Mesothelioma ciSplatin pemetrexed and beVACizumab

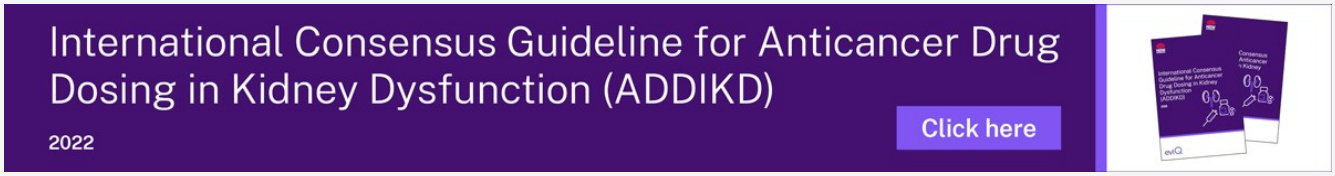
ID: 4022 v.1 **Endorsed**

Avastin® (bevacizumab) is no longer available on the PBS and alternative biosimilars are now available. The rapid infusion administration instructions for subsequent doses of bevacizumab included in eviQ protocols are based on studies conducted using Avastin® (bevacizumab).

Check for clinical trials in this patient group. Link to Australian Clinical Trials website

Link to Clinical practice guidelines for the treatment of lung cancer

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:

- Mesothelioma cARBOplatin pemetrexed and beVACizumab
- Mesothelioma ciSplatin and pemetrexed

Treatment schedule - Overview

Cycle 1 to 6

Drug	Dose	Route	Day
beVACizumab	15 mg/kg	IV infusion	1
Pemetrexed	500 mg/m^2	IV infusion	1
ciSplatin	75 mg/m^2 *	IV infusion	1

Cycle 7 and further cycles

Drug	Dose	Route	Day
beVACizumab	15 mg/kg	IV infusion	1

* In the clinical trial cisplatin was substituted with carboplatin AUC 5 in patients with grade 2 or greater cisplatin induced renal toxicity.[1]

Frequency: 21 days

Cycles: 6 with chemotherapy combination, followed by continuous treatment with bevacizumab until disease progression or unacceptable toxicity

Notes:
Cisplatin may be substituted with carboplatin as they have been shown to have similar efficacy from phase II trials.[2]

Drug status: All drugs in this protocol are on the PBS general schedule

Cost: ~ $1,670 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 6

Day before chemotherapy		
Dexamethasone	4 mg (PO)	TWICE a day with or after food *

Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	4 mg (PO)	TWICE a day with or after food *
beVACizumab	15 mg/kg (IV infusion)	in 100 mL sodium chloride 0.9% over 90 minutes (1st dose); if first dose is well tolerated subsequent doses may be administered over 30 minutes.**
Pemetrexed	500 mg/m^2 (IV infusion)	in 100 mL sodium chloride 0.9% over 10 minutes
ciSplatin	75 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes

Day 2		
Dexamethasone	4 mg (PO)	TWICE a day with or after food *

Day 3 and 4		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food

Cycle 7 and further cycles

Day 1		
beVACizumab	15 mg/kg (IV infusion)	in 100 mL sodium chloride 0.9% over 90 minutes (1st dose); if first dose is well tolerated subsequent doses may be administered over 30 minutes.**

* Dexamethasone premedication alternative dosing is 8 mg ONCE a day from day 1 as per reference committee consensus

** It is the consensus of the eviQ reference committee that it is safe to give the initial and subsequent doses of bevacizumab over 30 minutes.[3] The rapid infusion administration instructions for bevacizumab are based on studies conducted using Avastin® (bevacizumab). Refer to bevacizumab infusion times for more information.

Frequency: 21 days

Cycles: 6 with chemotherapy combination, followed by continuous treatment with bevacizumab until disease progression or unacceptable toxicity

Indications and patient population

Indications:

- Unresectable malignant pleural mesothelioma
  - ECOG performance status 0 to 2.

Cautions/Exclusions:

- pre existing neuropathies Grade 2 or greater
- moderate/severe renal impairment (creatinine clearance less than 60 mL/min.)
- significant hearing impairment/tinnitus.

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Premedication	Original pemetrexed trials included hydroxocobalamin and folic acid to commence 5 to 7 days prior to the first cycle of chemotherapy, however the PEMVITASTART (Singh et al 2019) trial has demonstrated that concurrent administration does not lead to increased haematological toxicity. It is the opinion of the reference committee that hydroxocobalamin and folic acid may be administered 5 to 7 days prior to, or simultaneously with, cycle 1 of pemetrexed based chemotherapy. Hydroxocobalamin (Vit B12) 1000 micrograms intramuscularly and repeat once every 3 cycles; Folic acid 500 micrograms PO once daily continuously until 21 days after the last dose of pemetrexed. Read more about PEMVITASTART Singh et al 2019
Emetogenicity HIGH	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. A steroid has been included both as an antiemetic and premedication for hypersensitivity in this protocol. 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
Hydration	Hydration helps to prevent cisplatin-induced nephrotoxicity. The default regimen is appropriate for patients with normal electrolytes, kidney function, fluid status etc. and should be adjusted according to individual requirements. Read more about cisplatin hydration regimens
Ototoxicity	Ototoxicity may occur with platinum-based therapy; patients should be monitored for signs and symptoms. Platinum compounds should be used with caution in patients with pre-existing conditions or risk factors. Ototoxicity may become more severe in patients being treated with other drugs with nephrotoxic potential e.g. aminoglycosides. An audiometry test should be performed if symptoms develop. Read more about ototoxicity - tinnitus and hearing loss
Peripheral neuropathy	Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool

Gastrointestinal perforation	Bevacizumab has been associated with serious cases of gastrointestinal (GI) perforation and should be permanently discontinued in patients who develop it.
Haemorrhage	Patients treated with bevacizumab have an increased risk of haemorrhage, especially tumour associated haemorrhage and minor mucocutaneous haemorrhage (e.g. epistaxis). Bevacizumab should be used with caution in patients at risk of bleeding.
Hypertension	Pre-existing hypertension should be adequately controlled prior to commencing bevacizumab and blood pressure should be monitored during therapy. Commence or adjust antihypertensive medication as clinically indicated.
Proteinuria	Patients may be at increased risk of developing proteinuria when treated with bevacizumab. Baseline urinalysis for proteinuria is recommended prior to commencement of therapy, and as clinically indicated. Routine testing prior to each treatment is no longer recommended, as dose reductions for low/intermediate levels of proteinuria are not recommended. Clinicians are advised to consider evaluating for proteinuria periodically (e.g. every 3 to 4 months) or in patients with clinical concerns (e.g. oedema/unexplained hypoalbuminemia) as treatment interruption may be required if proteinuria is significant (e.g. > 3 g/L). Read more about proteinuria
Reversible posterior leukoencephalopathy syndrome (RPLS)	Bevacizumab should be discontinued in patients who develop reversible posterior leukoencephalopathy syndrome (RPLS). The risk of reinitiating bevacizumab therapy in patients previously experiencing RPLS is not known. Read more about reversible posterior leukoencephalopathy syndrome (RPLS)
Thromboembolism	Both arterial and venous thromboembolic events have been observed in patients with this treatment. Therefore, use with caution in patients at increased risk or with a history of thrombotic events (i.e., cerebrovascular and cardiovascular disease)
Wound healing	Bevacizumab may adversely affect wound healing and should not be initiated in patients with a serious non-healing wound or ulcer. Elective surgery should not be undertaken within 6 weeks from the last dose of bevacizumab. Bevacizumab can be restarted 28 days after surgery provided wound healing is complete. Necrotising fasciitis, including fatal cases, has rarely been reported in patients treated with bevacizumab; usually secondary to wound healing complications, gastrointestinal perforation or fistula formation. Bevacizumab therapy should be discontinued in patients who develop necrotising fasciitis, and appropriate treatment should be promptly initiated.
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
Blood tests	FBC, EUC, eGFR, LFTs, calcium, magnesium and phosphate at baseline and prior to each treatment.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. 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

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well.
0.5 to less than 1.0	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and consider reducing pemetrexed and cisplatin by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing pemetrexed and cisplatin by 25% for subsequent cycles
Platelets x 10^9/L (pre-treatment blood test)	
75 to less than 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local institutional guidelines.
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and consider reducing pemetrexed and cisplatin by 25% for subsequent cycles
less than 50 with bleeding	Delay treatment until recovery and consider reducing pemetrexed and cisplatin by 50% for subsequent cycles

Renal impairment	
eGFR (CKI-EPI or MDRD) or eCrCl (Cockcroft Gault) (mL/min)*	
greater than or equal to 70	No dose modifications necessary
50 to less than 70	Reduce cisplatin by 25%
30 to less than 50	Reduce pemetrexed and cisplatin by 50% or consider substituting carboplatin for cisplatin
less than 30	Withhold chemotherapy

** Each method has its limitations; refer to Nephrotoxicity associated with cisplatin for more information.*

Hepatic impairment
No dose modifications necessary

Peripheral neuropathy	
Grade 2 which is present at the start of the next cycle	Reduce cisplatin by 25%; if persistent, reduce cisplatin by 50%
Grade 3 or Grade 4	Omit cisplatin

Mucositis and stomatitis	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce pemetrexed by 25% 3rd occurrence: Reduce pemetrexed by 50% 4th occurrence: Omit pemetrexed
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce pemetrexed by 50% 2nd occurrence: Omit pemetrexed

Diarrhoea	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce pemetrexed and cisplatin 25% 3rd occurrence: Reduce pemetrexed and cisplatin by 50% 4th occurrence: Omit pemetrexed and cisplatin
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: Reduce pemetrexed and cisplatin by 50% 2nd occurrence: Omit pemetrexed and cisplatin

Cease bevacizumab if any of the following occur:

- haemorrhagic event grade 3 or greater
- life threatening venous thromboembolic event, pulmonary embolism, cerebrovascular event or arterial insufficiency
- arterial thromboembolic event
- grade 4 hypertension or persisting grade 3 hypertension
- nephrotic syndrome
- gastrointestinal perforation or fistula formation
- episode of reversible posterior leukoencephalopathy syndrome (RPLS)

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*

Bevacizumab		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Anthracyclines	May enhance the cardiotoxic effect of anthracycline anti-cancer drugs	Monitor for increased cardiotoxicity (e.g. congestive heart failure)
Sunitinib	Microangiopathic haemolytic anaemia	Monitor for haemolytic anaemia, thrombocytopenia, hypertension, elevated creatinine and neurological symptoms
Sorafenib	Increased risk of toxicity, especially hand-foot syndrome	Monitor for increased toxicity
Anti-EGFR monoclonal antibodies (e.g. cetuximab, panitumumab)	Additive toxicity without additional treatment benefit	Avoid combination
Medications known to cause GI perforation (e.g. methylnaltrexone, NSAIDs, steroids)	Additive risk of GI perforation	Avoid combination

Cisplatin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing
Neurotoxic drugs (e.g. vincristine, paclitaxel)	Additive neurotoxicity	Monitor closely for neuropathy if combination used
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination
Carbamazepine, phenytoin, valproate	Decreased antiepileptic plasma levels	Monitor antiepileptic serum levels and seizure frequency for efficacy; adjust dosage as appropriate or select alternative antiepileptic (e.g. clonazepam, diazepam, lorazepam)

Pemetrexed		
	Interaction	**Clinical management**
NSAIDs (short acting e.g. ibuprofen, long acting e.g. piroxicam) **and** **Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)** **and** **Drugs secreted by the renal tubules (e.g. probenecid, penicillins etc.)**	Increased toxicity of pemetrexed possible due to reduced clearance	Avoid combination or monitor for increased pemetrexed toxicity (esp. myelosuppression, renal and gastrointestinal toxicities) Patients with mild to moderate kidney dysfunction should avoid short and long acting NSAIDs from 2 and 5 days respectively prior, until 2 days after, pemetrexed administration.

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	**Clinical management**
Dexamethasone	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of **antiemetic dexamethasone** by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of **antiemetic dexamethasone** has already been taken into account. If **dexamethasone is part of the chemotherapy protocol**, dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
Warfarin	Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant	INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant
Combined oral contraceptive	Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant	Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of NK-1 antagonist possible due to increased clearance	Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of NK-1 antagonist possible due to reduced clearance	Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation)
Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist	Avoid combination or monitor for increased toxicity especially with orally administered drugs

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 cycles 1 to 6

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

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 6 hours (initial); 5 hours (subsequent)

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify premedication taken or administer as prescribed.

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Bevacizumab

- bevacizumab is only compatible with sodium chloride 0.9%, ensure IV lines are flushed with sodium chloride 0.9% pre and post administration.

Prior to administration check:

- blood pressure
- baseline urinalysis for protein and repeat as clinically indicated (read more about proteinuria)

Administer bevacizumab:

- via IV infusion
- first dose over 90 minutes
  - the product information recommends giving the first dose over 90 minutes, it is the consensus of the eviQ reference committee that it is safe to give the initial and subsequent doses of bevacizumab over 30 minutes[3] (read more about the bevacizumab infusion times)
- observe for hypersensitivity reaction
- flush with ~ 50 mL of sodium chloride 0.9%.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate
- for severe reactions seek medical assistance immediately and do not restart infusion.

Chemotherapy - Time out

Pemetrexed

- administer pemetrexed 30 minutes prior to cisplatin infusion
- via IV infusion over 10 minutes
- may be administered concurrently with prehydration
- flush with ~ 50 mL of sodium chloride 0.9%
- continue with pre hydration fluids until administration of cisplatin.

Cisplatin

Commence prehydration for cisplatin:

- administer 10 mmol magnesium sulphate ($MgSO_4$) in 1000 mL sodium chloride 0.9% over 60 minutes
- followed by 200 mL of mannitol 20% over 15 minutes
  - mannitol should be administered via a controlled infusion
- mannitol 10% may be used as per institutional policy; there is much variation in the use of mannitol and although there is no conclusive evidence that mannitol should be used, many sites have used it routinely without renal toxicity. The routine use of frusemide to increase urine flow is not recommended. Refer to your institutional guidelines and medical orders.
- ensure patient has passed urine prior to cisplatin administration as per institutional policy.

Administer cisplatin (irritant):

- via IV infusion over 60 minutes
- flush with 100 mL of sodium chloride 0.9%.

Post hydration:

- 1000 mL sodium chloride 0.9% over 60 minutes.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

Antiemetics

- Antiemetics as prescribed.

Pemetrexed premedication

- Premedications as prescribed and written instructions on how to take them:
  - folic acid
  - hydroxocobalamin (vitamin B12)
  - dexamethasone

Patient information

- Ensure patient receives patient information sheet.

Administration cycle 7 onwards

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

Day 1

Approximate treatment time: 60 minutes

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each treatment.

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

Prime IV line(s) with sodium chloride 0.9%.

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Administer antiemetics if required

Treatment - Time out

Bevacizumab

- bevacizumab is only compatible with sodium chloride 0.9%, ensure IV lines are flushed with sodium chloride 0.9% pre and post administration.

Prior to administration check:

- blood pressure
- baseline urinalysis for protein and repeat as clinically indicated (read more about proteinuria)

Administer bevacizumab:

- via IV infusion
- first dose over 90 minutes
  - the product information recommends giving the first dose over 90 minutes, it is the consensus of the eviQ reference committee that it is safe to give the initial and subsequent doses of bevacizumab over 30 minutes[3] (read more about the bevacizumab infusion times)
- observe for hypersensitivity reaction
- flush with ~ 50 mL of sodium chloride 0.9%.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate
- for severe reactions seek medical assistance immediately and do not restart infusion.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Discharge information

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

Immediate (onset hours to days)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes
Headache	

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
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
Diarrhoea	Read more about treatment induced diarrhoea
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
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Gastrointestinal perforation	A rupture of the wall of the stomach, small intestine or large bowel. Symptoms include acute abdominal pain, tenderness and signs of sepsis.
Epistaxis	Acute bleeding from the nostril(s), nasal cavity, or nasopharynx.
Fatigue	Read more about fatigue
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
Nephrotoxicity	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.
Haemorrhage	
Thromboembolism	Arterial and venous thromboembolic events, including pulmonary embolism, deep vein thrombosis and cerebrovascular accidents can occur. Patients should be carefully assessed for risk factors, and consideration given for antithrombotic prophylaxis in high risk patients.
Proteinuria	Read more about proteinuria
Ototoxicity	Tinnitus and hearing loss may occur due to damage in the inner ear. Tinnitus is usually reversible, while hearing loss is generally irreversible. Hearing loss is dose-related, cumulative and may be worse in those with pre-existing hearing problems. Read more about ototoxicity - tinnitus and hearing loss
Hypertension	High blood pressure is commonly associated with many anti-cancer drugs. Pre-existing hypertension should be controlled prior to initiation of drugs capable of causing hypertension.
Reversible posterior leukoencephalopathy syndrome (RPLS)	A neurological disorder which may present with headache, seizures, lethargy, confusion, blindness and/or other visual and neurological disturbances. Mild to severe hypertension may also occur. Read more about reversible posterior leukoencephalopathy syndrome (RPLS)

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

The evidence supporting this protocol comes from a phase III multicentre, international, randomised trial – the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS) – involving 448 patients with previously untreated advanced malignant pleural mesothelioma comparing the addition of bevacizumab to the standard of care chemotherapy at the time, cisplatin and pemetrexed.[1]

Between February 2008 and January 2014, 223 patients were randomised to receive pemetrexed 500 mg/m^2, cisplatin 75 mg/m^2 plus bevacizumab 15 mg/kg intravenously every 3 weeks for up to 6 cycles. Bevacizumab was continued until disease progression or unacceptable toxicity (PCB arm). 225 patients were randomised to receive pemetrexed and cisplatin at the same dose every 3 weeks for up to 6 cycles (PC arm).

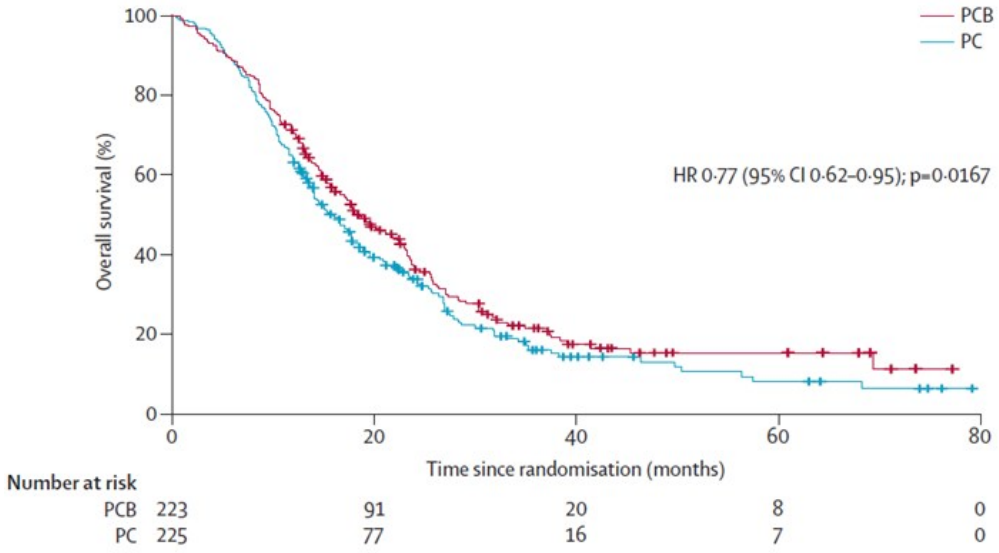
The primary endpoint was overall survival (OS), with secondary end-points of progression-free survival (PFS), quality of life (QoL) and safety.

Efficacy

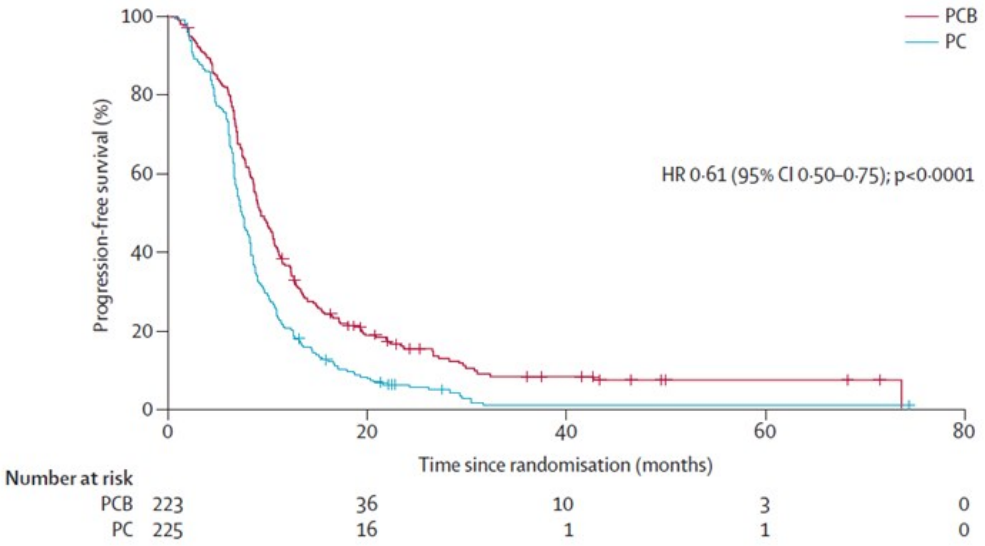
After a median follow-up of 39.4 months, the median OS was 18.8 months (95% confidence interval [CI] 15.9 - 22.6) in the PCB treatment arm, versus 16.1 months (95% CI 14.0 - 17.9) in the PC control arm (HR = 0.77, 95% CI 0.62 - 0.95; p = 0.0167). There was no significant difference when stratified by pre-planned prognostic factors including histological subtype.[1]

There was also improvement in median PFS with PCB compared to PC, 9.2 months (95% CI 8.5 - 10.5) versus 7.3 months (95% CI 6.7 - 8.0) respectively (HR = 0.61, 95% CI 0.50 - 0.75; p<0.0001).

Kaplan-Meier curve of overall survival[1]



Kaplan-Meier curve of progression-free survival[1]



Quality of life data was collected for over 54% of patients. Despite an increased toxicity profile in PCB, treatment groups did not differ significantly in QoL scores and global health status improved in over 20% of patients in both groups.[1]

Toxicity

Adverse events seen in MAPS are listed below. Grade 3 or higher adverse events occurred in 71% of patients in the PCB group compared to 62% in the control group.[1]

There was a higher rate of treatment discontinuation in the PCB arm compared to PC arm (24.3% versus 6.0% respectively, p < 0.0001). Adverse events leading to death occurred in 3 of 222 patients (1.4%) in the PCB arm and 2 of 224 patients (0.9%) in the chemotherapy arm. Specific bevacizumab toxicities were higher in the PCB group. Any-grade venous thromboembolism was 5.4% in the PCB group compared to 1.3% in the control group.

Adverse events[1]

	PCB (n=222)		PC (n=224)		Difference (%)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Neutropenia	173 (77·9%)	98 (44·1%)	177 (79·0%)	100 (44·6%)	−1·1% (−8·7 to 6·5)	−0·5% (−9·6 to 8·6)
Febrile neutropenia	4 (1·8%)	4 (1·8%)	7 (3·1%)	7* (3·1%)	−1·3% (−4·7 to 1·8)	−1·3% (−4·7 to 1·8)
Thrombocytopenia	130 (58·6%)	22 (9·9%)	119 (53·1%)	21 (9·4%)	5·4% (−3·8 to 14·5)	0·5% (−5·1 to 6·1)
Anaemia	163 (73·4%)	16 (7·2%)	187 (83·5%)	30 (13·4%)	−10·1% (−17·6 to −2·4)	−6·2% (−11·9 to −0·5)
Asthenia or fatigue	155 (69·8%)	30 (13·5%)	152 (67·9%)	28 (12·5%)	2·0% (−6·6 to 10·5)	1·0% (−5·3 to 7·3)
Weight loss	22 (9·9%)	0	22 (9·8%)	0	0·1% (−5·6 to 5·7)	0 (−1·7 to 1·7)
Anorexia	75 (33·8%)	5 (2·3%)	75 (33·5%)	9 (4·0%)	0·3% (−8·4 to 9·0)	−1·8% (−5·4 to 1·7)
Constipation	47 (21·2%)	2 (0·9%)	44 (19·6%)	1 (0·4%)	1·5% (−6·0 to 9·0)	0·5% (−1·5 to 2·4)
Diarrhoea	37 (16·7%)	1 (0·5%)	26 (11·6%)	2 (0·9%)	5·1% (−1·4 to 11·6)	−0·4% (−2·0 to 1·1)
Oral mucositis	37 (16·7%)	2 (0·9%)	33 (14·7%)	1 (0·4%)	1·9% (−4·9 to 8·7)	0·5% (−1·5 to 2·4)
Nausea or vomiting	174 (78·4%)	18 (8·1%)	172 (76·8%)	18 (8·0%)	1·6% (−6·1 to 9·3)	0·1% (−5·1 to 5·3)
Creatinine concentration increase	86 (38·7%)	8 (3·6%)	63 (28·1%)	4 (1·8%)	10·6% (1·9 to 19·1)	1·8% (−1·4 to 5·3)
Haemorrhage	91 (41·0%)	2† (0·9%)	16 (7·1%)	0	33·8% (26·3 to 41·0)	0·9% (−5·1 to 5·3)
Sepsis	3 (1·4%)	3‡ (1·4%)	3 (1·3%)	3 (1·3%)	<0·1% (−2·7 to 2·7)	<0·1% (−2·7 to 2·7)
Hepatic enzymes	5 (2·3%)	0	3 (1·3%)	1 (0·4%)	0·9% (−1·9 to 3·9)	−0·4% (−2·5 to 1·3)
Cardiovascular AEs	137 (61·7%)	64 (28·8%)	6 (2·7%)	2 (0·9%)	59·0% (51·8 to 65·3)	27·9% (21·9 to 34·2)
Hypertension	125 (56·3%)	51 (23·0%)	3 (1·3%)	0	55·0% (47·9–61·4)	23·0% (17·6 to 28·9)
Arterial and venous thromboembolic events	16 (7·2%)	13 (5·8%)	3 (1·3%)	2 (0·9%)	5·9% (2·2 to 10·1)	5·0% (1·6 to 8·9)

Data are n (%) or % (95% CI). PCB=pemetrexed plus cisplatin plus bevacizumab. PC=pemetrexed plus cisplatin. AE=adverse event. *Including one grade 5 febrile neutropenia case. †Including one fatal brain haemorrhage. ‡Including two toxic deaths.

References

1 Zalcman, G., J. Mazieres, J. Margery, et al. 2016. "Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial." Lancet 387(10026):1405-1414.

2 Ceresoli, G. L., P. A. Zucali, A. G. Favaretto, et al. 2006. "Phase II study of pemetrexed plus carboplatin in malignant pleural mesothelioma." J Clin Oncol 24(9):1443-1448.

3 Reidy, D. L., K. Y. Chung, J. P. Timoney, et al. 2007. "Bevacizumab 5 mg/kg can be infused safely over 10 minutes." J Clin Oncol. 25(19):2691-2695.

History

Version 1

Date	Summary of changes
20/05/2022	Protocol reviewed and approved by Medical Oncology Reference Committee
24/06/2022	Protocol published on eviQ. Review in 1 year.
21/10/2022	Bevacizumab treatment schedule note updated based on reference committee consensus to add that it is safe to give the initial dose of bevacizumab over 30 minutes.

First approved: 24 June 2022
Review due: 30 June 2023

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/4022
09 Aug 2023

Patient information - Mesothelioma - Cisplatin, pemetrexed and bevacizumab

Patient's name:

Your treatment

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

Cisplatin, pemetrexed and bevacizumab cycles 1 to 6

This treatment cycle is repeated every 21 days. You will have 6 treatments with bevacizumab, pemetrexed and cisplatin followed by bevacizumab alone.

Day	Treatment	How it is given	How long it takes
1	**Bevacizumab** (*be-vuh-SIZ-uh-mab*) **Pemetrexed** (*PEM-e-TREX-ed*) **Cisplatin** (*siss-PLAT-in*)	By a drip into a vein	About 6 hours for the first infusion. If no reactions, subsequent infusions may be given over a shorter amount of time.

Bevacizumab cycle 7 onwards

This treatment cycle is repeated every 21 days. You will have treatment with bevacizumab alone after completing 6 cycles of bevacizumab, pemetrexed and cisplatin. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	**Bevacizumab**	By a drip into a vein	About 60 minutes

When to get help

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

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

Surgery and wound healing

This treatment may affect wound healing. Tell your doctor if you are planning to have surgery or have a wound that has not healed.

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.
- **Pemetrexed premedication:** you will need to have some medications to help reduce the side effects of this treatment. You will be given more information about this from your doctor. The premedication consists of the following tablets and an injection

Medication	Dose	When to take
Vitamin B12	1000 micrograms	As an injection before the first chemotherapy treatment then every 3 cycles and stops with the last cycle of chemotherapy
Folic acid	500 micrograms	Start before the first treatment and take one tablet daily until 3 weeks after the last chemotherapy treatment
Dexamethasone	4 mg	Your doctor will tell you how and when to take these tablets

Tell your doctor or nurse if you have not started your premedication or if you forget to take the dexamethasone tablets before your treatment.

Side effects

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

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

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

Immediate (onset hours to days)	

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

Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.
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.**

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.**
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.**
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.**
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.

Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Bleeding into stomach or bowel	• This side effect is rare, but can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of these signs or symptoms:** ◦ **severe stomach pain** ◦ **swollen and hot skin around your stomach** ◦ **bleeding** ◦ **nausea or vomiting** ◦ **fever or chills** ◦ **a fast heartbeat** ◦ **you feel short of breath.**
Nose bleeds	• If your nose starts to bleed gently apply pressure on the soft part of nostrils below the bridge of the nose for at least 10 minutes. • It may help to put a cold pack over your forehead or the bridge of the nose. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if your nose will not stop bleeding.**
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.**
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.**
Kidney damage	• This treatment can cause changes to how your kidneys work. • You will have blood tests to make sure your kidneys are working properly. • You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this. • **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.**
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.**

Bleeding (haemorrhage)	• Tell your doctor or nurse if you have a wound that does not heal. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **unusual bleeding or bruising** ◦ **bright red or black, tarry bowel motions (stools, poo)** ◦ **stomach pain** ◦ **slurred speech** ◦ **shortness of breath** ◦ **a fast heartbeat.**
Blood clots (thromboembolism)	• Blood clots can occur with this 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:** ◦ **redness, heat or pain in your leg(s)** ◦ **numbness or weakness in your face, arm or leg** ◦ **chest pain** ◦ **sudden shortness of breath** ◦ **dizziness** ◦ **trouble speaking** ◦ **blurred vision** ◦ **severe headache** ◦ **unexplained falls or loss of balance.**
Kidney changes or damage	• This treatment may cause changes to how your kidneys work. This may cause protein in your urine. • This is not something that you will notice. • You will have blood and urine tests to check that your kidneys are working properly.
Hearing changes (ototoxicity)	• You may get ringing in your ears or loss of hearing. • You may have your hearing tested before and during your treatment. • **Tell your doctor or nurse as soon as possible if you notice any changes to your hearing.**
High blood pressure (hypertension)	• You may not have any signs or symptoms if you have high blood pressure. • If it is severe you may get headaches, shortness of breath or feel dizzy. • Your blood pressure will be taken regularly during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the signs or symptoms listed above.**
Changes in the way your brain works [reversible posterior leukoencephalopathy syndrome (RPLS)]	• This treatment can have an effect on your brain, but this is rare. • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **headaches or vision problems** ◦ **nausea and vomiting** ◦ **tiredness** ◦ **confusion** ◦ **fits (seizures)** ◦ **high blood pressure.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)
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 anti-inflammatory medicines known as NSAIDs (e.g. ibuprofen, diclofenac) may interact with your treatment. They should be stopped at least five days before each treatment and not restarted until two days after each treatment. Speak to your doctor if you are taking these medicines. However, do not stop taking any prescribed medicines (including low dose aspirin) without first speaking to your doctor
- Paracetamol is safe to take if you have a headache or other mild aches and pains.
- 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

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- 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.

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 Lung Foundation Australia on 1800 654 301

Mesothelioma information

- Asbestos Diseases Foundation of Australia Inc. (ADFA) – adfa.org.au
- Lung Foundation Australia – lungfoundation.com.au
- Lungevity – lungevity.org
- The Lung Cancer Network (formerly the Kylie Johnston Foundation) – lungcancernetwork.com.au/

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
- CHILL Cancer related hair loss - scalpcooling.org
- eviQ Cancer Treatments Online – eviQ.org.au
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information – patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer – targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

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

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

Additional notes:

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The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/4022
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