Multiple myeloma PAD (bortezomib DOXOrubicin and dexamethasone) upfront SUPERSEDED

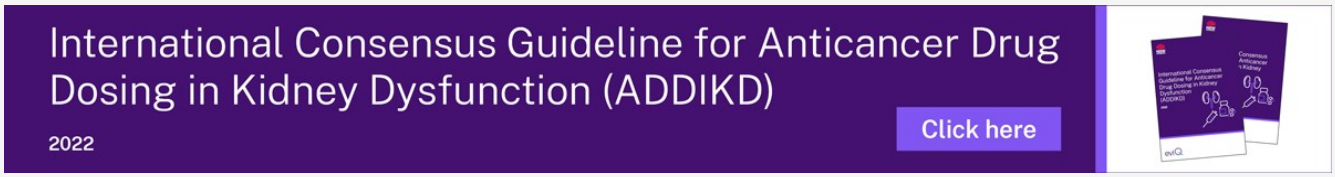
ID: 1431 v.3 **Superseded** Essential Medicine List

This protocol has been superseded as it is the consensus of the Haematology Reference Committee that there is limited evidence for use in upfront multiple myeloma, and is not commonly used in clinical practice.

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

Link to Medical Scientific Advisory Group (MSAG) Clinical Practice Guideline Multiple Myeloma

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.



Treatment schedule - Overview

Cycle 1 to 3

Drug	Dose	Route	Day
Dexamethasone	40 mg ONCE a day	PO	1 to 4, 9 to 12, 17 to 20
Bortezomib *	1.3 mg/m^2	Subcut	1, 4, 8, 11
DOXOrubicin **	36 mg/m^2	CIV via pump over 96 hours	1

* The once weekly bortezomib protocol with 1.5 mg/m^2 is associated with similar response rates to twice weekly bortezomib but with much less grade 3-4 events.[1]

** DOXOrubicin may alternatively be given at a dose of 20 mg/m^2 on days 1 AND 4 (total dose of 40 mg/m^2).[2]

Frequency: 28 days

Cycles: 3 followed by intensification with high dose melphalan and autologous stem cell transplant; followed by maintenance with bortezomib every 2 weeks for 2 years

Notes:
It is the consensus of the reference committee that a 20 mg/week starting dose of dexamethasone should be considered in patients > 75 years.[3]

Drug status: **Bortezomib**: PBS restricted benefit

Doxorubicin and dexamethasone: PBS general schedule

Dexamethasone is available as **0.5 mg** and **4 mg** tablets

Cost: ~ $1,620 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		
Dexamethasone	40 mg (PO)	ONCE a day. Take in the morning with food.
Palonosetron	0.25 mg (IV bolus)	30 minutes before chemotherapy
Bortezomib	1.3 mg/m^2 (Subcut)	via subcutaneous injection
DOXOrubicin	36 mg/m^2 (CIV)	via ambulatory infusion pump over 96 hours (equivalent to 9 mg/m^2/day)
Day 2 and 3		
Dexamethasone	40 mg (PO)	ONCE a day. Take in the morning with food.
Day 4		
Dexamethasone	40 mg (PO)	ONCE a day. Take in the morning with food.
Bortezomib	1.3 mg/m^2 (Subcut)	via subcutaneous injection
Day 8		
Bortezomib	1.3 mg/m^2 (Subcut)	via subcutaneous injection
Day 9 and 10		
Dexamethasone	40 mg (PO)	ONCE a day. Take in the morning with food.
Day 11		
Dexamethasone	40 mg (PO)	ONCE a day. Take in the morning with food.
Bortezomib	1.3 mg/m^2 (Subcut)	via subcutaneous injection
Day 12 and 17 to 20		
Dexamethasone	40 mg (PO)	ONCE a day. Take in the morning with food.

Notes:

- The once weekly bortezomib protocol with 1.5 mg/m^2 is associated with similar response rates to twice weekly bortezomib but with much less grade 3-4 events.[1]
- DOXOrubicin may alternatively be given at a dose of 20 mg/m^2 on days 1 AND 4 (total dose of 40 mg/m^2).[2]

Frequency: 28 days

Cycles: 3 followed by intensification with high dose melphalan and autologous stem cell transplant; followed by maintenance with bortezomib every 2 weeks for 2 years

Indications and patient population

- Induction therapy for upfront treatment of multiple myeloma prior to autologous stem cell transplantation

Clinical information

Venous access	Central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. As a steroid has been included as part of this protocol, additional antiemetic steroids are not required. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist may be available on the PBS in combination with a $5HT_3$ antagonist and steroid. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cumulative lifetime dose of anthracyclines	Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone). Criteria for reducing the total anthracycline cumulative lifetime dose include: • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation. Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion. Read more about cardiac toxicity associated with anthracyclines
Peripheral neuropathy	Peripheral neuropathy (PN), including grade 2 and 3 events are reported less frequently with subcutaneous (SC) dosing of bortezomib than with intravenous (IV) administration. All patients should be assessed regularly for symptoms of peripheral neuropathy. Most cases are reversible with dose modifications. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Orthostatic hypotension	Caution in patients with history of syncope or postural hypotension and those taking antihypertensive medications. Ensure patient is well hydrated prior to therapy.
Thrombocytopenia	Grade 3 and Grade 4 thrombocytopenia occur frequently. Usually transient and cyclical, recovering towards end of rest period. Platelet nadir occurs at approximately day 11. Dose delays and/or modifications may be required. Platelet support may be required. Read more about thrombocytopenia associated with bortezomib
Bone modifying agents	Use of a bone modifying agent (BMA) should be considered in all patients with symptomatic myeloma requiring treatment. For patients with newly diagnosed symptomatic myeloma, zoledronic acid, pamidronate or denosumab should be considered for monthly administration (adjust for kidney dysfunction where appropriate) for up to 2 years. A longer duration of therapy may be appropriate (MRC M IX trial).[4] For more information, please see the following protocols: ID 137 Multiple myeloma zoledronic acid ID 147 Multiple myeloma pamidronate ID 3964 Multiple myeloma denosumab - note denosumab is TGA approved but not PBS reimbursed for this indication.

Bisphosphonates and dental review	Caution should be taken with prolonged use of bisphosphonates due to the risk of osteonecrosis of the jaw (ONJ). A dental review prior to treatment is recommended, and all dental issues treated before the initiation of bisphosphonates. Dental review 6 to 12 monthly during treatment is advisable to minimise risk of ONJ. Concurrent daily oral supplements of calcium 500 mg and vitamin D 400 International Units are recommended. Read more about medication-related osteonecrosis of the jaw (MRONJ)
Corticosteroids	Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate. Read more about acute short term effects from corticosteroids
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	PJP prophylaxis is recommended e.g. trimethoprim/sulfamethoxazole 160/800 mg PO one tablet twice daily, twice weekly (e.g. on Mondays and Thursdays) OR one tablet three times weekly (e.g. on Mondays, Wednesdays and Fridays). Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Bortezomib is associated with a risk of Herpes Zoster infection (shingles). Antiviral prophylaxis is recommended to protect from HSV and VZV reactivation during active therapy including periods of neutropenia. Read about antiviral prophylaxis drugs and doses
Thromboprophylaxis	Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion. Read more about the prophylaxis of venous thromboembolism (VTE) in multiple myeloma
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, magnesium, phosphate and BSL at baseline and regularly throughout treatment. Weekly FBC is recommended for the first cycle, then prior to the start of each subsequent cycle or as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

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

Note: All dose reductions are calculated as a percentage of the starting dose

Bortezomib should be withheld at the onset of any Grade 4 haematological toxicity or any Grade 3 non-haematological, with the exception of neuropathy. On the resolution of the toxicity, bortezomib should be reinitiated at a 25% reduction of the previous dose as follows:

- 1.3 mg/m^2 reduced to 1 mg/m^2 and
- 1 mg/m^2 reduced to 0.7 mg/m^2

If the toxicity is not resolved or if it recurs at the lowest dose, discontinuation of bortezomib must be considered unless the benefit of treatment clearly outweighs the risk.

Haematological toxicity	
Any Grade 4 haematological toxicity	Withhold treatment; when the toxicity has resolved, recommence bortezomib at a 25% reduction of the previous dose.
Platelets ≤ 25 x 10^9/L on day 1 of any cycle	Consider withholding treatment until the platelet count is ≥50 x 10^9/L; recommence bortezomib at a 25% reduction of the previous dose.
Consider using G-CSF for neutropenia	

Bortezomib

Hepatic impairment	
Hepatic dysfunction	
Moderate or severe	Reduce bortezomib to 0.7 mg/m^2 per dose for the first cycle, then consider dose escalation to 1 mg/m^2 or further dose reduction to 0.5 mg/m^2 for subsequent cycles depending on patient tolerability

Doxorubicin

Hepatic impairment	
Hepatic dysfunction	
Mild	Reduce doxorubicin by 25%
Moderate	Reduce doxorubicin by 50%
Severe	Omit doxorubicin

Peripheral neuropathy	
Grade 1	No action
Grade 1 with pain or Grade 2	Reduce bortezomib to 1 mg/m^2

Peripheral neuropathy	
Grade 2 with pain or Grade 3	Withhold bortezomib therapy until toxicity resolves. Reinitiate with a reduced dose of bortezomib at 0.7 mg/m^2 and change treatment schedule to once per week. The pros and cons of continuing treatment in the presence of Grade 3 toxicity should be carefully considered.
Grade 4	Discontinue bortezomib

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*

Bortezomib		
	Interaction	**Clinical management**
Antihypertensives	Additive hypotensive effect	Monitor blood pressure. Ensure patient is well hydrated prior to bortezomib dose. Adjust antihypertensive dose as required
Strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir)	Potentially increased bortezomib toxicity due to reduced clearance	Monitor patients closely for bortezomib toxicity (thrombocytopenia, neutropenia, peripheral neuropathy)
Strong CYP3A4 and P-gp inducers (e.g. rifampin, St John's Wort)	Potentially reduced efficacy of bortezomib due to increased clearance	Monitor patients closely for decreased bortezomib efficacy
Other CYP3A4 inhibitors or inducers (e.g. azoles, grapefruit juice, macrolides, carbamazepine, phenytoin)	Low levels of evidence for interactions, coadministration has not been studied	Monitor patients closely for either toxicities or reduced efficacy
Oral hypoglycaemics	Hypoglycaemia or hyperglycaemia	Monitor blood glucose levels and adjust oral hypoglycaemic dose as required
Green tea	May diminish the anti-cancer effect of bortezomib	Avoid combination

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

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

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: 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 delay of treatment and review by medical officer before commencing treatment.

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Dexamethasone

- administer orally once daily in the morning, with food on **days 1 to 4, 9 to 12 and 17 to 20**

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

Chemotherapy - Time out

Bortezomib

- administer by subcutaneous injection
- rotate the injection site for each injection
- pain, inflammation and thrombophlebitis may occur at injection site
- doses of bortezomib must be at least 72 hours apart.

Doxorubicin

Administer doxorubicin continuous infusion (vesicant):

- Connect pump doxorubicin to port or CVC and administer over the correct time for the volume of drug in the pump
- verify the correct rate of infusion via the ambulatory infusion pump
- read more information about the different ambulatory infusion pumps.

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

Day 4

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 delay of treatment and review by medical officer before commencing treatment.

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Note: Dialysis patients: administer bortezomib either after the patient has been dialysed or a minimum of 4 hours prior to dialysis.

Dexamethasone

- administer orally ONCE a day in the morning, on **days 1 to 4**
- to be taken with or immediately after food.

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

Chemotherapy - Time out

Bortezomib

- administer by subcutaneous injection
- rotate the injection site for each injection
- pain, inflammation and thrombophlebitis may occur at injection site
- doses of bortezomib must be at least 72 hours apart.

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

Day 5

Approximate treatment time: 30 minutes

Safe handling and waste management

Disconnection of ambulatory infusion pump/infusor

Verify the ambulatory infusion pump/infusor is complete.

Disconnect the ambulatory infusion pump/infusor as per recommended procedure for type of pump/infusor.

Read more about ambulatory infusion pumps/infusors.

Deaccess TIVAD or CVAD.

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

Day 8

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 delay of treatment and review by medical officer before commencing treatment.

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Note: Dialysis patients: administer bortezomib either after the patient has been dialysed or a minimum of 4 hours prior to dialysis.

Chemotherapy - Time out

Bortezomib

- administer by subcutaneous injection
- rotate the injection site for each injection
- pain, inflammation and thrombophlebitis may occur at injection site
- doses of bortezomib must be at least 72 hours apart.

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

Days 9 and 10

This is an oral treatment

Dexamethasone

- administer orally once daily in the morning, with food on **days 1 to 4, 9 to 12 and 17 to 20**

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

Day 11

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 delay of treatment and review by medical officer before commencing treatment.

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Note: Dialysis patients: administer bortezomib either after the patient has been dialysed or a minimum of 4 hours prior to dialysis.

Dexamethasone

- administer orally once daily in the morning, with food on **days 1 to 4, 9 to 12 and 17 to 20**

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

Chemotherapy - Time out

Bortezomib

- administer by subcutaneous injection
- rotate the injection site for each injection
- pain, inflammation and thrombophlebitis may occur at injection site
- doses of bortezomib must be at least 72 hours apart.

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

Days 12 and 17 to 20

This is an oral treatment

Dexamethasone

- administer orally once daily in the morning, with food on **days 1 to 4, 9 to 12 and 17 to 20**

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

Discharge information

Dexamethasone tablets

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

Antiemetics

- Antiemetics as prescribed.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

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

Patient information

- Ensure patient receives patient information sheet.

Infusion pumps patient information sheet

- CADD-Legacy® 1 ambulatory infusion pump patient information sheet
- CADD-Legacy® Plus ambulatory infusion pump patient information sheet
- CADD® Solis VIP ambulatory infusion pump 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)	
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Hypotension	Low blood pressure is commonly associated with bortezomib treatment.
Injection-site reactions	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.

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	Thrombocytopenia is a reduction in the normal levels of functional platelets. It is associated with bortezomib treatment, particularly in patients who have had a number of prior therapies. However, it is rarely severe enough to postpone subsequent cycles. Read more about thrombocytopenia associated with bortezomib
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
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
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Radiation recall	Erythematous or inflammatory skin reaction resembling severe sunburn at sites previously treated with radiation therapy can occur with certain anti-cancer drugs. Symptoms include vesiculation, desquamation and ulceration of the skin. Read more about radiation recall
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Thromboembolism	Thromboembolic events, including pulmonary embolism, deep vein thrombosis and cerebrovascular accidents can occur. Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion. Read more about management of thromboembolism (VTE) in multiple myeloma

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

Delayed (onset months to years)	
Cardiotoxicity	Anthracyclines are the most frequently implicated anti-cancer drugs associated with cardiotoxicity, which typically manifests as a reduction in left ventricular ejection fraction (LVEF), cardiomyopathy, or symptomatic CHF. Anthracycline induced cardiotoxicity has been categorised into acute, early-onset chronic progressive and late-onset chronic progressive and is usually not reversible. The risk of clinical cardiotoxicity increases with a number of risk factors including higher total cumulative doses. Read more about cardiac toxicity associated with anthracyclines
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

This protocol has been superseded as it is the consensus of the Haematology Reference Committee that there is limited evidence for use in upfront multiple myeloma, and is not commonly used in clinical practice.

Oakervee et al. presented the initial sequential phase I/II study of bortezomib, doxorubicin and dexamethasone (PAD) in newly diagnosed, transplant-eligible myeloma patients (n=21) in 2005.[5] In this study, the maximum administered dose of doxorubicin was 9 mg/m^2, which was subsequently adopted in a second cohort of patients in the long-term follow-up study by Popat et al.,[6] and also used in the recently published randomised, multicentre phase III HOVON-65/GMMG-HD4 trial.[7]

Patients in the Oakervee/Popat studies received four 21-day cycles of PAD prior to autologous stem cell transplantation (ASCT), while a cohort of patients in the Popat study (n=20) received a lower dose of twice-weekly bortezomib (1.0 mg/m^2). Dexamethasone was administered on days 1 to 4 (plus days 8 to 11, 15 to 18 in cycle 1 only). There were no statistically significant differences in complete response (CR)/near complete response (nCR) and >very good partial response (VGPR) rates post-induction between PAD patients who received 1.0 mg/m^2 or 1.3 mg/m^2 of twice-weekly bortezomib (CR 11%/nCR 5%/VGPR 26% versus CR 24%/nCR 5%/VGPR 33%, respectively).

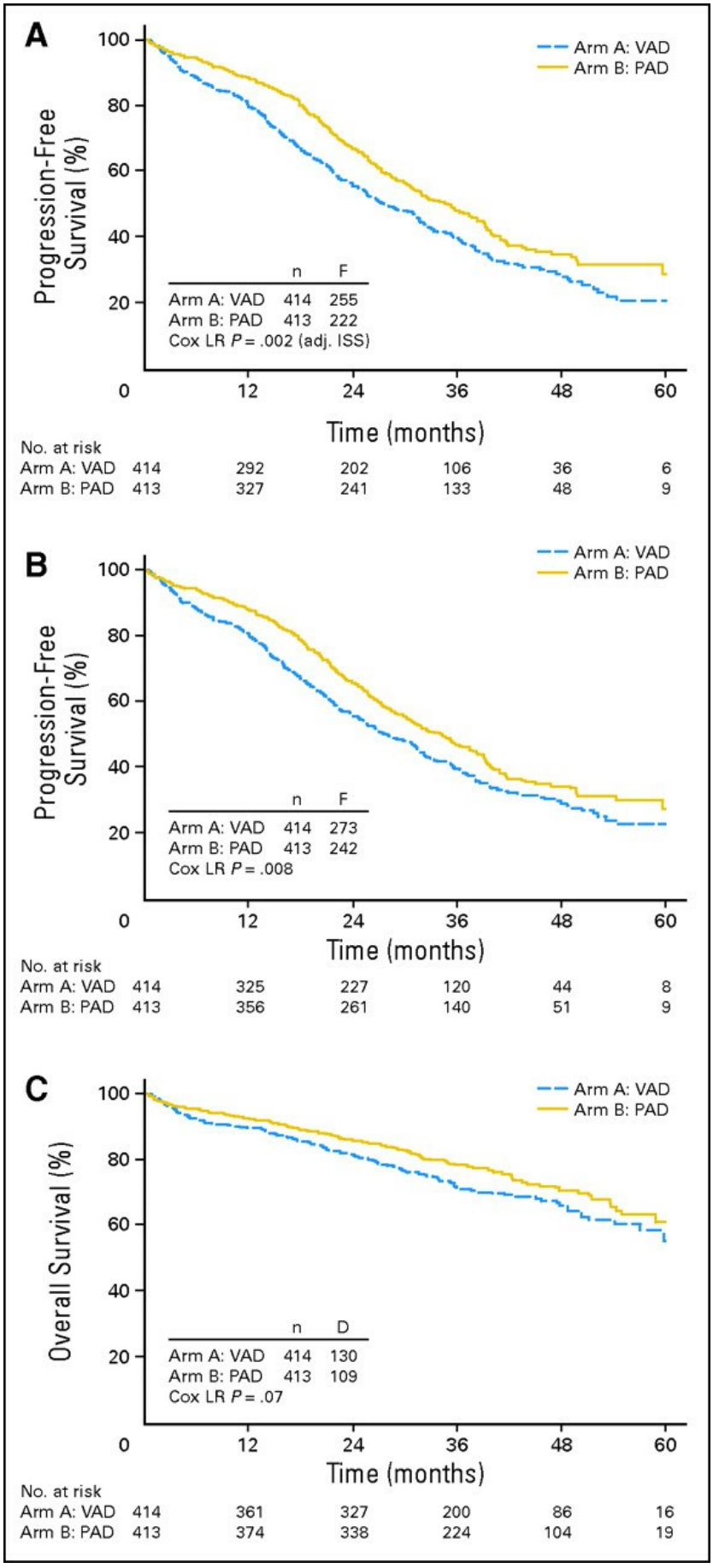
The HOVON-65/GMMG-HD4 Trial[7] enrolled 833 patients with newly diagnosed, transplant-eligible myeloma patients. Patients were randomised to three cycles of VAD induction, ASCT, followed by thalidomide 50 mg maintenance for 2 years or three cycles of PAD induction (bortezomib 1.3 mg/m^2 days 1, 4, 8, 11; doxorubicin 9 mg/m^2 days 1 to 4; dexamethasone 40 mg days 1 to 4, 9 to 12, 17 to 20 in a 28-day cycle), followed by ASCT and subsequent IV bortezomib 1.3 mg/m^2 every 2 weeks for 2 years. Of note, HOVON patients received single ASCT, while GMMG patients received tandem ASCTs, per institutional protocols. CR rates after induction were 24% with VAD vs. 36% with PAD (p=<0.001). Median progression-free survival (PFS) was 28 months for VAD arm vs. 35 months for PAD arm; in a multivariate analysis, PAD induction is associated with superior PFS (HR 0.74; 95% CI 0.62-0.89; p=0.001). Median overall survival (OS) was not reached after 66 months of follow-up in either arm, with 5-year OS of 55% (VAD arm) vs. 61% (PAD arm), p=0.07. Of note, GMMG patients had better OS overall (HR 0.75; 95% CI 0.57 -0.97; p=0.03), but when VAD vs. PAD patients were analysed within the GMMG group, there was no statistical difference in OS.

A small, phase II single-arm study published by Lee et al.[8] explored the use of short-course (two cycles) PAD induction in transplant-eligible South Korean patients to minimise toxicity. 32 patients received two 21-day cycles of PAD with bortezomib 1.3 mg/m^2 on days 1, 4, 8, 11; doxorubicin 9 mg/m^2 on days 1 to 4; and IV dexamethasone 40 mg on days 1 to 4 and 8 to 11. Patients were then mobilised with G-CSF only, followed by ASCT. After induction, CR was achieved in 19%, VGPR in 16% of patients. Post-ASCT, CR was achieved in 47% and VGPR in 27% of patients.

The use of liposomal doxorubicin in “PAD” has also been reported in 4 studies in the frontline treatment of myeloma. Most of these studies are small phase II trials with around 40 enrolled patients, most transplant eligible. In three of the trials, the patients received bortezomib 1.3 mg/m^2 on days 1, 4, 8, and 11; liposomal doxorubicin 30 mg/m^2 on day 4; dexamethasone 20 to 40 mg on days of and day after bortezomib therapy in a 21-day cycle,[9, 10] (one trial administered 40 mg day 1-4 only).[11] Most of these trials have limited patient follow-up, with an observed ORR 81-86% and nCR/CR 20 to 37.5% after 3-8 cycles of liposomal PAD. Given the small size of these phase II studies, the results should be interpreted with caution.

Efficacy

The use of PAD during induction therapy resulted in CR rates of 19 to 36% after 2 or 4 cycles, respectively. The HOVON-65/GMMG-HD4 showed that PAD was superior to VAD induction in respect to post-induction CR rates and PFS (refer to graph below). Median OS was not reached after 66 months of follow-up in either arm post-ASCT, with 5-year OS of 55% (VAD arm) vs. 61% (PAD arm), p=0.07.



Toxicity

Table A2.

Safety Profile and Toxicities

Variable	VAD (n = 414)				PAD (n = 413)			
	VAD Induction (n = 411)		Thalidomide Maintenance (n = 270)		PAD Induction (n = 410)		Bortezomib Maintenance (n = 229)	
	No.	%	No.	%	No.	%	No.	%
Any AE	401	98	260	96	400	98	222	97
AE grade 3 to 4	220	54	123	46	258	**63***	110	48
AE classified as SAE	148	36	61	23	187	**46***	77	**34***
AE leading to discontinuation, dose reduction, or delay of bortezomib	N/A	N/A	N/A	N/A	112	27	81	35
Death from AE	9	2	0	0	7	2	0	0
	All Grades	Grade 3 to 4	All Grades	Grade 3 to 4	All Grades	Grade 3 to 4	All Grades	Grade 3 to 4
Hematologic toxicities (%)								
Anemia	24	7	15	1	28	8	**27***	1
Neutropenia	2	1	4	1	4	3	2	0
Thrombocytopenia	18	5	19	2	**39†**	**10***	**37†**	4
Infections	49	21	61	18	56	26	**75***	24
Herpes zoster	0	0	1	0	**2‡**	0	2	0
Nonhematologic toxicities (%)								
Wasting, fatigue	28	4	20	1	27	4	20	1
GI symptoms	59	7	40	4	**67‡**	**11‡**	48	5
Cardiac disorders	24	5	13	2	27	8	19	3
Thrombosis	5	3	1	1	6	4	1	1
Peripheral neuropathy	26	10	**53†**	8	**37†**	**24†**	33	5

- NOTE. Bold numbers indicate a statistically significant higher proportion compared with the other arm.
- Abbreviations: AE, adverse event (including infection); N/A, not applicable; SAE, serious adverse event.
- *$P < .01$.
- †$P < .001$.
- ‡$P < .05$.

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History

Version 3

Date	Summary of changes
31/08/2012	New protocol taken to Haematology Reference Committee meeting; review in 2 years, category 2.
08/08/2013	Approved and published on eviQ.
13/03/2015	Decision at Haematology Reference Committee meeting to supersede PAD upfront due to limited evidence for use in upfront setting. Changed the route of bortezomib administration from IV to SC. Updated clinical information and treatment schedules to reflect SC administration.
31/05/2017	Transferred to new eviQ website. Version number change to v.3.
24/05/2019	Reviewed at Haematology Reference Committee meeting: • PBS information updated to Bortezomib authority and removed further wording. • Consensus to remain superseded.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.
29/11/2021 **20/01/2022**	Interactions updated.
24/01/2022	Pulmonary toxicity added to side effects.
14/10/2022	The following changes have been made with the consensus agreement of the Haematology Reference Committee: • Bone modifying agents block added to clinical information, related note removed from treatment schedule and linked pages removed • Link to Medical Scientific Advisory Group (MSAG) guidelines updated • Note regarding dexamethasone reduction in specific patient populations added to treatment schedule notes • Thromboprophylaxis information added to “Clinical information” section • Specific medications removed from G-CSF note in 'Dose modifications' section

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Last reviewed: 24 May 2019
Review due: 24 May 2021
Superseded: 13 March 2015

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/1431
13 Jun 2023

Patient information - Multiple myeloma - PAD (bortezomib, doxorubicin, dexamethasone) upfront

Patient's name:

Your treatment

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

PAD (bortezomib, doxorubicin, dexamethasone)			
This treatment cycle is repeated every 28 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 to 4, 9 to 12, 17 to 20	**Dexamethasone** (*dex-a-METH-a-sone*)	Take orally ONCE a day in the morning with food on days 1 to 4, 9 to 12 and 17 to 20 only. If you forget to take your tablets or vomit your tablets, contact your treating team.	
1, 4, 8, 11	**Bortezomib** (*bore-TEZ-oh-mib*)	By injection under the skin	About 5 minutes
1 to 4	**Doxorubicin** (*dox-oh-roo-bi-sin*)	By drip into a vein through a pump	For 4 days (96 hours) by pump at home.

When to get help

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

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

Pumps and central venous access devices (CVADs)

This treatment involves having chemotherapy through a pump. To have this, you will also need a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information see the eviQ patient information sheets on pumps and CVADs. At home you will need to look at your pump 3 to 4 times a day to check it is working. Your nurse will teach you how to do this.

Other medications given during this treatment

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

Superseded treatments

This treatment is superseded meaning that better treatments have taken its place. Uncommonly superseded treatments are still used. Your doctor will explain why this treatment has been selected for you.

Side effects

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

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

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

Immediate (onset hours to days)	
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.**
Low blood pressure (hypotension)	• You may get low blood pressure from the drug bortezomib. • You may feel dizzy or light-headed. • Tell your doctor if you are taking blood pressure medication. • Your doctor will monitor your blood pressure regularly while you are on this treatment. • Drink plenty of fluids (unless you are fluid restricted), especially before each dose of bortezomib. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Do not drive or operate machinery if you feel dizzy or light-headed. • Tell your doctor or nurse if you get any of the signs or symptoms listed above.
Injection-site reaction	• At the injection site you may get pain, redness, swelling or bruising. • These symptoms are usually not serious. • **Tell your doctor or nurse immediately if you notice any redness or pain during or after treatment.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Urine turning orange or red	• Your urine will turn an orange or red colour. • This is not harmful and should only last for up to 48 hours after treatment.

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 body. 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. • For minor pain take paracetamol. Do not take any medications containing aspirin or ibuprofen without talking to your doctor or nurse. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**

Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including: ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.
Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin reaction in an area previously treated with radiation therapy (radiation recall)	• In the area that was treated with radiation therapy, your skin may become: ◦ dry, red and itchy ◦ tender and swollen • It may also: ◦ peel or blister ◦ form ulcers • This usually happens weeks or months after chemotherapy treatment. • Avoid wearing tight clothing. • Avoid direct sunlight and very hot or cold temperatures. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • Tell your doctor or nurse if you get any of the symptoms listed above.
Side effects from steroid medication	• Steroid medication may cause: ◦ mood swings and behaviour changes ◦ an increased appetite ◦ weight gain ◦ swelling in your hands and feet ◦ stomach upsets ◦ trouble sleeping ◦ fragile skin and bruising ◦ an increase in your blood sugar level ◦ weak and brittle bones (osteoporosis) • Take your steroid medication with food to reduce stomach upset • If you have diabetes, your blood sugar levels may be tested more often. • Tell your doctor or nurse if you get any of the symptoms listed above.

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Late (onset weeks to months)	
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

Delayed (onset months to years)	
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems can occur months to years after treatment. • Tell your doctor if you have a history of heart problems or high blood pressure. • Before or during treatment, you may be asked to have a test to see how well your heart is working. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**
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 patients 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.
- You should not take any products containing vitamin C or green tea while you are having this treatment, they may make your treatment less effective.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

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

Diet and food safety

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

Fertility

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

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

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

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

Quitting smoking

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

Staying active

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

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

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – aci.health.nsw.gov.au/resources/blood-and-marrow-transplant
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information

and support to help you quit smoking. Talk to your treating team about any other questions you may have.

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

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