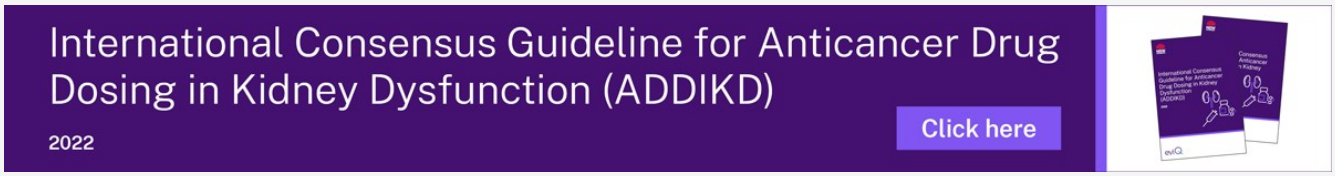
Acute lymphoblastic leukaemia Ph+ hyper CVAD part A and imatinib

ID: 1291 v.7 **Endorsed** Essential Medicine List

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 Ph+ hyper CVAD and imatinib part A and B/maintenance overview
- Acute lymphoblastic leukaemia Ph+ hyper CVAD part B and imatinib
- Acute lymphoblastic leukaemia Ph+ maintenance therapy (imatinib prednisolone vinCRISTine)

Treatment schedule - Overview

Cycle 1

Drug	Dose	Route	Day
Imatinib	600 mg ONCE a day	PO	1 to 14
Dexamethasone	40 mg ONCE a day	IV/PO	1 to 4 and 11 to 14
Mesna	600 mg/m^2	IV infusion	1 to 3
CYCLOPHOSPHamide	300 mg/m^2 TWICE a day	IV infusion	1 to 3
Methotrexate *	12 mg	Intrathecal	2
DOXOrubicin	50 mg/m^2	IV	4
vinCRISTine	2 mg	IV infusion	4 and 11
Filgrastim	10 micrograms/kg	Subcut	5 and continue daily until neutrophil recovery
Cytarabine (Ara-C) *	100 mg	Intrathecal	8

Cycle 3

Drug	Dose	Route	Day
Imatinib	600 mg ONCE a day	PO	1 to 21
Dexamethasone	40 mg ONCE a day	IV/PO	1 to 4 and 11 to 14
Mesna	600 mg/m^2	IV infusion	1 to 3
CYCLOPHOSPHamide	300 mg/m^2 TWICE a day	IV infusion	1 to 3

Drug	Dose	Route	Day
Methotrexate *	12 mg	Intrathecal	2
DOXOrubicin	50 mg/m^2	IV	4
vinCRISTine	2 mg	IV infusion	4 and 11
Filgrastim	10 micrograms/kg	Subcut	5 and continue daily until neutrophil recovery
Cytarabine (Ara-C) *	100 mg	Intrathecal	8

Cycle 5 and 7

Drug	Dose	Route	Day
Imatinib	600 mg ONCE a day	PO	1 to 21
Dexamethasone	40 mg ONCE a day	IV/PO	1 to 4 and 11 to 14
Mesna	600 mg/m^2	IV infusion	1 to 3
CYCLOPHOSPHamide	300 mg/m^2 TWICE a day	IV infusion	1 to 3
DOXOrubicin	50 mg/m^2	IV	4
vinCRISTine	2 mg	IV infusion	4 and 11
Filgrastim	10 micrograms/kg	Subcut	5 and continue daily until neutrophil recovery

* The total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol (i.e. intrathecal therapy on cycles 1 and 3). The IT dose of methotrexate when given via an Ommaya reservoir is 6 mg.[1] Link to intrathecal CNS prophylaxis schedule .

Frequency: 21 days

Cycles: 4 cycles of Part A (Cycles 1, 3, 5, 7) alternating with 4 cycles of Part B (Cycles 2, 4, 6, 8) for a total of 8 cycles, followed by maintenance therapy for 2 years. Commence next cycle after 21 days OR earlier if WCC >3 x10^9 and platelets >60 x10^9.

Notes:
Hyperhydration can be given in place of mesna as per local guidelines.[2, 3] Please see the haemorrhagic cystitis document for more information.

Rituximab: in patients with CD 20+ disease, strong consideration should be given to including rituximab 375 mg/m^2 on days 1 and 11 of cycles 1 to 4 of Hyper CVAD chemotherapy.[4]

Drug status: **Imatinib** and **Filgrastim** are PBS authority

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

Imatinib is available as **100 mg** and **400 mg** tablets

Cost: ~ $3150 (cycle 1); $4400 (cycles 3, 5, 7)

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

Day 1		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Mesna	600 mg/m^2 (IV infusion)	by continuous IV infusion for 24 hours, starting 1 hour before the first dose of cyclophosphamide and ending 12 hours after completion of last dose of cyclophosphamide.
CYCLOPHOSPHamide	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours)

Day 2		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Mesna	600 mg/m^2 (IV infusion)	by continuous IV infusion for 24 hours, starting 1 hour before the first dose of cyclophosphamide and ending 12 hours after completion of last dose of cyclophosphamide.
CYCLOPHOSPHamide	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours)
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy. Total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol - see CNS prophylaxis schedule below* (dose is 6 mg if given via an Ommaya reservoir)

Day 3		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Mesna	600 mg/m^2 (IV infusion)	by continuous IV infusion for 24 hours, starting 1 hour before the first dose of cyclophosphamide and ending 12 hours after completion of last dose of cyclophosphamide.
CYCLOPHOSPHamide	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours)

Day 4		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
DOXOrubicin	50 mg/m^2 (IV)	over 5 to 15 minutes
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag

Day 5		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Filgrastim	10 micrograms/kg (Subcut)	inject subcutaneously once daily starting day 5 and

Day 5		
		continue until neutrophil recovery.
Day 6 and 7		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Day 8		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Cytarabine (Ara-C)	100 mg (Intrathecal)	adhere to local institution intrathecal policy. Total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol - see CNS prophylaxis schedule below*
Day 9 and 10		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Day 11		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Day 12 to 14		
Imatinib	600 mg (PO)	ONCE a day on days 1 to 14 with food
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.

Cycle 3

Day 1		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Mesna	600 mg/m^2 (IV infusion)	by continuous IV infusion for 24 hours, starting 1 hour before the first dose of cyclophosphamide and ending 12 hours after completion of last dose of cyclophosphamide.
CYCLOPHOSPHamide	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours)
Day 2		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Mesna	600 mg/m^2 (IV infusion)	by continuous IV infusion for 24 hours, starting 1 hour before the first dose of cyclophosphamide and ending 12 hours after completion of last dose of cyclophosphamide.
CYCLOPHOSPHamide	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a

Day 2		
		day (every 12 hours)
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy. Total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol - see CNS prophylaxis schedule below* (dose is 6 mg if given via an Ommaya reservoir)
Day 3		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Mesna	600 mg/m^2 (IV infusion)	by continuous IV infusion for 24 hours, starting 1 hour before the first dose of cyclophosphamide and ending 12 hours after completion of last dose of cyclophosphamide.
CYCLOPHOSPHamide	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours)
Day 4		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
DOXOrubicin	50 mg/m^2 (IV)	over 5 to 15 minutes
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Day 5		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Filgrastim	10 micrograms/kg (Subcut)	inject subcutaneously once daily starting day 5 and continue until neutrophil recovery.
Day 6 and 7		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Day 8		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Cytarabine (Ara-C)	100 mg (Intrathecal)	adhere to local institution intrathecal policy. Total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol - see CNS prophylaxis schedule below*
Day 9 and 10		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8

Day 11		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag

Day 12 to 14		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.

Day 15 to 21		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8

Cycle 5 and 7

Day 1 to 3		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Mesna	600 mg/m^2 (IV infusion)	by continuous IV infusion for 24 hours, starting 1 hour before the first dose of cyclophosphamide and ending 12 hours after completion of last dose of cyclophosphamide.
CYCLOPHOSPHamide	300 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours)

Day 4		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
DOXOrubicin	50 mg/m^2 (IV)	over 5 to 15 minutes
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag

Day 5		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Filgrastim	10 micrograms/kg (Subcut)	inject subcutaneously once daily starting day 5 and continue until neutrophil recovery.

Day 6 to 10		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8

Day 11		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2

Day 11		
		to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
vinCRISTine	2 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
Day 12 to 14		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food or by IV infusion on days 1 to 4 and days 11 to 14.
Day 15 to 21		
Imatinib	600 mg (PO)	ONCE a day with food, continuously throughout cycles 2 to 8

Notes:

- * The total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol (i.e. intrathecal therapy on cycles 1 and 3). The IT dose of methotrexate when given via an Ommaya reservoir is 6 mg.[1] Link to intrathecal CNS prophylaxis schedule .
- Hyperhydration can be given in place of mesna as per local guidelines.[2, 3, 3, 2, 3] Please see the haemorrhagic cystitis document for more information.

Frequency: 21 days

Cycles: 4 cycles of Part A (Cycles 1, 3, 5, 7) alternating with 4 cycles of Part B (Cycles 2, 4, 6, 8) for a total of 8 cycles, followed by maintenance therapy for 2 years. Commence next cycle after 21 days OR earlier if WCC >3 x10^9 and platelets >60 x10^9.

Indications and patient population

- Philadelphia chromosome positive (Ph^+) acute lymphoblastic leukaemia
  - This protocol is intended for patients 25 years of age and older; an alternate protocol should be considered for patients younger than than 25 years

Clinical information

Safety alert vincristine administration	For safe administration of vincristine refer to the safety alert issued by the Australian Commission on Safety and Quality in Health Care
Venous access	Central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
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

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
Cumulative lifetime dose of anthracyclines	Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone). Criteria for reducing the total anthracycline cumulative lifetime dose include: • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation. Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion. Read more about cardiac toxicity associated with anthracyclines
Cardiac toxicity	Imatinib has been associated with cardiac complications (i.e. left ventricular ejection fraction (LVEF) dysfunction and heart failure). For patients with pre existing cardiac disease, measure LVEF at baseline and as clinically indicated. Monitor patient for signs and symptoms of congestive heart failure. In patients with hypereosinophilic syndrome and cardiac involvement, cardiogenic shock and left ventricular dysfunction have been associated with initiation of imatinib. The condition was reported to be reversible with the administration of systemic steroids, circulatory support measures, and temporary withholding of imatinib. Read more about cardiac toxicity associated with anti-cancer drugs
Gastrointestinal toxicity	Diarrhoea is a common side effect of tyrosine kinase inhibitors (TKI) (e.g imatinib and dasatinib). If severe diarrhoea occurs, discontinue TKI until condition improves or resolves. Constipation has also been commonly reported with these regimens possibly related to the use of vinca alkaloids. Patients should be monitored closely, and prophylactic or symptom control anti-diarrhoeal/laxatives prescribed accordingly.
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
Hypothyroidism	Hypothyroidism has been reported in thyroidectomy patients undergoing thyroxine replacement during treatment with imatinib. Monitor for signs and symptoms of hypothyroidism in thyroidectomy patients.
Fluid retention/oedema	Patients may experience an increased incidence of fluid retention and periorbital oedema. Monitor for signs and symptoms of fluid retention and if severe fluid retention occurs treatment should be withheld until resolved. Periorbital oedema is a common side effect of imatinib which is usually mild to moderate and managed conservatively.

Efficacy of therapy	Measure efficacy of therapy using a standardised RT-PCR assay for BCR-ABL transcripts. Assess after the first cycle, at 2 to 4 month intervals while on hyper CVAD, and at 4 to 6 month intervals thereafter. Alternate therapies should be considered for patients who do not achieve a major molecular remission (defined as BCR-ABL less than 0.1% in the marrow) by 3 months and for those who lose their initial response on serial monitoring.
Corticosteroids	Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate. Read more about acute short term effects from corticosteroids
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
Tumour lysis risk	Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended. Read more about the prevention and management of tumour lysis syndrome.
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. **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.
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC, LFTs, LDH, calcium, magnesium and phosphate at baseline and prior to each cycle. TSH and BSL at baseline 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 .

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).

Note:

- All dose reductions are calculated as a percentage of the starting dose
- All imatinib dose modifications are taken directly from the imatinib product information and should be considered at the discretion of the treating Haematologist

Haematological toxicity
Prolonged haematological toxicity in the absence of bone marrow involvement may require a dose reduction at the discretion of the Haematologist

Renal impairment	
Creatinine clearance (mL/min)	
10 to 50	No dose reduction
less than 10	Reduce cyclophosphamide dose by 25%

Mesna dosing schedule should be repeated each day high-dose cyclophosphamide (50 mg/kg or 2 g/m^2) is received. If the cyclophosphamide dose is adjusted (decreased or increased), the intravenous mesna dose should also be modified to maintain the mesna-to-cyclophosphamide ratio (1.0 - 1.5 x the daily dose of cyclophosphamide).[3]

Imatinib and its metabolites are not significantly excreted via the kidney, therefore a decrease in free drug clearance is not expected in renal insufficiency. The product information does however recommend that patients with mild, moderate or severe renal dysfunction start with a reduced daily dose of 400 mg.

Hepatic impairment	
Hepatic dysfunction	
Mild	Reduce doxorubicin and vincristine by 25%; reduce imatinib to 400 mg daily
Moderate	Reduce doxorubicin and vincristine by 50%; reduce imatinib to 400 mg daily

Hepatic impairment	
Severe	Omit doxorubicin and vincristine; reduce imatinib starting dose to 300 mg daily. If severe hepatotoxicity develops, attributable to imatinib, withhold imatinib until resolution, then it may be resumed at a reduced daily dose. It is recommended that the daily dose is reduced from 600 mg to 400 mg or from 400 mg to 300 mg

Elevations in liver function tests occur with both standard and high dose cytarabine. Significant liver function abnormalities may require discontinuation or a dose reduction.

Peripheral neuropathy	
Grade 2	Reduce vincristine by 50%
Grade 3 or Grade 4	Omit vincristine

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

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

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

Imatinib		
	Interaction	**Clinical management**
Gemfibrozil	Increased toxicity OR reduced efficacy of imatinib possible due to inhibition of CYP2C8-mediated metabolism of imatinib OR reduced imatinib absorption and impaired CYP2C8-mediated conversion of imatinib to its active metabolite by gemfibrozil	Avoid combination Caution advised if other CYP2C8 inhibitors are to be used (e.g. trimethoprim, glitazones, montelukast etc.)
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of imatinib possible due to reduced clearance	Monitor for imatinib toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of imatinib possible due to increased clearance	Avoid combination or monitor for decreased clinical response to imatinib
Drugs metabolised by CYP3A4 (e.g. atorvastatin, benzodiazepines, calcineurin inhibitors, clarithromycin, dihydroergotamine, simvastatin, etc.)	Increased effect/toxicity of these drugs possible due to inhibition of CYP3A4 by imatinib resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity of interacting drugs
Levothyroxine (thyroxine, Oroxine®, Eutroxsig®)	Reduced efficacy of thyroid replacement therapy resulting in hypothyroid symptoms; possibly due to induction of levothyroxine metabolism by imatinib and subsequent TSH elevation	Monitor closely for signs and symptoms of hypothyroidism, serum thyroxine and TSH levels; increase levothyroxine dose if needed
Paracetamol	Risk of liver toxicity due to inhibition of metabolism of paracetamol by imatinib	Avoid combination or monitor liver function closely

Mesna
No specific or clinically significant drug interactions

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 Cycle 1

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

product information monographs via the TGA website for further information.

Day 1

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s).

Access CVAD.

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Hydration

Administer appropriate intravenous hydration to reduce the incidence of tumour lysis syndrome e.g. sodium chloride at 50 - 100 mL/hour.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Mesna

- administer via IV infusion over 24 hours
- starting 1 hour before the first dose of cyclophosphamide and continue until 12 hours after the last dose of cyclophosphamide.

Note: hyperhydration alone can be given in place of mesna with hyperhydration as per local guidelines.[2, 3] Please see the haemorrhagic cystitis document for more information.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 3 hours
- 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.

Administer the second dose of cyclophosphamide 12 hours after the first dose.

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

Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Hydration

Administer appropriate intravenous hydration to reduce the incidence of tumour lysis syndrome e.g. sodium chloride at 50 - 100 mL/hour.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
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  - stir until tablet dissolves
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  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Mesna

- administer via IV infusion over 24 hours
- starting 1 hour before the first dose of cyclophosphamide and continue until 12 hours after the last dose of cyclophosphamide.

Note: hyperhydration alone can be given in place of mesna with hyperhydration as per local guidelines.[2, 3] Please see the haemorrhagic cystitis document for more information.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 3 hours
- 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.

Administer the second dose of cyclophosphamide 12 hours after the first dose.

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)

Day 3

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Hydration

Administer appropriate intravenous hydration to reduce the incidence of tumour lysis syndrome e.g. sodium chloride at 50 - 100 mL/hour.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Mesna

- administer via IV infusion over 24 hours
- starting 1 hour before the first dose of cyclophosphamide and continue until 12 hours after the last dose of cyclophosphamide.

Note: hyperhydration alone can be given in place of mesna with hyperhydration as per local guidelines.[2, 3] Please see the haemorrhagic cystitis document for more information.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 3 hours
- 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.

Administer the second dose of cyclophosphamide 12 hours after the first dose.

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

Day 4

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Hydration if prescribed

- continue daily weigh

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Doxorubicin

Administer doxorubicin (vesicant):

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

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

Vincristine

Administer vincristine (vesicant)

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

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

Day 5

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Filgrastim

- administer filgrastim by subcutaneous injection on day 5 once daily and continue until neutrophil recovery

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

Days 6 and 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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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 8

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Chemotherapy - Time out

Intrathecal cytarabine

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

Cytarabine intrathecal

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

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

Post intrathecal care:

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

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

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

Days 9 and 10

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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 11

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.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Vincristine

Administer vincristine (vesicant)

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

Deaccess CVAD.

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

Days 12 to 14

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
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  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

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

Discharge information

Imatinib tablets

- With written instructions on how to take them .
- Advise patients to weigh themselves regularly and to report any increase by more than 1 to 2 kg in a week.

Dexamethasone tablets

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

Antiemetics

- Antiemetics as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

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

Patient information

- Ensure patient receives patient information sheet.

Administration Cycle 3

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Day 1

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s).

Access CVAD.

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
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Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Mesna

- administer via IV infusion over 24 hours
- starting 1 hour before the first dose of cyclophosphamide and continue until 12 hours after the last dose of cyclophosphamide.

Note: hyperhydration alone can be given in place of mesna with hyperhydration as per local guidelines.[2, 3] Please see the haemorrhagic cystitis document for more information.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 3 hours
- 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.

Administer the second dose of cyclophosphamide 12 hours after the first dose.

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

Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
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Note: if a dose is forgotten or vomited, contact treating team.

Chemotherapy - Time out

Mesna

- administer via IV infusion over 24 hours
- starting 1 hour before the first dose of cyclophosphamide and continue until 12 hours after the last dose of cyclophosphamide.

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Administer the second dose of cyclophosphamide 12 hours after the first dose.

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)

Day 3

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Mesna

- administer via IV infusion over 24 hours
- starting 1 hour before the first dose of cyclophosphamide and continue until 12 hours after the last dose of cyclophosphamide.

Note: hyperhydration alone can be given in place of mesna with hyperhydration as per local guidelines.[2, 3] Please see the haemorrhagic cystitis document for more information.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 3 hours
- 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.

Administer the second dose of cyclophosphamide 12 hours after the first dose.

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

Day 4

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.

- continue daily weigh

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Hydration if prescribed

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Doxorubicin

Administer doxorubicin (vesicant):

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

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

Vincristine

Administer vincristine (vesicant)

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

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

Day 5

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Filgrastim

- administer filgrastim by subcutaneous injection on day 5 once daily and continue until neutrophil recovery

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

Days 6 and 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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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 8

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Chemotherapy - Time out

Intrathecal cytarabine

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

Cytarabine intrathecal

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

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

Post intrathecal care:

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

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

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

Days 9 and 10

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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 11

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.

- weigh patient before each treatment

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Vincristine

Administer vincristine (vesicant)

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

Deaccess CVAD.

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

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

Days 15 to 21

Safe handling and waste management

Safe administration

This is an oral treatment

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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)

Discharge information

Imatinib tablets

- With written instructions on how to take them .

- Advise patients to weigh themselves regularly and to report any increase by more than 1 to 2 kg in a week.

Dexamethasone tablets

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

Antiemetics

- Antiemetics as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

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

Patient information

- Ensure patient receives patient information sheet.

Administration Cycles 5 and 7

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.

Days 1 to 3

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s).

Access CVAD.

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

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation

- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Mesna

- administer via IV infusion over 24 hours
- starting 1 hour before the first dose of cyclophosphamide and continue until 12 hours after the last dose of cyclophosphamide.

Note: hyperhydration alone can be given in place of mesna with hyperhydration as per local guidelines.[2, 3] Please see the haemorrhagic cystitis document for more information.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 3 hours
- 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.

Administer the second dose of cyclophosphamide 12 hours after the first dose.

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

Day 4

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew

- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Doxorubicin

Administer doxorubicin (vesicant):

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

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

Vincristine

Administer vincristine (vesicant)

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

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

Day 5

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to

- place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
- stir until tablet dissolves
- to drink straight away
- to rinse glass and drink this too

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

Filgrastim

- administer filgrastim by subcutaneous injection on day 5 once daily and continue until neutrophil recovery

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

Days 6 to 10

This is an oral treatment

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.

Safe handling and waste management

Safe administration

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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 11

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.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
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  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

Chemotherapy - Time out

Vincristine

Administer vincristine (vesicant)

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

Deaccess CVAD.

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

Days 12 to 14

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1 to 4** and **11 to 14** of each cycle **OR**

- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

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

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

Days 15 to 21

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.

Treatment - Time out

Imatinib

- administer orally ONCE a day on **days 1 to 14** in **cycle 1 only** and **days 1 to 21** in **cycles 3, 5, 7**
- to be swallowed whole; do not break, crush or chew
- to be taken with a large glass of water and food to minimise GI irritation
- if difficulty is experienced swallowing the tablet advise patient to
  - place tablets in a glass of water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)
  - stir until tablet dissolves
  - to drink straight away
  - to rinse glass and drink this too

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)

Discharge information

Imatinib tablets

- With written instructions on how to take them .
- Advise patients to weigh themselves regularly and to report any increase by more than 1 to 2 kg in a week.

Dexamethasone tablets

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

Antiemetics

- Antiemetics as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Prophylaxis medications

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

Growth factor support

- Arrangements for administration if prescribed.

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

Immediate (onset hours to days)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.
Cardiotoxicity	Anthracyclines (e.g. daunorubicin, doxorubicin, epirubicin, idarubicin etc.) may cause acute cardiotoxicities such as arrhythmias, pericarditis-myocarditis syndrome and cardiac failure.
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Flare reaction	Anthracycline flare reaction is caused by a localised allergic reaction. It is characterised by erythematous vein streaking, urticaria and pruritus which may occur during drug administration and is often associated with too rapid an infusion. Extravasation must be ruled out if flare occurs.
Flu-like symptoms	
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
Headache	Mild headache is common with this treatment.
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
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
Cardiotoxicity	Cardiotoxicity may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, hypertension, cardiac ischaemia and congestive heart failure (CHF). The risk of cardiotoxicity is increased by a number of factors, particularly a history of heart disease and electrolyte imbalances. Read more about cardiotoxicity associated with anti-cancer drugs
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
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
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.
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
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

Late (onset weeks to months)	
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about nail toxicities
Periorbital oedema	Accumulation of fluid in the tissue surrounding the eye sockets (orbits).

Delayed (onset months to years)	
Cardiotoxicity	Anthracyclines can cause damage to the heart, this is commonly dose related.
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

Evidence and Efficacy

Philadelphia positive acute lymphoblastic leukaemia has historically responded poorly to induction chemotherapy regimens with lower CR rates than Philadelphia negative ALL and a median overall survival of 8 months.[5] The addition of imatinib to standard protocols has demonstrated efficacy in comparison to historical controls however dosing strategies vary. This review will summarise the data from recent trials and provide a recommendation for the optimal dosing strategy of imatinib in combination with hyper CVAD in patients deemed able to tolerate intensive induction chemotherapy.

More than 800 patients have been enrolled in multiple trials examining the use of imatinib in ALL. Studies by Yanada et al,[6] de Labarathe et al,[7] Thomas et al,[8] Bassan et al,[9] Wassman et al,[10] Chalandon et al[11] and Lim et al[12] have all demonstrated CR rates of 90 to 95%. These protocols used a variety of imatinib dosing schedules allied to various chemotherapy regimens during the induction, consolidation and maintenance phases.

Yanada et al reported on 80 patients receiving a JALSG protocol using imatinib 600 mg from day 8 to day 63 in combination with chemotherapy as induction, with consolidation consisting of alternating imatinib and chemotherapy followed by vincristine, prednisone and imatinib 600 mg for up to 2 years.[6] The final analysis of the JALSG study included 99 patients with a CR of 97% and a 5-year overall and disease-free survival of 50 and 43% respectively.[13] Wassman et al examined imatinib in doses from 400 to 600 mg using a variation of the GMALL protocol.[10] The French GRAAPH-2005 study[11] achieved a CR rate of 98% in the arm randomized to imatinib/prednisone/doxorubicin compared to 91% in those receiving imatinib with a hyper-CVAD part A cycle. Induction deaths were lower with less intensive therapy but 5 year OS and DFS rates were similar, indicating that tyrosine kinase inhibition may allow a reduction in the intensity of chemotherapy.

Thomas et al at MD Anderson demonstrated a 75% OS at 2 years using imatinib at a dose of 400 mg on days 1 to 14 of each cycle of Hyper CVAD followed by 600 mg for 13 months.[8] Only 20 patients were enrolled in the trial. A final report was published in 2015 describing an expanded cohort of 54 patients untreated or minimally treated, (age 17-84, median 51 years) who received the protocol with the final modified version of imatinib 600 mg days 1 to 14 of induction cycle 1, then 600 mg continuously with courses 2 to 8, followed by escalation to imatinib 800 mg as tolerated during 24 months of maintenance therapy with monthly vincristine and prednisone interrupted by 2 intensifications with hyper CVAD and imatinib, then imatinib indefinitely.[14] Allogeneic stem cell transplant was performed in CR1 where feasible at the treating clinician's discretion. 5 year disease free survival rates were 63% vs 43% with or without SCT, respectively. Minimal residual disease monitoring was with quantitative RT-PCR on bone marrow samples. These were obtained after the first cycle, at 2-4 month intervals while on hyper CVAD, and at 4-6 month intervals thereafter. Patients who had not achieved a major molecular response (MMR; defined as BCR-ABL < 0.1% in the marrow) had an inferior 5-year disease free survival compared to those who achieved at least this depth of response (60% vs. 25%).

Imatinib dose intensity was investigated by Lim et al[12] who used continuous imatinib at a dose of 600 mg commencing day 8 of induction then followed through five courses of consolidation or allogeneic haematopoietic cell transplant (age 16-71, median 41 years). Although, the hyper CVAD chemotherapy backbone was not included. Patients who were not transplanted were maintained

on imatinib for two years. Among the 82 patients in CR, the 5 year cumulative incidence of relapse and OS rates were 59% and 52% respectively. The group analysed patients based on initial imatinib dose intensity (IDI), calculated by dividing the total administered dose of imatinib over the first eight weeks of induction by the intended dose of imatinib for the eight weeks. An IDI >90% compared to <90% was associated with a median 5 year RFS and OS of 70 months versus 14 months and 39 months versus 17 months respectively. This suggests maintaining imatinib dose intensity >90% during the early phase of treatment was an important factor in longer remission free period and improved survival.

Notable differences to the current eviQ Philadelphia negative ALL hyper CVAD protocol include omission of methotrexate in the POMP maintenance schedule and intensification with hyper CVAD and imatinib at months 6 and 13 in 2004 schedule (details not published) (or 6 and 13 in the R-hyper CVAD protocol[4]).

Toxicity

Toxicity with Hyper CVAD and imatinib were similar to toxicities experienced with Hyper CVAD only. The following table is from the initial report on 20 patients.[8]

Table 3. Toxicities of hyper-CVAD and imatinib mesylate in 91 postinduction courses

Parameter	No. (%)* Grades 1-2	Grades 3-4
Infections (overall)†	—	23 (25)
FUO	—	7 (8)
Pneumonia	—	6 (7)
Bacterial	—	3 (3)
Atypical	—	2 (2)
Fungal/presumed fungal	—	1 (1)
Sepsis	—	9 (10)
GNR bacteremia	—	5 (5)
Catheter-related bacteremia	—	4 (4)
Other	—	8 (9)
Sinusitis	—	3 (3)
Osteomyelitis	—	2 (2)
Herpes zoster	—	2 (2)
Upper respiratory infections (RSV)	—	1 (1)
Cardiovascular		
Fluid retention	5 (25)	1 (5)
Arrythmia (supraventricular)	2 (10)	2 (10)
Deep venous thrombosis	—	2 (10)
Syncope	—	2 (10)
Reduction in ejection fraction	2 (10)	—
Hepatic		
Increase in bilirubin	5 (25)	—
Increase in transaminases	5 (25)	—
Neuromuscular		
Fatigue	6 (30)	2 (10)
Peripheral neuropathy	6 (30)	1 (5)
Headaches (postlumbar puncture)	2 (10)	2 (10)
Bone pain	3 (15)	—
Myalgias	2 (10)	—
Fracture (femur/vertebral)	—	2 (10)
Gastrointestinal		
Stomatitis	5 (25)	—
Constipation	4 (20)	1 (5)
Diarrhea	2 (10)	2 (10)
Nausea	2 (10)	1 (5)
Reflux	1 (5)	2 (10)
Ileus	—	1 (5)
Coagulopathy		
Hypofibrinogenemia	2 (10)	1 (5)
Hemorrhage		
Gastrointestinal	—	1 (5)
Skin		
Rash	2 (10)	—
Renal		
Increase in creatinine	5 (25)	—
Hyponatremia	—	1 (5)

GNR indicates gram-negative rod; —, not applicable.
*Incidence of infections episodes/courses; all other toxicities according to occurrence by patient since usually intermittent in nature (no. at risk = 20).
†Refer to Table 2 for infections specific for induction (course 1).

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Notable toxicities reported in the final report on the extended cohort include the following.[4]

Description	Prevalence (%)
Infections in induction	52
Infections in consolidation	70
Hyperglycaemia	43

Description	Prevalence (%)
Hypophosphataemia	59
DVT	7

References

1 Kantarjian, H., D. Thomas, S. O'Brien, et al. 2004. "Long-term follow-up results of hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (Hyper-CVAD), a dose-intensive regimen, in adult acute lymphocytic leukemia." Cancer. 101(12):2788-2801.

2 Hensley ML, Hagerty KL, Kewalramani T et al. 2009 " American Society of Clinical Oncology 2008 clinical practice guideline update: use of chemotherapy and radiation therapy protectants". J Clin Oncol. Jan 1;27(1):127-45.

3 Apperley J, Carreras E, Gluckman E, et al. 2012. "The EBMT-ESH Handbook: Haematopoietic Stem Cell Transplantation". Sixth Edition.

4 Thomas, D. A., S. O'Brien, S. Faderl, et al. 2010. "Chemoimmunotherapy with a modified hyper-CVAD and rituximab regimen improves outcome in de novo Philadelphia chromosome-negative precursor B-lineage acute lymphoblastic leukemia." J Clin Oncol 28(24):3880-3889.

5 Secker-Walker, L. M., J. M. Craig, J. M. Hawkins, et al. 1991. "Philadelphia positive acute lymphoblastic leukemia in adults: age distribution, BCR breakpoint and prognostic significance." Leukemia 5(3):196-199.

6 Yanada, M., J. Takeuchi, I. Sugiura, et al. 2006. "High complete remission rate and promising outcome by combination of imatinib and chemotherapy for newly diagnosed BCR-ABL-positive acute lymphoblastic leukemia: a phase II study by the Japan Adult Leukemia Study Group." J Clin Oncol 24(3):460-466.

7 de Labarthe, A., P. Rousselot, F. Huguet-Rigal, et al. 2007. "Imatinib combined with induction or consolidation chemotherapy in patients with de novo Philadelphia chromosome-positive acute lymphoblastic leukemia: results of the GRAAPH-2003 study." Blood 109(4):1408-1413.

8 Thomas, D. A., S. Faderl, J. Cortes, et al. 2004. "Treatment of Philadelphia chromosome-positive acute lymphocytic leukemia with hyper-CVAD and imatinib mesylate." Blood 103(12):4396-4407.

9 Bassan, R., G. Rossi, E. M. Pogliani, et al. 2010. "Chemotherapy-phased imatinib pulses improve long-term outcome of adult patients with Philadelphia chromosome-positive acute lymphoblastic leukemia: Northern Italy Leukemia Group protocol 09/00." J Clin Oncol 28(22):3644-3652.

10 Wassmann, B., H. Pfeifer, N. Goekbuget, et al. 2006. "Alternating versus concurrent schedules of imatinib and chemotherapy as front-line therapy for Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL)." Blood 108(5):1469-1477.

11 Chalandon, Y., X. Thomas, S. Hayette, et al. 2015. “Randomized study of reduced-intensity chemotherapy combined with imatinib in adults with Ph-positive acute lymphoblastic leukemia.” Blood 125(24):3711-3719

12 Lim, S. N., Y. D. Joo, K. H. Lee, et al. 2015. "Long-term follow-up of imatinib plus combination chemotherapy in patients with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia." Am J Hematol 90(11):1013-1020.

13 Hatta, Y., S. Mizuta, K. Matsuo, et al. 2018. "Final analysis of the JALSG Ph+ALL202 study: tyrosine kinase inhibitor-combined chemotherapy for Ph+ALL." Ann Hematol 97(9):1535-1545.

14 Daver, N., D. Thomas, F. Ravandi, et al. 2015. “Final report of a phase II study of imatinib mesylate with hyper-CVAD for the front-line treatment of adult patients with Philadelphia chromosome-positive acute lymphoblastic leukemia” Haematologica 100(5):653-661.

History

Version 7

Date	Summary of changes
22/09/2020	Biosimilar drug added to clinical information. Version number changed to V.7
23/10/2020	Protocol reviewed electronically by Haematology Reference Committee, no changes. Review in 2 years.
06/08/2021	Note added to treatment schedule for addition of rituximab in CD20+ disease.
20/01/2022	Interactions updated.
21/01/2022	Blood tests updated in clinical information. Pulmonary toxicity added to side effects.

Version 6

Date	Summary of changes
16/04/2020	'Mesna dosing and administration' block added to clinical information. Version number changed to v.6

Version 5

Date	Summary of changes
04/05/2012	New protocol taken to Haematology Reference Committee meeting.
23/01/2013	Approved and published on eviQ.
31/07/2014	Protocol reviewed by email survey. Added link to ALLG and ANZCTR with statement 'Patients with ALL should be considered for inclusion into clinical trials'. Changed pegfilgrastim to filgrastim. Next review in 2 years.
20/05/2016	Reviewed at the Haematology Reference Committee meeting: - added note about the methotrexate IT dose if an ommaya reservoir is used - phosphate levels included in the blood test clinical information block - efficacy of therapy clinical information block added - evidence updated
22/05/2017	Oral mesna removed from treatment schedules, drug status section, notes section, administration and patient information as per the Kantarjian et al. and Thomas et al. trials.
31/05/2017	Transferred to new eviQ website. Version number change to V.4. Other changes include: • diluent volume of vincristine changed from '50 to 100 mL' to '50 mL' as per Australian Injectable Handbook Sixth Edition.
14/05/2018	Protocol information updated to include the option of hyper-hydration with high dose cyclophosphamide.
21/09/2018	Protocol reviewed by the Haematology Reference Committee with the following changes: • treatment schedule filgrastim dose aligned with Thomas et al. 2004 study • dose modifications updated • wording adjusted for CYP 3A4 inhibitor and imatinib interaction • evidence reviewed and updated • constipation clinical information block replaced with gastrointestinal toxicity block • version change to V.5.
03/05/2019	Hydration regimen in administration section modified to align with study references.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.

First approved: 23 January 2013
Last reviewed: 23 October 2020
Review due: 31 December 2022

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/1291
28 Jun 2023

Patient information - Acute lymphoblastic leukaemia (ALL) - hyper CVAD part A and imatinib

Patient's name:

Your treatment

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

Hyper CVAD part A and imatinib

This treatment cycle alternates with Hyper CVAD part B and imatinib, and usually continues for a total of 8 cycles of chemotherapy. When you receive your next treatment cycle depends on how long it takes for your blood counts recover.

Day	Treatment	How it is given	How long it takes
	Imatinib (*im-AT-in-ib*)	Take orally ONCE a day with food and a large glass of water on day 1 to 14 in **cycle 1,** then ONCE daily continuously in **cycle 2 to 8**. Tablet(s) should be swallowed whole. If you are unable to swallow the tablets whole they may be dissolved in water and the solution swallowed (see directions in *Other information about your treatment*).	
1 to 4 and 11 to 14	**Dexamethasone** (*dex-a-METH-a-sone*)	By a drip into a vein **OR** take orally ONCE a day in the morning with food on days 1 to 4 and days 11 to 14 only.	About 15 minutes if given by a drip
1	**Cyclophosphamide** (*SYE-kloe-FOS-fa-mide*)	By a drip into a vein	About 3 hours TWICE a day
	Mesna (*MES-na*)	By a drip into a vein	For 24 hours
2	**Cyclophosphamide**	By a drip into a vein	About 3 hours TWICE a day
	Mesna	By a drip into a vein	For 24 hours
	Methotrexate (m*eth-o-TREX-ate*)	By injection into your spine (this may not be every cycle - check with your doctor)	About 4 hours
3	**Cyclophosphamide**	By a drip into a vein	About 3 hours TWICE a day
	Mesna	By a drip into a vein	For 24 hours
4	**Doxorubicin** (*dox-oh-roo-bi-sin*)	By a drip into a vein	About 15 minutes
	Vincristine (*vin-KRIS-teen*)	By a drip into a vein	About 10 minutes
5	**Granulocyte Colony Stimulating Factor** (*G-CSF*)	By injection under the skin	About 5 minutes
8	**Cytarabine** (*sye-TARE-a-been*)	By injection into your spine (this may not be every cycle - check with your doctor)	About 4 hours
11	**Vincristine**	By a drip into a vein	About 10 minutes

Missed doses:

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

When to get help

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

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

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

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

Other information about your treatment

Changes to your dose or treatment delays

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

Blood tests and monitoring

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

Central venous access devices (CVADs)

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

Treatment with cyclophosphamide

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

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Laxatives:** you may be given some medication to prevent or treat constipation. Your doctor or nurse will tell you how and when to take the laxatives.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you will be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover.
- **Mesna**: you will be given a drug called mesna with this treatment. Mesna helps to protect your bladder from the chemotherapy. It can be given by mouth as a tablet or by injection through your drip. Your doctor or nurse will tell you how and when to take the mesna tablets.

Instructions for dissolving imatinib tablets:

- Imatinib tablets should not be crushed, cut or chewed. For patients with swallowing difficulties imatinib tablets can be dissolved.
- You (or whoever is dissolving the tablets) should wear disposable gloves and try to minimise touching the tablets.
- Place the imatinib tablet(s) in a glass of water or apple juice (using approximately 50 mL for 100 mg tablet and approximately 200mL for 400mg tablet).
- Stir until tablet dissolves.
- Drink straight away.
- Rinse glass and drink this too.

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.

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

Immediate (onset hours to days)	
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**

Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<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.**
Bone pain after G-CSF injection	• You may have discomfort or a dull ache in your pelvis, back, arms or legs. • To reduce the pain, take paracetamol before each injection. • **Tell your doctor or nurse as soon as possible if your pain is not controlled.**
Heart problems	Heart problems are uncommon. You have a higher risk if you have had high blood pressure, chemotherapy or radiation therapy to your chest. You may be asked to have a test to see how your heart is working before and during treatment. If you develop shortness of breath, an irregular heart beat or chest pain go to your nearest hospital emergency department.
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.**
Redness and itching along vein	• You may get redness and itching along the vein where your chemotherapy is being infused. • This will usually go away within 30 minutes of stopping the injection. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above. Your nurse will check to make sure the drug has not leaked out of the vein.**
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • Tell your doctor or nurse if you get any of the symptoms listed above. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.**
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.**
Headache	• Talk to your doctor or nurse about what you can take if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Urine turning orange or red	• Your urine will turn an orange or red colour. • This is not harmful and should only last for up to 48 hours after treatment.

Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

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

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

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**

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.**

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.**

Side effects from steroid medication	• Steroid medication may cause:
	  ◦ mood swings and behaviour changes
	  ◦ an increased appetite
	  ◦ weight gain
	  ◦ swelling in your hands and feet
	  ◦ stomach upsets
	  ◦ trouble sleeping
	  ◦ fragile skin and bruising
	  ◦ an increase in your blood sugar level
	  ◦ weak and brittle bones (osteoporosis)
	• Take your steroid medication with food to reduce stomach upset
	• If you have diabetes, your blood sugar levels may be tested more often.
	• 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.**

Late (onset weeks to months)	
Hair loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**

Nail changes	• Your nails may:
	  ◦ grow more slowly
	  ◦ become darker
	  ◦ develop ridges or white lines
	  ◦ become brittle and flaky
	• In some cases, you may lose your nails completely.
	• Keep your nails clean and short.
	• Avoid things like biting your fingernails, getting a manicure, pedicure or false nails.
	• Wear gloves when you wash the dishes, work in the garden, or clean the house.

Swelling around the eyes	• You may get:
	  ◦ swelling or heaviness around your eyes
	  ◦ irritated eyes
	  ◦ eye discharge
	  ◦ changes to your vision.
	• **Tell your doctor or nurse if you get any of these symptoms.**

Delayed (onset months to years)	
Heart problems	Heart problems can occur months to years after treatment. You have a higher risk if you have had high blood pressure, chemotherapy or radiation therapy to your chest. You may be asked to have a test to see how your heart is working before and during treatment. If you develop shortness of breath, an irregular heart beat or chest pain go to your nearest hospital emergency department.
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.
- Some pain medications, e.g. paracetamol, can interact with your treatment. Check with your doctor or pharmacist before taking any medications for a headache or mild pain.
- 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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