Acute lymphoblastic leukaemia CALGB course II early intensification SUPERSEDED

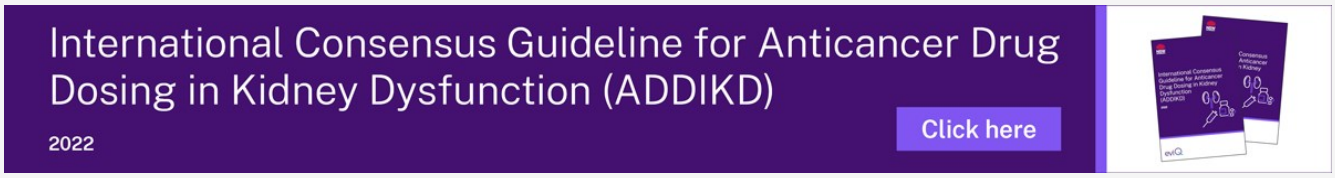
ID: 791 v.4 **Superseded** Essential Medicine List

The Haematology Reference Committee decided to supersede this protocol at the 2022 meeting as superior alternatives are available.

⚠ Asparaginase drug supply:
Native E-coli asparaginase (colaspase) ceased being manufactured in 2019. The Haematology Reference Committee recommends using protocols with evidence for the use of pegaspargase (from clinical trials) rather than substituting pegaspargase into native E-coli asparaginase containing protocols.

Patients with leukaemia should be considered for inclusion into clinical trials. Link to ALLG website and ANZCTR website.

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



Related pages:

- Acute lymphoblastic leukaemia CALGB overview SUPERSEDED
- Management of asparaginase therapy

- Overall CALGB treatment schema

Treatment schedule - Overview

Cycle 1 and 2

Drug	Dose	Route	Day
mercaptOPURine	60 mg/m^2 ONCE a day	PO	1 to 14
CYCLOPHOSPHamide	1,000 mg/m^2	IV infusion	1
Cytarabine (Ara-C)	75 mg/m^2	Subcut	1 to 4 and 8 to 11
Methotrexate	15 mg	Intrathecal	1
vinCRISTine	2 mg	IV infusion	15 and 22
Asparaginase (colaspase) *	6,000 International Units/m^2	Subcut	15, 18, 22, 25

* The manufacturers of Leunase® brand of asparaginase (colaspase) have confirmed that one Kyowa Unit (KU) is equivalent to one International Unit (IU). Alternative formulations and routes of administration may be used depending on local institution policies. Link to asparaginase document for equivalent dosing.

- Administer asparaginase after vincristine on the days that both drugs are administered to reduce vincristine toxicity.

Frequency: 28 days
Commence on count recovery.

Cycles: 2
Course II is repeated once i.e. IIA and IIB.

Notes:
Consider thiopurine methyltransferase (TPMT) testing prior to administration of mercaptopurine.

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

All other drugs in this protocol are on the PBS general schedule

Mercaptopurine is available as **50 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.*

Cycle 1 and 2

Day 1		
mercaptOPURine	60 mg/m^2 (PO)	ONCE a day. Take on an empty stomach at least one hour before or two hours after food.
CYCLOPHOSPHamide	1,000 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Cytarabine (Ara-C)	75 mg/m^2 (Subcut)	via subcutaneous injection
Methotrexate	15 mg (Intrathecal)	adhere to local institution intrathecal policy
Day 2 to 4		
mercaptOPURine	60 mg/m^2 (PO)	ONCE a day. Take on an empty stomach at least one hour before or two hours after food.
Cytarabine (Ara-C)	75 mg/m^2 (Subcut)	via subcutaneous injection
Day 5 to 7		
mercaptOPURine	60 mg/m^2 (PO)	ONCE a day. Take on an empty stomach at least one hour before or two hours after food.
Day 8 to 11		
mercaptOPURine	60 mg/m^2 (PO)	ONCE a day. Take on an empty stomach at least one hour before or two hours after food.
Cytarabine (Ara-C)	75 mg/m^2 (Subcut)	via subcutaneous injection
Day 12 to 14		
mercaptOPURine	60 mg/m^2 (PO)	ONCE a day. Take on an empty stomach at least one hour before or two hours after food.
Day 15		
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Asparaginase (colaspase)	6,000 International Units/m^2 (Subcut)	via subcutaneous injection. Administer asparaginase after vincristine on the days that both drugs are

Day 15		
		administered. *
Day 18		
Asparaginase (colaspase)	6,000 International Units/m^2 (Subcut)	via subcutaneous injection. Administer asparaginase after vincristine on the days that both drugs are administered. *
Day 22		
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Asparaginase (colaspase)	6,000 International Units/m^2 (Subcut)	via subcutaneous injection. Administer asparaginase after vincristine on the days that both drugs are administered. *
Day 25		
Asparaginase (colaspase)	6,000 International Units/m^2 (Subcut)	via subcutaneous injection. Administer asparaginase after vincristine on the days that both drugs are administered. *

* The manufacturers of Leunase® brand of asparaginase (colaspase) have confirmed that one Kyowa Unit (KU) is equivalent to one International Unit (IU). Alternative formulations and routes of administration may be used depending on local institution policies. Link to asparaginase document for equivalent dosing.

Frequency: 28 days
Commence on count recovery.

Cycles: 2
Course II is repeated once i.e. IIA and IIB.

Indications and patient population

- Acute lymphoblastic leukaemia in older adult patients

Clinical information

Safety alert vincristine administration	For safe administration of vincristine refer to the safety alert issued by the Australian Commission on Safety and Quality in Health Care
Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Venous access	Central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection

Hypersensitivity/infusion related reaction	High risk with asparaginase. Acute anaphylactoid reactions are the most common dose-limiting toxicity, particularly with IV administration. Patients that develop hypersensitivity to the E. coli derived formulation may be able to switch to Erwinia asparaginase. The Leunase brand of asparaginase (colaspase) is the only formulation for which the manufacturer advises an intradermal test dose prior to the initial dose or when a week or more has elapsed between doses. A negative skin reaction does not preclude the development of an allergic reaction and therefore the practice of a test dose is controversial. Read more about Management of asparaginase therapy Read more about Hypersensitivity reaction
Antiemetics for multi-day protocols	Antiemetic therapy should be administered throughout the duration of the chemotherapy protocol and to cover delayed nausea. The acute and delayed emetic risk of multi-day chemotherapy protocols will overlap depending on the individual drugs and their sequence of administration. More or less antiemetic cover may be required. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Thiopurine-S-methyltransferase (TPMT) enzyme deficiency	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. Consider assessing thiopurine-S-methyltransferase (TPMT) activity prior to administration of thiopurines.
Asparaginase	Asparaginase is associated with numerous toxicities including hypersensitivity, hepatotoxicity, coagulation abnormalities, pancreatitis, hyperlipidaemia, hyperglycaemia and CNS effects. Therefore routine monitoring and assessment of several parameters are required throughout treatment. There are several different formulations of asparaginase available, each with different dosing and administration recommendations. For comprehensive information on formulations, dosing, interactions, adverse reactions and specific monitoring parameters for asparaginase, see Management of asparaginase therapy document.
Pancreatitis	Pancreatitis can occur despite normal serum amylase, and can be fatal. In cases of clinical pancreatitis (unequivocal diagnosis based on lipase/amylase elevation, ultrasound and clinical findings) asparaginase treatment should be ceased and must not be resumed. Mild asymptomatic biochemical pancreatitis does not warrant discontinuing asparaginase therapy.
Peripheral neuropathy	Assess prior to each treatment. Based on clinical findings, temporary omission, dose reduction or cessation of the vinca alkaloid may be indicated; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Constipation	Prescribe prophylactic laxatives to prevent constipation related to the use of vinca alkaloids.
Hyperglycaemia	Hyperglycaemia has been observed with this treatment. Close monitoring of blood sugar levels is recommended. Initiation of antidiabetic therapy may be required. In patients with pre-existing diabetes, dose adjustment of oral antidiabetic medications or insulin may be required.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	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). Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients

Antiviral prophylaxis	Antiviral prophylaxis is recommended. Read more about antiviral prophylaxis drugs and doses
Antifungal prophylaxis	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. **Note**: Extended spectrum azole antifungals (e.g. posaconazole, voriconazole and itraconazole) should be avoided with vinca alkaloids. Metabolism is inhibited by azoles and neurotoxicity can be potentiated. Read more about antifungal prophylaxis drugs and doses.
Blood product support	The use of FFP and cryoprecipitate may be required to maintain fibrinogen levels to a normal range. Read more about Management of asparaginase therapy
Blood tests	FBC, EUC, LFTs, BSL, at baseline and prior to each treatment. Monitor pancreatic lipase and serum amylase, lipids and uric acid prior to and regularly during asparaginase therapy. Monitor fibrinogen levels, INR, APTT and PT at least once or twice weekly and consider monitoring antithrombin levels.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

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

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. References & Disclaimer

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

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

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

Cytarabine

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

Mercaptopurine		
	Interaction	**Clinical management**
Allopurinol	Increased toxicity of mercaptopurine due to reduced clearance as a result of inhibition of xanthine oxidase	If the combination is used the dose of mercaptopurine must be reduced by 75 % (i.e. only one quarter of the usual mercaptopurine dose is used)
Methotrexate, aminosalicylate derivatives (e.g. balsalazide, olsalazine, mesalazine, sulfasalazine)	Increased toxicity of mercaptopurine possible due to reduced clearance	Avoid combination or monitor closely for mercaptopurine toxicity
Ribavirin	Increased toxicity and reduced efficacy of mercaptopurine possible due to metabolic enzyme inhibition by ribavirin	Avoid combination or monitor closely for toxicity of and decreased clinical response to mercaptopurine

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

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

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

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 7 to 8 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Prime IV line(s).

Access CVAD.

- weigh patient on each visit
- urinalysis each visit

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 1 to 14**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken preferably on an empty stomach, one hour before or at least two hours after food
- avoid concomitant consumption of milk or dairy products

Note: missed doses should not be replaced, if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Prehydration

Administer 1000 mL sodium chloride 0.9% over 2 hours.

Cyclophosphamide

Administer cyclophosphamide:

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

Hydration if prescribed.

Cytarabine

- administer via subcutaneous injection on **days 1 to 4** and **8 to 11**
- localised reactions at the injection site can occur
  - treat with warm compress
- rotate the injection site each time.

Intrathecal methotrexate

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

Read more about the procedure for intrathecal methotrexate administration.

Post intrathecal care:

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

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

Deaccess CVAD.

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

Days 2 to 4

Approximate treatment time: 30 minutes

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.

- weigh patient on each visit
- urinalysis each visit

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 1 to 14**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken preferably on an empty stomach, one hour before or at least two hours after food
- avoid concomitant consumption of milk or dairy products

Note: missed doses should not be replaced, if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Cytarabine

- administer via subcutaneous injection on **days 1 to 4** and **8 to 11**
- 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)

Days 5 to 7

This is an oral treatment

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.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 1 to 14**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken preferably on an empty stomach, one hour before or at least two hours after food
- avoid concomitant consumption of milk or dairy products

Note: missed doses should not be replaced, if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

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

Days 8 to 11

Approximate treatment time: 30 minutes

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.

- weigh patient on each visit
- urinalysis each visit

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 1 to 14**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken preferably on an empty stomach, one hour before or at least two hours after food
- avoid concomitant consumption of milk or dairy products

Note: missed doses should not be replaced, if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Cytarabine

- administer via subcutaneous injection on **days 1 to 4** and **8 to 11**
- 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)

Days 12 to 14

This is an oral treatment

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.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 1 to 14**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken preferably on an empty stomach, one hour before or at least two hours after food
- avoid concomitant consumption of milk or dairy products

Note: missed doses should not be replaced, if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

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

Day 15

Approximate treatment time: 30 minutes

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.

- weigh patient on each visit
- urinalysis each visit

Hydration if prescribed.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

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

Vincristine

Administer vincristine (vesicant)

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

Asparaginase (colaspase)

Administer asparaginase (colaspase)

- via subcutaneous injection.

Deaccess CVAD.

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

Day 18

Approximate treatment time: 30 minutes

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.

- weigh patient on each visit
- urinalysis each visit

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Asparaginase (colaspase)

Administer asparaginase (colaspase)

- via subcutaneous injection.

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

Day 22

Approximate treatment time: 30 minutes

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.

- weigh patient on each visit
- urinalysis each visit

Hydration if prescribed.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

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

Vincristine

Administer vincristine (vesicant)

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

Asparaginase (colaspase)

Administer asparaginase (colaspase)

- via subcutaneous injection.

Deaccess CVAD.

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

Day 25

Approximate treatment time: 30 minutes

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.

- weigh patient on each visit
- urinalysis each visit

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Asparaginase (colaspase)

Administer asparaginase (colaspase)

- via subcutaneous injection.

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

Discharge information

Cytarabine subcutaneous injections

- Cytarabine subcutaneous injections with written instruction on how to administer.

Mercaptopurine tablets

- Mercaptopurine tablets with written instructions on how to take.

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)	
Injection-site reactions	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Constipation	
Cytarabine (Ara-C) syndrome	Flu-like symptoms including fever, myalgia and malaise can occur 6 to 12 hours after cytarabine administration. Symptoms generally resolve within 24 hours of completing therapy.
Diarrhoea	Read more about treatment induced diarrhoea
Pancreatitis	Inflammation of the pancreas with impairment of function is associated with asparaginase formulations.
Fatigue	Read more about fatigue
Haemorrhagic cystitis	An inflammatory process, characterised by diffuse bladder mucosal inflammation resulting in haemorrhage. Patients are at risk following blood and marrow transplant (BMT) or treatment with cyclophosphamide, ifosfamide and/or radiation therapy. Read more about haemorrhagic cystitis
Hyperglycaemia	High blood sugar, an excess of glucose in the blood stream.
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)

Delayed (onset months to years)	
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

The Haematology Reference Committee decided to supersede this protocol at the 2022 meeting as superior alternatives are available.

The key evidence for this protocol comes from two consecutive studies, CALGB 8811 and CALGB 9111.[1, 2] CALGB 8811 studied the efficacy of a 5 drug combination regimen for the induction, of adult patients with de novo acute lymphoblastic leukaemia followed by intensive consolidation. CALGB 9111 studied the addition of G-CSF to the 8811 regimen.

In CALGB 8811, 197 patients aged 16 to 80 years, were enrolled. All received induction chemotherapy comprising of cyclophosphamide, daunorubicin, vincristine, prednisolone and L-asparaginase. 85% (167) achieved complete remission (CR), 7% (13) had persistent disease and 9% (17) died during induction. Patients who achieved CR received consolidation with a multi-agent regimen, CNS prophylaxis, late intensification and maintenance therapy for a total of 2 years. The study concluded that this intensive regimen confers a high remission rate with a high proportion of long-term remissions in adult patients with ALL. After the first 76 patient were treated it was noted that patients older than 60 years had very high rates of death during induction (6 of 10). Subsequently, patients greater than 60 received reduced doses of cyclophosphamide, daunorubicin and prednisone during induction with a resultant reduction in early death rate.[1]

In CALGB 9111, G-CSF was added to the 8811 protocol. 198 adult patients (aged 16 to 83) with de novo ALL were randomised to receive placebo or G-CSF 5 micrograms/kg/day subcutaneously from day +5 until the ANC was > 1 x 10^9/L for 2 consecutive days. The study concluded that although patients who received G-CSF had higher remission rates and lower mortality, its use did not impact on the disease free survival. All CALGB ALL protocols now include the use of G-CSF in the induction phase only.

Efficacy

In CALGB 8811, CR rates were age dependent - 94% in those patients less than 30 years old, 85% in those aged 30 to 59 and 39% for those patients equal to or greater than 60 years (p-<0.001). Patients who had a mediastinal mass (100%) or blasts of T-cell origin (97% vs 80% for those with B-cell lineage) demonstrated a higher CR rate than other patients. After a median follow-up of 43 months the median survival was 36 months. For those patients who achieved CR, median remission duration was 29 months.

In CALGB 9111, there were 41 patients over 60 years old. The CR rate was 87% for patients less than 60 years and 77% for patients 60 years and older.[2] There was no statistically significant differences in CR rates with the addition of G-CSF however the older patients who received G-CSF had more rapid platelet recovery (median 17 vs 26 days, p=0.04).

With a median follow up of 4.7 years after CALGB 9111, there was a median overall survival (OS) of 2.3 years and disease free survival (DFS) of 2.4 years in those patients who received G-CSF. In the placebo arm, median OS was 1.7 years and median DFS was 1.8 years, but these differences were not statistically significant.

Toxicity

In the CALGB 8811 study[1] myelosuppression and infection were the most frequent major toxicities. 9% (17) patients died during induction mostly from infection (gram-negative, Streptococcus pnemonia, Candida); 9 were over 60 years old. One patient died from tumour lysis syndrome-induced renal failure during induction.

During the consolidation or maintenance phases a further 11 patients died, including 3 who died of haemorrhagic events. The major toxicities for this study are summarised in the table below. It was found that the addition of G-CSF from day 5 of chemotherapy (CALGB 9111), did not significantly reduce the non-haematological toxicities and also, because of the incidence of infections, did not enable patients to complete the first 3 months of chemotherapy any more rapidly than those who received the placebo.[2]

Toxicity from Larson et al:[1]

	Induction	Intensification	Maintenance
Leukopenia (<2,000 μL)	98%	97%	75%
Thrombocytopenia (<50,000/μL)	94	84	32
Anemia (Hgb <8 g/dL)	65	84	26
Hemorrhage	5 (1)	4 (2)	0
Infection	54 (7)	49 (4)	25
Fever without infection	4	8	2
Nausea/vomiting	8	17	8
Stomatitis	7	9	7
Diarrhea	4	3	1
Hepatic	25	28	30
Pulmonary	8	5 (1)	4
Cardiac	5 (1)	1	6
Genitourinary	8 (1)	2	1
CNS	6	13	6
Peripheral nervous system	7	12	7
Skin	4	1	2
Allergy	0	1	1

The table lists the frequencies (%) of grade 3 and 4 toxicities during each phase of treatment using the CALGB Expanded Common Toxicity Criteria. The percentage of patients with lethal toxicity is shown in parentheses.

References

1 Larson, R. A., R. K. Dodge, C. P. Burns, et al. 1995. "A five-drug remission induction regimen with intensive consolidation for adults with acute lymphoblastic leukemia: cancer and leukemia group B study 8811." Blood 85(8):2025-2037.

2 Larson, R. A., R. K. Dodge, C. A. Linker, et al. 1998. "A randomized controlled trial of filgrastim during remission induction and consolidation chemotherapy for adults with acute lymphoblastic leukemia: CALGB study 9111." Blood 92(5):1556-1564.

History

Version 4

Date	Summary of changes
11/03/2022	Reviewed by Haematology Reference Committee. Protocol to be superseded as superior alternatives are available.
22/05/2023	Protocol superseded. Review in 4 years.

Version 3

Date	Summary of changes
04/05/2012	New protocol taken to Haematology Reference Committee meeting
11/02/2013	Approved and published on eviQ
30/07/2014	Protocol reviewed by email survey. Added link to ALLG and ANZCTR with statement 'Patients with ALL should be considered for inclusion into clinical trials'. Added asparaginase monitoring. Next review in 2 years.
20/05/2016	Protocol reviewed at the Haematology Reference Committee meeting. The Haematology Reference Committee decided to supersede this protocol at the May 2016 meeting due to its low priority in clinical practice. It remains available for viewing on eviQ however it will no longer be maintained with ongoing literature review or other revisions.
31/05/2017	Transferred to new eviQ website. Version number change to v.3. Other changes include: • diluent volume of vincristine changed from '50 to 100 mL' to '50 mL' as per Australian Injectable Handbook Sixth Edition. • added in patient information: 'Information for patients on allopurinol'. • L- asparaginase (colaspase) changed to asparaginase (colaspase) per TGA update, to align with names used

Date	Summary of changes
	internationally https://www.tga.gov.au/updating-medicine-ingredient-names-list-affected-ingredients#active
24/11/2017	Discussed at RCM, decision to reinstate protocol due to feedback that the protocol is still used in clinical practice.
29/08/2019	Clinical information for consideration of thiopurine methyltransferase (TPMT) testing prior to administration of mercaptopurine added.
23/10/2020	Protocol reviewed electronically by Haematology Reference Committee. Asparaginase flag added to protocol. Review in 2 years.
21/01/2022	Pulmonary toxicity added to side effects.
29/07/2022	Clinical information block updated: Thiopurine-S-methyltransferase (TPMT) enzyme deficiency.

First approved: 11 February 2013
Last reviewed: 22 May 2023
Review due: 30 June 2027

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/791
26 Jun 2023

Patient information - CALGB course II early intensification

Patient's name:

Your treatment

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

CALGB course II early intensification			
This treatment cycle is repeated twice.			
Day	**Treatment**	**How it is given**	**How long it takes**
1 to 14	**Mercaptopurine** (*mer-KAP-toe-PURE-een*)	Take orally ONCE a day on days 1 to 14 on an empty stomach, at least one hour before or two hours after food. Swallow whole with a glass of water, do not break, crush or chew. Avoid taking with dairy products as they may decrease its absorption. If you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.	
1	**Cyclophosphamide** (*SYE-kloe-FOS-fa-mide*)	By a drip into a vein	About 1 hour
	Cytarabine (*sye-TARE-a-been*)	By injection under the skin	About 5 minutes
	Methotrexate (*Meth-o-TREX-ate*)	By injection into your spine	About 4 hours
2 to 4 and 8 to 11	**Cytarabine**	By injection under the skin	About 5 minutes
15	**Vincristine** (*vin-KRIS-teen*)	By a drip into a vein	About 10 minutes
	Asparaginase (*as-PAR-a-jin-ase*)	By injection under the skin	About 5 minutes
18	**Asparaginase**	By injection under the skin	About 5 minutes
22	**Vincristine**	By a drip into a vein	About 10 minutes
	Asparaginase	By injection under the skin	About 5 minutes
25	**Asparaginase**	By injection under the skin	About 5 minutes

When to get help

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

IMMEDIATELY go to your nearest hospital	Emergency contact details

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

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

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

Other information about your treatment

Information for patients on allopurinol

Tell your doctor, nurse or pharmacist if you are taking allopurinol tablets (including Progout®, Zyloprim® and Allosig®). This treatment contains mercaptopurine, and allopurinol can increase the levels of this drug in the body. This can cause low white blood cells and increase your risk of infection. If you need to take both medicines, your doctor will reduce your dose of mercaptopurine and monitor your blood counts more regularly.

Changes to your dose or treatment delays

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

Blood tests and monitoring

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

Central venous access devices (CVADs)

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

Treatment with cyclophosphamide

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

Other medications given during this treatment

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

- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication.

Superseded treatments

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

Side effects

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

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

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

Immediate (onset hours to days)	
Injection-site reaction	• At the injection site you may get pain, redness, swelling or bruising. • These symptoms are usually not serious. • **Tell your doctor or nurse immediately if you notice any redness or pain during or after treatment.**
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.
Early (onset days to weeks)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Liver problems	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**

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

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.

Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass.
	• You may also get:
	  ◦ bloating, cramping or pain
	  ◦ a loss of appetite
	  ◦ nausea or vomiting.
	• Drink plenty of fluids (unless you are fluid restricted).
	• Eat plenty of fibre-containing foods such as fruit, vegetables and bran.
	• Take laxatives as directed by your doctor.
	• Try some gentle exercise daily.
	• **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**

Flu-like symptoms from cytarabine	• You may get a fever, skin rash, aches and pains or increased sweating. • These symptoms are caused by the drug cytarabine. • Symptoms usually happen 6 to 12 hours after your dose, and may last until 24 hours after your treatment has finished. • To reduce any pain or fever, take paracetamol, if needed. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if these symptoms do not get better after 24 hours.

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Inflamed pancreas (pancreatitis)	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get:** ◦ **abdominal (stomach) pain** ◦ **a swollen stomach** ◦ **nausea or vomiting** ◦ **fever or chills** ◦ **a fast heartbeat.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Bladder irritation (haemorrhagic cystitis)	• You may get: ◦ blood in your urine, sometimes with blood clots ◦ pain or burning when you urinate ◦ the urge to urinate more than normal ◦ stomach or pelvic pain or discomfort. • When you go home, make sure you drink plenty of fluids (unless you are fluid restricted). • Empty your bladder often. • **Tell your doctor or nurse as soon as possible if you notice any blood in your urine.**
High blood sugar level (hyperglycaemia)	• You may feel thirsty and need to urinate more often than normal. • You may get repeated infections, especially thrush. • 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. • **Tell your doctor or nurse if you get any of the signs or symptoms listed above.**
Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including: ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.

Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.

Delayed (onset months to years)	

Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.
	• You may get:
	  ◦ shortness of breath
	  ◦ fever
	  ◦ dry cough
	  ◦ wheezing
	  ◦ fast heartbeat
	  ◦ chest pain.
	• Your doctor will monitor how well your lungs are working during your treatment.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.

- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

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

Other medical and dental treatment

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

Diet and food safety

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

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

Risk of developing a second cancer

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

Quitting smoking

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

Staying active

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

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

Where to get more information

Telephone support

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

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – 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
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

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

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information - patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

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