Indication	The treatment of relapsed or refractory multiple myeloma following 3 prior lines of systemic treatment to include a proteosome inhibitor and an immunomodulatory agent. The patient must have not received previous treatment with daratumumab, or an anti-CD38 antibody, unless they have been previously treated with daratumumab as part of induction therapy pre-transplant and responded to daratumumab. NB NHS England does not fund daratumumab for patients with primary amyloidosis. NB: Induction chemotherapy and stem cell transplant is considered to be 1 line of therapy.
Treatment Intent	Disease Modification
Frequency and number of cycles	Every 28 days. Continue until progressive disease or unacceptable toxicity or patient choice, whichever occurs first. A formal medical review as to whether treatment with daratumumab should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment.
Monitoring Parameters pre-treatment	• Check virology status prior to cycle 1 • Consider flu and pneumococcal vaccination pre-therapy. • Monitor FBC, U&Es & LFTs at each cycle. • BP baseline • Limited data in patients >120kg, give at clinicians discretion. • **Dose reduction** • Dose reductions of daratumumab are not recommended. Dose delay may be required to allow recovery of blood cell counts in the event of haematological toxicity. • **Renal or hepatic impairment:** No dose adjustments necessary. • **Interference with tests**: Daratumumab binds to CD38 on red blood cells and results in a positive Indirect Antiglobulin Test (Coombs test) which may persist for up to 6 months after the last injection. Send a blood sample for group/ direct antiglobulin/phenotype testing prior to treatment. Daratumumab may be detected on SPE and IFE assays resulting in false positive results for patients with IgG kappa myeloma protein impacting initial assessment of complete responses. • **Contraception:** To avoid exposure to the foetus, women of reproductive potential should use effective contraception during treatment and for 3 months after cessation of daratumumab treatment • **Missed dose:** 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. • **Daratumumab injection related reactions (IRRs):** • Daratumumab can cause severe injection reactions which may result in admission to hospital. Pre-meds must be given 1-3 hours before the injection. • Patients should be pre-medicated with chlorphenamine, dexamethasone and paracetamol as well as monitored (vital signs before and after the injection) and counselled regarding IRRs, especially during and following the first and second injections. If an anaphylactic reaction or life-threatening (Grade 4) reactions occur, appropriate emergency care should be initiated immediately. Daratumumab therapy should be discontinued immediately and permanently. Patients should be observed for 6 hours post the 1st injection, 2 hours after 2nd dose and then 15 minutes observation after subsequent doses.

	• If the patient experiences no major IRRs after 3 doses of sub cut administration, post injection corticosteroids may be discontinued at the clinician's discretion. • The use of post-infusion medications (e.g. inhaled corticosteroids, short and long acting bronchodilators) should be considered for patients with a history of chronic obstructive pulmonary disease to manage respiratory complications should they occur. • **Administration:** o Inject 15 mL into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the navel over approximately 3-5 minutes. Do not inject at other sites of the body as no data are available. Injection sites should be rotated for successive injections. o Daratumumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars. o Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by slowing down the injection, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose. o During treatment with daratumumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site as daratumumab.
References	HAEM-MYEL-040 v1 SPC accessed online08.02.2022 Blueteq form accessed online 08.02.2022

NB For funding information, refer to CDF and NICE Drugs Funding List

Dosing schedule for daratumumab (28 day cycle)

Cycle	Daratumumab due on day:
1	1, 8, 15 &22
2	1, 8, 15 &22
3	1 & 15
4	1 & 15
5	1 & 15
6	1 & 15
7 onwards	1

Repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration
See table above	Dexamethasone	**20mg first 2 administrations** only then reduce to **12mg**	PO	stat	To be administered 1-3 hours prior to daratumumab. NB review dose of dexamethasone and increase back to 20mg where clinically indicated. (dispensed as TTO pack)
	Paracetamol	1gm	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Montelukast	10mg **First administration only**	PO	stat	
	DARATUMUMAB	**1800mg**	SC	bolus	Inject 15 mL into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the navel over approximately 3-5 minutes. Do not inject at other sites of the body as no data are available. Injection sites should be rotated for successive injections

TTOs: Repeat every 28 days

TTOs	Drug	Dose	Route	Directions
	Dexamethasone	4mg	PO	To be taken in the morning for 2 days starting the day after daratumumab treatment. NB if no major IRR after 3 doses of subcut daratumumab this can be stopped (see notes above).
	Aciclovir	400mg	PO	BD continuously (plus 3 more months after completion of last treatment dose)
	Co-trimoxazole	480mg	PO	TWICE daily on Mondays, Wednesdays and Fridays (plus 3 more months after completion of last treatment dose)
	Omeprazole	20mg	PO	OD Omit from cycle 3
	Allopurinol	300mg	PO	OD and review after 4 weeks. Prescribe continuing supply if required from cycle 2 onwards.
	Metoclopramide	10mg	PO	Take 10mg up to TDS when required. Do not take for more than 5 days continuously. On Cycle 1 only, then prescribe as required.
	Loperamide	2mg	PO	Take two capsules (4mg) after first loose stool, then one capsule (2mg) after each loose stool when required. (Maximum 16mg per day). Dispense on Cycle 1 only, and then prescribe as required.
	Consider the use of prophylactic anti-fungals			
	Pre Med TTO packs to be dispensed.			