

Daratumumab SC Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
As monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy	C90	00604a	ODMS 01/07/2020

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Treatment with daratumumab is administered as a subcutaneous injection according to the dosing schedule in Table 1 and Treatment Table 2 below until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Table 1: Dosing schedule of daratumumab

Schedule	Weeks ^a
Weekly (total of 8 doses)	Weeks 1 to 8
Every two weeks (total of 8 doses)	Weeks 9 to 24 ^b
Every four weeks	Week 25 onwards until disease progression ^c
^a Weeks 1 to 8 = Cycles 1 to 8 (1 cycle = 1 week) Weeks 9 to 24 = Cycles 9 to 16 (1 cycle = 2 weeks) Week 25 onwards = Cycle 17 onwards (1 cycle = 4 weeks)	
^b First dose of the every-2-week dosing schedule is given at Week 9	
^c First dose of the every-4-week dosing schedule is given at Week 25	

Table 2: Treatment table for daratumumab

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Daratumumab	1800mg	S.C	Over 3 to 5 minutes	As per Table 1 dosing schedule
If a planned dose of daratumumab is missed, the dose should be administered as soon as possible and the dosing schedule should be adjusted accordingly, maintaining the treatment interval.					

NCCP Regimen: Daratumumab SC Monotherapy	Published: 23/07/2020 Review: 20/09/2026	Version number: 2
Tumour Group: Myeloma NCCP Regimen Code: 00604	IHS Contributor: NCCP Plasma Cell Disorder Clinical Advisory Group	Page 1 of 6
The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens		

ELIGIBILITY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to daratumumab or any of the excipients
- Pregnancy
- Breastfeeding
- Severe uncontrolled asthma/obstructive airways disease

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies

TESTS:

Baseline tests:

- FBC, renal, liver and bone profile
- Uric acid
- Urine pregnancy testing for pre-menopausal women < 55 years
- Inform patient and transfusion laboratory that patient is due to commence daratumumab. Send a 'Group and Save' sample to the transfusion laboratory for red cell phenotyping as all cross matching will be positive following treatment with Daratumumab due to binding of daratumumab to red cells.
- Virology Screen: EBV, CMV, Hep B, Hep C and HIV
Hepatitis B Reactivation: Patients should be tested for both HBsAg and HBcoreAb as per local policy. See Adverse Effects/Regimen Specific Complications re Hepatitis B Reactivation.

Regular tests:

- FBC, renal and liver profile monthly

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

NCCP Regimen: Daratumumab SC Monotherapy	Published: 23/07/2020 Review: 20/09/2026	Version number: 2
Tumour Group: Myeloma NCCP Regimen Code: 00604	IHS Contributor: NCCP Plasma Cell Disorder Clinical Advisory Group	Page 2 of 6
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- No dose reductions of daratumumab are recommended.
- Dose delay may be required to allow recovery of blood cell counts in the event of haematological toxicity.
- Consider supportive care with transfusions or growth factors.

Renal and Hepatic Impairment:

Table 3: Dose modification of daratumumab in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
No formal studies of daratumumab in patients with renal impairment have been conducted. Based on a population pharmacokinetic (PK) analysis no dosage adjustment is necessary for patients with renal impairment	No formal studies of daratumumab in patients with hepatic impairment have been conducted. Based on population PK analyses, no dosage adjustments are necessary for patients with hepatic impairment

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal (Refer to local policy).

PRE AND POST INJECTION MEDICATIONS:

- Pre-dose medications (oral or intravenous) should be administered to reduce the risk of infusion related reactions (IRRs) to all patients 1-3 hours prior to every dose of daratumumab as suggested in Table 4.
- Consider use of montelukast 10mg PO 60 minutes pre-daratumumab before the first dose only to reduce the incidence of infusion-related reactions
- For the prevention of delayed IRRs, oral corticosteroid (20 mg methylprednisolone or equivalent dose of an intermediate-acting or long-acting corticosteroid in accordance with local policy) should be administered on each of the two days following all injections (beginning the day after the injection).
- If the patient experiences no major IRRs after the first three injections, post-injection corticosteroids (excluding any background regimen corticosteroids) may be discontinued.
- Following the first four injections, if the patient experiences no major IRRs, these inhaled post-injection medications may be discontinued at the discretion of the physician.

NCCP Regimen: Daratumumab SC Monotherapy	Published: 23/07/2020 Review: 20/09/2026	Version number: 2
Tumour Group: Myeloma NCCP Regimen Code: 00604	IHS Contributor: NCCP Plasma Cell Disorder Clinical Advisory Group	Page 3 of 6
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

Table 4: Suggested medications for pre and post daratumumab administration

Day	Drugs	Dose	Route	Timing	Cycle
1	Dexamethasone	20mg	PO	1-3 hours prior to daratumumab injection	1-2
2,3	Dexamethasone	4mg	PO		All cycles
1	Dexamethasone	12mg	PO	1-3 hours prior to daratumumab injection	From cycle 3 onwards
1	Paracetamol	1g	PO	1-3 hours	All cycles
1	Chlorphenamine ^a	4mg	PO	1-3 hours prior to daratumumab injection	All cycles

^aOr equivalent oral or intravenous antihistamine

See other supportive care for recommended post-injection medications

OTHER SUPPORTIVE CARE:

- Anti-viral prophylaxis should be considered for the prevention of herpes zoster virus reactivation. **(Refer to local policy).**
- Bisphosphonates should be considered in all patients with myeloma related bone disease.
- Tumour lysis syndrome prophylaxis **(Refer to local policy).**
- H2 antagonist or proton pump inhibitor **(Refer to local policy).**
- Consider PJP prophylaxis **(Refer to local policy).**
- Influenza vaccination in appropriate patients.
- **Recommended post-injection medications for patients with a history of obstructive pulmonary disorder:**
 - The use of post-injection medications including short and long acting bronchodilators, and inhaled corticosteroids should be considered.
- Women of child-bearing potential should use effective contraception during, and for 3 months after cessation of daratumumab treatment.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Daratumumab is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

- **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 daratumumab administration. It should be recognised that daratumumab bound to RBCs may mask detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted. Patients should be typed and screened prior to starting daratumumab treatment. Phenotyping may be considered prior to starting daratumumab treatment as per local practice. Red blood cell genotyping is not impacted by daratumumab and may be performed at any time. In the event of a planned transfusion blood transfusion centres should be notified of this interference with indirect antiglobulin tests. If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given per local blood bank practices.

NCCP Regimen: Daratumumab SC Monotherapy	Published: 23/07/2020 Review: 20/09/2026	Version number: 2
Tumour Group: Myeloma NCCP Regimen Code: 00604	IHS Contributor: NCCP Plasma Cell Disorder Clinical Advisory Group	Page 4 of 6
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

- **Interference with determination of Complete Response:** Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both, the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.
 - Consider use of daratumumab-specific IFE reflex assay (DIRA) to distinguish the therapeutic from the patient's M protein. The DIRA assay can be used to determine whether additional testing, including determination of the sFLC ratio and BM evaluation, is warranted in patients with IgG-κ band and low measurable M protein (≤ 2 g/L) to assess the presence of (stringent) CR.
- **Hepatitis B Reactivation:** Hepatitis B virus reactivation, in some cases fatal, has been reported in patients treated with daratumumab. HBV screening should be performed in all patients before initiation of treatment with daratumumab. For patients with evidence of positive HBV serology, monitor for clinical and laboratory signs of HBV reactivation during, and for at least six months following the end of daratumumab treatment. Manage patients according to current clinical guidelines. Consider consulting a hepatitis disease expert as clinically indicated. In patients who develop reactivation of HBV while on daratumumab, suspend treatment with daratumumab and institute appropriate treatment. Resumption of daratumumab treatment in patients whose HBV reactivation is adequately controlled should be discussed with physicians with expertise in managing HB.

DRUG INTERACTIONS:

- No interaction studies have been performed.
- Current drug interaction databases should be consulted for more information

REFERENCES

1. Mateos NV, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial *Lancet Haematol* 2020, 7(5) 370-380.
2. Van de Donk NWCJ, Richardson PG, Malavasi F. CD38 antibodies in multiple myeloma: back to the future. *Blood*. 2018 Jan 4; 131 (1):13-29. doi: 10.1182/blood-2017-06-740944. Epub 2017 Nov 8. Review. PubMed PMID: 29118010
3. Subcutaneous daratumumab (DARA) in patients (Pts) with relapsed or refractory multiple myeloma (RRMM): Part 2 update of the open-label, multicenter, dose escalation phase 1b study (PAVO). *Blood* (2018) 132 (Supplement 1): 1995.
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V3 2021. Available at: <https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf>
5. HPRA Direct Healthcare professional communication 26/06/2019. Daratumumab (DARZALEX®) and risk of reactivation of hepatitis B virus: Hepatitis B virus status to be established in patients receiving DARZALEX® Available at: [https://www.hpra.ie/docs/default-source/default-document-library/important-safety-information---darzalex-\(daratumumab\).pdf?sfvrsn=0](https://www.hpra.ie/docs/default-source/default-document-library/important-safety-information---darzalex-(daratumumab).pdf?sfvrsn=0)

NCCP Regimen: Daratumumab SC Monotherapy	Published: 23/07/2020 Review: 20/09/2026	Version number: 2
Tumour Group: Myeloma NCCP Regimen Code: 00604	IHS Contributor: NCCP Plasma Cell Disorder Clinical Advisory Group	Page 5 of 6
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

6. Daratumumab (DARZALEX®) Summary of Product Characteristics. Accessed August 2021. Available at:
https://www.ema.europa.eu/en/documents/product-information/velcade-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	23/07/2020		NCCP Plasma Cell Disorder Clinical Advisory Group
2	20/09/2021	Regimen review Update of premedication table in supportive care to include recommended pre and post injection medications	NCCP Plasma Cell Disorder Clinical Advisory Group

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

NCCP Regimen: Daratumumab SC Monotherapy	Published: 23/07/2020 Review: 20/09/2026	Version number: 2
Tumour Group: Myeloma NCCP Regimen Code: 00604	IHS Contributor: NCCP Plasma Cell Disorder Clinical Advisory Group	Page 6 of 6
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		