Reference number(s)
4232-A

Standard Medicare Part B Management Darzalex

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Darzalex	daratumumab

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1]

Darzalex is indicated for the treatment of adult patients with multiple myeloma:

- in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy.
- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant.
- in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant.
- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy.
- in combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy.

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- in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.
- as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

Compendial Uses[2-4]

- Multiple myeloma
- Systemic light chain amyloidosis
- T-cell acute lymphoblastic leukemia (T-ALL)
- POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome
- Monoclonal immunoglobulin deposition disease (MIDD)
- Monoclonal gammopathy of renal significance (MGRS)
- Human immunodeficiency virus (HIV)-related B-cell lymphomas

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

Documentation of testing or laboratory results confirmation t(11:14) translocation, where applicable.

Coverage Criteria

Multiple Myeloma[1-4]

Authorization of 12 months may be granted for the treatment of multiple myeloma when used in combination with cyclophosphamide, bortezomib, and dexamethasone.

Authorization of 12 months may be granted for the treatment of multiple myeloma as primary therapy when any of the following criteria is met:

- The member has asymptomatic high risk smoldering disease.
- The member is ineligible for a transplant or transplant-deferred and the requested medication will be used in combination with lenalidomide and dexamethasone.
- The member is ineligible for a transplant and the requested medication will be used in combination with bortezomib, melphalan, and prednisone.

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- The member is eligible for transplant and the requested medication will be used in combination with either of the following:
  - Bortezomib, thalidomide, and dexamethasone for a maximum of 16 doses
  - Carfilzomib, lenalidomide, and dexamethasone
- The requested medication will be used in combination with bortezomib, lenalidomide, and dexamethasone

Authorization of 12 months may be granted for the treatment of previously treated multiple myeloma when any of the following criteria is met:

- The requested medication will be used in combination with lenalidomide and dexamethasone in members who are bortezomib-refractory.
- The requested medication will be used in combination with bortezomib and dexamethasone in members who are lenalidomide-refractory.
- The requested medication will be used in combination with carfilzomib and dexamethasone in members who are bortezomib-refractory or lenalidomide-refractory.
- The requested medication will be used in combination with teclistamab-cqyv (Tecvayli) in members who are bortezomib- refractory or lenalidomide-refractory.
- The requested medication will be used in combination with carfilzomib, pomalidomide, and dexamethasone.
- The requested medication will be used in combination with pomalidomide and dexamethasone in members who have received at least one prior therapy including a proteasome inhibitor (PI) and an immunomodulatory agent.
- The requested medication will be used in combination with selinexor and dexamethasone.
- The requested medication will be used in combination with venetoclax and dexamethasone for members with documented t(11:14) translocation.
- The requested medication will be used as a single agent in members who have received at least three prior therapies, including a PI and an immunomodulatory agent.
- The requested medication will be used as a single agent in members who are double refractory to a PI and an immunomodulatory agent.

Authorization of 12 months may be granted for maintenance therapy of symptomatic multiple myeloma for transplant candidates when either of the following criteria is met:

- The requested medication will be used in combination with lenalidomide and the member has high risk disease.
- The requested medication will be used as a single agent.

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POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes) Syndrome, Monoclonal Immunoglobulin Deposition Disease (MIDD), and Monoclonal Gammopathy of Renal Significance (MGRS)[2,4]

Authorization of 12 months may be granted for the treatment of POEMS syndrome, plasma cell-related MIDD, and plasma cell-related MGRS.

Systemic Light Chain Amyloidosis[2,3]

Authorization of 12 months may be granted for the treatment of systemic light chain amyloidosis if either of the following criteria is met:

- The requested medication will be used in combination with bortezomib, cyclophosphamide and dexamethasone or as a single agent.
- The member has relapsed or refractory disease when any of the following criteria is met:
  - The requested medication will be used in combination with venetoclax and the member has a documented t(11:14) translocation.
  - The requested medication will be used in combination with lenalidomide and dexamethasone.
  - The requested medication will be used in combination with dexamethasone.
- The requested medication will be used in combination with bortezomib and dexamethasone.

T-Cell Acute Lymphoblastic Leukemia (T-ALL)[2]

Authorization of 12 months may be granted for treatment for relapsed/refractory T-cell acute lymphoblastic leukemia (T-ALL).

Human Immunodeficiency Virus (HIV)-Related B-cell Lymphomas[2]

Authorization of 12 months may be granted for the treatment of HIV-related plasmablastic lymphoma when the requested medication will be used in combination with dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin).

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Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.Multiple Myeloma

Authorization for 12 months may be granted for multiple myeloma when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member meets any of the following criteria:
    - The requested drug will be used in combination with bortezomib, thalidomide, and dexamethasone and the member has not received a maximum of 16 doses.
    - The member is receiving benefit from therapy. Benefit is defined as:
        - No evidence of unacceptable toxicity while on the current regimen or
        - No evidence of disease progression while on the current regimen

Human Immunodeficiency Virus (HIV)-Related B-cell Lymphomas, POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes) Syndrome, Monoclonal Immunoglobulin Deposition Disease (MIDD), Monoclonal Gammopathy of Renal Significance (MGRS), Systemic Light Chain Amyloidosis, and T-Cell Acute Lymphoblastic Leukemia (T-ALL)

Authorization for 12 months may be granted for HIV-related B-cell lymphomas, POEMS syndrome, monoclonal immunoglobulin deposition disease (MIDD), monoclonal gammopathy of renal significance (MGRS), systemic light chain amyloidosis, and T-cell Acute lymphoblastic leukemia (T-ALL) when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen or
    - No evidence of disease progression while on the current regimen

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Darzalex.

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- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service-Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- NCCN Guideline: Systemic light chain amyloidosis
- NCCN Guideline: Multiple myeloma
- NCCN Guideline: Acute Lymphoblastic Leukemia
- NCCN Guideline: Pediatric Acute Lymphoblastic Leukemia
- NCCN Guideline: B-Cell Lymphomas

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Darzalex are covered in addition to the following:

- Multiple myeloma
- Systemic light chain amyloidosis
- T-cell acute lymphoblastic leukemia (T-ALL)
- POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome
- Monoclonal immunoglobulin deposition disease (MIDD)
- Monoclonal gammopathy of renal significance (MGRS)
- Human immunodeficiency virus (HIV)-related B-cell lymphomas

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Darzalex to treat multiple myeloma, POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome, monoclonal immunoglobulin deposition disease (MIDD), monoclonal gammopathy of renal significance (MGRS), systemic light chain amyloidosis, T-cell acute lymphoblastic leukemia (T-ALL), and Human immunodeficiency virus (HIV)-related B-cell lymphomas can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).
Support for using Darzalex to treat relapsed or refractory systemic light chain amyloidosis can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

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References

1. Darzalex [package insert]. Horsham, PA: Janssen Biotech, Inc.; April 2025.
2. The NCCN Drugs & Biologics Compendium® ©2026 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 3, 2026.
3. Micromedex® (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ Accessed: September 30, 2025.
4. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 5.2026) 2026 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 3, 2026.

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