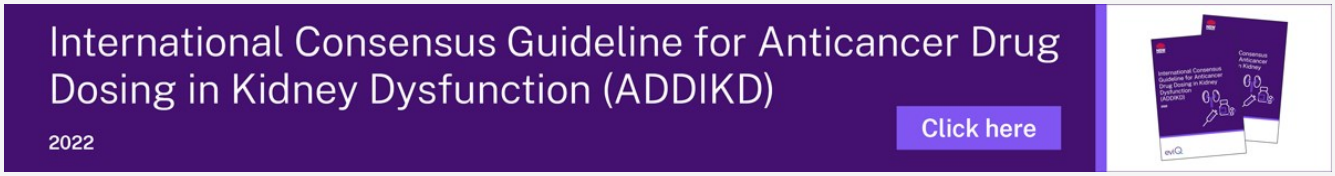
# Multiple myeloma CyBorD (CYCLOPHOSPHamide bortezomib dexamethasone) twice weekly

**ID: 556** v.6 **Endorsed** Essential Medicine List

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.




**Related pages:**

- Multiple myeloma CyBorD (CYCLOPHOSPHamide bortezomib dexamethasone) weekly

## Treatment schedule - Overview

### Cycle 1 to 4

| Drug | Dose | Route | Day |
|---|---|---|---|
| Dexamethasone * | 40 mg ONCE a day | PO | 1, 4, 8, 11 |
| CYCLOPHOSPHamide ** | 300 mg/m$^2$ ONCE a week | PO | 1, 8, 15 |
| Bortezomib | 1.3 mg/m$^2$ | Subcut | 1, 4, 8, 11 |

* The dexamethasone dose may alternatively be administered as 20 mg on the day of and day after bortezomib (days 1, 2, 4, 5, 8, 9, 11 and 12) as per Kropff et al. 2007[1]

** The cyclophosphamide dose may alternatively be administered as a 50 mg per day dose,[2] 500 mg/m$^2$ on D1, 8, 15,[3] 500 mg on D1, 8, 15 as per clinical practice, 900 mg/m$^2$ IV on D1 only,[4] or omitted in frail and/or elderly patients.

**Frequency:** 21 days

**Cycles:** 4 cycles prior to transplant; up to 13 cycles for transplant ineligible patients; and up to 11 cycles for relapsed patients.

**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. [5]

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

**Cyclophosphamide** and **dexamethasone**: PBS general schedule

Cyclophosphamide is available as **50 mg** tablets
Dexamethasone is available as **0.5 mg** and **4 mg** tablets

**Cost:** ~ $1,610 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 4

| Day 1 | | |
|---|---|---|
| Granisetron | 2 mg (PO) | 60 minutes before chemotherapy |
| Dexamethasone | 40 mg (PO) | ONCE a day on days 1, 4, 8 and 11. Take in the morning with food. |
| CYCLOPHOSPHamide | 300 mg/m$^2$ (PO) | ONCE a week on days 1, 8 and 15. Take in the morning. |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |

| Day 4 | | |
|---|---|---|
| Dexamethasone | 40 mg (PO) | ONCE a day on days 1, 4, 8 and 11. Take in the morning with food. |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |

| Day 8 | | |
|---|---|---|
| Granisetron | 2 mg (PO) | 60 minutes before chemotherapy |
| Dexamethasone | 40 mg (PO) | ONCE a day on days 1, 4, 8 and 11. Take in the morning with food. |
| CYCLOPHOSPHamide | 300 mg/m$^2$ (PO) | ONCE a week on days 1, 8 and 15. Take in the morning. |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |

| Day 11 | | |
|---|---|---|
| Dexamethasone | 40 mg (PO) | ONCE a day on days 1, 4, 8 and 11. Take in the morning with food. |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |

| Day 15 | | |
|---|---|---|
| Granisetron | 2 mg (PO) | 60 minutes before chemotherapy |
| CYCLOPHOSPHamide | 300 mg/m$^2$ (PO) | ONCE a week on days 1, 8 and 15. Take in the morning. |

**Notes:**

- The dexamethasone dose may alternatively be administered as 20 mg on the day of and day after bortezomib (days 1, 2, 4, 5, 8, 9, 11 and 12) as per Kropff et al. 2007[1]
- The cyclophosphamide dose may alternatively be administered as a 50 mg per day dose,[2] 500 mg/m$^2$ on D1, 8, 15,[3] 500 mg on D1, 8, 15 as per clinical practice, 900 mg/m$^2$ IV on D1 only,[4] or omitted in frail and/or elderly patients.

**Frequency:** 21 days

**Cycles:** 4 cycles prior to transplant; up to 13 cycles for transplant ineligible patients; and up to 11 cycles for relapsed patients.

## Indications and patient population

- Newly diagnosed or relapsed/refractory multiple myeloma

## Clinical information

| | |
|---|---|
| **Caution with oral anti-cancer drugs** | Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs.<br>Read more about the COSA guidelines and oral anti-cancer therapy |
| **Emetogenicity MODERATE** | Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy.<br>As a steroid has been included as part of this protocol, additional antiemetic steroids are not required.<br>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.<br>Ensure that patients also have sufficient antiemetics for breakthrough emesis:<br>Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR<br>Prochlorperazine 10 mg PO every 6 hours when necessary.<br>Read more about preventing anti-cancer therapy induced nausea and vomiting |
| **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.<br>Read more about peripheral neuropathy<br>Link to chemotherapy-induced peripheral neuropathy screening tool |
| **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.<br>Read more about thrombocytopenia associated with bortezomib |
| **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. |
| **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).[6]<br>For more information, please see the following protocols:<br>ID 137 Multiple myeloma zoledronic acid<br>ID 147 Multiple myeloma pamidronate<br>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.<br>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.<br>Read more about acute short term effects from corticosteroids |

| | |
|---|---|
| **Tumour lysis risk** | Assess patient for risk of developing tumour lysis syndrome.<br>Read more about prevention and management of tumour lysis syndrome. |
| **Thromboprophylaxis** | Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion.<br>Read more about the prophylaxis of venous thromboembolism (VTE) in multiple myeloma |
| **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).<br>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.<br>Read about antiviral prophylaxis drugs and doses |
| **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.<br>Access the PBS website |
| **Blood tests** | FBC, EUC, LFTs, calcium, magnesium, phosphate and BSL 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.<br>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.<br>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.<br>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.<br>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

| Dose reduction steps for bortezomib | |
|---|---|
| **Bortezomib** should be withheld at the onset of Grade 4 haematological toxicity or any Grade 3 non-haematological toxicity, with the exception of neuropathy. Upon resolution of the toxicity, bortezomib should be reinitiated at a 25% reduction of the previous dose as follows: | |
| Starting dose | 1.3 mg/m$^2$ |
| Dose level -1 | 1 mg/m$^2$ |
| Dose level -2 | 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 | |
|---|---|
| **ANC, Platelets x 10$^9$/L** | |
| Grade 3 haematological toxicity | Consider withholding bortezomib and cyclophosphamide.<br><br>Consider dose reduction for cyclophosphamide in subsequent cycles. |
| Grade 4 haematological toxicity | Withhold bortezomib and cyclophosphamide. When toxicity has resolved, recommence with bortezomib at a 25% reduction of the previous dose and cyclophosphamide at a 30% reduction of the previous dose. |
| Platelets 25 or less on Day 1 of any cycle | Consider withholding treatment until the platelet count is 50 or higher; recommence bortezomib at a 25% reduction of the previous dose. |

| Renal impairment | |
|---|---|
| **Creatinine clearance (mL/min)** | |
| less than 20 * | Omit cyclophosphamide |

** Kropff et al.[1] exclusion criteria.*

| 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. |

| Peripheral neuropathy | |
|---|---|
| Grade 1 | No action |
| Grade 1 with pain<br>or Grade 2 | Reduce bortezomib to 1 mg/m$^2$ |
| Grade 2 with pain<br>or Grade 3 | Withhold bortezomib 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 |

| Cyclophosphamide | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)** | Increased toxicity of cyclophosphamide possible due to increased conversion to active (and inactive) metabolites | Avoid combination or monitor for cyclophosphamide toxicity |
| **CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)** | Reduced efficacy of cyclophosphamide possible due to decreased conversion to active (and inactive) metabolites | Avoid combination or monitor for decreased clinical response to cyclophosphamide |
| **Amiodarone** | Possible additive pulmonary toxicity with high-dose cyclophosphamide (i.e. doses used prior to stem cell transplant; 60 mg/kg daily or 120 to 270 mg/kg over a few days) | Avoid combination or monitor closely for pulmonary toxicity |
| **Allopurinol, hydrochlorothiazide, indapamide** | Delayed effect. Increased risk of bone marrow depression; probably due to reduced clearance of active metabolites of cyclophosphamide | Avoid combination, consider alternative antihypertensive therapy or monitor for myelosuppression |
| **Ciclosporin** | Reduced efficacy of ciclosporin due to reduced serum concentration | Monitor ciclosporin levels; adjust dosage as appropriate; monitor response to ciclosporin |
| **Suxamethonium** | Prolonged apnoea due to marked and persistent inhibition of cholinesterase by cyclophosphamide | Alert the anaesthetist if a patient has been treated with cyclophosphamide within ten days of planned general anaesthesia |

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

| 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.<br><br>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.<br><br>Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors.<br><br>Dabigatran: avoid combination with strong P-gp inducers and inhibitors.<br><br>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.<br>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.<br>If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia).<br>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.<br>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.

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.

- baseline weight

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

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

**Note:** dexamethasone is given on days 1, 4, 8 and 11; cyclophosphamide is given on days 1, 8, 15; bortezomib is given on days 1, 4, 8 and 11 of each cycle.

### Dexamethasone

- administer orally ONCE a day in the morning
- to be taken with or immediately after food.

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

### Chemotherapy - Time out

### Cyclophosphamide

- administer orally ONCE a week in the morning on **days 1, 8 and 15** every 21 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- patients should be well hydrated and be encouraged to void frequently during treatment to prevent cyclophosphamide induced bladder irritation.

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

### 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 4

**Approximate treatment time: 30 minutes**

Safe handling and waste management

Safe administration

General patient assessment prior to each day of 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.

**Note:** dexamethasone is given on days 1, 4, 8 and 11; cyclophosphamide is given on days 1, 8, 15; bortezomib is given on days 1, 4, 8 and 11 of each cycle.

### Dexamethasone

- administer orally ONCE a day in the morning
- 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)**

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## Day 8

**Approximate treatment time: 30 minutes**

Safe handling and waste management

Safe administration

General patient assessment prior to each day of 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.

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

**Note:** dexamethasone is given on days 1, 4, 8 and 11; cyclophosphamide is given on days 1, 8, 15; bortezomib is given on days 1, 4, 8 and 11 of each cycle.

### Dexamethasone

- administer orally ONCE a day in the morning
- to be taken with or immediately after food.

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

### Chemotherapy - Time out

### Cyclophosphamide

- administer orally ONCE a week in the morning on **days 1, 8 and 15** every 21 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- patients should be well hydrated and be encouraged to void frequently during treatment to prevent cyclophosphamide induced bladder irritation.

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

### 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)**

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## Day 11

**Approximate treatment time: 30 minutes**

Safe handling and waste management

Safe administration

General patient assessment prior to each day of 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.

**Note:** dexamethasone is given on days 1, 4, 8 and 11; cyclophosphamide is given on days 1, 8, 15; bortezomib is given on days 1, 4, 8 and 11 of each cycle.

### Dexamethasone

- administer orally ONCE a day in the morning
- 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)**

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## Day 15

**This is an oral treatment**

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

**Note:** dexamethasone is given on days 1, 4, 8 and 11; cyclophosphamide is given on days 1, 8, 15; bortezomib is given on days 1, 4, 8 and 11 of each cycle.

### Chemotherapy - Time out

### Cyclophosphamide

- administer orally ONCE a week in the morning on **days 1, 8 and 15** every 21 days

- to be swallowed whole with a glass of water; do not break, crush or chew
- patients should be well hydrated and be encouraged to void frequently during treatment to prevent cyclophosphamide induced bladder irritation.

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

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

## Discharge information

### Dexamethasone and cyclophosphamide tablets

- Dexamethasone and cyclophosphamide 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.

# 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) | |
|---|---|
| **Hypotension** | Low blood pressure is commonly associated with bortezomib treatment. |
| **Nausea and vomiting** | Read more about prevention of treatment induced nausea and vomiting |
| **Taste and smell alteration** | Read more about taste and smell changes |

| Early (onset days to weeks) | |
|---|---|
| **Neutropenia** | Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively.<br>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.<br>Read more about thrombocytopenia associated with bortezomib |
| **Arthralgia and myalgia** | Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation.<br>Read more about arthralgia and myalgia |
| **Constipation** | |
| **Diarrhoea** | Read more about treatment induced diarrhoea |
| **Fatigue** | Read more about fatigue |
| **Haemorrhagic cystitis** | An inflammatory process, characterised by diffuse mucosal inflammation with haemorrhage involving the entire bladder. Patients are at risk following treatment with cyclophosphamide, ifosfamide and radiation therapy.<br>Read more about haemorrhagic cystitis |
| **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.<br>Read more about peripheral neuropathy |
| **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.<br>Read more about skin rash |

| Late (onset weeks to months) | |
|---|---|
| **Anaemia** | Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood.<br>Read more about anaemia |
| **Alopecia - partial** | Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out.<br>Read more about alopecia and scalp cooling |
| **Cognitive changes (chemo fog)** | Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'.<br>Read more about cognitive changes (chemo fog) |

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

## Evidence

The haematology reference committee was influenced by a number of trials with variation in terms of cycle length and dosing of cyclophosphamide and dexamethasone. It was felt that there is no need for separate protocols for CyBorD for newly diagnosed and relapsed multiple myeloma, given the limited number of trials supporting each individually.

A meta-analysis comparing VCD (CyBorD) (bortezomib, cyclophosphamide and dexamethasone) to VTD (bortezomib, thalidomide and dexamethasone) published in the British Journal of Haematology 2014 highlighted the heterogeneity in terms of treatment dosing and schedule. VCD is given two times per week in all trials except for Reeder's[7] once weekly regimen. There is variability in the dosing of dexamethasone between 480 mg/cycle over 28 days,[7] 120 mg/cycle over 21 days[8] and 320 mg/cycle over 21 days.[9]

It was the consensus of the haematology reference committee was that dexamethasone dosing as per the original Reeder protocol resulted in significant intolerance and hence may be dosed as D1, 4, 8, 11 (with option to split to 20 mg on D1, 2, 4, 5, 8, 9, 11, 12).[9, 10, 1]

Cyclophosphamide doses also vary, between 50 mg daily,[2] 300 mg/m$^2$ every week, 500 mg/m$^2$ every week[3], 500 mg weekly as per clinical practice and cyclophosphamide 900 mg/m$^2$ on day 1.[4, 11] It was also the consensus of the reference committee to give cyclophosphamide as a weekly dose of 300 mg/m$^2$ on D1, 8 and 15 as per clinical practice.

Based on 5 clinical trials involving VCD, a total of 157 patients have been treated with bortezomib, cyclophosphamide and dexamethasone between 2009 and 2012 for management of myeloma upfront. Cycle length has varied between 21 days and 28 days.[12]

The primary and secondary end points for these studies was to compare early response rates and toxicity profiles, as well as progression free survival (PFS) and overall survival (OS).

## Efficacy

### Untreated patients

In the randomised MM5 German study,[4] 3 cycles of VCD was compared with PAD in 504 newly diagnosed, transplant eligible myeloma patients. VCD has non-inferior response rate (37% vs 34.3% having ≥ very good partial response (VGPR), p=0.0001), lower rates of progressive disease (0.4% vs 4.8%, p=0.003), lower neuropathy (8.4% vs 14.9%, p=0.03), severe adverse events (24.0% vs 32.7%, p=0.04) and thromboembolic events (0.4% vs 2.8%, p=0.04). The study favours the use of VCD over PAD as initial induction therapy for transplant-eligible myeloma patients.

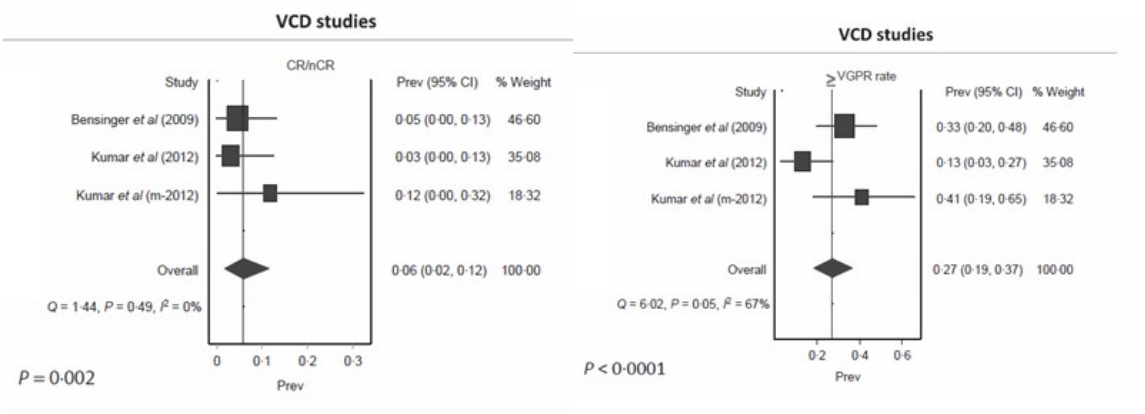
In another randomised French IFM 2013-04 study,[3] 4 cycles of VCD was compared with VTD in 340 newly diagnosed, transplant eligible patients. VCD has lower VGPR or better response (66.3% vs 56.2%, p=0.05) and lower overall response rate (ORR) (92.3% vs 83.4%, p=0.01), although no differences was noted in rate of complete remission (CR). VCD had higher grade 3 to 4 cytopenias (33.1% vs 18.9%, p=0.003), but VTD had higher rate of grade 2-4 peripheral neuropathy (21.9% vs 12.9%, p=0.008). In contrast, an earlier integrated analysis comparing VTD to VCD trials[12] found that VTD had significantly higher post-induction CR/nCR rates (34% vs 6%, OR 3.9, 95% CI 1.5-11.3; p= 0.002) and VGPR rates (62% vs 7%, OR = 4.3, 95% CI 2.5- 7.2, p<0.0001) but no significant difference in ORR (90% vs 88%, p= 0.74).

**Table and graphs - post-induction response rates and adverse events**

**Table III.** Combined post-induction response rates and adverse events for the VTD and VCD Induction groups are shown prior to the integrated analysis.

| | VTD (%) | VCD (%) |
|---|---|---|
| ORR | 91 | 83 |
| CR/nCR | 34 | 17 |
| ≥VGPR | 62 | 40 |
| PR | 31 | 43 |
| Overall AE ≥ grade 3 | 57 | 51 |
| Neuropathy ≥ grade 3 | 9 | 6 |
| ISS II-III | 61 | 59 |
| High risk cytogenetics | 37 | 21 |
| ASCT | 87 | 51 |

VTD Velcade thalidomide, dexamethasone; VCD, Velcade cyclophosphamide dexamethasone; ISS, International Staging system; CR, complete response; nCR, near complete response; VGPR, very good partial response; PR, partial response; ORR, overall response rate; AE, adverse event; ASCT, autologous stem cell transplantation.






Further evidence regarding the efficacy is present in the 2019 published VCAT Study[13] which investigated the role of bortezomib, thalidomide and prednisone consolidation in newly diagnosed transplant eligible myeloma patients. In this study all patients received initial therapy with 3 cycles of bortezomib (1.3mg/$m^2$ D1,4,8,11), cyclophosphamide (300mg/$m^2$ D1,8,15), and dexamethasone (20mg D1,2,4,5,8,9,11,12). Of the 256 patients enrolled in the trial, 250 patients completed 3 cycles of VCD with an VGPR rate post induction of 18.1% and a partial response (PR) rate of 53.5%. Peripheral neuropathy (PN) rates following 3 cycles of induction were reported at 39%, however ≥ grade 3 PN account for 3.5% of patients.

### Primary refractory or relapsed disease

Several phase II trials utilised VCD in the relapsed-refractory setting. De Waal et al[14] administered 6 cycles of VCD with 50 mg daily cyclophosphamide, followed by 1 year of bortezomib and cyclophosphamide maintenance, and showed an ORR of 71%, and a median PFS and OS of 18.4 months and 28.1 months respectively. Earlier, Kropff et al[1] used VCD with twice weekly bortezomib for 8 cycles, followed by weekly bortezomib for another 5 cycles. An ORR of 90% was achieved, with a median EFS and OS of 12 months and 22 months respectively.

Following encouraging results of phase 2 trials, a randomised controlled trial comparing bortezomib and dexamethasone with or without cyclophosphamide in patients with primary refractory or relapsed myeloma was performed.[15] The trial was prematurely terminated, due to lack of recruitment. 96 patients were randomised into 2 groups. The updated results demonstrated a median time to progression of 9.9 months in the VCD arm, compared with 12.6 months in the VD arm. Overall response rates were similar (70% in VCD arm and 74% in VD arm).[15]

## Toxicity

The most common treatment-emergent non-haematologic adverse events reported have included peripheral neuropathy, fatigue, diarrhoea and constipation.

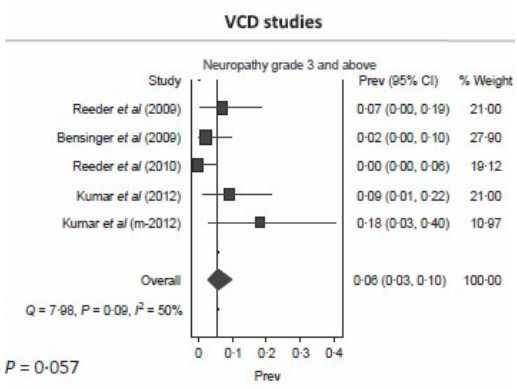


Table 2. Major hematologic and non-hematologic toxicities.

| | CVD (n=16) | VD (n=20) | V (n=11) |
|---|---|---|---|
| New grade 3/4 thrombocytopenia | 7 (44%) | 10 (50%) | 7 (64%) |
| Grade 3 baseline thrombocytopenia | 3 | 4 | 2 |
| Thrombocytopenia (grade 3/4) | 10 | 14 | 9 |
| New grade 3/4 neutropenia | 3 (19%) | 3 (15%) | 5 (45%) |
| Grade 3/4 baseline neutropenia | 0 | 1 | 3 |
| Neutropenia (grade 3/4) | 3 | 4 | 8 |
| Grade 3 infection | 2 (13%) | 6 (30%) | 2 (18%) |
| Peripheral neuropathy (new/worse) | 6 (5/1) (37%) | 12 (6/6) (60%) | 1 (1/0) (9%) |
| New neuropathy (grade 1-2/3-4) | 4/1 (25%/6%) | 6/0 (30%/0) | 1/1 (9%/9%) |
| Worsening neuropathy (grade 3 above) | 1 (6%) | 6 (30%) | 0 |
| Postural hypotension | 1 | 3 | 0 |
| Shingles/chickenpox/herpes simplex | 1 (6%) | 7 (35%) | 1 (9%) |



### Subcutaneous vs intravenous administration and toxicity

Mode of administration of bortezomib has been studied in both new diagnosis and relapsed disease settings. Merz et al[16] analysed patients with newly diagnosed myeloma in the MM5 study and found that grade 2 or more peripheral neuropathy were higher in patients having intravenous bortezomib compared with subcutaneous route (8% vs 2%, p=0.001), whilst ORR were similar. Moreau et al[17] showed in the relapsed setting, that subcutaneous bortezomib has lower incidence of peripheral neuropathy than intravenous route, whilst time to progression and OS were similar. Subcutaneous administration is therefore considered the standard practice for bortezomib.

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## History

### Version 6

| Date | Summary of changes |
|---|---|
| **19/03/2010** | New protocol presented at Haematology Reference Group Meeting. |
| **20/05/2010** | Approved and published on eviQ. |
| **20/02/2012** | New format to allow for export of protocol information.<br>Protocol version number changed to v.2.<br>Antiemetics and premedications added to the treatment schedule.<br>Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations.<br>Drug specific information placed behind the drug name link. |
| **06/03/2012** | PHC view added. |

| Date | Summary of changes |
|---|---|
| **10/05/2012** | Reviewed at Haematology Reference Committee Meeting; categorised as category 1 requiring full review, then review again in 2 years. |
| **21/05/2012** | Palonosetron added as default 5HT3 antagonist antiemetic in treatment schedule. |
| **15/11/2012** | Default antiemetic changed to granisetron - repeat palonosetron doses should not be administered within a 7 day interval. |
| **19/06/2013** | Added new bisphosphonate clinical information block. |
| **22/08/2013** | Published review 2 years post Haematology Reference Committee Meeting. |
| **13/03/2015** | Reviewed at Haematology Reference Committee Meeting:<br>• Removed relapsed from the title.<br>• Added relapsed and upfront into the indications.<br>• Decision to use generic drug names so CVD will now be named CyBorD.<br>• Dexamethasone dose changed to 40 mg on D1, 4, 8 and 11.<br>• Changed IV bortezomib to subcutaneous (SC) administration.<br>• Evidence updated. |
| **31/05/2017** | Transferred to new eviQ website. Version number change to v.4. |
| **24/11/2017** | Reviewed at Haematology Reference Committee Meeting:<br>• Version number increased to v.5<br>• Treatment schedule:<br>◦ Cyclophosphamide dose changed from 500 mg to 300 mg/$m^2$ as per clinical practice and consensus decision of the reference committee.<br>◦ Palonosetron IV changed to granisetron PO as per clinical practice.<br>• Notes under treatment schedule edited.<br>• Evidence updated.<br>• Next review in 2 years. |
| **24/05/19** | Reviewed at Haematology Reference Committee Meeting:<br>• Version number increase to v.6.<br>• PBS information updated to indicate bortezomib is authority and removed information from the note.<br>• Indication wording updated.<br>• Evidence updated.<br>• Next review in 2 years. |
| **02/08/2019** | Updated cyclophosphamide hydration recommendations. |
| **10/10/2019** | Clinical information updated with PBS expanded indications for G-CSF. |
| **15/05/2020** | Reformatted dose modification section for bortezomib; step down dose reductions now in table. No information has change and reformatted for clarity only. |
| **26/07/2021** | Protocol reviewed at March Haematology Reference Committee Meeting. Discussion continued over email and protocol published with the following changes:<br>• Protocol name updated to include 'twice-weekly'.<br>• Bortezomib drug status changed as per PBS.<br>• Evidence updated.<br>• For review in 2 years. |
| **29/11/2021**<br>**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:<br>• Bone modifying agents block added to clinical information, related note removed from treatment schedule and linked pages removed<br>• Link to Medical Scientific Advisory Group (MSAG) guidelines updated<br>• Note regarding dexamethasone reduction in specific patient populations added to treatment schedule notes |

| Date | Summary of changes |
| --- | --- |
| | • Thromboprophylaxis assessment information added to “Clinical information” section |



**First approved:** 20 May 2010
**Last reviewed:** 26 July 2021
**Review due:** 30 June 2023

***The currency of this information is guaranteed only up until the date of printing, for any updates please check:***
*https://www.eviq.org.au/p/556*
*09 Jun 2023*

# Patient information - Multiple myeloma - CyBorD (cyclophosphamide, bortezomib and dexamethasone)

**Patient's name:**

## Your treatment

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

| CyBorD (cyclophosphamide, bortezomib and dexamethasone) | | | |
|---|---|---|---|
| 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, 4, 8 and 11 | **Dexamethasone** (*dexa-METH-a-sone*) | Take orally ONCE a day in the morning with food on days 1, 4, 8 and 11 only. | |
| 1, 8 and 15 | **Cyclophosphamide** (*SYE-kloe-FOS-fa-mide*) | Take orally ONCE a week in the morning on days 1, 8 and 15 only. Swallow whole, do not break, crush or chew tablets. | |
| 1, 4, 8 and 11 | **Bortezomib** (*BORE-tez-oh-mib*) | By injection under the skin. | About 5 minutes |

**Missed doses:**

- **Dexamethasone**: if you forget to take your tablets or vomit your tablets, contact your treating team.
- **Cyclophosphamide**: if you forget to take your tablets or vomit your tablets, take your normal dose the next time it is due. Do not take an extra dose.

## 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**<br><br>Ask your doctor or nurse from your treating team who to contact if you have a problem |
|---|---|
| • a temperature of 38°C or higher<br>• chills, sweats, shivers or shakes<br>• shortness of breath<br>• uncontrolled vomiting or diarrhoea<br>• pain, tingling or discomfort in your chest or arms<br>• you become unwell. | Daytime:<br>Night/weekend:<br>Other instructions: |

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

- pain, stinging, swelling or redness around the injection site
- 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.

### Treatment with cyclophosphamide

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

### Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **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.

## 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) | |
|---|---|
| **Low blood pressure (hypotension)** | • You may get low blood pressure from the drug bortezomib.<br>• You may feel dizzy or light-headed.<br>• Tell your doctor if you are taking blood pressure medication.<br>• Your doctor will monitor your blood pressure regularly while you are on this treatment.<br>• Drink plenty of fluids (unless you are fluid restricted), especially before each dose of bortezomib.<br>• 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.<br>• Do not drive or operate machinery if you feel dizzy or light-headed.<br>• Tell your doctor or nurse if you get any of the signs or symptoms listed above. |
| **Nausea and vomiting** | • You may feel sick (nausea) or be sick (vomit).<br>• Take your anti-sickness medication as directed even if you don't feel sick.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat small meals more frequently.<br>• Try food that does not require much preparation.<br>• Try bland foods like dry biscuits or toast.<br>• Gentle exercise may help with nausea.<br>• Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment.<br>• **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.<br>• These changes are likely to go away with time.<br>• Do your mouth care regularly.<br>• Chew on sugar-free gum or eat sugar-free mints.<br>• Add flavour to your food with sauces and herbs.<br>• Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment. |

| Early (onset days to weeks) | |
|---|---|
| **Infection risk (neutropenia)** | • This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening.<br>• Wash your hands often.<br>• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.<br>• Do your mouth care regularly.<br>• Inspect your central line site (if you have one) daily for any redness, pus or swelling.<br>• Limit contact with people who are sick.<br>• Learn how to recognise the signs of infection.<br>• Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:**<br>◦ **a temperature of 38°C or higher**<br>◦ **chills, shivers, sweats or shakes**<br>◦ **a sore throat or cough**<br>◦ **uncontrolled diarrhoea**<br>◦ **shortness of breath**<br>◦ **a fast heartbeat**<br>◦ **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<br>• Try not to bruise or cut yourself.<br>• Avoid contact sport or vigorous exercise.<br>• Clear your nose by blowing gently.<br>• Avoid constipation.<br>• Brush your teeth with a soft toothbrush.<br>• For minor pain take paracetamol. Do not take any medications containing aspirin or ibuprofen without talking to your doctor or nurse.<br>• **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.** |
| **Joint and muscle pain and stiffness** | • You may get muscle, joint or general body pain and stiffness.<br>• Applying a heat pack to affected areas may help.<br>• Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain. |
| **Constipation** | • You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass.<br>• You may also get:<br>◦ bloating, cramping or pain<br>◦ a loss of appetite<br>◦ nausea or vomiting.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat plenty of fibre-containing foods such as fruit, vegetables and bran.<br>• Take laxatives as directed by your doctor.<br>• Try some gentle exercise daily.<br>• **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.<br>• You may also get bloating, cramping or pain.<br>• Take your antidiarrhoeal medication as directed by your doctor.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat and drink small amounts more often.<br>• Avoid spicy foods, dairy products, high fibre foods, and coffee.<br>• Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment.<br>• **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.<br>• Do not drive or operate machinery if you are feeling tired.<br>• Nap for short periods (only 1 hour at a time)<br>• Prioritise your tasks to ensure the best use of your energy.<br>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).<br>• Try some gentle exercise daily.<br>• Allow your friends and family to help.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above.** |
| **Bladder irritation (haemorrhagic cystitis)** | • You may get:<br>◦ blood in your urine, sometimes with blood clots<br>◦ pain or burning when you urinate<br>◦ the urge to urinate more than normal<br>◦ stomach or pelvic pain or discomfort.<br>• When you go home, make sure you drink plenty of fluids (unless you are fluid restricted).<br>• Empty your bladder often.<br>• **Tell your doctor or nurse as soon as possible if you notice any blood in your urine.** |

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| **Nerve damage (peripheral neuropathy)** | • You may notice a change in the sensations in your hands and feet, including:<br>  ◦ tingling or pins and needles<br>  ◦ numbness or loss of feeling<br>  ◦ pain.<br>• You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects.<br>• Test water temperature with your elbow when bathing to avoid burns.<br>• Use rubber gloves, pot holders and oven mitts in the kitchen.<br>• Wear rubber shoes or boots when working in the garden or garage.<br>• Keep rooms well lit and uncluttered.<br>• Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment.<br>• Tell your doctor or nurse if you get any of the symptoms listed above. |
| **Side effects from steroid medication** | • Steroid medication may cause:<br>  ◦ mood swings and behaviour changes<br>  ◦ an increased appetite<br>  ◦ weight gain<br>  ◦ swelling in your hands and feet<br>  ◦ stomach upsets<br>  ◦ trouble sleeping<br>  ◦ fragile skin and bruising<br>  ◦ an increase in your blood sugar level<br>  ◦ weak and brittle bones (osteoporosis)<br>• Take your steroid medication with food to reduce stomach upset<br>• If you have diabetes, your blood sugar levels may be tested more often.<br>• 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.<br>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.<br>• Do not scratch your skin.<br>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.<br>• **Talk to your doctor or nurse about other ways to manage your skin rash.** |

| **Late (onset weeks to months)** | |
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| **Low red blood cells (anaemia)** | • You may feel dizzy, light-headed, tired and appear more pale than usual.<br>• Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.** |
| **Hair thinning** | • Your hair may become dry and may break easily.<br>• You may lose some of your hair.<br>• Use a gentle shampoo and a soft hairbrush.<br>• Take care with hair products like hairspray, hair dye, bleaches and perms.<br>• Protect your scalp from the cold with a hat or scarf.<br>• Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher.<br>• Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au) |
| **Chemo brain (chemotherapy-related cognitive impairment)** | • You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory.<br>• These symptoms usually improve once treatment is completed.<br>• Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain).<br>• Tell your doctor or nurse if you get any of the symptoms listed above. |

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

## General advice for people having cancer treatment

### Chemotherapy safety

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

### Blood clot risk

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

### Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- 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

**Additional notes:**

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***The currency of this information is guaranteed only up until the date of printing, for any updates please check:***
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