Multiple myeloma daratumumab

ID: 3371 v.1 **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.

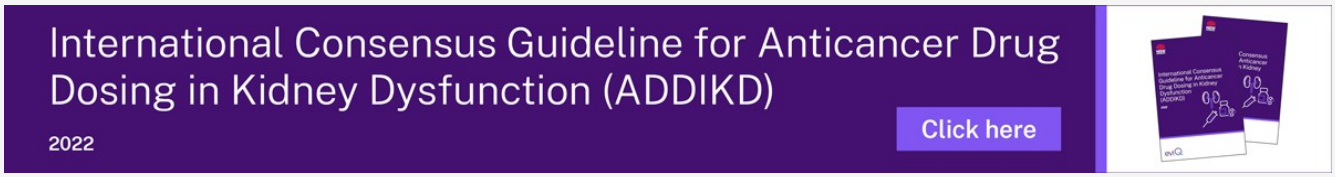
If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices. Please refer to the ANZSBT/MSAG position paper. [1]

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

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

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 daratumumab subcutaneous

Treatment schedule - Overview

Cycle 1 and 2

Drug	Dose	Route	Day
Daratumumab	16 mg/kg	IV infusion	1, 8, 15, 22 *

Cycle 3 to 6

Drug	Dose	Route	Day
Daratumumab	16 mg/kg	IV infusion	1 and 15

Cycle 7 and further cycles

Drug	Dose	Route	Day
Daratumumab	16 mg/kg	IV infusion	1

* 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.

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity.

Notes:

- Daratumumab may be administered subcutaneously as a flat dose of 1,800 mg. For more information see ID 4084 Multiple myeloma daratumumab subcutaneous.
- 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.[2]

Drug status: **Daratumumab**: PBS authority

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)	1 to 3 hours before treatment. * As per treating clinician's discretion
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 2 and 3		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion
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 (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
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 9 and 10		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion
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 (IV)	1 to 3 hours before treatment. * As per treating

Day 15		
		clinician's discretion
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 and 17		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion

Day 22		
Paracetamol	1,000 mg (PO)	1 to 3 hours before treatment
Loratadine	10 mg (PO)	1 to 3 hours before treatment
Dexamethasone	12 mg (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
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 23 and 24		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion

Cycle 2

Day 1		
Paracetamol	1,000 mg (PO)	1 to 3 hours before treatment
Loratadine	10 mg (PO)	1 to 3 hours before treatment
Dexamethasone	12 mg (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
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 2 and 3		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion

Day 8		
Paracetamol	1,000 mg (PO)	1 to 3 hours before treatment
Loratadine	10 mg (PO)	1 to 3 hours before treatment
Dexamethasone	12 mg (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
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 9 and 10		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion

Day 15		
Paracetamol	1,000 mg (PO)	1 to 3 hours before treatment

Day 15		
Loratadine	10 mg (PO)	1 to 3 hours before treatment
Dexamethasone	12 mg (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
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 and 17		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion
Day 22		
Paracetamol	1,000 mg (PO)	1 to 3 hours before treatment
Loratadine	10 mg (PO)	1 to 3 hours before treatment
Dexamethasone	12 mg (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
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 23 and 24		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion

Cycle 3 to 6

Day 1		
Paracetamol	1,000 mg (PO)	1 to 3 hours before treatment
Loratadine	10 mg (PO)	1 to 3 hours before treatment
Dexamethasone	12 mg (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
Daratumumab	16 mg/kg (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate^
Day 2 and 3		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion
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 (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
Daratumumab	16 mg/kg (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate^
Day 16 and 17		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion

Cycle 7 and further cycles

Day 1		
Paracetamol	1,000 mg (PO)	1 to 3 hours before treatment
Loratadine	10 mg (PO)	1 to 3 hours before treatment
Dexamethasone	12 mg (IV)	1 to 3 hours before treatment. * As per treating clinician's discretion
Daratumumab	16 mg/kg (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate^

Day 2 and 3		
Dexamethasone	4 mg (PO)	ONCE a day with or after food. ** As per treating clinician's discretion

* Dexamethasone 20 mg (or equivalent) is given intravenously (IV) for the first 2 doses of daratumumab, followed by dexamethasone 12 mg (or equivalent) intravenously or orally (IV/PO) for all subsequent doses for the prevention of infusion-related reactions (IRRs).

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

*** 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.

^ Refer to daratumumab infusion table for detailed administration instructions

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity.

Indications and patient population

- Relapsed/refractory multiple myeloma after at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD) or refractory to both a PI and an IMiD

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion-related reaction	High risk with daratumumab. 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.[3] Close monitoring during and after administration is recommended.[4]
Pre and post-treatment medication	The product information states that pre- and post-treatment medication is required for this treatment. Please refer to the treatment schedule for the suggested pre- and post-treatment medication regimen. This may be substituted to reflect institutional policy. 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. Read more about daratumumab rapid infusion
Emetogenicity MINIMAL	No antiemetics should be routinely administered before treatment in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
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. 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. Extended red cell phenotyping and RBC antibody screen should be done for patients prior to starting daratumumab. 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. 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.
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).[5] For more information, please see the following protocols: ID 137 Multiple myeloma zoledronic acid ID 147 Multiple myeloma pamidronate ID 3964 Multiple myeloma denosumab - note denosumab is TGA approved but not PBS reimbursed for this indication.
Bisphosphonates and dental review	Caution should be taken with prolonged use of bisphosphonates due to the risk of osteonecrosis of the jaw (ONJ). A dental review prior to treatment is recommended, and all dental issues treated before the initiation of bisphosphonates. Dental review 6 to 12 monthly during treatment is advisable to minimise risk of ONJ. Concurrent daily oral supplements of calcium 500 mg and vitamin D 400 International Units are recommended. Read more about medication-related osteonecrosis of the jaw (MRONJ)
Corticosteroids	Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate. Read more about acute short term effects from corticosteroids
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Thromboprophylaxis	Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion. Read more about the prophylaxis of venous thromboembolism (VTE) in multiple myeloma

Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC, LFTs, calcium, magnesium 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. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

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

Note: The modifications in this section are as recommended in the product information.[2]

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.

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*

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

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration cycles 1 and 2

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

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of 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.

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

Note: ensure the patient has dexamethasone for TWO days post-daratumumab if prescribed.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Day 2 and 3

This is an oral treatment

Dexamethasone

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

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

Day 8

Approximate treatment time: initial infusion 7 hours, second infusion 5 hours and subsequent infusions 4 hours

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of 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.

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

Note: ensure the patient has dexamethasone for TWO days post-daratumumab if prescribed.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Day 9 and 10

This is an oral treatment

Dexamethasone

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

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

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.

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.

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

Note: ensure the patient has dexamethasone for TWO days post-daratumumab if prescribed.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Day 16 and 17

This is an oral treatment

Dexamethasone

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

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

Day 22

Approximate treatment time: 4 hours

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of 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.

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

Note: ensure the patient has dexamethasone for TWO days post-daratumumab if prescribed.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Day 23 and 24

This is an oral treatment

Dexamethasone

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

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

Discharge information

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 3 to 6

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

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of 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.

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

Note: ensure the patient has dexamethasone for TWO days post-daratumumab if prescribed.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Day 2 and 3

This is an oral treatment

Dexamethasone

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

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

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.

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.

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

Note: ensure the patient has dexamethasone for TWO days post-daratumumab if prescribed.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Day 16 and 17

This is an oral treatment

Dexamethasone

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

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

Discharge information

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 cycle 7 onwards

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

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of 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.

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

Note: ensure the patient has dexamethasone for TWO days post-daratumumab if prescribed.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Day 2 and 3

This is an oral treatment

Dexamethasone

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

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

Discharge information

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. Read more about hypersensitivity reaction

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
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. Read more about arthralgia and myalgia
Fatigue	Read more about fatigue
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
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.
Thromboembolism	Thromboembolic events, including pulmonary embolism, deep vein thrombosis and cerebrovascular accidents can occur. Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion. Read more about management of thromboembolism (VTE) in multiple myeloma

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea

Evidence

The evidence supporting this protocol is provided by a combined analysis of two phase 1/2 open-label studies (GEN501 and SIRIUS studies) involving 148 patients with relapsed and/or refractory multiple myeloma (MM), who were treated with daratumumab monotherapy.[6]

GEN501 was an open label, multicentre, phase I/2, dose escalation and dose expansion study that included patients with at least 2 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD). SIRIUS was an open-label multicentre phase II study that included patients with MM with at least 3 prior lines of therapy (including PI and IMiD) or who were double refractory to PI and IMiD. For the combined analysis, data from all patients who received daratumumab 16 mg/kg in GEN501 part 2 and SIRIUS were included.

Between March 2008 and December 2015, 148 patients received daratumumab, 16 mg/kg IV, per week for 8 weeks, every 2 weeks for 16 weeks, then once every 4 weeks until disease progression.

The primary end point for the combined analysis was overall response rate (ORR) and secondary end points were duration of response, progression free survival and overall survival.

Daratumumab monotherapy demonstrated rapid, deep and durable responses with a median OS that was better than what was expected for this particular group of heavily pretreated patients and a clinical survival benefit that extended to patients with responses that were <PR (ie. stable disease and minor responses).

A search of the literature found limited evidence to support the use of daratumumab for the treatment of multiple myeloma. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by the trials analysed by Usmani et al.[6, 7]

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Usmani et al, 2016[6, 7]	**Yes**	Yes	
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	October 2017	**Yes**	N/A	-
BCCA	N/A	**N/A**	N/A	-
CCO	October 2017	**Yes**	Yes	-
MSAG	March 2017	**Yes**	N/A	-

Efficacy

In the combined analysis of the SIRIUS and GEN501 studies, after a median follow up of 20.7 months, the median OS was 20.1 months (95% CI 7.4 months to NE). This is favourable compared to the expected median OS of 7.9 months in real-world data of patients who have had at least 3 prior lines of therapy including an immunomodulatory drug (IMiD) and a proteasome inhibitor (PI), or patients who are double refractory to an IMiD and a PI,[7] as was the case for the majority of patients in the SIRIUS and GEN501 studies. Thirty-one percent of patients achieved at least a partial response (PR), of which 43% achieved at least a very good partial response (VGPR). The rate of CR or better was 4.7%. Importantly, a survival benefit was seen (med OS 18.5 months) even patients who achieved <PR (ie stable disease or minor responses).

Table 1: Summary of responses in the combined daratumumab 16 mg/kg group.

	Patients receiving daratumumab 16 mg/kg (N = 148)		
Response	**No.**	**%**	**95% CI**
ORR	46	31.1	23.7-39.2
Clinical benefit (ORR + MR)	55	37.2	29.4-45.5
VGPR or better	20	13.5	8.5-20.1
CR or better	7	4.7	1.9-9.5
sCR	3	2.0	0.4-5.8
CR	4	2.7	0.7-6.8
VGPR	13	8.8	4.8-14.6
PR	26	17.6	11.8-24.7
MR	9	6.1	2.8-11.2
SD	68	45.9	37.7-54.3
PD	18	12.2	7.4-18.5
NE	7	4.7	1.9-9.5

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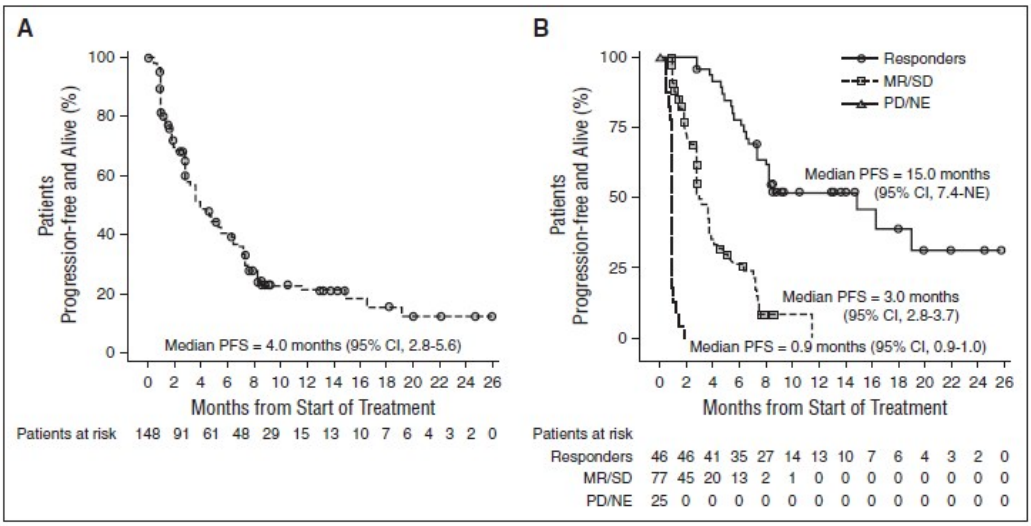

Figure 1: PFS in the combined daratumumab 16 mg/kg group. At a median follow-up of 20.7 months, the median PFS of patients in (A) the combined data set and (B) stratified by response category are shown.

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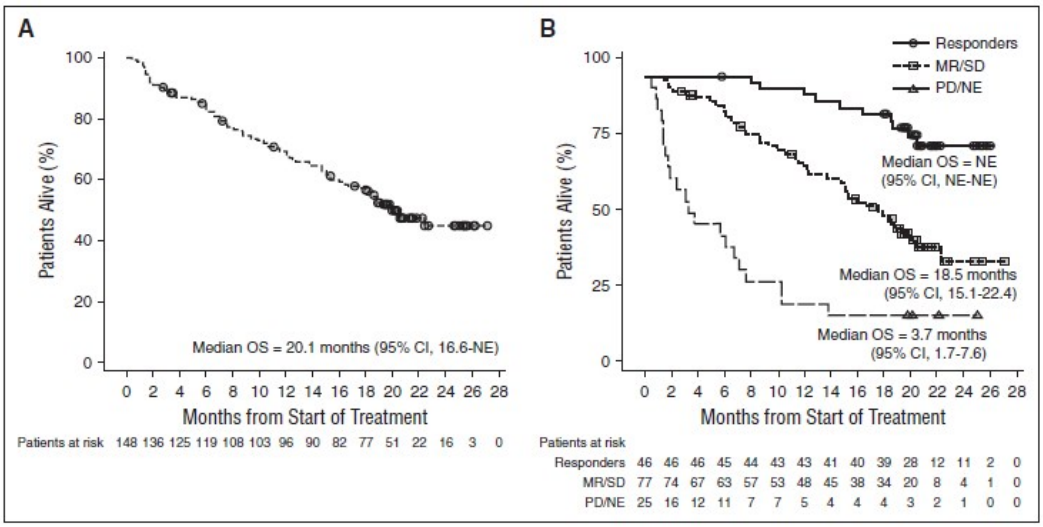

Figure 2: OS in the combined daratumumab 16 mg/kg group. The median OS of patients in (A) the combined data set and (B) stratified by response category are shown.

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The final results of the pooled analysis was presented as ASH 2017, with median follow-up of patients of approximately 3 years. Median overall survival (OS) was 20.5 months (95% CI 16.6-28.1), and the 3-year OS was 36.5% (95% CI 28.4-44.6). Amongst responders, the median duration of response was 8.0 months (95% CI 6.5-14.7). 19.6% of responders remained progression-free at 3 years.[8]

No quality of life (QoL) data was collected in these phase I/II studies. In general, treatment was very well tolerated.

Toxicity

The most common treatment related adverse events (AEs) are summarised in table 1. Infusion related reactions (IRRs) occurred in 48% of patients, the majority of which were grade 1 and 2, the symptoms of which mainly included nasal congestions, cough, allergic rhinitis, throat irritability and dyspnoea. Ninety-six percent of IRRs occurred in the first infusion, with decreasing incidence in subsequent infusions (7% during the second, and 7% during subsequent infusions). IRRs were safety managed with pre (+/- post) medications including antihistamines, corticosteroids and paracetamol.

Thirty-one percent of patients required blood transfusions. As CD38 is weakly expressed on red blood cells (RBCs), daratumumab is known to weakly bind to RBCs and interferes with the indirect antiglobulin tests in pretransfusion immunohaematology testing. While no direct AEs related to blood transfusion reaction were reported in these studies, as a result pretransfusion intereference by daratumumab, it is recommended that all patients have extended red cell phenotyping prior to the first dose of daratumumab (or genotyping at any time) to allow dispensing of extended phenotype matched blood if daratumumab interference in pretransfusion testing cannot be resolved by recommended methods.[1] Communications to blood transfusion laboratory is important to enable this. Patients should be encouraged to carry an alert card indicating their daratumumab treatment, extended red cell phenotype and

presence of any known red cell alloantibodies for at least 6 months after the last dose of daratumumab.

Table 1: Overall treatment emergent adverse events.

	All grades		Grade 3		Grade 4	
TEAE	No.	%	No.	%	No.	%
Fatigue	62	41.9	3	2.0	0	
Nausea	44	29.7	0		0	
Anemia	42	28.4	26	17.6	0	
Back pain	40	27.0	4	2.7	0	
Cough	38	25.7	0		0	
Thrombocytopenia	32	21.6	13	8.8	8	5.4
Upper respiratory tract infection	32	21.6	1	0.7	0	
Neutropenia	31	20.9	11	7.4	4	2.7

References

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4 King, T. A., J. Jagger, J. Wood, et al. 2018. "Best Practice for the Administration of Daratumumab in Multiple Myeloma: Australian Myeloma Nurse Expert Opinion." Asia Pac J Oncol Nurs

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6 Usmani, S. Z., B. M. Weiss, T. Plesner, et al. 2016. "Clinical efficacy of daratumumab monotherapy in patients with heavily pretreated relapsed or refractory multiple myeloma." Blood 128(1):37-44.

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History

Version 1

Date	Summary of changes
24/11/2017	New eviQ protocol presented at Haematology Reference Group meeting
16/04/2018	New protocol published on eviQ v.1.

Date	Summary of changes
24/05/2019	Protocol reviewed at Haematology Reference Committee meeting. Evidence updated. Review in 5 years.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.
23/04/2021	Daratumumab rapid infusion link added to clinical information and administration, note added to treatment schedule about first daratumumab infusion split dose
14/10/2022	The following changes have been made with the consensus agreement of the Haematology Reference Committee: • Link to Medical Scientific Advisory Group (MSAG) guidelines updated • Note regarding subcutaneous daratumumab added to treatment schedule • Bone modifying agents block added to "Clinical information" section, related note removed from treatment schedule and linked pages removed • Pre and post-treatment medication block streamlined • Thromboprophylaxis information added to “Clinical information” section • Discharge thromboprophylaxis information removed from “Administration” section • Thromboembolism side effect updated • "Administration" section reformatted

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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/3371
13 Jun 2023

Patient information - Daratumumab

Patient's name:

Your treatment

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

Daratumumab			
This treatment cycle is repeated every 28 days. 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, 15 and 22	**Daratumumab** *(dara-toom-oo-mab)*	By a drip into a vein	About 7 to 8 hours
Cycle 2			
Day	**Treatment**	**How it is given**	**How long it takes**
1, 8, 15 and 22	**Daratumumab**	By a drip into a vein	About 4 to 5 hours
Cycles 3 to 6			
Day	**Treatment**	**How it is given**	**How long it takes**
1 and 15	**Daratumumab**	By a drip into a vein	About 4 to 5 hours
Cycle 7 and further cycles			
Day	**Treatment**	**How it is given**	**How long it takes**
1	**Daratumumab**	By a drip into a vein	About 4 to 5 hours

When to get help

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

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath	Daytime:..... Night/weekend:..... Other instructions:.....

- uncontrolled vomiting or diarrhoea
- pain, tingling or discomfort in your chest or arms
- you become unwell.

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.
	• **If you feel unwell during the infusion or shortly after it, or:**
	  ◦ **get a fever, shivers or shakes**
	  ◦ **feel dizzy, faint, confused or anxious**
	  ◦ **start wheezing or have difficulty breathing**
	  ◦ **have a rash, itch or redness of the face**
	
	While you are in hospital: Tell your doctor or nurse immediately.
	After you leave: Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.

Early (onset days to weeks)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening.
	• Wash your hands often.
	• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.
	• Do your mouth care regularly.
	• Inspect your central line site (if you have one) daily for any redness, pus or swelling.
	• Limit contact with people who are sick.
	• Learn how to recognise the signs of infection.
	• Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:**
	  ◦ **a temperature of 38°C or higher**
	  ◦ **chills, shivers, sweats or shakes**
	  ◦ **a sore throat or cough**
	  ◦ **uncontrolled diarrhoea**
	  ◦ **shortness of breath**
	  ◦ **a fast heartbeat**
	  ◦ **become unwell even without a temperature.**

Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.

Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Anti-sickness medication is usually not needed but may help in some people. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Side effects from steroid medication	• Steroid medication may cause: ◦ mood swings and behaviour changes ◦ an increased appetite ◦ weight gain ◦ swelling in your hands and feet ◦ stomach upsets ◦ trouble sleeping ◦ fragile skin and bruising ◦ an increase in your blood sugar level ◦ weak and brittle bones (osteoporosis) • Take your steroid medication with food to reduce stomach upset • If you have diabetes, your blood sugar levels may be tested more often. • Tell your doctor or nurse if you get any of the symptoms listed above.

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**

General advice for people having cancer treatment

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

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