Daratumumab (Darzalex®)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

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

FDA-Approved Indications

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.
- 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

- 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 are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

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

COVERAGE CRITERIA

Multiple Myeloma

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.
- 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.

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

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

Authorization of 12 months may be granted for the treatment of systemic light chain amyloidosis when 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)

Authorization of 12 months may be granted for the treatment of relapsed/refractory T-cell acute lymphoblastic leukemia (T-ALL) when the requested medication will be used in combination with either of the following:

- Vincristine, pegaspargase, doxorubicin, and prednisone or dexamethasone
- Vincristine, calaspargase. doxorubicin, and prednisone or dexamethasone

Human Immunodeficiency Virus (HIV)-Related B-cell Lymphomas

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).

CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when either of the following regimen or indication-specific criteria is met:

- All members (including new members) requesting the requested medication in combination with bortezomib, thalidomide, and dexamethasone for multiple myeloma must meet all requirements in the coverage criteria section.

- For all other regimens and indications listed in the coverage criteria section, there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Darzalex (Daratumumab)	Multiple Myeloma or POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes) Syndrome	Route of Administration: Intravenous 16mg/kg per dose (dosing schedule varies by regimen)
Darzalex (Daratumumab)	Systemic Light Chain Amyloidosis	Route of Administration: Intravenous 16mg/kg every week for 8 doses, followed by every 2 weeks for 8 doses, then every 4 weeks
Darzalex (Daratumumab)	T-cell Acute Lymphoblastic Leukemia (T-ALL)	Route of Administration: Intravenous 16mg/kg every week for 8 doses, followed by every 2 weeks for 8 doses, then every 4 weeks

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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. 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.
4. Micromedex® (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ Accessed: September 30, 2025.

EFFECTIVE DATE 7/31/2026