Medical Drug Clinical Criteria

Subject:	Darzalex (daratumumab) and Darzalex Faspro (daratumumab and hyaluronidase-fihj)		
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Overview

This document addresses the use of Darzalex (daratumumab) and Darzalex Faspro (daratumumab and hyaluronidase-fihj). Daratumumab is a human anti-CD38 monoclonal antibody that is FDA approved for newly diagnosed and relapsed/refractory multiple myeloma (MM). Darzalex is administered intravenously, with weight based dosing, over hours. Darzalex Faspro is a subcutaneous dosage form that allows for flat dosing and is administered over 3-5 minutes. The National Comprehensive Cancer Network® (NCCN) provides category 2A recommendations for the use of daratumumab. Approved and recommended uses are listed below.

Newly diagnosed multiple myeloma:

- *Ineligible for stem cell transplant:*
  - In combination with bortezomib, melphalan, and prednisone
  - In combination with lenalidomide and dexamethasone
  - In combination with cyclophosphamide, bortezomib, and dexamethasone (NCCN 2A)
  - In combination with carfilzomib, lenalidomide, and dexamethasone (DP BIIa)
- *Eligible for stem cell transplant:*
- In combination with bortezomib, thalidomide, and dexamethasone
- In combination with bortezomib, lenalidomide, and dexamethasone (Label, NCCN 2A)
- In combination with cyclophosphamide, bortezomib, and dexamethasone (NCCN 2A)
- In combination with carfilzomib, lenalidomide, and dexamethasone (NCCN 2A)

Relapsed or refractory multiple myeloma:

- In combination with lenalidomide and dexamethasone
- In combination with bortezomib and dexamethasone
- In combination with pomalidomide and dexamethasone in those who have received at least 2 prior therapies (or 1 prior line of therapy) including lenalidomide and a proteasome inhibitor (Label, NCCN 2A)
- As a single agent in those who have received at least three prior lines of therapy including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
- In combination with carfilzomib and dexamethasone
- In combination with cyclophosphamide, bortezomib, and dexamethasone (NCCN 2A)
- In combination with carfilzomib, pomalidomide, and dexamethasone (NCCN 2A)
- In combination with selinexor and dexamethasone (NCCN 2A)
- In combination with venetoclax and dexamethasone for patients with t(11;14) (NCCN 2A)

Maintenance therapy for multiple myeloma:

- Daratumumab/lenalidomide (two-drug maintenance recommended for high-risk disease) for transplant candidates after response to primary myeloma therapy or for response or stable disease following transplant (NCCN 1/2A)

Emerging data from prospective and retrospective studies indicate Darzalex and/or Darzalex Faspro produce clinically meaningful responses in patients with systemic light chain amyloidosis. Most recently, the FDA has approved Darzalex Faspro for the treatment of light chain amyloidosis in combination with bortezomib, cyclophosphamide, and dexamethasone. This indication is under accelerated approval and continued approval may be contingent upon confirmatory trials. It is not indicated and not recommended for treatment of light chain amyloidosis in individuals who have NYHA class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials. There is also evidence to support Darzalex as a single agent, in combination with lenalidomide and dexamethasone, or in combination with dexamethasone with or without bortezomib in relapsed or refractory systemic light chain amyloidosis (Kimmich 2020, Roussel 2020). NCCN additionally recommends daratumumab for the management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome and Pediatric Acute Lymphoblastic Leukemia.

Definitions and Measures

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Multiple myeloma: A type of cancer that begins in plasma cells (white blood cells that produce antibodies).

Plasma cell leukemia: A rare and aggressive form of multiple myeloma characterized by high levels of plasma cells in the peripheral blood.

Proteasome inhibitors: A class of drugs used to treat multiple myeloma that work by blocking the action of proteasomes which are cellular complexes that break down proteins. Examples include bortezomib, carfilzomib and ixazomib.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Darzalex (daratumumab) and Darzalex Faspro (daratumumab and hyaluronidase-fihj)

Requests for Darzalex (daratumumab) or Darzalex Faspro (daratumumab and hyaluronidase-fihj) may be approved if the following criteria are met:

I. Individual has a diagnosis of multiple myeloma, including plasma cell leukemia; **AND**
II. Individual is using for one of the following:
    A. Newly diagnosed multiple myeloma for those who are ineligible for stem cell transplantation:
        1. In combination with melphalan, prednisone and a proteasome inhibitor (PI) (for example, bortezomib); **OR**
        2. In combination with lenalidomide and dexamethasone;

    OR
    B. Newly diagnosed multiple myeloma for those who are eligible for stem cell transplant, in combination with bortezomib, dexamethasone, and either thalidomide or lenalidomide (Label, NCCN 2A);
    OR
    C. Newly diagnosed multiple myeloma in combination with carfilzomib, lenalidomide, and dexamethasone;
    OR
    D. Newly diagnosed multiple myeloma in combination with cyclophosphamide, bortezomib, and dexamethasone;
    OR
    E. Relapsed or refractory multiple myeloma (Label, NCCN 2A):
        1. As a single agent following therapy with at least two prior lines of therapy including a PI (for example, bortezomib, carfilzomib, or ixazomib) and an immunomodulatory agent (for example, thalidomide, lenalidomide, or pomalidomide); **OR**
        2. In combination with cyclophosphamide, bortezomib, and dexamethasone; **OR**
        3. In combination with carfilzomib, pomalidomide, and dexamethasone (NCCN 2A); **OR**
        ~~3.~~4. In combination with selinexor and dexamethasone; **OR**
        ~~4.~~5. In combination with venetoclax and dexamethasone for patients with t(11:14); **OR**
        ~~5.~~6. As combination therapy following treatment with at least one prior line of therapy when used with one of following:
            a. A PI (for example, bortezomib, carfilzomib, or ixazomib) and dexamethasone; **OR**
            b. An immunomodulatory agent (for example, thalidomide, lenalidomide, or pomalidomide) and dexamethasone;

    OR
    F. As single-agent maintenance therapy for multiple myeloma in transplant candidates (NCCN 2A); **OR**
    G. In combination with lenalidomide for maintenance therapy of high-risk multiple myeloma in transplant candidates (NCCN 2A);

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OR

III. Individual has a diagnosis of systemic light chain amyloidosis; **AND**

IV. Individual is using as a single agent (NCCN 2A);

OR

V. Individual is using in combination:

A. Bortezomib, cyclophosphamide, and dexamethasone; **OR**

B. In combination with carfilzomib, pomalidomide, and dexamethasone (NCCN 2A); **OR**

~~B.~~C. Dexamethasone with or without bortezomib (DP B IIa);

OR.

VI. Individual has a diagnosis of pediatric Acute Lymphoblastic Leukemia (ALL), as T-ALL (NCCN 2A); **AND**

VII. Individual is using a daratumumab-containing regimen (e.g. daratumumab, vincristine, pegaspargase or calaspargase, doxorubicin, and prednisone or dexamethasone) for relapsed/refractory T-ALL;

OR

~~VII.~~VIII. Individual has a diagnosis of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome (NCCN 2A).

Requests for Darzalex (daratumumab) or Darzalex Faspro (daratumumab and hyaluronidase-fihj) may not be approved if the above criteria are not met and for all other indications not included above.

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Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9145	Injection, daratumumab, 10 mg [DARZALEX]
J9144	Injection, daratumumab, 10 mg and hyaluronidase-fihj [Darzalex Faspro]

ICD-10 Diagnosis

C90.00-C90.32	Multiple myeloma and malignant plasma cell neoplasms
C91.00-C91.02	Acute lymphoblastic leukemia
~~E85.0-E85.9~~	~~Amyloidosis~~
~~Z51.11-Z51.12~~	~~Encounter for antineoplastic chemotherapy and immunotherapy~~
~~Z85.79~~	~~Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues~~
~~T86.5~~	~~Complications of stem cell transplant~~
~~Z94.84~~	~~Stem cells transplant status~~
D47.2	Monoclonal gammopathy [Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes (POEMS)]
E85.3	Secondary systemic amyloidosis
E85.4	Organ-limited amyloidosis
E85.81	Light chain (AL) amyloidosis
E85.89	Other amyloidosis
E85.9	Amyloidosis, unspecified
T86.5	Complications of stem cell transplant
Z51.11-Z51.12	Encounter for antineoplastic chemotherapy and immunotherapy
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues
Z94.84	Stem cells transplant status

Document History

Revised: 08/15/2025
Document History:

- 08/15/2025 – Annual Review: Add combination use with carfilzomib, pomalidomide, and dexamethasone in multiple myeloma and combination use with lenalidomide and dexamethasone in systemic light chain amyloidosis per NCCN; add diagnoses of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome per NCCN. Coding Reviewed: Removed ICD-10-CM E85.0-E85.2, E85.82. Added ICD-10-CM D47.2.
- 08/16/2024 – Annual Review: Add combination use with venetoclax for consistency. Coding Reviewed: No changes.
- 11/17/2023 – Annual Review: Add NCCN recommendations for combination use with selinexor and maintenance therapy in multiple myeloma; add pediatric acute lymphoblastic leukemia per NCCN. Coding Reviewed: Added ICD-10-CM C91.00-C91.02.
- 02/24/2023 – Annual Review: Remove requirement for no prior anti-CD38 treatment; update combination therapy language to be more general per NCCN; add combination use with carfilzomib, lenalidomide, and dexamethasone for newly diagnosed multiple myeloma. Coding Reviewed; No changes.
- 05/20/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/21/2021 – Annual Review: Update multiple myeloma criteria to include combination use with cyclophosphamide, bortezomib, and dexamethasone; update criteria to allow primary therapy with lenalidomide, bortezomib, and dexamethasone; add additional combination regimens for systemic light chain amyloidosis; wording and formatting changes. Coding Reviewed: No changes.
- 03/15/2021 – Select Review: Update criteria for light chain amyloidosis per FDA label. Coding Reviewed: No changes.
- 06/08/2020 – Select Review: Add new dosage form Darzalex Faspro to clinical criteria document. Coding Review: Removed ICD-10-CM D46.4, Expanded E85.0-E85.9, Added Z51.11-Z51.12. Effective 10/1/2020 Add HCPCS J9999, C9062 for Darzalex Faspro. Delete HCPCS C9399 on 9/30/20. Effective 1/1/2021 Added J9144, Removed J9999, C9062 12/31/2020.
- 05/15/2020 – Annual Review: Add criteria for use in systemic light chain amyloidosis; wording and formatting changes. Coding Review: Added ICD-10-DX: E85.81, D46.4
- 11/15/2019 – Select Review: Add criteria for new FDA indication of first-line use in combination with bortezomib, thalidomide, and dexamethasone. Coding Reviewed: Added ICD-10 DX T86.5, Z94.84
- 08/16/2019 – Select Review: Add criteria for new FDA indication of first-line use in combination with lenalidomide and dexamethasone. Remove HIV and hepatitis reference in may not be approved section for consistency. Coding reviewed. No changes.
- 05/17/2019 – Annual Review: First review of Darzalex clinical criteria. Minor wording and formatting updates. Add references for off-label criteria. Coding Reviewed: no changes.

References

1. Chari A, Martinez-Lopez J, Mateos M, et al. Daratumumab in combination with carfilzomib and dexamethasone in lenalidomide-refractory patients with relapsed multiple myeloma: Subgroup analysis of MMY1001. J Clin Oncol. 2018; 36(15):8002-8002
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: June 18, 2025.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Jakubowiak A, Chari A, Lonial S, et al. Daratumumab in combination with carfilzomib, lenalidomide and dexamethasone in patients with newly diagnosed multiple myeloma (MMY1001). J Clin Oncol. 2017; 35(15):8000-8000.
5. Kimmich CR, Terzer T, Benner A, et al: Daratumumab for systemic AL amyloidosis: prognostic factors and adverse outcome with nephrotic-range albuminuria. Blood 2020; 135(18):1517-1530.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
7. Roussel M, Merlini G, Chevret S, et al. A prospective phase II of daratumumab in previously treated systemic light chain amyloidosis (AL) patients. Blood. 2020; 135: 1531-1540.
8. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed June 2025.
    a. Multiple Myeloma. V2.2025. Revised April 11, 2025.
    b. Systemic Light Chain Amyloidosis. V1.2026. Revised June 11, 2025.
    c. Pediatric Acute Lymphoblastic Leukemia. V3.2025. Revised March 17, 2025.