukemia." *Blood* 115(2):206-214.
- 7 Ribera, J., A. Oriol, M. Sanz. et al. 2008. "Comparison of the results of the treatment of adolescents and young adults with standard-risk acute lymphoblastic leukemia with the Programa Espanol de Tratamiento en Hematologia Pediatric-based Protocol ALL-96". *Journal of Clinical Oncology* 10;26(11): 1843-9
- 8 Huguet, F., T. Leguay, E. Raffoux, et al. 2009. "Pediatric-inspired therapy in adults with Philadelphia chromosome-negative acute lymphoblastic leukemia: the GRAALL-2003 study." *Journal of Clinical Oncology* 27(6):911-918.
- 9 Greenwood, M. T. Trahair, M. Osborn. et al. 2019. "Intensive Paediatric Therapy is as Deliverable in Adolescents and Young Adults as Children with ALL - Preliminary Results of the Australasian Leukaemia and Lymphoma Group (ALLG) ALL06 Study. EHA Poster presentation.

## History

### Version 2

Date	Summary of changes
29/11/2022	Protocol reviewed electronically by Haematology Reference Committee. Updates include: <ul style="list-style-type: none"> <li>• New clinical information block added: Thiopurine-S-methyltransferase (TPMT) enzyme deficiency.</li> <li>• Pegaspargase interactions block updated.</li> <li>• Evidence update - study data published for ALL06.</li> <li>• Removed 'interim' from protocol title..</li> </ul>
15/05/2023	Approved and published as version number v.2.  For review in 2 years

### Version 1

Date	Summary of changes
23/10/2020	New protocol taken to Haematology Reference Committee meeting
29/03/2021	Approved and published on eviQ. Version 1. Review in 1 year.
12/11/2021	Protocol flow diagram updated.
20/01/2022	Interactions updated.
21/01/2022	Pulmonary toxicity added to side effects.

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)

**First approved:** 29 March 2021  
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***The currency of this information is guaranteed only up until the date of printing, for any updates please check:***

<https://www.eviq.org.au/p/3900>

28 Jun 2023



# Patient information - Acute lymphoblastic leukaemia (ALL) - ALL06 Protocol II

Patient's name:

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## Your treatment

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

ALL06 Protocol II			
This treatment cycle is given once only.			
Day	Treatment	How it is given	How long it takes
1 to 21	<b>Dexamethasone</b> ( <i>dex-a-METH-a-son</i> e)	Take orally TWICE a day on days 1 to 21. To be taken with or immediately after food.  From day 22, you should reduce the dose of dexamethasone gradually ('taper') and then stop as per your doctor's instructions.	
1	<b>Pegaspargase</b> ( <i>peg-AS-par-jase</i> )	By injection into a large muscle	About 5 to 10 minutes
8, 15, 22 and 29	<b>Doxorubicin</b> ( <i>dox-oh-roo-bi-sin</i> )	By a drip into a vein	About 15 minutes
	<b>Vincristine</b> ( <i>vin-KRIS-teen</i> )	By a drip into a vein	About 5 to 10 minutes
36 to 49	<b>Tioguanine</b> ( <i>THIGH-oh-GWAHN-ee</i> n)	Take orally ONCE a day on days 36 to 49. Swallow whole with a glass of water, do not break, crush or chew.	
36	<b>Cytarabine</b> ( <i>sy</i> e-TARE-a-been)	By injection under the skin	About 5 minutes
	<b>Cyclophosphamide</b> ( <i>SYE-kloe-FOS-fa-mide</i> )	By a drip into a vein	About 1 hour
	<b>Mesna</b> ( <i>MES-na</i> )	By a drip into a vein	About 15 minutes
	<b>Methotrexate</b> * ( <i>meth-o-TREX-ate</i> )	By injection into your spine	About 4 hours
37 to 39	<b>Cytarabine</b>	By injection under the skin	About 5 minutes
43	<b>Cytarabine</b>	By injection under the skin	About 5 minutes
	<b>Methotrexate</b> *	By injection into your spine	About 4 hours
44 to 46	<b>Cytarabine</b>	By injection under the skin	About 5 minutes


\* You may have additional methotrexate doses. Your doctor will advise if you require these.

### Missed doses:

- **Dexamethasone** and **tioguanine**: if you forget to take your tablets or vomit your tablets, contact your treating team.

## 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.

### Treatment with cyclophosphamide

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

### 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.

## 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>Headache</b>	<ul style="list-style-type: none"> <li>You can take paracetamol if you have a headache.</li> <li><b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.</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>get a fever, shivers or shakes</li> <li>feel dizzy, faint, confused or anxious</li> <li>start wheezing or have difficulty breathing</li> <li>have a rash, itch or redness of the face</li> </ul> </li> </ul> <p><b>While you are in hospital: Tell your doctor or nurse immediately.</b></p> <p><b>After you leave: Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.</b></p>
<b>Injection-site reaction</b>	<ul style="list-style-type: none"> <li>At the injection site you may get pain, redness, swelling or bruising.</li> <li>These symptoms are usually not serious.</li> <li><b>Tell your doctor or nurse immediately if you notice any redness or pain during or after treatment.</b></li> </ul>
<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>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>Heart problems</b>	<p>Heart problems are uncommon. You have a higher risk if you have had high blood pressure, chemotherapy or radiation therapy to your chest. You may be asked to have a test to see how your heart is working before and during treatment. If you develop shortness of breath, an irregular heart beat or chest pain go to your nearest hospital emergency department.</p>

<b>Constipation</b>	<ul style="list-style-type: none"> <li>• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass.</li> <li>• You may also get: <ul style="list-style-type: none"> <li>◦ bloating, cramping or pain</li> <li>◦ a loss of appetite</li> <li>◦ nausea or vomiting.</li> </ul> </li> <li>• Drink plenty of fluids (unless you are fluid restricted).</li> <li>• Eat plenty of fibre-containing foods such as fruit, vegetables and bran.</li> <li>• Take laxatives as directed by your doctor.</li> <li>• Try some gentle exercise daily.</li> <li>• <b>Tell your doctor or nurse if you have not opened your bowels for more than 3 days.</b></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>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>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>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>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>◦ <b>abdominal (stomach) pain</b></li> <li>◦ <b>a swollen stomach</b></li> <li>◦ <b>nausea or vomiting</b></li> <li>◦ <b>fever or chills</b></li> <li>◦ <b>a fast heartbeat.</b></li> </ul> </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>
<b>Blood clots (thromboembolism)</b>	<ul style="list-style-type: none"> <li>• Blood clots can occur with this treatment.</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>redness, heat or pain in your leg(s)</b></li> <li>◦ <b>numbness or weakness in your face, arm or leg</b></li> <li>◦ <b>chest pain</b></li> <li>◦ <b>sudden shortness of breath</b></li> <li>◦ <b>dizziness</b></li> <li>◦ <b>trouble speaking</b></li> <li>◦ <b>blurred vision</b></li> <li>◦ <b>severe headache</b></li> <li>◦ <b>unexplained falls or loss of balance.</b></li> </ul> </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>Skin colour changes</b>	<ul style="list-style-type: none"> <li>You may have darkening of your skin, especially in areas that are exposed to the sun.</li> <li>You may also notice darkening of your tongue, gums and over your finger joints.</li> <li>These skin changes may fade over time.</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> </ul>

Delayed (onset months to years)	
<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>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>



### Chemotherapy safety

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

### Blood clot risk

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

### Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

### Other medical and dental treatment

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

### Diet and food safety

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

### Fertility

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

### Pregnancy and breastfeeding

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

### Sex life and sexuality

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

### Risk of developing a second cancer

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

you the specific risks of your treatment.

### Quitting smoking

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

### Staying active

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

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

## Where to get more information

### Telephone support

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

### 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)

