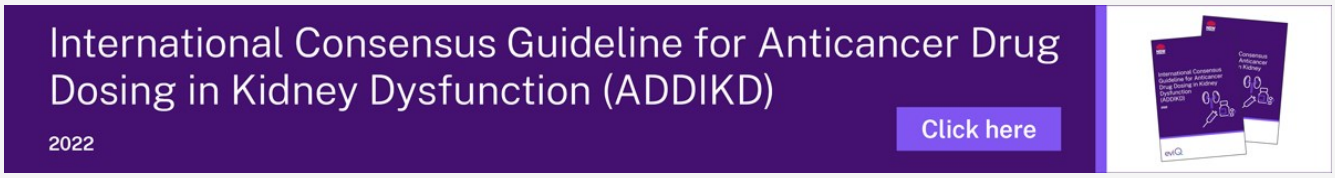
Acute promyelocytic leukaemia APML4 maintenance

ID: 1938 v.3 **Endorsed**

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 promyelocytic leukaemia APML4 overview

Treatment schedule - Overview

Cycle 1 to 8

Drug	Dose	Route	Day
Tretinoin (ATRA)	45 mg/m^2 divided in TWO equal doses *	PO	1 to 14
Methotrexate	5 mg/m^2 ONCE a week, titrate to neutrophil count **	PO	15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85
mercaptOPURine	50 mg/m^2 ONCE a day titrate to neutrophil count **	PO	15 to 90

* ATRA doses should be rounded to the nearest 10mg.

** Methotrexate (5 - 15 mg/m^2 weekly) and mercaptopurine (50 - 90 mg/m^2/daily) are adjusted to target a neutrophil count of 1 - 2 x 10^9/L

Frequency: 90 days

Cycles: 8. Maintenance therapy may begin 3 to 4 weeks after completion of consolidation 2 therapy. It is continuous for 2 years and consists of eight 3-monthly cycles. Tretinoin is administered alone for the first 2 weeks of each cycle.

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

It is the consensus of the reference committee that alternative consolidation therapies may be appropriate for use in high-risk patients. See evidence section for alternative consolidation treatment options.

Drug status: **Tretinoin** is TGA registered but not PBS listed for this indication

Mercaptopurine and **methotrexate** are on the PBS general schedule

Mercaptopurine is available as **50 mg** tablets
Methotrexate is available as **2.5 mg** and **10 mg** tablets
Tretinoin is available as **10 mg** capsules

Cost: ~ $1,280 per cycle

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 to 8

Day 1 to 14		
Tretinoin (ATRA)	45 mg/m^2 (PO)	in TWO equally divided doses daily (round to the nearest 10 mg).

Day 15		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 16 to 21		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 22		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 23 to 28		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 29		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 30 to 35		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 36		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 37 to 42		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 43		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 44 to 49		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 50		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 51 to 56		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 57		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 58 to 63		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 64		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 65 to 70		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 71		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 72 to 77		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 78		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 79 to 84		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 85		
Methotrexate	5 mg/m^2 (PO)	ONCE a week on days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85. Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count .*
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Day 86 to 90		
mercaptOPURine	50 mg/m^2 (PO)	ONCE a day Take on an empty stomach at least one hour before or two hours after food. Up titrate according to neutrophil count. *

Notes:

* Methotrexate (5-15 mg/m^2 weekly) and mercaptopurine (50-90 mg/m^2/daily) are adjusted to target a neutrophil count of 1-2 x 10^9/L

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

Frequency: 90 days

Cycles: 8. Maintenance therapy may begin 3 to 4 weeks after completion of consolidation 2 therapy. It is continuous for 2 years and consists of eight 3-monthly cycles. Tretinoin is administered alone for the first 2 weeks of each cycle.

Indications and patient population

- Acute promyelocytic leukaemia (APML)

Note:

It is the consensus of the reference committee that alternative consolidation therapies without maintenance may be appropriate for use in high-risk patients. See evidence section.

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Teratogenic effects	This treatment can cause severe congenital disabilities or death to an unborn baby. All patients of reproductive potential must use at least one reliable contraceptive method for at least 4 weeks before starting treatment, during treatment (including dose interruptions), and for 4 weeks after stopping treatment. In female patients of reproductive potential (if sexually active), a pregnancy test should be carried out prior to initiating treatment (after 4 weeks of contraception use), weekly during the first month of treatment and monthly thereafter. Effective contraception methods and adequate contraception timeframes should be discussed with all patients of reproductive potential.
Thiopurine-S-methyltransferase (TPMT) enzyme deficiency	Patients with an inherited deficiency of the TPMT enzyme are at an increased risk of, and prone to developing, rapid bone marrow depression which may lead to severe, life-threatening myelosuppression when undergoing treatment with thiopurines (azathioprine, mercaptopurine, tioguanine). This may be exacerbated by coadministration with drugs that inhibit TPMT, such as olsalazine, mesalazine or sulfasalazine. Consider assessing thiopurine-S-methyltransferase (TPMT) activity prior to administration of thiopurines.

Hyperleukocytosis	Treatment related hyperleukocytosis (WBC greater or equal to 100 x 10^9/L) develops in approximately 50% of arsenic trioxide treated patients. Peak WBC count occurs at about 20 days post first arsenic trioxide dose and usually resolves at a median of 10.5 days after the peak, despite continuation of arsenic trioxide. It may be managed with careful observation, checking particularly for emerging APML differentiation syndrome. Hydroxycarbamide (hydroxyurea) has been used to treat marked hyperleukocytosis associated with arsenic trioxide, but its benefit is unclear.
Pseudotumour cerebri	Headaches are common on ATRA therapy, although the possibility of intracranial haemorrhage, particularly during induction always needs to be considered. Pseudotumour cerebri is more common in young patients less than 20, and may be associated with severe headache, nausea and vomiting. It may necessitate temporary discontinuation of ATRA and recommencement at a lower dose.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Depending on dose and duration of steroid therapy, PJP prophylaxis may be appropriate (at clinician's discretion). Read about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antifungal and antiviral prophylaxis	Antifungal and antiviral prophylaxis should be determined according to individual institutional policy. Note that azole antifungals may contribute to QTc prolongation. Read more about antiviral and antifungal prophylaxis
Blood tests	FBC, EUC, eGFR, LFTs, APTT, PT and fibrinogen level at baseline, then 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 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. 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 .

No dose reductions are recommended.

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*

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

Methotrexate		
	Interaction	**Clinical management**
Ciprofloxacin **NSAIDS** **Probenecid** **Proton pump inhibitors (e.g. esomeprazole, omeprazole, pantoprazole)**	Increased toxicity of methotrexate possible due to reduced clearance	Avoid combination or monitor for methotrexate toxicity Important note: with high-dose methotrexate therapy, many of these drug combinations are *contraindicated*
Sulphonamides and penicillins (e.g. sulfamethoxazole (in Bactrim®, Septrin®), piperacillin (in Tazocin®) etc.)	Increased toxicity of methotrexate possible due to displacement from serum protein binding	Avoid combination or monitor for methotrexate toxicity
Trimethoprim	Increased toxicity of methotrexate possible due to additive antifolate activity	Avoid combination or monitor for methotrexate toxicity
Mercaptopurine	Increased toxicity of mercaptopurine possible due to reduced clearance	Avoid combination or monitor for mercaptopurine toxicity
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Hepatotoxic drugs (e.g. azathioprine, leflunomide, retinoids, sulfasalazine)	Additive hepatotoxicity	Avoid combination or monitor liver function closely
Folic acid (e.g. as in multivitamins) **Asparaginase (administered immediately prior or concurrently)**	Reduced efficacy of methotrexate possible due antagonism of its action	Avoid combination or monitor for decreased clinical response to methotrexate Note: asparaginase administered shortly after methotrexate can enhance its efficacy and reduce its toxicity

Tretinoin (ATRA)		
	Interaction	**Clinical management**
Cytochrome p450 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of tretinoin possible due to decreased clearance	Avoid combination or monitor for tretinoin toxicity
Cytochrome p450 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of tretinoin possible due to increased clearance	Avoid combination or monitor for decreased clinical response to tretinoin
Antifibrinolytic agents (e.g. tranexamic acid and aprotinin)	Cases of fatal thrombotic complications have been reported rarely in patients concomitantly treated with tretinoin and antifibrinolytic agents.	Avoid combination or closely monitor
Tetracyclines	Elevation of intracranial pressure/pseudotumour cerebri may be caused by tetracyclines and retinoids. Patients treated with tretinoin and tetracyclines in combination might be at a greater risk of experiencing this condition.	Avoid combination or monitor for elevation of intracranial pressure/pseudotumour cerebri
Vitamin A	Combination with vitamin A may cause or exacerbate the symptoms of hypervitaminosis A.	Combination is contraindicated

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

Administration

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

product information monographs via the TGA website for further information.

Days 1 to 14 (tretinoin)

This is an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each treatment.

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Tretinoin (ATRA)

- administer orally in TWO equal divided doses on **days 1 to 14**
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken with or without food
- protect skin from sunlight

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

Notify medical team if the patient reports weight gain, shortness of breath and/or temperature as this may be symptoms of differentiation syndrome.

Read more about APML differentiation syndrome

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78 and 85 (methotrexate)

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Methotrexate

- administer orally ONCE a week on **days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78** and **85**
- swallow tablets whole

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 90 (mercaptopurine)

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Mercaptopurine

- administer orally ONCE a day on **days 15 to 90**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken preferably on an empty stomach, one hour before or at least two hours after food
- avoid concomitant consumption of milk or dairy products

Note: missed doses should not be replaced; if a tablet 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

Tretinoin capsules

- Tretinoin capsules with written instructions on how to take them

Methotrexate tablets

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

Mercaptopurine tablets

- Mercaptopurine tablets with written instructions on how to take.

Antiemetics

- Antiemetics as 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)	
Headache	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

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
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Hyperglycaemia	High blood sugar, an excess of glucose in the blood stream.
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.
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.
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

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

Evidence

Acute promyelocytic leukaemia (APML) is a biologically and clinically distinct variant of acute myeloid leukaemia characterised by t(15;17) translocation resulting in a PML-RARA fusion protein. The impaired myeloid differentiation resulting from the translocation may be restored by pharmacologic doses of all-trans-retinoic acid (ATRA).

Arsenic trioxide (ATO) acts synergistically with ATRA to degrade PML-RARA. APML4 was a phase 2 study that aimed to exploit ATO/ATRA synergy in order to minimise exposure to anthracyclines. Idarubicin is given on days 2, 4, 6, and 8 of induction along with

prednisolone and ATO/ATRA, followed by two “chemotherapy-free” ATO/ATRA-only consolidation cycles and 2 years of oral maintenance (ATRA, weekly methotrexate, and 6-mercaptopurine).

Notable inclusion criteria included age > 1 year (but no upper limit; age range was 19-73), ECOG performance status 0-3, normal left ventricular ejection fraction, and Q-Tc interval < 500 milliseconds. Idarubicin dosing was age-adjusted. Molecular monitoring of bone marrow was mandated for assessment of treatment efficacy.[1]

Chemotherapy-free consolidation without maintenance has been found to be beneficial in standard-risk patients, it has been utilised to a limited extent in the National Cancer Research Institute (NCRI) AML17 trial[2] and by the MD Anderson group[3] for high-risk adult patients following induction with ATO/ATRA, combined with gemtuzumab ozogamicin (GO). However, GO is currently not TGA-approved for use in APML. The Children’s Oncology Group (COG) AAML1331 study[4] is a nonrandomised, noninferiority trial that looked at survival outcomes in 154 paediatric patients with APML. The patients, aged between 1 and 21 years, received ATRA and arsenic throughout induction and intermittently throughout 4 cycles of consolidation. The high-risk patients (56/154) received 4 doses of idarubicin (similar to APML4). The duration of treatment was approximately 9 months without any maintenance. Shah et al.[5] reported a retrospective analysis of 10 high-risk APML patients, median age 44.5 years, with 7 patients receiving induction as per APML4 with idarubicin and all patients receiving consolidation with ATO/ATRA without maintenance, as per the APL0406 study[1]. The TUD-APOLLO-64 study (NCT02688140) is currently underway, a randomised phase 3 study of high-risk APML patients, comparing standard ATRA and anthracycline-based chemotherapy regimens with ATO/ATRA in combination with low-doses of idarubicin during induction, followed by 4 cycles of ATO/ATRA consolidation therapy. However, there are no results of this study published to date. Despite the absence of published trials for high-risk adults with APML, which involve standard of care induction combined with chemotherapy-free consolidation without maintenance, it is the consensus of the reference committee that based on the above studies, high-risk patients may receive chemotherapy-free consolidation as per ID 1943 Acute promyelocytic leukaemia standard risk (chemotherapy free) consolidation.

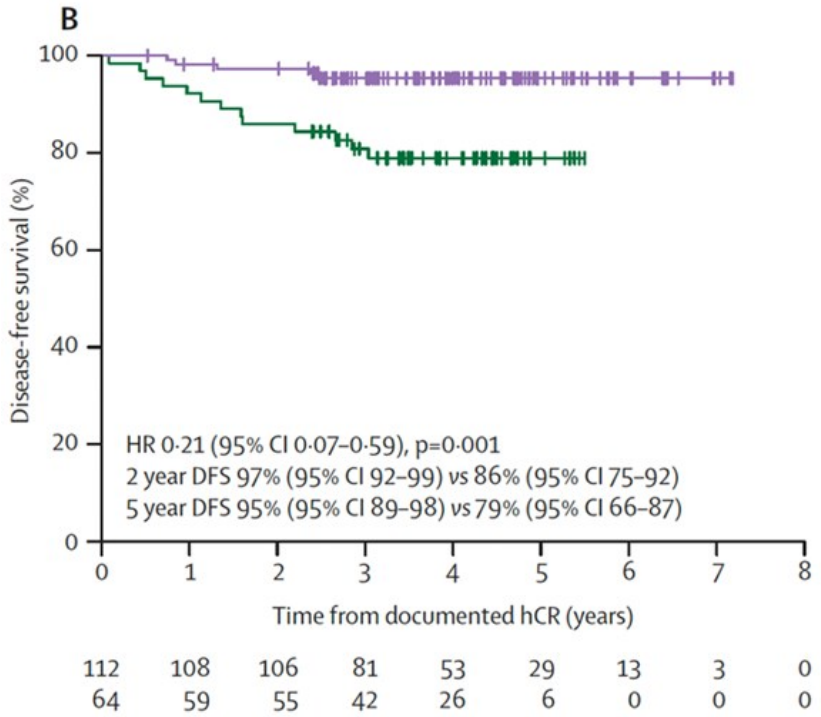
Efficacy

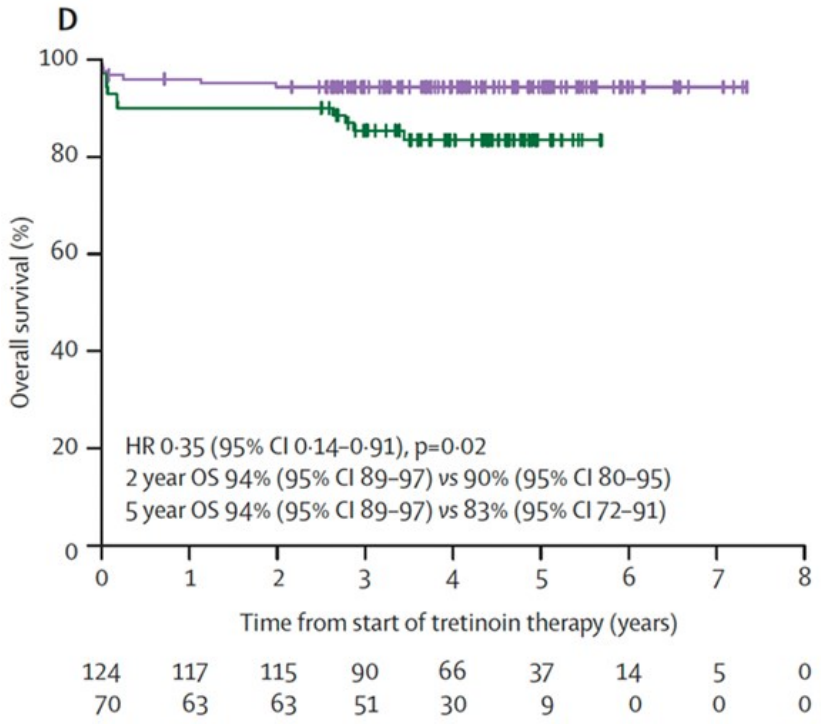
There were 124 evaluable patients with 4 deaths (1 myocardial ischaemia, 2 intracerebral haemorrhage, and 1 cerebral oedema), and 2 withdrawals from the study during induction. The remaining 118/124 (95%) entered haematological complete remission (hCR). 112/118 hCR patients proceeded to consolidation, each of whom attained molecular remission.[1]

In the final analysis, there had been a total of 5 relapses and there was one off-study death. The 5-year outcome data showed 95% freedom from relapse (FFR) and disease-free survival (DFS), 90% event-free survival (EFS), and 94% overall survival (OS).[6] The FFR, DFS, EFS, and OS results were all statistically significantly superior to the ALLG's prior APML3 study which used ATRA and idarubicin (but no arsenic) in induction and consolidation.

In the Children’s Oncology Group (COG) AAML1331 study the median follow-up duration was 24.7 months for patients with standard-risk APML and 22.8 months for patients with high-risk APML. The 2-year EFS and OS for standard-risk patients was 98% and 99% respectively, and for high-risk patients 2-year EFS was 96.4% and OS 100%.[4]

Figure 1. Kaplan-Meier DFS and OS curves from the APML4 (purple) and APML3 (green) treatment protocols[6]





Toxicity

Most patients received at least 80% of the maximum specified dosing of idarubicin, ATRA, and ATO. During induction, 14% experienced Q-Tc prolongation greater than 500 ms, 44% developed grade 3/4 hepatic changes, and 76% developed grade 3/4 infections.[1] Grade 3/4 differentiation syndrome developed in 14%, with no resulting deaths. No case of differentiation syndrome or deaths were reported during either consolidation cycle.

In comparison with the 2-year interim APML4 data, there were no major differences in grade 3–4 non-haematologic toxic effects during induction and consolidation.[6] Toxic effects declined with successive treatment cycles, being the highest in induction and lowest in the second cycle of consolidation. Myelotoxic effects in consolidation were dependent on the arsenic trioxide schedule, with grade 3–4 neutropenia seen in 69 (62%) of 112 patients in the first consolidation cycle compared with 30 (27%) of 112 patients in the second cycle. No grade 3–4 thrombocytopenia occurred in either cycle of consolidation. During the maintenance period, the most frequent grade 3–4 adverse events were increased concentrations of alanine or aspartate aminotransferase and neutropenia.

Table 1. Number of patients experiencing grade 3-4 non-haematologic adverse events during induction and consolidation[1]

	Induction	Con 1*	Con 2†	*P* (Induction vs Con 1)	*P* (Con 1 vs Con 2)
No. of patients for whom AE data are available	120 (97%)	112 (100%)	110 (98%)		
Cardiac‡	1 (1%)	1 (1%)	0 (0%)	1.0	1.0
Prolonged Q-Tc interval	17 (14%)	10 (9%)	4 (4%)	.17	.11
Hepatic§	53 (44%)	13 (12%)	2 (2%)	< .0001	.01
Gastrointestinal¶	33 (28%)	3 (3%)	1 (1%)	< .0001	.62
Infection#	91 (76%)	21 (19%)	3 (3%)	< .0001	.0005
Differentiation syndrome	17 (14%)	0 (0%)	0 (0%)	.0005	
Neurological**	7 (6%)	2 (2%)	0 (0%)	.29	.48
Headache	4 (3%)	2 (2%)	0 (0%)	.68	.48
Dermatological	5 (4%)	1 (1%)	0 (0%)	.48	
Respiratory††	2 (2%)	1 (1%)	0 (0%)	1.0	1.0
Metabolic‡‡	19 (16%)	4 (4%)	4 (4%)	.002	1.0
Second malignancy	0 (0%)	1 (1%)§§	0 (0%)	1.0	1.0

*Consolidation cycle 1.
†Consolidation cycle 2.
‡Conduction abnormalities other than Q-Tc prolongation or left ventricular systolic dysfunction.
§Clinical liver failure or elevation of bilirubin, ALT, AST, or GGT.
¶Nausea, vomiting, diarrhea, mucositis, or enterocolitis.
#Documented infection or febrile neutropenia.
**Dizziness, mood alteration, musculoskeletal pain, or seizure.
††Dyspnea or hypoxia not attributed to differentiation syndrome.
‡‡Hyperglycemia, hypertriglyceridemia, hypoalbuminemia, hypokalemia, hypophosphatemia, or renal failure.
§§Squamous cell carcinoma (SCC) of skin. Because the latency of skin cancer related to arsenic exposure is usually measured in years or decades (Levine T, Marcus W, Chen C. US Environmental Protection Agency Risk Assessment Forum: Special Report on Ingested Inorganic Arsenic. Available from: http://www.epa.gov/raf/publications/pdfs/EPA_625_3-87_013.PDF. Accessed April 2, 2012), it is unlikely that this SCC was a consequence of the therapeutic ATO used in this protocol.

References

1 Iland, H. J., K. Bradstock, S. G. Supple, et al. 2012. "All-trans-retinoic acid, idarubicin, and IV arsenic trioxide as initial therapy in acute promyelocytic leukemia (APML4)." Blood 120(8):1570-1580; quiz 1752.

2 Burnett, A. K., N. H. Russell, R. K. Hills, et al. 2015. "Arsenic trioxide and all-trans retinoic acid treatment for acute promyelocytic leukaemia in all risk groups (AML17): results of a randomised, controlled, phase 3 trial." Lancet Oncol 16(13):1295-1305.

3 Abaza, Y., H. Kantarjian, G. Garcia-Manero, et al. 2017. "Long-term outcome of acute promyelocytic leukemia treated with all-trans-retinoic acid, arsenic trioxide, and gemtuzumab." Blood 129(10):1275-1283.

4 Kutny, M. A., T. A. Alonzo, O. Abla, et al. 2022. "Assessment of Arsenic Trioxide and All-trans Retinoic Acid for the Treatment of Pediatric Acute Promyelocytic Leukemia: A Report From the Children's Oncology Group AAML1331 Trial." JAMA Oncol 8(1):79-87.

5 Shah, G., F. M. Mikhail, K. Bachiasvili, et al. 2020. "Outcomes of high-risk acute promyelocytic leukemia patients treated with arsenic trioxide (ATO)/all trans retinoic acid (ATRA) based induction and consolidation without maintenance phase: A case Series." Hematol Oncol Stem Cell Ther 13(3):143-146.

6 Iland, H. J., M. Collins, K. Bradstock, et al. 2015. "Use of arsenic trioxide in remission induction and consolidation therapy for acute promyelocytic leukaemia in the Australasian Leukaemia and Lymphoma Group (ALLG) APML4 study: a non-randomised phase 2 trial." Lancet Haematol 2(9):e357-366.

History

Version 3

Date	Summary of changes
24/02/2023	Protocol reviewed by the Haematology Reference Committee at the Leukaemia RCM.
18/10/2023	Protocol updated with the following changes: • addition of note regarding alternate consolidation treatment options

	• update of evidence Version increased to V3. Review in 2 years.

Version 2

Date	Summary of changes
20/05/2016	New protocol taken to Reference Committee meeting.
05/10/2016	Approved and published on eviQ.
13/06/2017	Added in patient information: 'Information for patients on allopurinol'.
31/05/2017	Transferred to new eviQ website. Version number change to v.2.
21/09/2018	Protocol reviewed at Haematology Reference Committee meeting. Evidence updated to include paragraph on maintenance therapy in low/intermediate risk patients.Removed ATRA 'with food' from protocol for consistency with patient information. Review in 2 years.
29/08/2019	Clinical information for consideration of thiopurine methyltransferase (TPMT) testing prior to administration of mercaptopurine added.
23/10/2020	Protocol reviewed electronically by the Haematology Reference Committee, no changes. Review in 2 years.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.
24/01/2022	Pulmonary toxicity added to side effects.
29/07/2022	New clinical information block added: Thiopurine-S-methyltransferase (TPMT) enzyme deficiency.

First approved: 5 October 2016
Last reviewed: 24 February 2023
Review due: 30 June 2025

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/1938
18 Oct 2023

Patient information - Acute promyelocytic leukaemia (APML) - APML4 maintenance

Patient's name:

Your treatment

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

APML4 maintenance

This treatment cycle is repeated every 90 days, continuously for 2 years. You will have 8 cycles. It is usually started 3 to 4 weeks after you have finished consolidation 2 treatment.

Day	Treatment	How it is given
1 to 14	**Tretinoin (ATRA)** *(TRET-i-NO-in)*	Take orally TWICE a day with or without food on day 1 to 14 only. Swallow whole with a glass of water, do not break, crush or chew.
15, 22, 29, 36, 43, 50, 57, 64, 71, 78 and 85	**Methotrexate** *(Meth-o-TREX-ate)*	Take orally ONCE a week only (day 15, 22, 29, 36, 43, 50, 57, 64, 71, 78 and 85 only). Swallow whole with a glass of water on an empty stomach at least one hour before or two hours after food.
15 to 90	**Mercaptopurine** *(mer-KAP-toe-PURE-een)*	Take orally ONCE a day on an empty stomach, at least one hour before or two hours after food on day 15 to 90 only. Swallow whole with a glass of water, do not break, crush or chew. Avoid taking with dairy products as they may decrease its absorption.

Missed doses:

- **Tretinoin** or **mercaptopurine**: if you forget to take a dose or vomit a dose, take your normal dose the next time it is due. Do not take an extra dose.
- **Methotrexate**: as this is only to be taken ONCE a week, if you forget to take a tablet or vomit a tablet, call your doctor for further instructions.

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:

Other information about your treatment

Information for patients on allopurinol

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

Blood tests and monitoring

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

Other medications given during this treatment

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

Side effects

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

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

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

Immediate (onset hours to days)	
Headache	• You can take paracetamol 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.**
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.**
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.
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.**
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.**
High blood sugar level (hyperglycaemia)	• You may feel thirsty and need to urinate more often than normal. • You may get repeated infections, especially thrush. • If you are a diabetic you will need to have your blood sugar levels checked more often. You may also need to have your diabetes medication increased. • **Tell your doctor or nurse if you get any of the signs or symptoms listed above.**
Low blood magnesium, potassium and calcium levels (hypomagnesaemia, hypokalaemia, hypocalcaemia)	• This may be found from your routine blood tests and treated by your doctor. • If it is severe you may get: ◦ muscle cramps or twitches ◦ numbness or tingling in your fingers, toes or around your mouth ◦ constipation ◦ an irregular heartbeat ◦ sleepy, drowsy or confused • **Tell your doctor or nurse as soon as possible if you get any of the signs or symptoms listed above.**
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.**
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.**

Delayed (onset months to years)	

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

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

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

Other medical and dental treatment

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

Diet and food safety

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

Fertility

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

Pregnancy and breastfeeding

- This treatment can cause major congenital disabilities or death 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. You must use contraception while having this treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

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

Quitting smoking

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

Staying active

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

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

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (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 – https://aci.health.nsw.gov.au/networks/bmtct
- 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
- Carer Help - carerhelp.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

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

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

Additional notes:

First approved: 5 October 2016
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18 Oct 2023