Daratumumab
Adjudication Guideline

Rule Category: Pharmaceutical	**Ref: No:** 2023-PH-27	**Version Control:** Version No. V1.0	**Effective Date:** 25th August 2023	**Last Update:** 25th July 2023
Approved by: Daman	**Responsible:** Medical Standards & Research	**Related Adjudication Guidelines:** NA		

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1. Abstract

1.1 For Members

Daratumab belongs to a group of medicines called "monoclonal antibodies".[4]
Monoclonal antibodies are proteins that have been designed to recognise and attach to specific targets in the body. Daratumumab has been designed to attach to specific cancer cells in your body, so that your immune system can destroy the cancer cells.[4]

1.2 For Medical Professionals

Daratumumab is an immunoglobulin G1 kappa (IgG1k) human monoclonal antibody against CD38 antigen, produced in a mammalian cell line using recombinant DNA technology.

CD38 is a transmembrane glycoprotein (48 kDa) expressed on the surface of hematopoietic cells, including multiple myeloma and other cell types and tissues and has multiple functions, such as receptor mediated adhesion, signaling, and modulation of cyclase and hydrolase activity.

2. Scope

This adjudication rule highlights the coverage details for medically necessary indications for Daratumumab as per the policy terms and conditions of each health insurance plan administered by Daman.

3. Adjudication Policy

3.1 Eligibility / Coverage Criteria

Daman considers the use of Daratumumab medically necessary for the following indications:

1. **Multiple myeloma:**

- **Newly diagnosed:**[6,8,19]

  - Treatment of newly diagnosed multiple myeloma (in combination with bortezomib, thalidomide, and dexamethasone) in adults who are eligible for autologous stem cell transplant.
  - Treatment of newly diagnosed multiple myeloma (in combination with bortezomib, melphalan, and prednisone) in adults who are ineligible for autologous stem cell transplant.
  - Treatment of newly diagnosed multiple myeloma (in combination with lenalidomide and dexamethasone) in adults who are ineligible for autologous stem cell transplant.

- **Refractory:**[6,8,19]

  - Treatment of relapsed or refractory multiple myeloma (in combination with dexamethasone and lenalidomide) in adults who have received at least 1 prior therapy.
  - Treatment of relapsed or refractory multiple myeloma (in combination with dexamethasone and bortezomib) in adults who have received at least 1 prior therapy.
  - Treatment of relapsed or refractory multiple myeloma (in combination with dexamethasone and carfilzomib) in patients who have received 1 to 3 prior therapies.

- Treatment of relapsed or refractory multiple myeloma (in combination with dexamethasone and pomalidomide) in adults who have received at least 2 prior therapies, including lenalidomide and a proteasome inhibitor.
- Treatment of relapsed or refractory multiple myeloma (as monotherapy) in adults who have received at least 3 prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent or who are double refractory to a proteasome inhibitor and an immunomodulatory agent.

2. Light Chain Amyloidosis [17,18, 19]

- Light chain (AL) amyloidosis in combination with bortezomib, cyclophosphamide and dexamethasone in newly diagnosed patients. Daratumumab can be used for both relapsed or refractory disease.

3.2 Requirements for Coverage

- ICD and CPT / Drug codes must be coded to the highest level of specificity.

Recommended dosage for Daratumumab Intravenous infusion:[19]16 mg/kg actual body weight according to the following schedule.

- The usual starting dose of Daratumumab is 16 mg per kg of body weight/dose dependednt on body weight.

- Daratumumab injection for intravenous use is available as 100 mg/5ml and 400 mg/20 ml single-dose vials.The recommended dose is 16 mg/kg actual body weight according to the following schedule.

Table 1: [19]
Daratumumab injection Dosing Schedule in Combination With Lenalidomide or Pomalidomide (4-Week Cycle) and Low-Dose Dexamethasone and for Monotherapy.

Weeks	Schedule
Weeks 1 to 8	weekly (total of 8 doses)
Weeks 9 to 24[a]	weeks (total of 8 doses)
Week 25 onwards until disease progression[b]	every four week
a) First dose of the every-2-week dosing schedule is given at week 9. b) First dose of the every-4-week dosing schedule is given at week 25.	

Table 2: [19]
Daratumumab injection Dosing Schedule in Combination With Bortezomib, Melphalan and Prednisone ([VMP], 6-Week Cycle).

Weeks	Schedule
Weeks 1 to 6	weekly (total of 6 doses)
Weeks 7 to 54[a]	weeks (total of 16 doses)
Week 55 onwards until disease progression[b]	every four week
a) First dose of the every-3-week dosing schedule is given at week 7. b) First dose of the every-4-week dosing schedule is given at week 55.	

Table 3: [19]
Daratumumab injection Dosing Schedule in Combination With Bortezomib, Thalidomide and Dexamethasone ([VTd]; 4-Week Cycle).

Treatment Phase	Weeks	Schedule
Induction	Weeks 1 to 8	weekly (total of 8 doses)
	Weeks 9 to 16[a]	weeks (total of 4 doses)
Stop for high dose chemotherapy and ASCT		
Consolidation	Weeks 1 to 8[b]	Every two weeks (total of 4 doses)

a) First dose of the every-2-week dosing schedule is given at week 9.
b) First dose of the every-2-week dosing schedule is given at week 1 upon re-initiation of treatment following ASCT.

Table 4: [19]
Daratumumab injection Dosing Schedule With Bortezomib and Dexamethasone (3-Week Cycle).

Weeks	Schedule
Weeks 1 to 9	weekly (total of 9 doses)
Weeks 9 to 24[a]	weeks (total of 9 doses)
Week 25 onwards until disease progression[b]	every four week

a) First dose of the every-3-week dosing schedule is given at week 10.
b) First dose of theevery-4-week dosing schedule is given at week 25.

Table 5: [19]
Daratumumab injection Dosing Schedule With Carfilzomib and Dexamethasone (4-Week Cycle).

Weeks	Dose [c]	Schedule
Weeks 1	8 mg/Kg	Days 1 and 2 (total 2 doses)
Weeks 2 to 8	16 mg/Kg	Weekly (total of 7 doses)
Week 9 to 24[a]	16mg/Kg	Every two weeks (Total of 8 doses)
Week 25 onwards until disease progression[b]	16mg/Kg	every four week

a) First dose of the every-3-week dosing schedule is given at week 9.
b) First dose of theevery-4-week dosing schedule is given at week 25.
c) Based on Actual Body weight.

Table 6: [19]
Infusion Rates for Daratumumab injection (16 mg/kg) Administration.

Week	Dilution Volume	Initial Rate (first hour)	Rate Increment	Maximum Rate
Week 1 Infusion				
Option 1 (single dose infusion)				
Week 1 Day 1 (16mg /Kg)	1,000mL	50 mL/hour	50 mL/hour every hour	200 mL/hour
Option 2 (Split dose infusion)				
Week 1 Day 1 (8mg/Kg)	500 mL	50 mL/hour	50 mL/hour every hour	200 mL/hour
Week 1 Day 2 (8 mg/Kg)	500 mL	50 mL/hour	50 mL/hour every hour	200 mL/hour
Week 2 (16 mg/Kg) [b]	500 mL	50 mL/hour	50 mL/hour every hour	200 mL/hour
Week 3 onwards (16 mg/Kg) [c]	500 mL	100 mL/hour	50 mL/hour every hour	200 mL/hour

a) Consider incremental escalation of the infusion rate only in the absence of infusion-related reactions.
b) Use a dilution volume of 500 mL for the 16 mg/kg dose only if there were no infusion-related reactions the previous week. Otherwise, use a dilution volume of 1,000 ml.
c) Use a modified initial rate (100 mL/hour) for subsequent infusions (i.e., Week 3 onwards) only if there were no infusion-related reactions during the previous infusion. Otherwise, continue to use instructions indicated in the table for the Week 2 infusion rate.

Recommendation Dosage for Daratumumab Subcutaneous injection [19]:

The recommended dose is 1,800 mg of Daratumumab for subcutaneous injection, which is administered over approximately 3-5 minutes according to the following dosing schedule.

Tables 1 to 4 recommend dosage for Muliple Myeloma as monotherapy or as part of a combination therapy.

Table 1: [19]
Daratumumab dosing schedule in combination with lenalidomide, pomalidomide or carfilzomib and dexamethasone (4-week cycle) and for monotherapy.

Weeks	Schedule
Weeks 1 to 8	Weekly (total of 8 doses)
Weeks 9 to 24[a]	Every two weeks (total of 8 doses)
Week 25 onwards until disease progression[b]	Every four weeks
a) First dose of the every-2-week dosing schedule is given at week 9. b) First dose of theevery-4-week dosing schedule is given at week 25.	

Table 2: [19]
Daratumumab dosing schedule in combination with bortezomib, melphalan and prednisone (6-week cycle).

Weeks	Schedule
Weeks 1 to 6	Weekly (total of 6 doses)
Weeks 7 to 54[a]	Every three weeks (total of 16 doses)
Week 55 onwards until disease progression[b]	Every four weeks
a) First dose of the every-3-week dosing schedule is given at week 7. b) First dose of theevery-4-week dosing schedule is given at week 55.	

Table 3: [19]
Daratumumab dosing schedule in combination with bortezomib, thalidomide and dexamethasone (4-week cycle).

Treatment Phase	Weeks	Schedule
Induction	Weeks 1 to 8	Weekly (total of 8 does)
	Weeks 9 to 16a	Every two weeks (total of 4 doses)
Stop for High dose chemotherapy and ASCT		
Consolidation	Weeks 1 to 8[b]	Every two weeks (total of 4 doses).
a) First dose of the every-2-week dosing schedule is given at week 9. b) First dose of the every-2-week dosing schedule is given at week 1 upon re-initiation of treatment following ASCT.		

Table 4: [19]
Daratumumab dosing schedule in combination with bortezomib and dexamethasone (3- week cycle).

Weeks	Schedule
Weeks 1 to 9	Weekly (total of 9 doses)
Weeks 10 to 24[a]	Every three weeks (total of 5 doses)
Week 25 onwards until disease progression[b]	Every four weeks
a) First dose of the every-3-week dosing schedule is given at week 10. b) First dose of theevery-4-week dosing schedule is given at week 25.	

2. Recommended Dosage for Light Chain Amyloidosis[19]

Daratumumab injection dosing schedule in combination with bortezomib, cyclophosphamide and dexamethasone (4-week cycle)

Weeks	Schedule
Weeks 1 to 8	Weekly (total of 8 doses)
Weeks 9 to 24[a]	Every three weeks (total of 8 doses)
Week 25 onwards until disease progression[b]	Every four weeks
a) First dose of the every-2-week dosing schedule is given at week 9. b) First dose of theevery-4-week dosing schedule is given at week 25.	

Eligible clinician Speciality

Eligible clinician Speciality
Internal Medicine
Cardiology
Oncology
Nephrology

Questionnaire Link: ***https://www.damanhealth.ae/main/pdf/support/Questionnaire/Pre-approval%20Form%20for%20Daratumumab.pdf***

3.3 Non-Coverage

Daratumumab will not be covered by Daman (for any plan) if it fails to fulfill the coverage criteria

Plan	Coverage
Visitor plan	Not covered.
Basic Plan	Covered as per medical Criteria and member SOB.
Enhanced Plan	Covered as per medical Criteria and member SOB.
Thiqa	Covered as per medical Criteria and member SOB.

3.4 Payment and Coding Rules

Please apply DOH payment rules and regulations and relevant coding manuals for ICD, CPT, etc.

4. Denial Codes

Code	Code Description
MNEC-003	Service is not clinically indicated based on good clinician practice.
MNEC-004	Service is not clinically indicated based on good clinician practice, without additional supporting diagnosis /activities.
CODE-010	Activity/diagnosis inconsistent with clinician specialty
CODE-014	Activity/diagnosis inconsistent with clinician specialty
AUTH-001	Prior approval is required and was not obtained

5. Appendices

5.1 References

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20. *https://clinicaltrials.gov/ct2/show/NCT03871829*

5.2 Revision History

Date	Change(s)
25/07/2023	Release of V1.0