Testicular germ cell metastatic BEP (bleomycin etoposide ciSplatin)

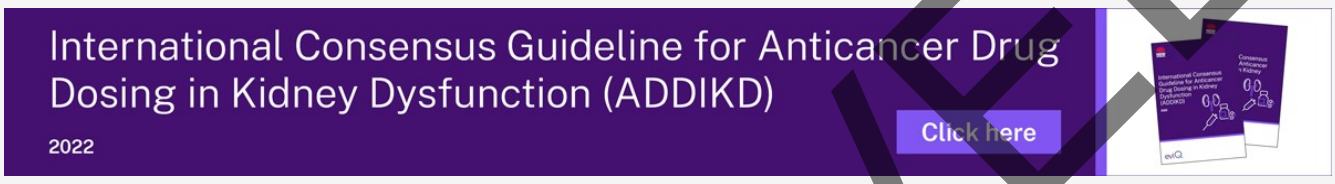
ID: 320 v.6 **Endorsed** Essential Medicine List

Clinicians are advised to consult with a medical oncologist from a tertiary treatment centre with high volume experience in testicular cancer prior to use of this regimen.

Link to ANZUP testicular cancer surveillance recommendations

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

- Testicular germ cell metastatic VIP (etoposide iFOSFamide ciSplatin)
- Autologous conditioning germ cell tumour TICE overview

- Risk classification of metastatic germ cell tumours

Treatment schedule - Overview

Cycle 1 to 3

Drug	Dose	Route	Day
Bleomycin #	30,000 International Units	IM/IV	1, 8, 15
ciSplatin ^	20 mg/m^2	IV infusion	1 to 5
Etoposide ^*	100 mg/m^2	IV infusion	1 to 5
Pegfilgrastim **	6 mg	Subcut	6

#Bleomycin dose equivalence: 1,500 International Units is equivalent to 1.5 USP units and approximately equivalent to 1.5mg (by potency) or 1mg (by weight)[1]

^ Dose should be calculated based on actual BSA, and should not be capped or modified, due to the risk of under dosing.

* Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.

** The risk of neutropenia without G-CSF prophylaxis is ~ 10 to 20% and therefore may not be required.[2] However, in order to maintain dose intensity, many clinicians have chosen to give it as primary prophylaxis.

Frequency: 21 days

Cycles: 3 for good-risk disease (4 cycles for intermediate or poor-risk disease - see notes section below)

Notes:
Fertility issues including preservation (e.g. sperm banking) should be discussed with the patient prior to initiating chemotherapy

This is the 5 day 'US PEB' regimen discussed in the key evidence.[3] The number of cycles depends on the category of risk (Risk classification of metastatic germ cell tumours):

- **good prognosis**: 3 cycles (total bleomycin 270,000 International Units)
- **intermediate prognosis**: 4 cycles (bleomycin is sometimes omitted in Cycle 4 because of decrease in lung function; if no bleomycin in Cycle 4, total bleomycin 270,000 International Units)
- **poor prognosis**: 4 cycles (total bleomycin 360,000 International Units).

Drug status: All drugs in this protocol are on the PBS general schedule. **Pegfilgrastim** is PBS authority

Cost: ~ $1,170 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 3

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	8 mg (PO)	60 minutes before chemotherapy**
Bleomycin	30,000 International Units (IM/IV)	in 5 mL to 10 mL sodium chloride 0.9% over 10 minutes (when given intramuscularly mix with 1 to 2 mL lignocaine 1%)
ciSplatin	20 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes (dose should be calculated based on actual BSA, and should not be capped or modified, due to the risk of under dosing)
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes

Day 2 and 3		
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy**
ciSplatin	20 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes (dose should be calculated based on actual BSA, and should not be capped or modified, due to the risk of under dosing)
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes

Day 4		
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	8 mg (PO)	60 minutes before chemotherapy**

Day 4		
ciSplatin	20 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes (dose should be calculated based on actual BSA, and should not be capped or modified, due to the risk of under dosing)
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Day 5		
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy**
ciSplatin	20 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes (dose should be calculated based on actual BSA, and should not be capped or modified, due to the risk of under dosing)
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Day 6		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food
Pegfilgrastim	6 mg (Subcut)	Inject subcutaneously on day 6, at least 24 hours after chemotherapy
Day 7		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food
Day 8		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food
Bleomycin	30,000 International Units (IM/IV)	in 5 mL to 10 mL sodium chloride 0.9% over 10 minutes (when given intramuscularly mix with 1 to 2 mL lignocaine 1%)
Day 15		
Bleomycin	30,000 International Units (IM/IV)	in 5 mL to 10 mL sodium chloride 0.9% over 10 minutes (when given intramuscularly mix with 1 to 2 mL lignocaine 1%)

- Bleomycin dose equivalence: 1,500 International Units is equivalent to 1.5 USP units and approximately equivalent to 1.5mg (by potency) or 1mg (by weight)[1]
- Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.
- The risk of neutropenia without G-CSF prophylaxis is ~ 10 to 20% and therefore G-CSF may not be required.[2] However, in order to maintain dose intensity, many clinicians have chosen to give it as primary prophylaxis.
- * Non-PBS, dosing extrapolated from trials and as per reference committee consensus.[4, 5]
- ** The dose of dexamethasone on day 1 is 8 mg as per eviQ RC consensus but may be increased to 12 mg at the clinician's discretion. Link to ID 7 Prevention of antineoplastic induced nausea and vomiting.

Frequency: 21 days

Cycles: 3 for good-risk disease (4 cycles for intermediate or poor-risk disease - see notes section below)

Indications and patient population

Indications:

- Metastatic germ cell tumours

Cautions/exclusions:

- In patients aged over 40 there is increased risk of bleomycin toxicity, consider alternate regimens:
  - good risk disease 4 cycles of EP
  - intermediate risk or poor risk disease 4 cycles of VIP.

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
Hypersensitivity/infusion related reaction	High risk with bleomycin and etoposide. Note: a hypersensitivity reaction can occur with any dose of bleomycin, regardless of whether a test dose has been performed.
Premedication	A corticosteroid may reduce severity of fever/chills related to bleomycin (note: dexamethasone/prednisolone is included as an antiemetic in this protocol); paracetamol may be used to reduce fever.
Emetogenicity HIGH	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. Note: On day 15, no antiemetics should be routinely administered before treatment in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen. 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
Etoposide conversion factor	Note: Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.
Pulmonary toxicity	Bleomycin has been associated with severe and life threatening respiratory complications. The risk of bleomycin pulmonary toxicity appears higher in patients aged over 40 years. The total cumulative dose of bleomycin should NOT exceed 400,000 international units. The risk of pulmonary toxicity increases beyond a cumulative dose of 300,000 international units. Check the cumulative dose prior to each treatment. Baseline clinical assessment, pulmonary function tests (including DL_{CO}) and routine monitoring is recommended. Read more about pulmonary toxicity associated with anti-cancer drugs.
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 review by medical officer before commencing treatment as alternate regimen may be considered. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool

Tumour marker monitoring	AFP and BHCG should be monitored on day 1, 8 and 15 of first cycle and then as clinically indicated
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC, LFTs, calcium and magnesium at baseline and prior to each cycle.
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 fathering a child	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and contraception timeframe should be discussed with all patients of reproductive potential. 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: Delay and dose reductions are not recommended as the efficacy of this treatment may be greatly compromised - clinicians are advised to consult with a medical oncologist from a tertiary treatment centre with high volume experience in testicular cancer if dose delay or reduction due to toxicities or renal or hepatic dysfunction is being contemplated; an alternative treatment regimen may need to be considered.

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*

Bleomycin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Bleomycin toxicity may result from delayed clearance due to induced kidney dysfunction; including when low doses used	Avoid combination or monitor kidney function for increased bleomycin toxicity. Administer bleomycin before cisplatin in regimens using the combination
Oxygen during anaesthesia	Bleomycin causes sensitisation of lung tissue to oxygen	If oxygen is required, the use of low concentration (e.g. 25%) is recommended. Fluid replacement should be carefully monitored, with emphasis on administration of colloid rather than crystalloid, to avoid interstitial pulmonary oedema
Colony stimulating factors	May increase the risk of bleomycin induced pulmonary toxicity, especially at higher doses; this has not been confirmed in clinical trials	Monitor patients closely for signs of pulmonary toxicity if the combination is used

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)

Etoposide and Etoposide Phosphate		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin etc.)	Increased toxicity of etoposide possible due to reduced clearance	Avoid combination or monitor for etoposide toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of etoposide possible due to increased clearance	Avoid combination or monitor for decreased clinical response to etoposide
Glucosamine	Reduced efficacy of etoposide (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II)	Avoid combination or monitor for decreased clinical response to etoposide
Grapefruit juice	Reduced efficacy of oral etoposide possible due to possible alteration of P-gp mediated intestinal transport of etoposide	Avoid combination or monitor for decreased clinical response to etoposide

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

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: 4.5 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool.

Any toxicity greater than grade 2 should be reviewed by medical officer, however delay and dose reductions are not recommended as the efficacy of the treatment may be greatly compromised- clinicians are advised to consult with a medical oncologist from a tertiary treatment centre with high volume experience in testicular cancer if dose delay or reduction is being contemplated. An alternative treatment regimen may need to be considered.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Chemotherapy - Time out

Note: It is recommended to administer bleomycin prior to cisplatin as cisplatin may reduce the renal clearance of bleomycin, enhancing bleomycin toxicities.

Bleomycin

Administer bleomycin (irritant):

- over 10 minutes
  - via a minibag **OR**
  - by IV bolus via a side port of a freely flowing IV infusion
- flush with ~ 50 mL of sodium chloride 0.9%
- observe for hypersensitivity reaction especially during the first and second doses
- hypersensitivity reaction can occur with any dose of bleomycin regardless of whether a test dose has been administered.

Note: If bleomycin is to be given by IM injection bleomycin must be mixed with lignocaine, if platelet count less than 100 x 10^9/L, consult medical officer prior to IM injection.

- Read more about the safe administration of intramuscular cytotoxic drugs.

Cisplatin

Commence prehydration for cisplatin:

- administer 10 mmol magnesium sulphate ($MgSO_4$) in 1000 mL sodium chloride 0.9% over 60 minutes
- 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%.

Etoposide

Administer etoposide (irritant):

- via IV infusion over 30 to 60 minutes
- rapid infusion may cause hypotension

- observe for hypersensitivity
- flush with ~ 100 mL sodium chloride 0.9%
- if using etoposide phosphate administer in ~ 50 mL sodium chloride 0.9% or glucose 5% over ~15 minutes.

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.

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

Day 2 to 5

Approximate treatment time: 4 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool.

Any toxicity greater than grade 2 should be reviewed by medical officer, however delay and dose reductions are not recommended as the efficacy of the treatment may be greatly compromised- clinicians are advised to consult with a medical oncologist from a tertiary treatment centre with high volume experience in testicular cancer if dose delay or reduction is being contemplated. An alternative treatment regimen may need to be considered.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Chemotherapy - Time out

Cisplatin

Commence prehydration for cisplatin:

- administer 10 mmol magnesium sulphate ($MgSO_4$) in 1000 mL sodium chloride 0.9% over 60 minutes
- 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%.

Etoposide

Administer etoposide (irritant):

- via IV infusion over 30 to 60 minutes
- rapid infusion may cause hypotension
- observe for hypersensitivity
- flush with ~ 100 mL sodium chloride 0.9%
- if using etoposide phosphate administer in ~ 50 mL sodium chloride 0.9% or glucose 5% over ~15 minutes.

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.

Note: ensure arrangements have been made for the administration of growth factor on day 6 (24 hours post day 5 chemotherapy).

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

Day 8 and 15

Approximate treatment time: 30 minutes

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Bleomycin

Administer bleomycin (irritant):

- over 10 minutes
  - via a minibag **OR**
  - by IV bolus via a side port of a freely flowing IV infusion
- flush with ~ 50 mL of sodium chloride 0.9%
- observe for hypersensitivity reaction especially during the first and second doses
- hypersensitivity reaction can occur with any dose of bleomycin regardless of whether a test dose has been administered.

Note: If bleomycin is to be given by IM injection bleomycin must be mixed with lignocaine, if platelet count less than 100 x 10^9/L, consult medical officer prior to IM injection.

- Read more about the safe administration of intramuscular cytotoxic drugs.

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.

Growth factor support

- Arrangements for administration if prescribed.

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

Immediate (onset hours to days)	
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
Flu-like symptoms	
Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.

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
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Fatigue	Read more about fatigue
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
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.
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
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Hyperpigmentation	Darkening of an area of skin caused by the overproduction of melanin.
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation.
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about nail toxicities

Evidence

This replaced the previous standard of cisplatin, vinblastine and bleomycin in 1987 when it was shown to have similar (low risk disease) or greater (high risk disease) efficacy and less toxicity, particularly neuromuscular.[6] Multiple phase II and III trials attempting to define superior regimens in higher risk disease have not shown benefit over BEP. Strategies including the use of alternative or additional chemotherapy agents,[7, 8] more complex multi-drug regimens,[9, 10, 11, 12] and most recently, very high dose chemotherapy with stem cell support[13] are more toxic but no more effective than BEP.

A randomised trial conducted by the Australia New Zealand Germ Cell Trials Group (ANZGCTG, now incorporated in the Australian and New Zealand Urogenital and Prostate Cancer Trials Group Ltd [ANZUP]), has shown that the dose and dose intensity of BEP is important. A survey of treatment patterns in Australia conducted by the(ANZGCTG) in the early 1990s demonstrated considerable variations in management at participating centres. Approximately half of the centres used a five-day chemotherapy regimen incorporating etoposide 500 mg/m^2/cycle, as used in the United States (US). The remaining centres generally used a three-day chemotherapy regimen incorporating etoposide at a dose of 360 mg/m^2/cycle, based on regimens commonly used in Britain. Based on the results of a previous ANZGCTG study almost all centres used bleomycin, but many investigators were uncertain about the optimal dose and schedule in view of the unpredictable toxicity of this drug.

The ANZGCTG decided to compare two "standard" regimens of chemotherapy, each incorporating cisplatin, etoposide and bleomycin, in a randomised clinical trial for good-prognosis disease as defined by modified Memorial Sloan-Kettering criteria.[3] The first regimen was based on treatment recommendations from Indiana University, and referred to as "US PEB", and comprised 3 cycles of cisplatin 20 mg/m^2 days 1 to 5, etoposide 100 mg/m^2 days 1 to 5, and bleomycin 30,000 International Units days 1, 8 and 15, repeated every 21 days ($3B_{90}E_{500}P$).

The second regimen was based on the control arm of a published European clinical trial, and referred to as "European BEP", and comprised 4 cycles of cisplatin 100 mg/m^2 day 1, etoposide 120 mg/m^2 days 1 to 3, and bleomycin 30,000 International Units day 1, repeated every 21 days ($4B_{30}E_{360}P$).

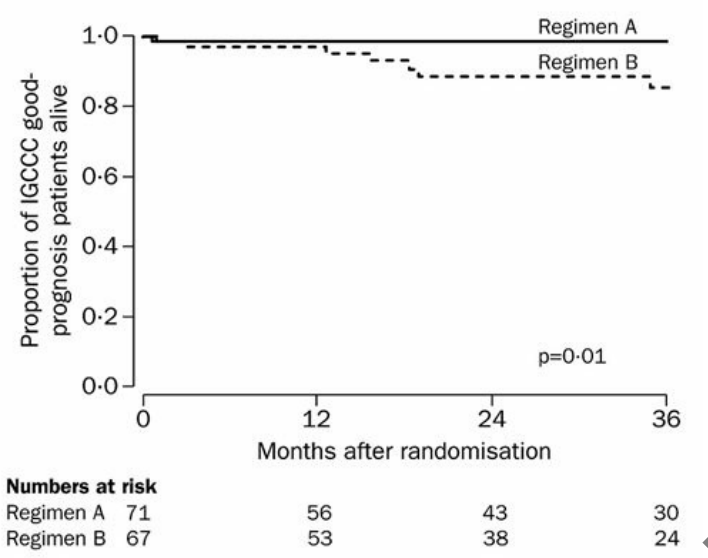
The trial was stopped after the second planned interim analysis met predefined stopping rules. 166 patients were randomised, 83 to each arm. Baseline characteristics were reasonably balanced between the 2 arms.

After a median follow up of 8.5 years, the OS rate at 8 years remained superior in patients treated with $3B_{90}E_{500}P$ vs the $4B_{30}E_{360}P$ regimen (92% vs 83%; HR=0.38; p=0.037). The PFS rate at 8 years was better with $3B_{90}E_{500}P$ than the $4B_{30}E_{360}P$ regimen, but the difference did not reach statistical significance.[14]

Efficacy

From multiple studies, it has been shown that prognostic groups as defined by the International Germ Cell Consensus Classification[15] dictate response. Good-risk patients have a 90% cure rate with BEP. Intermediate-risk patients have a 80% cure rate with BEP. Poor-risk patients such as non-Seminomatous Germ Cell Tumours (NSGCT) with high tumour markers, nonpulmonary visceral metastases, or a mediastinal primary site at presentation only have a 50% cure rate with BEP. Consider alternative regimens on trial for intermediate and poor-risk patients.

Overall Survival (all patients):[3]



Toxicity

Toxicity[3]	Regimen A (%)	Regimen B (%)	*p*-value
Grade 3 and 4			
Anaemia	1	7	0.1
Leucopenia	31	33	1.0
Neutropenia	59	65	0.5
Thrombocytopenia	2	8	0.2
Grade 2, 3 and 4			
Nausea and vomiting	57	74	0.02
Pulmonary	12	8	0.6
Peripheral Neuropathy	10	8	1.0
Renal	1	0	1.0
Tinnitus	2	6	0.3
Other*	35	24	0.2

** includes constipation, headache, indigestion, lethargy and dizziness*

Regimen A: 3 cycles of cisplatin 20 mg/m^2 on days 1 to 5, etoposide 100 mg/m^2 days 1 to 5 and bleomycin 30,000 International units days 1, 8 and 15 repeated every 21 days

Regimen B: 4 cycles of cisplatin 100 mg/m^2 day 1, etoposide 120 mg/m^2 days 1 to 3 and bleomycin 30,000 International units day 1 and repeated every 21 days

Four deaths (2 in each group) were related to the study treatment. Three deaths in the $3B_{90}E_{500}P$ group and ten deaths in the $4B_{30}E_{360}P$ group were associated with disease progression.

HRQL scores for eight side effects associated with chemotherapy (as assessed by the GLQ-8 questionnaires were available for 149 patients (90%)). HRQL scores were similar for both regimens.

The primary differences in HRQL between the groups at 3, 6, and 12 weeks occurred in scores for numbness or pins-and-needles sensations (p=0.003), hair loss (p=0.04), and Spitzer Quality of Life Index (p=0.05), which were better in the $3B_{90}E_{500}P$ group. Scores for most scales returned to baseline levels at 6 months.[14]

Also consider potential long-term toxicity of BEP including infertility, ototoxicity, Raynaud's phenomenon, peripheral neuropathy, lung disease, cardiovascular disease and secondary malignancies.[16]

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History

Version 6

Date	Summary of changes
18/11/2021	Protocol reviewed by Medical Oncology Reference Committee. Cisplatin changed from moderately to highly emetogenic as per NCCN, MASCC/ESMO and ASCO guidelines and medical oncology reference committee consensus. Treatment schedule antiemetics and clinical information updated to reflect the change. Indications updated to include cautions and exclusions. Clinical information pulmonary toxicity- risk increase with age over 40 added. NK-1 antagonist added to interactions. Version number changed to V.6.
31/08/2022	Bleomycin extravasation category updated to align with extravasation clinical resources update.

Version 5

Date	Summary of changes
04/09/2020	Biosimilar drug added to clinical information. Version number changed to V.5.

Version 4

Date	Summary of changes
08/10/2019	Clinical information updated with PBS expanded indications for GCSF. Treatment schedule note updated.

Version 3

Date	Summary of changes
15/05/2007	Patient sheet updated.
07/12/2007	Bleomycin dose information added.
15/12/2007	Further information about bleomycin dose equivalence added.
08/03/2010	Review, new dose modifications and transferred to eviQ.
15/06/2010	Blood tests for FBC removed from "Key Administration Points" table for Days 2 to 5 and Days 8 and 15.
13/08/2010	Pegfilgrastim added to treatment schedule.
02/11/2010	Evidence reviewed and updated.
21/07/2011	New format to allow for export of protocol information. Protocol version number changed to *V.2.* Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
16/01/2012	PHC view updated.
05/04/2013	Reviewed by reference committee via email. No change. 2 year review.
10/7/2013	Dose modifications for cisplatin updated.
09/05/2014	Reviewed at Medical Oncology Reference Committee meeting. Dose modifications changed. PHC view removed. Review 2 years.
31/03/2017	Protocol discussed and decided to have a 5 year review period. Next due for review in 2019.

Date	Summary of changes
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.3.
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
25/03/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 15/03/2019. ANZUP surveillance recommendations added as related page. Next review in 5 years.

First approved: 13 September 2005
Last reviewed: 15 March 2019
Review due: 30 June 2024

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/320
19 Jun 2023

Patient information - Testicular cancer metastatic - BEP (bleomycin, etoposide, cisplatin)

Patient's name:

Your treatment

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

BEP (bleomycin, etoposide, cisplatin)

This treatment cycle is repeated every 21 days. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	**Bleomycin** (*blee-oh-MYE-sin*)	By a drip into a vein or by injection into your muscle	About 4.5 hours
	Etoposide (*e-TOE-poe-side*) **Cisplatin** (*siss-PLAT-in*)	By a drip into a vein	
2 to 5	**Etoposide** **Cisplatin**	By a drip into a vein	About 4 hours
6	**Pegfilgrastim** (*peg-fil-GRA-stim*)	By injection under the skin	About 5 minutes
8 and 15	**Bleomycin**	By a drip into a vein or by injection into your muscle	About 30 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.

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

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.

Flu-like symptoms	• You may get:
	  ◦ a fever
	  ◦ chills or sweats
	  ◦ muscle and joint pain
	  ◦ a cough
	  ◦ headaches.
	• The drug bleomycin can cause a fever or flu-like illness within the first day of having the treatment.
	• You can take paracetamol to help settle these symptoms.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if the symptoms do not settle or you become unwell.**

Bone pain after G-CSF injection	• You may have discomfort or a dull ache in your pelvis, back, arms or legs. • To reduce the pain, take paracetamol before each injection. • **Tell your doctor or nurse as soon as possible if your pain is not controlled.**
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.**
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.
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.**

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 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.**

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.**
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.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
Skin colour changes	• You may have darkening of your skin, especially in areas that are exposed to the sun. • You may also notice darkening of your tongue, gums and over your finger joints. • These skin changes may fade over time. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.
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 you doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.** • Ask your doctor or nurse for eviQ patient information about lung damage from bleomycin treatment.
Nail changes	• Your nails may: ◦ grow more slowly ◦ become darker ◦ develop ridges or white lines ◦ become brittle and flaky • In some cases, you may lose your nails completely. • Keep your nails clean and short. • Avoid things like biting your fingernails, getting a manicure, pedicure or false nails. • Wear gloves when you wash the dishes, work in the garden, or clean the house.

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

- 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.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to 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.

Fathering a child

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that your partner could be pregnant.
- Do not try to 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 fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.

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

Testicular cancer information

- Healthy Male Andrology Australia – healthymale.org.au
- Livestrong – livestrong.org

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
- 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:

First approved: 13 September 2005
Last reviewed: 15 March 2019
Review due: 30 June 2024

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/320
16 Jun 2023