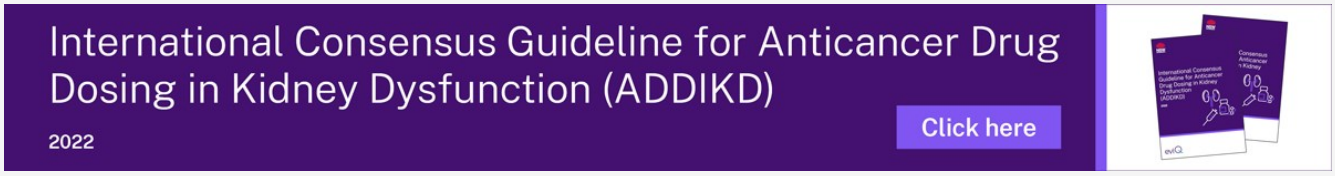
Acute lymphoblastic leukaemia BFM 2000 consolidation protocol 1B SUPERSEDED

ID: 1269 v.5 **Superseded** Essential Medicine List

This protocol has been superseded as native form L-asparaginase is no longer available in Australia.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

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

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



Related pages:

- Acute lymphoblastic leukaemia BFM 2000 overview SUPERSEDED

- Overall BFM 2000 treatment schema
- Overall BFM 2000 protocol flow diagram

Treatment schedule - Overview

Drug	Dose	Route	Day
mercaptOPURine *	60 mg/m^2 ONCE a day	PO	1 to 28
CYCLOPHOSPHamide **	1,000 mg/m^2	IV infusion	1 and 29
Mesna	400 mg/m^2 at 0, 4 and 8 hours after the start of each cyclophosphamide dose***	IV infusion	1 and 29
Cytarabine (Ara-C) ****	75 mg/m^2	Subcut	3 to 6, 10 to 13, 17 to 20, 24 to 27
Methotrexate	12 mg	Intrathecal	10 and 24

*If a cytarabine block is delayed, then mercaptopurine is suspended. Omitted mercaptopurine doses should be made up until the total of 28 doses (total 1680 mg/m^2) is reached.

**For second cyclophosphamide dose WCC should be >1.0 x 10^9/L, neutrophils ≥0.3 x 10^9/L and platelets ≥50 x 10^9/L

*** 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.

****Start 2nd, 3rd and 4th cytarabine blocks if WCC ≥0.5 x 10^9/L and platelets ≥30 x 10^9/L

Criteria for starting Protocol IB:

- if initial CNS involvement, the CNS must show complete remission
- if initial mediastinal tumour, reduction to <30% initial mass
- good general condition with no serious infections
- creatinine/creatinine clearance within normal limits

If in bone marrow CR at day 33, the following haematological criteria apply prior to the commencement of further therapy:

- WCC $\geq$2.0 x 10^9/L
- neutrophils $\geq$0.5 x 10^9/L
- platelets $\geq$50 x 10^9/L

If not in CR at day 33, proceed with therapy without waiting for haematological recovery.

Duration: 29 days

Cycles: 1
Ideally day 1 of this protocol is day 36 as calculated from the start of Induction Protocol IA.

Notes:

- This treatment should only be carried out in a major centre as intense monitoring and support is required.
- Consider thiopurine methyltransferase (TPMT) testing prior to administration of mercaptopurine.
- Units are encouraged to enrol eligible patients (age 15 to 40) on the currently active ALLG ALL6 protocol, which is very close to BFM2000 and currently the ANZCHOG paediatric protocol.

Drug status: All 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.*

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 **
Mesna	400 mg/m^2 (IV infusion)	in 100 mL sodium chloride 0.9% over 15 to 30 minutes at 0, 4 and 8 hours after the start of each 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.
Day 2		
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 3 to 6		
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 3 to 6		
Cytarabine (Ara-C)	75 mg/m^2 (Subcut)	via subcutaneous injection***
Day 7 to 9		
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 10		
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***
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy
Day 11 to 13		
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 14 to 16		
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 17 to 20		
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 21 to 23		
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 24		
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***
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy
Day 25 to 27		
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 28		
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 29		
CYCLOPHOSPHamide	1,000 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes **
Mesna	400 mg/m^2 (IV infusion)	in 100 mL sodium chloride 0.9% over 15 to 30 minutes at 0, 4 and 8 hours after the start of each cyclophosphamide dose (first dose may be loaded in

Day 29		
		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.

* If a cytarabine block is delayed, then mercaptopurine is suspended. Omitted mercaptopurine doses should be made up until the total of 28 doses (total 1680 mg/m^2) is reached. Consider thiopurine methyltransferase (TPMT) testing prior to administration of mercaptopurine.

** For second cyclophosphamide dose WCC should be >1.0 x 10^9/L, neutrophils ≥0.3 x 10^9/L and platelets ≥50 x 10^9/L

*** Start 2nd, 3rd and 4th cytarabine blocks if WCC ≥0.5 x 10^9/L and platelets ≥30 x 10^9/L

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If in bone marrow CR at day 33, the following haematological criteria apply prior to the commencement of further therapy:

- WCC ≥2.0 x 10^9/L
- neutrophils ≥0.5 x 10^9/L
- platelets ≥50 x 10^9/L

If not in CR at day 33, proceed with therapy without waiting for haematological recovery.

Duration: 29 days

Cycles: 1
Ideally day 1 of this protocol is day 36 as calculated from the start of Induction Protocol IA.

Indications and patient population

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

Clinical information

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

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.
Haemorrhagic cystitis associated with high dose chemotherapy	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. Read more about haemorrhagic cystitis
Mesna dosing and administration	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. Read more about haemorrhagic cystitis
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. posaconazole 300 mg PO twice daily for one day then 300 mg PO daily. 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, LDH and BSL at baseline, prior to each cycle and regularly throughout treatment as clinically indicated.
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*

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		
	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

Mesna
No specific or clinically significant drug interactions

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

Administration

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

product information monographs via the TGA website for further information.

Day 1

Safe handling and waste management

Safe administration

General patient assessment prior to each 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.

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

- baseline weight
- baseline urinalysis
- strict fluid balance input and output

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 1 to 28**
- 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.

- 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.

Deaccess CVAD.

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

Days 3 to 6

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

Mercaptopurine

- administer orally ONCE a day on **days 1 to 28**
- 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
- 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)

Day 10

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 1 to 28**
- 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
- 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

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

Days 11 to 13 and 17 to 20

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 28**
- 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
- 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)

Day 24

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 28**
- 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
- 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)

Days 25 to 27

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 28**
- 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
- 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)

Day 29

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.

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

- baseline weight
- baseline urinalysis
- strict fluid balance input and output

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Prehydration

Administer 1000 mL sodium chloride 0.9% over 2 hours.

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

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.

Deaccess CVAD.

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

Discharge information

Mercaptopurine tablets

- Mercaptopurine tablets with written instructions on how to take.

Cytarabine subcutaneous injections

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

Antiemetics

- Antiemetics as prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) e.g. PJP prophylaxis, antifungals, antivirals.

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

Immediate (onset hours to days)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Injection-site reactions	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
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)	
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
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
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
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Arthralgia and myalgia	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 arthralgia and myalgia
Fatigue	Read more about fatigue
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.
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 - partial	Hair thinning and/or patchy hair loss. 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)
Hyperpigmentation	Darkening of an area of skin caused by the overproduction of melanin.

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

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

In most published studies, adolescent patients with ALL achieve better results when treated with paediatric rather than adult

protocols.[1, 2, 3] It is unclear as to the relative contributions of the composition of paediatric protocols, disease differences between children and older patients, the hospital settings in which they are delivered or the effects of selection bias.

A collaborative French study[4] retrospectively analysed patients aged between 15 and 20 who had been treated with either an adult ALL protocol (LALA94) or a paediatric protocol (FRALLE-93) showing a 5 year event free survival (EFS) advantage in favour of FRALLE-93 (67% versus 41% 5 year EFS, P<0.001) as well as an advantage for the paediatric protocol in overall survival (78% versus 45% at 5 years, P<0.001). Pui et al 2011 reported an event free survival at 5 years of 86.4% for adolescent patients aged 15 to 18 treated with a paediatric protocol (total therapy study XV, st Jude).

Moricke et al 2008[5] reported the results of 2169 paediatric and adolescent patients up to age 18 treated for ALL with the ALL-BFM95 protocol. Overall event free survival was estimated to be 79.6% at 6 years. Patients were stratified and treated according to risk (standard, medium and high risk). The 6 year EFS in the MR patients was 79.7% and 49.2% in the HR patients, and 58.3% for all patients aged 15 and older. Minimal residual disease criteria were not used for risk stratification in the ALL-BFM95 regimen. The published results of the ALL-BFM95 study did not demonstrate a benefit from the two randomisations (cytarabine in the intensification phase and pulse during maintenance).[6]

One retrospective Finnish study[7] did not show any improvement in the survival for patients aged 10 to 25 treated on a paediatric rather than an adult protocol, with a 5 year event free survival of 67% for the paediatric and 60% for the adult.

The ALL-BFM95 regimen was used as the standard arm of ALL-BFM 2000 with the incorporation of the minimal residual disease testing in patients with precursor B ALL. With this ALL- BFM 2000 regimen, the 5 year event free survival in this pre-B ALL subpopulation were 92.3%, 77.6% and 50.1% for the standard (42% of patients), intermediate (52% of patients) and high risk patients (6% of patients).[8]

The ALL- BFM 2000 standard arm has been used as the treatment regimen in this protocol, since it is common to both ALL-BFM95 and ALL- BFM 2000 regimens. If minimal residual disease (MRD) testing is available, then the incorporation of these results appears justified on the published data, at least for the pre-B ALL group.[8]

The selection of asparaginase preparations is reviewed in the Asparaginase document. Leunase® (colaspase, E. coli preparation) is the most commonly used preparation and the default option as presented in these protocols. Pegasparaginase is given as an alternative preparation and has the advantage of longer half life, lower immunogenicity and more efficient asparaginase depletion than standard preparatations.[9, 10] All patients on the ongoing MRC UKALL 14 protocol receive pegylated asparaginase. The doses employed in the current treatment protocol are in line with those employed in the ongoing ANZCHOG, ALLG ALL6 and MRC UKALL 14 studies.

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

Toxicity

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

References

1 Seibel, N. L. 2008. "Treatment of acute lymphoblastic leukemia in children and adolescents: peaks and pitfalls." Hematology Am Soc Hematol Educ Program:374-380.

2 Wood, W. A. and S. J. Lee. 2011. "Malignant hematologic diseases in adolescents and young adults." Blood 117(22):5803-5815.

3 Taizo AN &Hunger SP. Blood consult: therapeutic strategy and complications in the adolescent and young adult with acute lymphoblastic leukemia. Blood 2012; DOI 10.1182/blood-2011-10-36712

4 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.

5 Ching-Hon P et al. "Improved Prognosis for Older Adolescents With Acute Lymphoblastic Leukemia." J Clin Oncol 2010;

29:386-391.

6 Moricke, A., A. Reiter, M. Zimmermann, et al. 2008. "Risk-adjusted therapy of acute lymphoblastic leukemia can decrease treatment burden and improve survival: treatment results of 2169 unselected pediatric and adolescent patients enrolled in the trial ALL-BFM 95." Blood 111(9):4477-4489.

7 Usvasalo, A., R. Raty, S. Knuutila, et al. 2008. "Acute lymphoblastic leukemia in adolescents and young adults in Finland." Haematologica 93(8):1161-1168.

8 Conter, V., C. R. Bartram, M. G. Valsecchi, et al. 2010. "Molecular response to treatment redefines all prognostic factors in children and adolescents with B-cell precursor acute lymphoblastic leukemia: results in 3184 patients of the AIEOP-BFM ALL 2000 study." Blood 115(16):3206-3214.

9 Stock, W., D. Douer, D. J. DeAngelo, et al. 2011. "Prevention and management of asparaginase/pegasparaginase-associated toxicities in adults and older adolescents: recommendations of an expert panel." Leuk Lymphoma 52(12):2237-2253.

10 Wetzler M et al. "Effective asparagine depletion with pegylated asparaginase results in improved outcomes in adult acute lymphoblastic leukemia: Cancer and Leukemia Group B Study 9511." Blood 2007;109:4164-4167

History

Version 5

Date	Summary of changes
30/03/2021	Protocol reviewed electronically by Haematology Reference Committee in September 2020 with consensus to supersede once the ALL06 protocol is published given L-asparaginase is no longer available. Version number increased to 5. 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.

Version 4

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

Version 3

Date	Summary of changes
04/05/2012	New protocol taken to Haematology Committee meeting
18/12/2012	Approved and published on eviQ
27/06/2014	Protocol reviewed by email survey. Added link to ALLG and ANZCTR with statement 'Patients with ALL should be considered for inclusion into clinical trials'. Next review in 2 years.
20/05/2016	Protocol reviewed at Haematology Reference Committee meeting. Added - Consider thiopurine methyltransferase (TPMT) testing prior to administration of mercaptopurine. No other changes, review in 2 years.
26/05/2017	Administration of mesna aligned with clinical trial.
31/05/2017	Transferred to new eviQ website. Version number change to V.3.
12/04/2019	Reviewed at the September 2018 Haematology Reference Committee meeting with no significant changes, review in 2 years.
29/08/2019	Clinical information for consideration of thiopurine methyltransferase (TPMT) testing prior to administration of mercaptopurine added.

First approved: 18 December 2012
Last reviewed: 23 September 2020
Review due: 31 December 2022
Superseded: 30 March 2021

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/1269
26 Jun 2023

Patient information - BFM 2000 consolidation protocol 1B

Patient's name:

Your treatment

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

BFM 2000 consolidation protocol 1B			
This treatment cycle is given once only.			
Day	**Treatment**	**How it is given**	**How long it takes**
1 to 28	**Mercaptopurine** (*mer-KAP-toe-PURE-een*)	Take orally ONCE a day on days 1 to 28 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 and 29	**Cyclophosphamide** (*SYE-kloe-FOS-fa-mide*)	By a drip into a vein	About 1 hour
	Mesna (*MES-na*)	By a drip into a vein	About 15 minutes
3 to 6, 10 to 13, 17 to 20 and 24 to 27	**Cytarabine** (*sye-TARE-a-been*)	By injection under the skin	About 5 minutes
10 and 24	**Methotrexate** (*meth-o-TREX-ate*)	By injection into your spine	About 4 hours

When to get help

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

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

- pain, tingling or discomfort in your chest or arms
- you become unwell.

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

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.
- **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.

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)	

Allergic reaction	• Allergic reactions are uncommon but can be life threatening.
	• **If you feel unwell during the infusion or shortly after it, or:**
	  ◦ **get a fever, shivers or shakes**
	  ◦ **feel dizzy, faint, confused or anxious**
	  ◦ **start wheezing or have difficulty breathing**
	  ◦ **have a rash, itch or redness of the face**
	
	While you are in hospital: Tell your doctor or nurse immediately.
	After you leave: Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.

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.**
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)	

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.**

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.**
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.**
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.

Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.
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.**
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.**
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 thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)
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.
Skin colour changes	• You may have darkening of your skin, especially in areas that are exposed to the sun. • You may also notice darkening of your tongue, gums and over your finger joints. • These skin changes may fade over time. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.

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

Additional notes:

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https://www.eviq.org.au/pi/1269
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