# Multiple myeloma DVd (daratumumab bortezomib dexamethasone)

**ID: 3611** v.3 **Endorsed**

**⚠ Blood transfusion warning:**

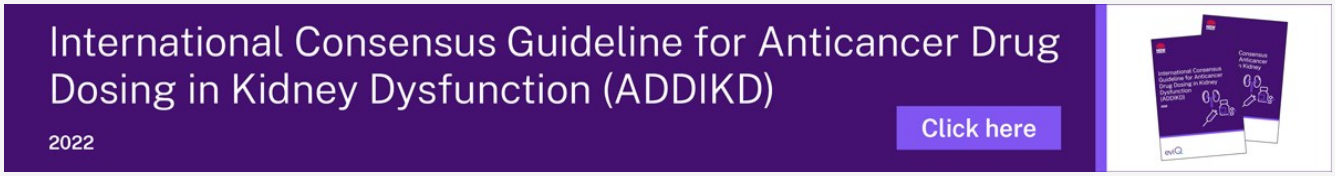
Interference with indirect antiglobulin tests may occur. Please notify your blood transfusion laboratory and send a blood sample for extended red blood cell phenotype and RBC antibody screen BEFORE the first dose of daratumumab.

If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices. Please refer to the ANZSBT/MSAG position paper. [1]

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 DVd (daratumumab bortezomib dexamethasone) overview
- Multiple myeloma daratumumab maintenance
- Multiple myeloma DVd (daratumumab subcutaneous bortezomib dexamethasone) overview

## Treatment schedule - Overview

### Cycle 1

| Drug | Dose | Route | Day |
|---|---|---|---|
| Dexamethasone | 20 mg | IV infusion | 1 |
| Daratumumab | 16 mg/kg | IV infusion | 1 * |
| Bortezomib | 1.3 mg/m$^2$ | Subcut | 1, 4, 8, 11 ** |
| Dexamethasone | 20 mg | PO | 2, 4 and 5, 8 and 9, 11 and 12 *** |
| Daratumumab | 16 mg/kg | IV infusion | 8 and 15 |

### Cycle 2 and 3

| Drug | Dose | Route | Day |
|---|---|---|---|
| Dexamethasone | 20 mg | PO | 1 and 2, 4 and 5, 8 and 9, 11 and 12 ** |
| Daratumumab | 16 mg/kg | IV infusion | 1, 8, 15 |

| Drug | Dose | Route | Day |
|---|---|---|---|
| Bortezomib | 1.3 mg/m$^2$ | Subcut | 1, 4, 8, 11 |

### Cycle 4 to 8

| Drug | Dose | Route | Day |
|---|---|---|---|
| Dexamethasone | 20 mg | PO | 1 and 2, 4 and 5, 8 and 9, 11 and 12 ** |
| Daratumumab | 16 mg/kg | IV infusion | 1 |
| Bortezomib | 1.3 mg/m$^2$ | Subcut | 1, 4, 8, 11 |

* First dose of daratumumab on day 1 of cycle 1 may be administered as a split dose infusion over two consecutive days. See daratumumab Product Information for details.
** The eviQ reference committee considers that the use of weekly bortezomib is acceptable to minimise the risk of peripheral neuropathy. A weekly schedule of bortezomib 1.3 mg/m$^2$ (together with subcutaneous administration) appears to significantly reduce neurotoxicity compared to the twice weekly bortezomib schedule.[2]
*** Dexamethasone dose may be reduced to 20 mg/week for patients > 75 years, BMI < 18.5, poorly controlled diabetes mellitus or prior intolerance to steroid therapy. For patients on a reduced dexamethasone dose, the entire 20 mg dose should be given as pre-infusion medication.

**Frequency:** 21 days

**Cycles:** 8

**Notes:**

- Daratumumab may be administered subcutaneously as a flat dose of 1,800 mg. For more information see ID 4144 Multiple myeloma DVd (daratumumab subcutaneous bortezomib dexamethasone).
- For patients with a history of chronic obstructive pulmonary disease or asthma, consider the use of post-infusion medications, including short and long-acting bronchodilators, and inhaled corticosteroids. Inhaled post-infusion medications may be discontinued following the fourth infusion, at the discretion of the treating clinician if the patient experiences no major IRRs.[3]
- For patients with a history of chronic obstructive pulmonary disease, or other pre-existing lung conditions, consider using oral montelukast 10 mg prior to daratumumab on day 1 of cycle 1.

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

**Daratumumab**: PBS authority

**Dexamethasone**: PBS general schedule
Dexamethasone is available as **0.5 mg** and **4 mg** tablets

## 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

| Day 1 | | |
|---|---|---|
| Paracetamol | 1,000 mg (PO) | 1 to 3 hours before treatment |
| Loratadine | 10 mg (PO) | 1 to 3 hours before treatment |
| Dexamethasone | 20 mg (IV infusion) | 1 to 3 hours before treatment |
| Daratumumab | 16 mg/kg (IV infusion) | in sodium chloride 0.9% as per graded administration rate. * Note: first infusion (cycle 1 day 1) is in 1000 mL. |

| Day 1 | | |
|---|---|---|
| | | If no reaction, all subsequent infusions in 500 mL. |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 2** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.* |
| **Day 4** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.* |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 5** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.* |
| **Day 8** | | |
| Paracetamol | 1,000 mg (PO) | 1 to 3 hours before treatment |
| Loratadine | 10 mg (PO) | 1 to 3 hours before treatment |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.* |
| Daratumumab | 16 mg/kg (IV infusion) | in sodium chloride 0.9% as per graded administration rate. *** Note: first infusion (cycle 1 day 1) is in 1000 mL. If no reaction, all subsequent infusions in 500 mL |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 9** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.* |
| **Day 11** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.* |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 12** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.* |

| Day 15 | | |
|---|---|---|
| Paracetamol | 1,000 mg (PO) | 1 to 3 hours before treatment |
| Loratadine | 10 mg (PO) | 1 to 3 hours before treatment |
| Dexamethasone | 12 mg (PO) | 1 to 3 hours before treatment |
| Daratumumab | 16 mg/kg (IV infusion) | in sodium chloride 0.9% as per graded administration rate. *** Note: first infusion (cycle 1 day 1) is in 1000 mL. If no reaction, all subsequent infusions in 500 mL |

| Day 16 | | |
|---|---|---|
| Dexamethasone | 4 mg (PO) | ONCE a day with or without food.*** As per treating clinician's discretion |

## Cycle 2 and 3

| Day 1 | | |
|---|---|---|
| Paracetamol | 1,000 mg (PO) | 1 to 3 hours before treatment |
| Loratadine | 10 mg (PO) | 1 to 3 hours before treatment |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Daratumumab | 16 mg/kg (IV infusion) | in sodium chloride 0.9% as per graded administration rate. * Note: first infusion (cycle 1 day 1) is in 1000 mL. If no reaction, all subsequent infusions in 500 mL. |
| Bortezomib | 1.3 mg/$m^2$ (Subcut) | via subcutaneous injection |

| Day 2 | | |
|---|---|---|
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |

| Day 4 | | |
|---|---|---|
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Bortezomib | 1.3 mg/$m^2$ (Subcut) | via subcutaneous injection |

| Day 5 | | |
|---|---|---|
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |

| Day 8 | | |
|---|---|---|
| Paracetamol | 1,000 mg (PO) | 1 to 3 hours before treatment |
| Loratadine | 10 mg (PO) | 1 to 3 hours before treatment |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Daratumumab | 16 mg/kg (IV infusion) | in sodium chloride 0.9% as per graded administration |

| Day 8 | | |
|---|---|---|
| | | rate. * Note: first infusion (cycle 1 day 1) is in 1000 mL. If no reaction, all subsequent infusions in 500 mL. |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 9** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| **Day 11** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 12** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| **Day 15** | | |
| Paracetamol | 1,000 mg (PO) | 1 to 3 hours before treatment |
| Loratadine | 10 mg (PO) | 1 to 3 hours before treatment |
| Dexamethasone | 12 mg (PO) | 1 to 3 hours before treatment |
| Daratumumab | 16 mg/kg (IV infusion) | in sodium chloride 0.9% as per graded administration rate. * Note: first infusion (cycle 1 day 1) is in 1000 mL. If no reaction, all subsequent infusions in 500 mL. |
| **Day 16** | | |
| Dexamethasone | 4 mg (PO) | ONCE a day with or without food.*** As per treating clinician's discretion |

### Cycle 4 to 8

| Day 1 | | |
|---|---|---|
| Paracetamol | 1,000 mg (PO) | 1 to 3 hours before treatment |
| Loratadine | 10 mg (PO) | 1 to 3 hours before treatment |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Daratumumab | 16 mg/kg (IV infusion) | in 500 mL sodium chloride 0.9% as per graded administration rate *** |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 2** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 |

| | | |
|---|---|---|
| **Day 2** | | |
| | | hours before treatment.** |
| **Day 4** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 5** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| **Day 8** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 9** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| **Day 11** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |
| Bortezomib | 1.3 mg/m$^2$ (Subcut) | via subcutaneous injection |
| **Day 12** | | |
| Dexamethasone | 20 mg (PO) | ONCE a day. Take in the morning with food. On the days of daratumumab administration, dexamethasone dose should be given as a pre-infusion medication 1 to 3 hours before treatment.** |

* Refer to daratumumab infusion table for detailed administration instructions.

** Dexamethasone dose may be reduced to 20 mg/week for patients > 75 years, BMI < 18.5, poorly controlled diabetes mellitus or prior intolerance to steroid therapy. For patients on a reduced dexamethasone dose, the entire 20 mg dose should be given as pre-infusion medication.

*** For those who are at high risk for post infusion reaction or with a history of COPD or asthma.

**Note:**

- First dose of daratumumab (i.e. day 1 of cycle 1) may be administered as a split dose infusion over two consecutive days. See daratumumab Product Information for details.
- For patients with a history of chronic obstructive pulmonary disease, or other pre-existing lung conditions, consider using oral montelukast 10 mg prior to daratumumab on day 1 of cycle 1.

- The eviQ reference committee considers that the use of weekly bortezomib is acceptable to minimise the risk of peripheral neuropathy. A weekly schedule of bortezomib 1.3 mg/m$^2$ (together with subcutaneous administration) appears to significantly reduce neurotoxicity compared to the twice weekly bortezomib schedule.[2]

**Frequency:** 21 days

**Cycles:** 8

## Indications and patient population

- Relapsed/refractory multiple myeloma after at least one prior line of therapy.

## Clinical information

| | |
|---|---|
| **Venous access required** | IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment.<br>Read more about central venous access device line selection |
| **Hypersensitivity/infusion-related reaction** | High risk with daratumumab.<br>Infusion-Related Reactions (IRRs) can occur with administration of IV or SC daratumumab. Hypersensitivity risk is greatest with the first dose of daratumumab, and is higher in IV than SC administration.[4]<br>Close monitoring during and after administration is recommended.[5] |
| **Pre and post-treatment medication** | The product information states that pre- and post-treatment medication is required for this treatment.<br>Please refer to the treatment schedule for the suggested pre- and post-treatment medication regimen. This may be substituted to reflect institutional policy.<br>For patients with a history of chronic obstructive pulmonary disease, consider the use of post-treatment medications including short and long acting bronchodilators, and inhaled corticosteroids. Following the first four infusions or injections, if the patient experiences no major infusion-related reactions (IRRs), these inhaled post-treatment medications may be discontinued at the discretion of the treating clinician. |
| **Daratumumab rapid infusion** | Administration of daratumumab by rapid infusion is not in line with the product monograph, however published literature indicates that it can be completed safely.<br>Read more about daratumumab rapid infusion |
| **Emetogenicity LOW to MODERATE** | Antiemetics may be required before treatment. If a patient experiences nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen.<br>Read more about preventing anti-cancer therapy induced nausea and vomiting |
| **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) |
| **Interference with indirect antiglobulin test (indirect Coombs test)** | Daratumumab binds to CD38 found at low levels on red blood cells (RBCs) and may result in a positive indirect Coombs test.<br>Daratumumab-mediated positive indirect Coombs test may persist for up to 6 months after the last dose of daratumumab. Daratumumab bound to RBCs may cause panagglutination during pretransfusion indirect Coombs tests and may therefore mask detection of alloantibodies to red blood antigens in the patient's serum.<br>Extended red cell phenotyping and RBC antibody screen should be done for patients prior to starting daratumumab.<br>Please refer to the ANZSBT/MSAG position paper. [1] |
| **Interference with serum protein electrophoresis and immunofixation tests** | Daratumumab may be detected on serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for monitoring disease monoclonal immunoglobulins (M protein), which can lead to false positive assay results in patients with IgG kappa myeloma protein. The initial assessment of complete responses by the International Myeloma Working Group (IMWG) criteria may be affected.<br>For patients with persistent very good partial response other methods to evaluate the depth of response should be considered if it was to impact on management strategy. |
| **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 |
| **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. |
| **Pneumocystis jirovecii pneumonia (PJP) prophylaxis** | 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 |
| **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 |
| **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 and phosphate at baseline and prior to each treatment. |

| | |
|---|---|
| **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

### Daratumumab:[3]

- No dose reductions are recommended for daratumumab. Dose may be delayed until blood cell count recovery if haematological toxicity occurs.
- Infusion-related reactions (IRRs)
  - For IRRs of any grade/severity, immediately interrupt the daratumumab infusion and manage symptoms.
  - Management of IRRs may further require reduction in the rate of infusion, or treatment discontinuation of daratumumab.

### Bortezomib:

- Bortezomib should be withheld at the onset of any Grade 4 haematological toxicity or any Grade 3 non-haematological, with the exception of neuropathy (see below). Upon resolution of the toxicity, bortezomib should be reinitiated at a 25% reduction of the previous dose as follows:
  - 1.3 mg/m$^2$ reduced to 1 mg/m$^2$ and
  - 1 mg/m$^2$ reduced to 0.7 mg/m$^2$.
- If the toxicity is not resolved or if it recurs at the lowest dose, discontinuation of bortezomib must be considered unless the benefit of treatment clearly outweighs the risk.

| Haematological toxicity | |
|---|---|
| **ANC x $10^9$/L (pre-treatment blood test)** | |
| 0.5 to 1.0 (no complications) | No dose reduction is required, consider treatment with G-CSF |
| 0.5 to 1.0 with fever<br>OR<br>less than 0.5 | Withhold bortezomib until recovery to baseline OR ≤ Grade 2.<br><br>Upon recovery, restart bortezomib at current dose and consider G-CSF support. If recurrence is seen, reduce bortezomib by 25% of the previous dose. |
| **Platelets x $10^9$/L (pre-treatment blood test)** | |
| less than 50 with bleeding<br>OR<br>less than 25 | Withhold bortezomib until recovery to baseline OR ≤ Grade 2.<br><br>Upon recovery, reinitiated at a 25% reduction of the previous dose. |

| Hepatic impairment | |
|---|---|
| **Bilirubin level** | |
| > 1.5 x ULN | 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 |

| Daratumumab |
|---|
| No drug-drug interaction studies have been performed. Clinical pharmacokinetic assessments of daratumumab in combination with lenalidomide, pomalidomide, thalidomide, bortezomib and dexamethasone indicated no clinically-relevant drug-drug interaction |

| 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 cycles 1 to 3

*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: initial infusion 7 hours, second infusion 5 hours and subsequent infusions 4 hours**

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.

Prime required IV lines with sodium chloride 0.9%:

- low protein-binding polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre), polyurethane (PU), polybutadiene (PBD), polyvinyl chloride (PVC), polypropylene (PP) or polyethylene (PE) administration sets must be used for daratumumab.
- attach a second IV line via a luer lock connector as close as possible to the site of injection
  - this may be required in case of a hypersensitivity reaction.

Insert IV cannula or access TIVAD or CVAD.

- baseline weight

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### Dexamethasone

- administer intravenously for cycle 1, day 1 and orally ONCE a day in the morning for subsequent doses
- on the days of daratumumab administration, dexamethasone should be given as a pre-infusion medication 1 to 3 hours before treatment.

### Treatment - Time out

### Daratumumab

**Prior to administration:**

- check baseline observations
- verify premedication has been taken. If not, administer 1 to 3 hours prior to daratumumab administration:
  - paracetamol 1000 mg orally AND
  - loratadine 10 mg orally (or similar antihistamine)
  - a corticosteroid should be included as a premed according to local guidelines unless a regimen-specific corticosteroid is indicated

**First infusion in 1,000 mL sodium chloride 0.9%:**

- **commence daratumumab** infusion at 50 mL/hr for the first hour
- repeat observations prior to each rate increase
- **increase rate** by 50 mL/hr every hour, up to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

Link to daratumumab infusion table

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have completely resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

**Second infusion in 500 mL sodium chloride 0.9%:**

- check for any adverse events during previous infusion.  If previous reaction occurred, please refer to the daratumumab infusion table .
- **commence daratumumab** infusion at 50 mL/hr for the first hour
- repeat observations prior to each rate increase
- **increase rate** by 50 mL/hr every hour, up to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

**Subsequent infusions in 500 mL sodium chloride 0.9%:**

If previous reaction occurred, please refer to the daratumumab infusion table .

If **no** adverse event experienced with the first two infusions:

- **commence** daratumumab infusion at 100 mL/hr
- repeat observations prior to each rate increase
- **increase rate** by 50 mL/hr increments every hour to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about daratumumab rapid infusion

### 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.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

---

## Day 2

**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.

---

## Day 4

**Approximate treatment time: 60 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

Administer antiemetics if required

### 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.

### Chemotherapy - Time out

### Bortezomib

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

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

---

## Day 5

**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.

---

## Day 8

**Approximate treatment time: 5 hours (initial); 4 hours (subsequent)**

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool.

Any toxicity grade 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.

Prime required IV lines with sodium chloride 0.9%:

- low protein-binding polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre), polyurethane (PU), polybutadiene (PBD), polyvinyl chloride (PVC), polypropylene (PP) or polyethylene (PE) administration sets must be used for daratumumab.
- attach a second IV line via a luer lock connector as close as possible to the site of injection
  - this may be required in case of a hypersensitivity reaction.

Insert IV cannula or access TIVAD or CVAD.

- baseline weight

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### Dexamethasone

- administer orally ONCE a day in the morning
- on the days of daratumumab administration, dexamethasone should be given as a pre-infusion medication 1 to 3 hours before treatment.

### Treatment - Time out

### Daratumumab

**Prior to administration:**

- check baseline observations
- verify premedication has been taken. If not, administer 1 to 3 hours prior to daratumumab administration:
  - paracetamol 1000 mg orally AND
  - loratadine 10 mg orally (or similar antihistamine)
  - a corticosteroid should be included as a premed according to local guidelines unless a regimen-specific corticosteroid is indicated

**First infusion in 1,000 mL sodium chloride 0.9%:**

- **commence daratumumab** infusion at 50 mL/hr for the first hour
- repeat observations prior to each rate increase
- **increase rate** by 50 mL/hr every hour, up to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

Link to daratumumab infusion table

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have completely resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

**Second infusion in 500 mL sodium chloride 0.9%:**

- check for any adverse events during previous infusion.  If previous reaction occurred, please refer to the daratumumab infusion table .
- **commence daratumumab** infusion at 50 mL/hr for the first hour
- repeat observations prior to each rate increase
- **increase rate** by 50 mL/hr every hour, up to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

**Subsequent infusions in 500 mL sodium chloride 0.9%:**

If previous reaction occurred, please refer to the daratumumab infusion table .

If **no** adverse event experienced with the first two infusions:

- **commence** daratumumab infusion at 100 mL/hr
- repeat observations prior to each rate increase
- **increase rate** by 50 mL/hr increments every hour to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about daratumumab rapid infusion

## 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.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

---

## Day 9

**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.

---

## Day 11

**Approximate treatment time: 60 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

Administer antiemetics if required

### 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.

### Chemotherapy - Time out

### Bortezomib

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

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

---

## Day 12

**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.

---

## Day 15

**Approximate treatment time: 4 hours**

Handling of monoclonal antibodies 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.

Prime required IV lines with sodium chloride 0.9%:

- low protein-binding polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre), polyurethane (PU), polybutadiene (PBD), polyvinyl chloride (PVC), polypropylene (PP) or polyethylene (PE) administration sets must be used for daratumumab.
- attach a second IV line via a luer lock connector as close as possible to the site of injection
  - this may be required in case of a hypersensitivity reaction.

Insert IV cannula or access TIVAD or CVAD.

### Pre treatment medication

Administer antiemetics if required

### Treatment - Time out

### Daratumumab

#### Prior to administration:

- check for any adverse events during previous infusion. If previous reaction occurred, please refer to the daratumumab infusion table .
- check baseline observations
- verify premedication has been taken. If not, administer 1 to 3 hours prior to daratumumab administration:
  - paracetamol 1000 mg orally AND
  - loratadine 10 mg orally (or similar antihistamine)
  - a corticosteroid should be included as a premed according to local guidelines unless a regimen-specific corticosteroid is indicated

#### Subsequent infusions in 500 mL sodium chloride 0.9%:

If previous reaction occurred, please refer to the daratumumab infusion table .

If **no** adverse event experienced with previous infusions:

- **commence** daratumumab infusion at 100 mL/hr
- repeat observations prior to each rate increase
- **increase rate** by 50 mL/hr increments every hour to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about daratumumab rapid infusion

Remove IV cannula and/or deaccess TIVAD or CVAD.

## Discharge information

#### Dexamethasone tablets

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

#### Antiemetics

- Antiemetics as prescribed.

#### Growth factor support

- Arrangements for administration if prescribed.

#### Prophylaxis medications

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

#### Patient information

- Ensure patient receives patient information sheet.

## Administration cycles 4 to 8

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

### Day 1

**Approximate treatment time: 4 hours**

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.

Prime required IV lines with sodium chloride 0.9%:

- low protein-binding polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre), polyurethane (PU), polybutadiene (PBD), polyvinyl chloride (PVC), polypropylene (PP) or polyethylene (PE) administration sets must be used for daratumumab.
- attach a second IV line via a luer lock connector as close as possible to the site of injection
  - this may be required in case of a hypersensitivity reaction.

Insert IV cannula or access TIVAD or CVAD.

- baseline weight

#### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

#### Dexamethasone

- administer intravenously for cycle 1, day 1 and orally ONCE a day in the morning for subsequent doses
- on the days of daratumumab administration, dexamethasone should be given as a pre-infusion medication 1 to 3 hours before treatment.

#### Treatment - Time out

#### Daratumumab

**Prior to administration:**

- check for any adverse events during previous infusion. If previous reaction occurred, please refer to the daratumumab infusion table .
- check baseline observations
- verify premedication has been taken. If not, administer 1 to 3 hours prior to daratumumab administration:
  - paracetamol 1000 mg orally AND
  - loratadine 10 mg orally (or similar antihistamine)
  - a corticosteroid should be included as a premed according to local guidelines unless a regimen-specific corticosteroid is indicated

**Subsequent infusions in 500 mL sodium chloride 0.9%:**

If previous reaction occurred, please refer to the daratumumab infusion table .

If **no** adverse event experienced with previous infusions:

- **commence** daratumumab infusion at 100 mL/hr
- repeat observations prior to each rate increase

- **increase rate** by 50 mL/hr increments every hour to a maximum of 200 mL/hr if observations are stable
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about daratumumab rapid infusion

### 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.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

---

## Day 2

**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.

---

## Day 4

**Approximate treatment time: 60 minutes**

Safe handling and waste management

Safe administration

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.

### Chemotherapy - Time out

#### Bortezomib

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

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

---

## Day 5

**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.

---

## Day 8

**Approximate treatment time: 60 minutes**

Safe handling and waste management

Safe administration

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.

### Chemotherapy - Time out

### Bortezomib

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

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

---

## Day 9

**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.

---

## Day 11

**Approximate treatment time: 60 minutes**

Safe handling and waste management

Safe administration

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.

### Chemotherapy - Time out

#### Bortezomib

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

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

---

## Day 12

**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.

---

## Discharge information

### Dexamethasone tablets

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

### Antiemetics

- Antiemetics as prescribed.

### Growth factor support

- Arrangements for administration if prescribed.

### Prophylaxis medications

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

### Patient information

- Ensure patient receives patient information sheet.

# Side effects

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

| Immediate (onset hours to days) | |
|---|---|
| **Hypersensitivity reaction** | Anaphylaxis and infusion related reactions can occur with this treatment.<br>Read more about hypersensitivity reaction |
| **Hypotension** | Low blood pressure is commonly associated with bortezomib treatment. |

| 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 |
| **Dyspnoea** | |
| **Fatigue** | Read more about fatigue |
| **Fever** | |
| **Nausea and vomiting** | Read more about prevention of treatment induced nausea and vomiting |
| **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 |
| **Thromboembolism** | Thromboembolic events, including pulmonary embolism, deep vein thrombosis and cerebrovascular accidents can occur. Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion.<br>Read more about management of thromboembolism (VTE) in multiple myeloma |

| Late (onset weeks to months) | |
|---|---|
| **Anaemia** | Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood.<br>Read more about anaemia |
| **Anorexia** | Loss of appetite accompanied by decreased food intake.<br>Read more about anorexia |
| **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 CASTOR study[7] investigated the role of daratumumab when added to bortezomib and dexamethasone. In this randomised, Phase III open-label study, patients who had received at least one prior line of therapy were assigned to receive up to 8 cycles of subcutaneous bortezomib, given days 1, 4, 8 and 11 of a 21 day cycle, in combination with dexamethasone given on the day of, and day after, each bortezomib administration. Patients randomised to the experimental arm additionally received daratumumab once-weekly for the first 3 cycles, followed by 3-weekly doses (given on day 1 of each cycle) for cycles 4 to 8, followed by 4-weekly doses until progressive disease or discontinuation due to toxicity. Patients may have received prior bortezomib if they were not refractory to it and had not discontinued due to toxicity. The primary end-point was progression-free survival (PFS).

### Efficacy

251 patients were randomised to receive daratumumab (DVd); 247 were assigned to the control (Vd) group. After a median follow-up of 7.4 months, the median progression-free survival (PFS) was not reached (NR) in the daratumumab arm, and 7.2 months in the control group (HR 0.39, p<0.001). The 12 month PFS was 60.7% versus 26.9%, favouring the daratumumab arm. Overall response rate was 82.9% in the daratumumab group versus 63.2% in the control group (p<0.001). Similarly, complete response rates favoured the daratumumab arm (19.2% v 9.0%, p=0.001).

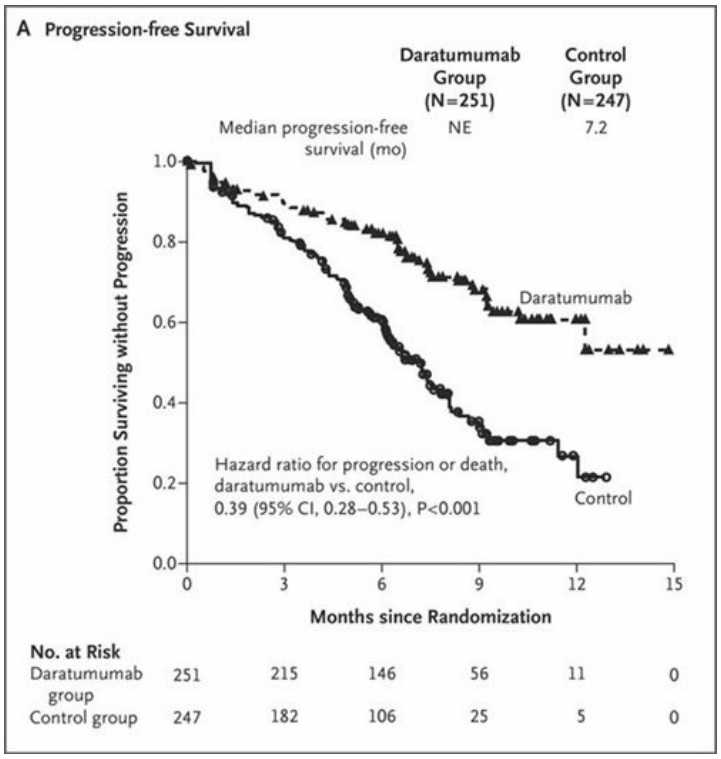


**Table 2. Summary of Responses among Patients Who Could Be Evaluated for Response.***

| Response Category | Daratumumab Group (N=240) | Control Group (N=234) | P Value† |
|---|---|---|---|
| Overall response | | | |
| No. with response | 199 | 148 | |
| Rate — % (95% CI) | 82.9 (77.5–87.5) | 63.2 (56.7–69.4) | <0.001 |
| Best overall response — no. (%) | | | |
| Complete response or better | 46 (19.2) | 21 (9.0) | 0.001 |
| Complete response | 35 (14.6) | 16 (6.8) | |
| Stringent complete response‡ | 11 (4.6) | 5 (2.1) | |
| Very good partial response or better | 142 (59.2) | 68 (29.1) | <0.001 |
| Very good partial response | 96 (40.0) | 47 (20.1) | |
| Partial response | 57 (23.8) | 80 (34.2) | |
| Minimal response | 10 (4.2) | 20 (8.5) | |
| Stable disease | 24 (10.0) | 47 (20.1) | |
| Progressive disease | 5 (2.1) | 16 (6.8) | |
| Response could not be evaluated | 2 (0.8) | 3 (1.3) | |

* Response was assessed on the basis of International Uniform Criteria Consensus recommendations (details on the criteria for disease responses are provided in the protocol). The population of patients who could be evaluated for response included patients who had a confirmed diagnosis of multiple myeloma and measurable disease at baseline or screening. In addition, patients must have received at least one dose of trial treatment and must have had at least one disease assessment after the baseline visit.
† P values were calculated with the use of the Cochran–Mantel–Haenszel chi-square test.
‡ Criteria for a stringent complete response include the criteria for a complete response plus a normal free light-chain ratio and absence of clonal plasma cells as assessed by immunohistochemical or immunofluorescence analysis or by two-color-to-four-color flow cytometry.



An update of CASTOR with three years of follow-up has been published[8], and a more recent abstract presentation confirmed ongoing efficacy at 4 years of follow-up.[9] With a median follow-up of 47 months, PFS remained significantly prolonged in the daratumumab arm compared to the control arm (median 16.7 vs 7.1 months, P <0.00001). 3-year overall survival was similar at 61% and 51% respectively.

A recent sub-analysis explored the effect of cytogenetic risk on outcomes in the CASTOR data.[10] In this analysis at median of 40 months follow-up, DVd prolonged PFS compared with Vd in both standard (16.6 vs 6.6 months, p<0.0001) and high (12.6 vs 6.2 months, p=0.0106) cytogenetic risk. Higher rates of MRD negativity and sustained MRD negativity were seen in the DVd group regardless of cytogenetic risk.

The use of once-weekly bortezomib in combination with daratumumab and dexamethasone has not been investigated in prospective studies. Small retrospective studies demonstrate efficacy and tolerability, particularly in patients with pre-existing neuropathy.[11]

## Toxicity

Overall rates of adverse events were similar in the two groups. Grades 3 and 4 events were more common in the daratumumab arm (76.1% v 62.4%), with haematological toxicity (thrombocytopenia, anaemia and neutropenia) being the most common adverse events with higher incidence rates. Rates of discontinuation were similar in the two groups. Infusion-related reactions were common, but almost all were Grades 1 and 2.[7]

No new safety signals were identified in the 4-year follow-up data, although noting the incidence of second primary malignancy was 4.9% in the daratumumab arm and 1.7% in the Vd arm.[9]

**Table 3. Most Common Adverse Events in the Safety Population.***

| Event | Daratumumab Group (N=243) | | Control Group (N=237) | |
|---|---|---|---|---|
| | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 |
| | *number of patients (percent)* | | | |
| Common hematologic adverse event | | | | |
| Thrombocytopenia | 143 (58.8) | 110 (45.3) | 104 (43.9) | 78 (32.9) |
| Anemia | 64 (26.3) | 35 (14.4) | 74 (31.2) | 38 (16.0) |
| Neutropenia | 43 (17.7) | 31 (12.8) | 22 (9.3) | 10 (4.2) |
| Lymphopenia | 32 (13.2) | 23 (9.5) | 9 (3.8) | 6 (2.5) |
| Common nonhematologic adverse events | | | | |
| Peripheral sensory neuropathy | 115 (47.3) | 11 (4.5) | 89 (37.6) | 16 (6.8) |
| Diarrhea | 77 (31.7) | 9 (3.7) | 53 (22.4) | 3 (1.3) |
| Upper respiratory tract infection | 60 (24.7) | 4 (1.6) | 43 (18.1) | 2 (0.8) |
| Fatigue | 52 (21.4) | 11 (4.5) | 58 (24.5) | 8 (3.4) |
| Cough | 58 (23.9) | 0 | 30 (12.7) | 0 |
| Constipation | 48 (19.8) | 0 | 37 (15.6) | 2 (0.8) |
| Dyspnea | 45 (18.5) | 9 (3.7) | 21 (8.9) | 2 (0.8) |
| Insomnia | 41 (16.9) | 0 | 35 (14.8) | 3 (1.3) |
| Peripheral edema | 40 (16.5) | 1 (0.4) | 19 (8.0) | 0 |
| Asthenia | 21 (8.6) | 2 (0.8) | 37 (15.6) | 5 (2.1) |
| Pyrexia | 38 (15.6) | 3 (1.2) | 27 (11.4) | 3 (1.3) |
| Pneumonia | 29 (11.9) | 20 (8.2) | 28 (11.8) | 23 (9.7) |
| Hypertension | 21 (8.6) | 16 (6.6) | 8 (3.4) | 2 (0.8) |
| Secondary primary cancer† | 6 (2.5) | NA | 1 (0.4) | NA |

* The safety population included all patients who received at least one dose of trial treatment. Adverse events of any grade that were reported in at least 15% of patients in either treatment group and grade 3 or 4 adverse events that were reported in at least 5% of patients in either treatment group are listed. NA denotes not applicable.
† The presence of a secondary primary cancer was prespecified in the statistical analysis plan as an adverse event of clinical interest. The other adverse events of clinical interest included infusion-related reactions, infections or infestations, peripheral neuropathies, and cardiac disorders.



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## History

### Version 3

| Date | Summary of changes |
|---|---|
| **3/05/2023** | Discussed at the 2022 eviQ Haematology Reference Committee meeting with the following changes:<br>• Link to Medical Scientific Advisory Group (MSAG) guidelines updated<br>• Notes regarding SC daratumumab and weekly dosing of bortezomib added to treatment schedule<br>• Bone modifying agents block added to "Clinical information" section, related note removed from treatment schedule and linked pages removed<br>• Pre and post-treatment medication block streamlined<br>• Thromboprophylaxis information added to “Clinical information” section<br>• Discharge thromboprophylaxis information removed from “Administration” section<br>• Thromboembolism side effect updated<br>• "Administration" section reformatted<br><br>Changed to v.3 and review date aligned with ID 4144 Multiple myeloma DVd (daratumumab subcutaneous bortezomib dexamethasone). |

### Version 2

| Date | Summary of changes |
|---|---|
| **30/04/2021** | Protocol reviewed by Haematology Reference Committee. Updates include:<br>• Evidence update to include CASTOR trial follow-up data.<br>• Added - daratumumab rapid infusion link to clinical information and administration, first daratumumab infusion split dose note, option for montelukast prior to C1D1 daratumumab.<br>• Administration timeline format change.<br><br>For review in 2 years. |
| **29/11/2021**<br><br>**20/01/2022** | Interactions updated. |
| **24/01/2022** | Pulmonary toxicity added to side effects. |

### Version 1

| Date | Summary of changes |
|---|---|

| Date | Summary of changes |
|---|---|
| **24/05/2019** | New eviQ protocol presented at Haematology Reference Committee meeting. |
| **08/07/2019** | New protocol published on eviQ v.1. Review in 1 year. |
| **10/10/2019** | Clinical information updated with PBS expanded indications for G-CSF. |



**First approved:** 24 May 2019
**Last reviewed:** 25 May 2021
**Review due:** 30 June 2024

***The currency of this information is guaranteed only up until the date of printing, for any updates please check:***
*https://www.eviq.org.au/p/3611*
*13 Jun 2023*

# Patient information - Multiple myeloma - DVd (daratumumab bortezomib dexamethasone)

**Patient's name:**

## Your treatment

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

| **DVd (daratumumab, bortezomib, dexamethasone)** | | | |
|---|---|---|---|
| This treatment cycle is repeated every 21 days for the first 8 cycles followed by maintenance daratumumab. Your doctor will advise you of the number of treatments you will have. | | | |
| **Cycle 1** | | | |
| **Day** | **Treatment** | **How it is given** | **How long it takes** |
| 1, 8 and 15 | **Daratumumab** *(dara-toom-oo-mab)* | By a drip into a vein | About 7 to 8 hours |
| 1 and 2, 4 and 5, 8 and 9, 11 and 12 | **Dexamethasone** (*dexa-METH-a-sone*) | Take orally ONCE a day in the morning with food on days 1 and 2, 4 and 5, 8 and 9, 11 and 12 only **Please note:** on cycle 1 day 1 your dexamethasone dose will be given by a drip into the vein prior to daratumumab administration | |
| 1, 4, 8 and 11 | **Bortezomib** (*BORE-tez-oh-mib*) | By injection under the skin | About 5 minutes |
| **Cycles 2 and 3** | | | |
| **Day** | **Treatment** | **How it is given** | **How long it takes** |
| 1, 8 and 15 | **Daratumumab** | By a drip into a vein | About 4 to 5 hours |
| 1 and 2, 4 and 5, 8 and 9, 11 and 12 | **Dexamethasone** | Take orally ONCE a day in the morning with food on days 1 and 2, 4 and 5, 8 and 9, 11 and 12 only | |
| 1, 4, 8 and 11 | **Bortezomib** | By injection under the skin | About 5 minutes |
| **Cycles 4 to 8** | | | |
| **Day** | **Treatment** | **How it is given** | **How long it takes** |
| 1 | **Daratumumab** | By a drip into a vein | About 4 to 5 hours |
| 1 and 2, 4 and 5, 8 and 9, 11 and 12 | **Dexamethasone** | Take orally ONCE a day in the morning with food on days 1 and 2, 4 and 5, 8 and 9, 11 and 12 only | |
| 1, 4, 8 and 11 | **Bortezomib** | 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.

## 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:..... |

Before starting daratumumab, my blood test results collected on (date) _____ were:

**Blood type:** ☐ A ☐ B ☐ AB ☐ O ☐ Rh+ ☐ Rh-

**Indirect Coombs test (antibody screen) was:** ☐ Negative ☐ Positive for the following antibodies:.....

Other:.....

Contact details of institution where the blood tests were performed:.....

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

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

## Other information about your treatment

### Treatment delays

There may 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. Your doctor will explain if you need any delays to your treatment and the reason why.

### Blood tests and monitoring

You will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

### Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the eviQ patient information sheets on CVADs.

### 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.
- **Daratumumab pre and post-treatment medication:** before your treatment with daratumumab you will need to take some tablets called a premedication to help prevent you from having a reaction. After your daratumumab infusion or injection you may be given some additional corticosteroid tablets called post-treatment medication to prevent further reactions.

## Side effects

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

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

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

| **Immediate (onset hours to days)** | |
|---|---|
| **Allergic reaction** | • Allergic reactions are uncommon but can be life threatening.<br>• **If you feel unwell during the infusion or shortly after it, or:**<br>◦ **get a fever, shivers or shakes**<br>◦ **feel dizzy, faint, confused or anxious**<br>◦ **start wheezing or have difficulty breathing**<br>◦ **have a rash, itch or redness of the face**<br><br>**<u>While you are in hospital:</u> Tell your doctor or nurse immediately.**<br>**<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.** |
| **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. |
| **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.** |
| **Shortness of breath** | • You may have a cough.<br>• You may feel short of breath.<br>• **Tell your doctor or nurse immediately if you feel you have a cough or feel short of breath.** |
| **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.** |
| **Fever** | • You may feel warm.<br>• Tell your doctor or nurse if you get this symptom. |
| **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.** |
| **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)** | |
|---|---|
| **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.** |
| **Appetite loss (anorexia)** | • You may not feel like eating.<br>• Try to avoid drinking fluids at meal times.<br>• Try to eat small meals or snacks regularly throughout the day.<br>• Try to eat food that is high in protein and calories.<br>• If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian. |
| **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)** | |
|---|---|
| **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.
- 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.
- 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 more 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
- 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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