UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Darzalex Intravenous Utilization Management Medical Policy
- Darzalex™ (daratumumab intravenous infusion – Janssen Biotech)

REVIEW DATE: 04/24/2024

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 the treatment of patients 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, for treatment of patients 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 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.
- 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.

Guidelines

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

- **Multiple Myeloma:** NCCN guidelines (version 3.2024 – March 8, 2024) recommend Darzalex in treatment regimens for primary therapy.[2-3] Darzalex/lenalidomide/bortezomib/dexamethasone, Darzalex/bortezomib/Thalomid/dexamethasone, Darzalex/Kyprolis/lenalidomide/dexamethasone, and Darzalex/cyclophosphamide/bortezomib/dexamethasone are among the recommended regimens for primary therapy for transplant candidates. For patients who are non-transplant candidates, Darzalex with: lenalidomide/dexamethasone (preferred; category 1), and bortezomib/melphalan/prednisone (category 1), and cyclophosphamide/bortezomib/dexamethasone are among the regimens for primary treatment. All other recommendation are category 2A. For previously treated multiple myeloma (one to three prior therapies), Darzalex/dexamethasone plus bortezomib (category 1), lenalidomide (category 1), Pomalyst, or Kyprolis (category 1) are among the Preferred regimens, whereas other Darzalex-containing regimens are listed as other or useful in certain circumstances. Darzalex ± lenalidomide has been added under "Useful in Certain Circumstances" for maintenance therapy in transplant candidates.

- **Pediatric Acute Lymphoblastic Leukemia:** NCCN guidelines (version 5.2024 – April 3, 2024) recommend Darzlex-containing regimen as one of the "Other Recommended Regimens" for relapsed/refractory disease (category 2A).[6]
- **Systemic Light Chain Amyloidosis:** The NCCN guidelines (version 2.2024 – December 12, 2023) list Darzalex Intravenous as a therapy for previously treated disease or for newly diagnosed disease (both category 2A).[4] In both settings Darzalex is recommended as a single agent. Of note, Darzalex Faspro is indicated and is specifically recommended as a preferred first-line therapy for systemic light chain amyloidosis, given in combination with cyclophosphamide and dexamethasone.

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.[4] 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.[7,8] 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 or ii):
  - **i.** Darzalex is used in combination with at least two other therapies; OR
    Note: Examples of therapies that may be used in combination with Darzalex include dexamethasone or prednisone, lenalidomide, Pomalyst (pomalidomide capsules), Thalomid (thalidomide capsules), melphalan, bortezomib, or Kyprolis (carfilzomib intravenous infusion).
  - **ii.** Patient meets ONE of the following (a or b):
    - **a)** Patient has tried at least three different regimens for multiple myeloma; OR

Note: Examples of agents used in other regimens include bortezomib, Kyprolis, lenalidomide, cyclophosphamide, Ninlaro (ixazomib capsules).

b) Darzalex is used as maintenance therapy in a transplant candidate; AND

C) The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets the following:

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. Pediatric Acute Lymphoblastic Leukemia. 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 has relapsed or refractory disease; AND

C) 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 ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient meets ONE of the following (i or ii):

i. The medication will be used as a single agent for newly diagnosed disease; OR

ii. The medication will be used as a single agent for relapsed/refractory disease; AND

C) The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets the following:

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 Intravenous 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 [prescribing information]. Horsham, PA: Janssen Biotech; January 2023.
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3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 3.2024 – March 8, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 15, 2024.
4. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2024 – December 12, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 15, 2024.
5. Kaufman GP, Schrier SL, Lafayette RA, et al. Daratumumab yields rapid and deep hematologic responses in patients with heavily pretreated AL amyloidosis. *Blood*. 2017;130(7):900-902.
6. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 5.2024 – April 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 17, 2024.
7. 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.
8. 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	**Multiple Myeloma:** Based on guidelines, changed requirement of combination therapies with Darzalex to at least "two other therapies". Previously, this was at least one other therapy. Added "dexamethasone or prednisone" as examples in Note for this criteria. Added new option for approval that "Darzalex is used as maintenance therapy in a transplant candidate." The requirement is either patient meets this new maintenance therapy criterion or has tried at least three different regimens.	04/12/2023
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