CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – CD38-Directed Cytolytic Antibody) – Darzalex Intravenous Utilization Management Medical Policy
- Darzalex™ (daratumumab intravenous infusion – Janssen)

REVIEW DATE: 11/12/2025

OVERVIEW

Darzalex, a CD38-directed cytolytic antibody, is indicated for treatment of **multiple myeloma** in the following situations:[1]

- in newly diagnosed patients, in combination with lenalidomide and dexamethasone, for those who are ineligible for autologous stem cell transplant and in relapsed/refractory disease, in combination with lenalidomide and dexamethasone in patients who have received at least one prior therapy.
- in newly diagnosed patients, in combination with bortezomib, melphalan, and prednisone in those ineligible for autologous stem cell transplant.
- in newly diagnosed patients, in combination with bortezomib, Thalomid® (thalidomide capsules), and dexamethasone, in those who are eligible for autologous stem cell transplant.
- in patients who have received at least one prior therapy, in combination with bortezomib and dexamethasone.
- in relapsed/refractory disease, in combination with Kyprolis® (carfilzomib intravenous infusion) and dexamethasone in patients who have received one to three prior lines of therapy.
- in patients who have received at least two prior therapies (including lenalidomide and a proteasome inhibitor), in combination with Pomalyst® (pomalidomide capsules) and dexamethasone.
- in patients who have received at least three 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), as monotherapy.

Guidelines

Darzalex is discussed in guidelines from the National Comprehensive Cancer Network (NCCN).

- **Acute Lymphoblastic Leukemia (ALL):** NCCN pediatric ALL guidelines (version 1.2026 – August 11, 2025) recommend Darzalex-containing regimen as one of the "Other Recommended Regimens" for relapsed/refractory disease (category 2A).[2] NCCN ALL guidelines (version 2.2025 – June 27, 2025) recommend Darzalex-containing regimen as one of the "Other Recommended Regimens" for relapsed/refractory disease (category 2B).[3]
- **Multiple Myeloma:** NCCN guidelines (version 3.2026 – November 3, 2025) recommend Darzalex in multiple regimens (with at least two other medications) as primary treatment and for previously treated disease. Darzalex monotherapy is recommended as primary treatment for asymptomatic high risk smoldering myeloma in select patients (category 1), for maintenance therapy in transplant candidates (category 2A), and for relapsed/refractory disease after at least three prior therapies (category 2A).[4-5]
- **Systemic Light Chain Amyloidosis:** NCCN guidelines (version 1.2026 – March 12, 2025) list Darzalex as a therapy for previously treated disease or for newly diagnosed disease as a single agent or in combination with other therapies (both category 2A).[6]

Dosing Information

Dosing varies depending on regimen prescribed. Refer to the prescribing information for more specific dosing for FDA-approved regimens. Dose reductions are not recommended. In cases of hematological toxicity, dose delay may be required to allow recovery of blood cell counts. When Darzalex Intravenous was evaluated in systemic light chain amyloidosis, the dose used was similar to multiple myeloma.[7] For Pediatric Acute Lymphoblastic Leukemia, the recommended dosing is Darzalex 16 mg/kg administered intravenously for a median of two cycles (range 1 to 3 cycles), 28-days for each cycle.[8,9] Since the range was maximum of 3 cycles, the dosing allows for up to 12 weeks of therapy.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Darzalex Intravenous. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the criteria and dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Darzalex Intravenous, as well as the monitoring required for adverse events and long-term efficacy, approval requires Darzalex Intravenous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Darzalex Intravenous is recommended in those who meet one of the following criteria:

FDA-Approved Indication

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1. Multiple Myeloma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i, ii, iii, or iv):
  - **i.** The medication is used in combination with at least two other therapies; OR
    Note: Examples of medications that may be used in combination with Darzalex include dexamethasone or prednisone, lenalidomide, Pomalyst (pomalidomide capsules), Thalomid (thalidomide capsules), melphalan, bortezomib, Kyprolis (carfilzomib intravenous infusion), cyclophosphamide, Venclexta (venetoclax tablets), or Xpovio (selinexor tablets).
  - **ii.** Patient has tried at least three different regimens for multiple myeloma; OR
    Note: Examples of medications used in other regimens include bortezomib, Kyprolis (carfilzomib intravenous infusion), lenalidomide, cyclophosphamide, Ninlaro (ixazomib capsules), Pomalyst (pomalidomide capsules), or Thalomid (thalidomide capsules).
  - **iii.** The medication is used as maintenance therapy in a transplant candidate; OR
  - **iv.** Patient has high-risk smoldering multiple myeloma; AND
- **C)** The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):

- **A)** The dose is 16 mg/kg per week given intravenously for up to nine weeks followed by 16 mg/kg doses separated by 2 or more weeks for up to 1 year; AND
  Note: The initial dose may be given as an 8 mg/kg intravenous infusion on Day 1 and Day 2.

B) After 1 year of therapy, the dose is 16 mg/kg with doses separated by at least 4 weeks.

Other Uses with Supportive Evidence

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2. Acute Lymphoblastic Leukemia. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient has relapsed or refractory disease; AND
- **B)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 16 mg/kg per week given intravenously for up to 12 weeks (3 cycles, 28-days each).

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3. Systemic Light Chain Amyloidosis. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
- **A)** The dose is 16 mg/kg intravenously, administered no more frequently than once weekly for up to eight infusions followed by infusions separated by 2 or more weeks; AND
- **B)** After 6 months of therapy, doses are separated by at least 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Darzalex is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Darzalex® intravenous infusion [prescribing information]. Horsham, PA: Janssen; April 2025.
2. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 1.2026 – August 11, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 10, 2025.
3. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2025 – June 27, 2025 © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 10, 2025.
4. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 10, 2025. Search term: daratumumab.
5. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 3.2026 – November 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 10, 2025.
6. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 1.2026 – June 11, 2025 © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 10, 2025.
7. Kaufman GP, Schrier SL, Lafayette R, et al. Daratumumab yields rapid and deep hematologic responses in patients with heavily pretreated AL amyloidosis. *Blood*. 2017;130(7):900-902.
8. Janssen Research & Development. A study to evaluate the efficacy and safety of Daratumumab in pediatric and young adult participants greater than or equal to 1 and less than or equal to 30 years of age with relapsed/refractory precursor B-cell or T-cell acute lymphoblastic leukemia or lymphoblastic lymphoma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2024 April 17]. Available at https://www.clinicaltrials.gov/study/NCT03384654?term=NCT03384654&rank=1&tab=results#participant-flow. NLM Identifier: NCT03384654.

9. Hogan LE, Bhatia T, Teachey DT, et al. Efficacy and safety of daratumumab (DARA) in pediatric and young adult patients (pts) with relapsed/refractory T-cell acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LL): Results from the phase 2 DELPHINUS study. *JCO* 40, 10001-10001(2022).

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Light Chain Amyloidosis:** Added qualifier "Systemic" to the condition name, to match guideline nomenclature. Added criterion that Darzalex can be used as a single agent for newly diagnosed disease. Deleted criterion "Patient has received at least one other regimen for this condition" and the Note with examples. Instead, added criterion that the medication will be used as a single agent for relapsed/refractory disease. **Pediatric Acute Lymphoblastic Leukemia:** Added new approval condition and criteria.	04/24/2024
Update	04/11/2025: The policy name was changed from "Oncology (Injectable) - Darzalex Intravenous UM Medical Policy" to "Oncology (Injectable - CD38-Directed Cytolytic Antibody) - Darzalex Intravenous UM Medical Policy"	N/A
Annual Revision	**Multiple Myeloma:** Cyclophosphamide, Venclexta (venetoclax tablets), and Xpovio (selinexor tablets) were added to the examples of therapies that may be used in combination with Darzalex. **Acute Lymphoblastic Leukemia:** Previously this condition of approval was worded as "Pediatric Acute Lymphoblastic Leukemia". The requirement that the patient is ≤ 18 years of age was removed. **Systemic Light Chain Amyloidosis:** The following wording "...for newly diagnosed disease" was removed from the requirement that the medication will be used as a single agent. The option for approval which states that the medication will be used as a single agent for relapsed/refractory disease was changed to "the medication is used in combination with at least two other therapies" and a Note with examples of other therapies was added.	04/30/2025
Early Annual Revision	**Multiple Myeloma:** An option for approval was added for a patient with high-risk smoldering multiple myeloma. Pomalyst (pomalidomide capsules), or Thalomid (thalidomide capsules), were added to the Note of examples of medications used in other regimens. **Systemic Light Chain Amyloidosis:** The requirements that the medication will be used as a single agent or in combination with at least two other therapies along with the Note of examples of therapies were removed.	11/12/2025