

Multiple myeloma (bortezomib and dexamethasone) relapsed SUPERSEDED

ID: 55 v.4 Superseded Essential Medicine List

This protocol has been superseded as triplet therapy appears to be more efficacious than single or doublet therapy. It is not commonly used in clinical practice. ID 556 Multiple myeloma CyBorD (CYCLOPHOSPHamide bortezomib dexamethasone) twice weekly is the preferred regimen.

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](#).

International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADIKD)

2022

[Click here](#)



Treatment schedule - Overview

Cycle 1 to 11

Drug	Dose	Route	Day
Dexamethasone	20 mg ONCE a day	PO	1 and 2, 4 and 5, 8 and 9, 11 and 12
Bortezomib *	1.3 mg/m ²	Subcut	1, 4, 8, 11

* For extended therapy of more than 8 cycles, bortezomib may be administered on a standard schedule or on a maintenance schedule of once weekly for 4 weeks, days 1, 8, 15, and 22 followed by a 13 day rest period (days 23 to 35). Maximum of 11 cycles total.¹

Frequency: 21 days

Cycles: 4 cycles initially, then if at least partial response continue to 8 cycles. Maximum of 11 cycles total.

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.²

Drug status: Bortezomib: [PBS restricted benefit](#)

Dexamethasone: [PBS general schedule](#)

Full prescribing information and Authority Application forms available from the [Department of Human Services](#) website

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

Cost: ~ \$1,510 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 11

Day 1		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.
Bortezomib	1.3 mg/m ² (Subcut)	via subcutaneous injection
Day 2		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.
Day 4		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.
Bortezomib	1.3 mg/m ² (Subcut)	via subcutaneous injection
Day 5		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.
Day 8		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.
Bortezomib	1.3 mg/m ² (Subcut)	via subcutaneous injection
Day 9		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.
Day 11		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.
Bortezomib	1.3 mg/m ² (Subcut)	via subcutaneous injection
Day 12		
Dexamethasone	20 mg (PO)	ONCE a day on the day of and the day after each bortezomib dose. Take in the morning with food.

Note: for extended therapy of more than 8 cycles, bortezomib may be administered on a standard schedule or on a maintenance schedule of once weekly for 4 weeks, days 1, 8, 15, and 22 followed by a 13 day rest period (days 23 to 35). Maximum of 11 cycles total.¹

Frequency: 21 days

Cycles: 4 cycles initially, then if at least partial response continue to 8 cycles. Maximum of 11 cycles total.

Indications and patient population

- Salvage treatment for patients with relapsed/refractory multiple myeloma

Clinical information

Emetogenicity LOW	<p>Antiemetics are not routinely required; however should a patient experience emesis:</p> <p>Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR</p> <p>Prochlorperazine 10 mg PO every 6 hours when necessary may be administered.</p> <p>Read more about preventing anti-cancer therapy induced nausea and vomiting</p>
Peripheral neuropathy	<p>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.</p> <p>Read more about peripheral neuropathy</p> <p>Link to chemotherapy-induced peripheral neuropathy screening tool</p>
Thrombocytopenia	<p>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.</p> <p>Read more about thrombocytopenia associated with bortezomib</p>
Orthostatic hypotension	<p>Caution in patients with history of syncope or postural hypotension and those taking antihypertensive medications. Ensure patient is well hydrated prior to therapy.</p>
Bone modifying agents	<p>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).³</p> <p>For more information, please see the following protocols:</p> <p>ID 137 Multiple myeloma zoledronic acid</p> <p>ID 147 Multiple myeloma pamidronate</p> <p>ID 3964 Multiple myeloma denosumab - note denosumab is TGA approved but not PBS reimbursed for this indication.</p>
Bisphosphonates and dental review	<p>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.</p> <p>Read more about medication-related osteonecrosis of the jaw (MRONJ)</p>
Corticosteroids	<p>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.</p> <p>Read more about acute short term effects from corticosteroids</p>
Tumour lysis risk	<p>Assess patient for risk of developing tumour lysis syndrome.</p> <p>Read more about prevention and management of tumour lysis syndrome.</p>
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	<p>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).</p> <p>Read more about prophylaxis of pneumocystis jirovecii (carinii) in cancer patients</p>

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
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
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. Upon resolution of the toxicity, bortezomib should be reinitiated at a 25% reduction of the previous dose as follows:

- 1.3 mg/m² reduced to 1 mg/m² and
- 1 mg/m² reduced to 0.7 mg/m².

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 x 10 ⁹ /L, Platelets x 10 ⁹ /L (pre-treatment blood test)	
Any Grade 4 haematological toxicity	Withhold treatment; when the toxicity has resolved, recommence bortezomib at a 25% 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.

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 or Grade 2	Reduce bortezomib to 1 mg/m ²
Grade 2 with pain 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

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	<p>Interaction with both CYP3A4 and P-gp inhibitors /inducers.</p> <p>DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).</p>	<p>Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers.</p> <p>Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors.</p> <p>Dabigatran: avoid combination with strong P-gp inducers and inhibitors.</p> <p>If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.</p>
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-HT ₃ receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	<p>Avoid combination.</p> <p>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</p>
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	<p>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.</p> <p>For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook</p>

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

Days 1 ,2, 4, 5, 8, 9, 11 and 12 (Dex)

This is an oral treatment

Dexamethasone

- administer orally ONCE a day in the morning on **days 1, 2, 4, 5, 8, 9, 11, and 12**
- to be taken with or immediately after food.

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

Days 1, 4, 8 and 11 (bortezomib)

[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.

Dexamethasone

- administer orally ONCE a day in the morning on **days 1, 2, 4, 5, 8, 9, 11, and 12**
- to be taken with or immediately after food.

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

Note: Bortezomib is given day 1, 4, 8 and 11 of each cycle.

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)

Discharge information

Dexamethasone tablets

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

Antiemetics

- Antiemetics as 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)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	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
Diarrhoea	Read more about treatment induced diarrhoea
Constipation	
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
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
Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Delayed (onset months to years)	
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

This protocol has been superseded as triplet therapy appears to be more efficacious than single or doublet therapy.

Studies that have evaluated the use of bortezomib agent alone or in combination with other agents:

- the SUMMIT trial,⁴ was an open-label, non-randomised, phase II multicentre study of bortezomib which included 202 patients who had received at least two prior therapies (median number 6; 64% had received haematopoietic cell transplantation or other high-dose therapy) and were progressing on the most recent therapy. Dexamethasone could be added for patients with a suboptimal response. For the 193 patients with measurable disease, the complete plus partial response rate was 28 percent. For responding patients, median time to progression and median overall survival were 14 and >23 months, respectively.^{4, 5}
- a randomised phase III multicentre trial compared bortezomib to treatment with high dose dexamethasone in 669 patients with relapsed/refractory myeloma (APEX™ trial).^{6, 7} Patients who had relapsed after one to three previous therapies were randomly assigned to receive one of the following two regimens:
 - Dexamethasone 40 mg orally on days 1 to 4, 9 to 12, and 17 to 20 every five weeks for four cycles, followed by 40 mg orally

on days 1 to 4 every 28 days for an additional five cycles.

- Bortezomib 1.3 mg/m² IV on days 1, 4, 8, and 11 every three weeks for eight cycles, followed by 1.3 mg/m² IV on days 1, 8, 15, and 22 every five weeks for an additional three cycles
- the CREST⁸ trial was a phase 2 open label study in 54 relapsed/refractory myeloma patients randomised to receive bortezomib 1 mg/m² IV or 1.3 mg/m² IV twice weekly for 2 weeks every 3 weeks for a maximum of 8 cycles. Oral dexamethasone was permitted in patients with progressive or stable disease after 2 or 4 cycles respectively.

Efficacy

Two prospective, phase II trials and one prospective randomised phase III trial have evaluated the efficacy of bortezomib in the treatment of patients with relapsed or refractory MM. Overall response rates for single agent bortezomib are approximately 30%. Bortezomib has also been evaluated in combination with dexamethasone with overall response rates of approximately 65%.

At a planned interim analysis, the APEX^{6,7} study was terminated early and patients receiving dexamethasone were offered therapy with bortezomib. At the time of early termination of the study, at a median follow-up of 8.3 months, patients receiving bortezomib experienced prolonged median time to progression of disease (6.2 versus 3.5 months), prolonged survival (hazard ratio 0.57), and higher response rates (complete or partial responses) (38 versus 18%) compared with those receiving dexamethasone. Overall survival was prolonged in patients receiving bortezomib, both for those who had received one prior treatment (hazard ratio 0.39) and for those who had received more than one prior treatment (hazard ratio 0.65). The median duration of response was 8 months in patients receiving bortezomib and 5.6 months in patients receiving dexamethasone. A higher response rate was observed in patients receiving bortezomib regardless of baseline β 2-microglobulin concentration.

256 patients with relapsed or refractory myeloma were enrolled in SUMMIT (n=202) and CREST (n=54). Overall 41% (n=106; 78 SUMMIT, 28 CREST) patients had dexamethasone added to the initial bortezomib therapy after the 2nd to 4th cycle. 13% of the patients in the SUMMIT study who received combination therapy demonstrated improved response, with 5 achieving PR following minimal or no response to bortezomib alone. Of the 28 patients on the CREST study who received combination therapy, 33% (9) demonstrated improved response. In relation to the timing of the addition of the dexamethasone, 14.7% of those who commenced on or before the 4th cycle demonstrated improved response, compared to 25.4% of those who commenced following cycle 4.⁹

Toxicity

In the APEX study,^{6,7} the incidence of grade >3 events and the discontinuation rate were similar in both arms. Patients receiving bortezomib experienced a greater frequency of grade 3 toxicity (61 versus 44%) than patients receiving dexamethasone. The most frequent adverse events (>25%) with bortezomib were thrombocytopenia, neutropenia, peripheral neuropathy, fatigue, anaemia, dyspnoea and GI symptoms. Non-haematological grade 3 events were rare.

The side-effect profile for bortezomib +/- dexamethasone from the SUMMIT and CREST studies is shown below:

Adverse Events⁹

Table 4. Most frequently reported adverse events (>30% in any single group).

Adverse event	Patients (%)				
	Bortezomib 1.3 mg/m ² (n=90)		Bortezomib 1.0 mg/m ² (n=16)		All grade 3 or 4 events (n=106)
	Alone	After DEX added	Alone	After DEX added	
Fatigue	56	24	63	25	8
Nausea	52	21	44	13	7
Diarrhea	42	22	25	0	8
Thrombocytopenia	38	24	31	19	33
Pyrexia	32	12	13	25	2
Anemia	32	14	25	13	9
Insomnia	26	19	31	31	3
Constipation	27	14	25	31	3
Headache	24	8	38	0	4
Arthralgia	23	13	31	50	5
Pain in limb	17	12	31	6	6
Bone pain	13	8	38	0	2
Back pain	9	6	31	13	4
Peripheral edema	8	3	31	6	0

DEX: dexamethasone.

© Haematologica 2006

References

- 1 Richardson, P. G., P. Sonneveld, M. W. Schuster, et al. 2009. "Reversibility of symptomatic peripheral neuropathy with bortezomib in the phase III APEX trial in relapsed multiple myeloma: impact of a dose-modification guideline." *Br J Haematol* 144(6):895-903.
- 2 Quach, H., M. H. Prince and S. Harrison on behalf of MSAG. 2022. "Clinical practice guideline multiple myeloma." Myeloma Foundation of Australia.
- 3 Morgan, G. J., J. A. Child, W. M. Gregory, et al. 2011. "Effects of zoledronic acid versus clodronic acid on skeletal morbidity in patients with newly diagnosed multiple myeloma (MRC Myeloma IX): secondary outcomes from a randomised controlled trial." *Lancet Oncol* 12(8):743-752.
- 4 Richardson, P. G., B. Barlogie, J. Berenson, et al. 2003. "A phase 2 study of bortezomib in relapsed, refractory myeloma." *N.Engl.J Med.* 348(26):2609-2617.
- 5 Richardson, P. G., B. Barlogie, J. Berenson, et al. 2006. "Extended follow-up of a phase II trial in relapsed, refractory multiple myeloma:: final time-to-event results from the SUMMIT trial." *Cancer* 106(6):1316-1319.
- 6 Richardson, P. G., P. Sonneveld, M. W. Schuster, et al. 2005. "Bortezomib or high-dose dexamethasone for relapsed multiple myeloma." *N Engl J Med* 352(24):2487-2498.
- 7 Richardson, P. G., P. Sonneveld, M. Schuster, et al. 2007. "Extended follow-up of a phase 3 trial in relapsed multiple myeloma: final time-to-event results of the APEX trial." *Blood.* 110(10):3557-3560.
- 8 Jagannath, S., B. Barlogie, J. Berenson, et al. 2004. "A phase 2 study of two doses of bortezomib in relapsed or refractory myeloma." *Br.J Haematol.* 127(2):165-172.
- 9 Jagannath, S., P. G. Richardson, B. Barlogie, et al. 2006. "Bortezomib in combination with dexamethasone for the treatment of patients with relapsed and/or refractory multiple myeloma with less than optimal response to bortezomib alone." *Haematologica.* 91(7):929-934.

History

Version 4

Date	Summary of changes
01/11/2007	PBS listing information added.
25/08/2008	Addition of dexamethasone to protocol. Addition of supporting evidence and information relevant to steroids.
07/09/2009	Reviewed and transferred to eviQ.
2/08/2010	Update of hepatic dose modifications in line with US bortezomib product information; PCP prophylaxis recommendations.
01/02/2012	New format to allow for export of protocol information. Protocol version number changed to v.2. Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
09/02/2012	PHC view added.
31/08/2012	Presented for review at the Haematology Reference Committee meeting. Added note in evidence: according to the original (APEX trial), bortezomib was given weekly on days 1, 8, 15 and 22 of cycles 9 to 11 (35 day cycles). S/C bortezomib information added.
19/06/2013	Added new bisphosphonate clinical information block.

Date	Summary of changes
21/08/2013	Evidence reviewed, no changes review in 2 years.
13/03/2015	Decision at Haematology Reference Committee meeting to supersede protocol, as triplet therapy appears to be more efficacious than single or doublet therapy. It is not commonly used in clinical practice and CyBorD (ID 556) is the preferred regimen. 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.4.
24/05/2019	Reviewed at Haematology Reference Committee meeting: - consensus to remain superseded
29/11/2021	Interactions updated.
20/01/2022	
24/01/2022	Pulmonary toxicity added to side effects.
12/10/2022	The following changes have been made with the consensus agreement of the Haematology Reference Committee: <ul style="list-style-type: none"> • Bone modifying agents block added to "Clinical information" section, 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

The information contained in this protocol is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to treatment. Any clinician (medical oncologist, haematologist, radiation oncologist, medical physicist, radiation therapist, pharmacist or nurse) seeking to apply or consult this protocol is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at www.eviQ.org.au

First approved: 8 January 2008
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/55>

12 Jun 2023

Patient information - Multiple myeloma - Bortezomib and dexamethasone (relapsed)

Patient's name:

Your treatment

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


Bortezomib and dexamethasone (relapsed)

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, 2, 4, 5, 8, 9, 11 and 12	Dexamethasone (<i>dex-a-METH-a-son</i> e)	Take orally ONCE a day in the morning with food on day 1, 2, 4, 5, 8, 9, 11, 12 only. If you forget to take your tablets or vomit your tablets, contact your treating team.	
1, 4, 8 and 11	Bortezomib (<i>bore-TEZ-oh-mib</i>)	By injection under the skin	About 5 minutes

When to get help

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

 IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	Emergency contact details Ask your doctor or nurse from your treating team who to contact if you have a problem
<ul style="list-style-type: none">• a temperature of 38°C or higher• chills, sweats, shivers or shakes• shortness of breath• uncontrolled vomiting or diarrhoea• pain, tingling or discomfort in your chest or arms• you become unwell.	Daytime:..... Night/weekend:..... Other instructions:.....

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

- 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.

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.

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)	
Nausea and vomiting	<ul style="list-style-type: none">• You may feel sick (nausea) or be sick (vomit).• Take your anti-sickness medication as directed even if you don't feel sick.• Drink plenty of fluids (unless you are fluid restricted).• Eat small meals more frequently.• Try food that does not require much preparation.• Try bland foods like dry biscuits or toast.• Gentle exercise may help with nausea.• Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment.• Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.
Early (onset days to weeks)	

Infection risk (neutropenia)	<ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> ◦ 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)	<ul style="list-style-type: none"> • 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.
Diarrhoea	<ul style="list-style-type: none"> • 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.
Constipation	<ul style="list-style-type: none"> • You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: <ul style="list-style-type: none"> ◦ 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.

Tiredness and lack of energy (fatigue)	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> You may notice a change in the sensations in your hands and feet, including: <ul style="list-style-type: none"> 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.
Side effects from steroid medication	<ul style="list-style-type: none"> Steroid medication may cause: <ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> 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.

Delayed (onset months to years)

Lung problems

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

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

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

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

