UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – CD38 - Directed Cytolytic Antibody) – Darzalex Faspro Utilization Management Medical Policy

- Darzalex Faspro® (daratumumab and hyaluronidase-fihj subcutaneous injection – Janssen)

REVIEW DATE: 04/30/2025

OVERVIEW

Darzalex Faspro, a CD38-directed cytolytic antibody and endoglycosidase, is approved for use in adults in the following situations:[1]

- **Light chain amyloidosis**, in newly diagnosed patients, in combination with bortezomib, cyclophosphamide, and dexamethasone. It is a limitation of use that Darzalex Faspro is not indicated and is not recommended in patients with New York Heart Association Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of clinical trials.
- **Multiple myeloma**:
  - in newly diagnosed patients, in combination with bortezomib, lenalidomide, and dexamethasone for induction and consolidation for those who are eligible for autologous stem cell transplant.
  - 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 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 patients who have received at least one prior therapy (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.

Darzalex Faspro is a fixed combination of daratumumab and hyaluronidase (recombinant human). It contains the identical molecular antibody of daratumumab available in Darzalex intravenous, but hyaluronidase has been added to facilitate systemic delivery. Darzalex Faspro should be administered under the care of a healthcare provider as a 3 to 5 minute subcutaneous injection. The dose of Darzalex Faspro is fixed regardless of the patient's body surface area; dose reductions are not recommended. Safety and efficacy is not established in patients < 18 years of age.

Guidelines

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

- **Systemic Light Chain Amyloidosis:** NCCN guidelines (version 2.2025 – March 12, 2025) list daratumumab 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). The guidelines state that for any regimen that includes daratumumab, this could be Darzalex or Darzalex Faspro.
- **Multiple Myeloma:** NCCN guidelines (version 2.2025 – April 11, 2025) include Darzalex Faspro in the recommendations for all of the daratumumab-containing regimens.[3] NCCN does recommend Darzalex intravenous or Faspro in multiple regimens both as primary treatment and in previously treated disease. For primary therapy for transplant candidates, Darzalex/lenalidomide/bortezomib/dexamethasone is a "Preferred Regimen" (category 1); Darzalex/Kyprolis/lenalidomide/dexamethasone and Darzalex/bortezomib/ cyclophosphamide/dexamethasone are listed as "useful in certain circumstances" (both category 2A). In this setting, Darzalex/lenalidomide is recommended as maintenance therapy (category 2A). Darzalex/lenalidomide/dexamethasone is recommended for the management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome as induction therapy for transplant eligible patients (category 2A). Primary therapy for patients who are non-transplant candidates include Darzalex/lenalidomide/dexamethasone as a "Preferred Regimen" (category 1), and Darzalex/cyclophosphamide/bortezomib/dexamethasone as "useful in certain circumstances: (category 2A). For previously treated multiple myeloma that is relapsed or refractory after one to three prior therapies, Darzalex/Kyprolis/dexamethasone or Darzalex/lenalidomide/dexamethasone are recommended for bortezomib-refractory patients; Darzalex/Kyprolis/dexamethasone and Darzalex/bortezomib/dexamethasone are recommended for lenalidomide-refractory patients (all category 1). Darzalex/Pomalyst/dexamethasone is listed for both bortezomib-refractory patients and lenalidomide-refractory patients after one prior therapy including lenalidomide and a proteasome inhibitor (category 1). Other regimens that include Darzalex are also listed as "other recommended regimens" and "useful in certain circumstances" (category 2A).

Dosing Information

Darzalex Faspro is available as a single-dose vial containing 1,800 mg of daratumumab and 30,000 units of hyaluronidase per 15 mL.[1] Dosing schedule varies depending on regimen prescribed. Refer to the prescribing information for more specific FDA-approved regimens. Dose reductions are not recommended. In cases of myelosuppression, dose delay may be required to allow recovery of blood cell counts.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Darzalex Faspro. 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 Faspro, as well as the monitoring required for adverse events and long-term efficacy, approval requires Darzalex Faspro 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 Faspro is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. 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 does NOT have severe heart failure, according to the prescriber; AND
  Note: Severe heart failure is defined as New York Heart Association Class IIIB or IV cardiac disease or Mayo Stage IIIB.
- **C)** The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets ALL of the following (A, B, and C):
- **A)** The dose is 1,800 mg/30,000 units; AND
- **B)** Darzalex Faspro is administered no more frequently than once weekly for up to eight subcutaneous injections followed by subcutaneous injections separated by 2 or more weeks; AND
- **C)** After 6 months of therapy, doses are separated by at least 4 weeks.

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2. 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.** 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 Faspro include dexamethasone or prednisone, lenalidomide capsules, Pomalyst (pomalidomide capsules), Thalomid (thalidomide capsules), melphalen, bortezomib, Kyprolis (carfilzomib intravenous infusion), cyclophosphamide, Venclexta (venetoclax tablets), or Xpovio (selinexor tablets).
  - **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 injection, Kyprolis (carfilzomib injection), lenalidomide capsules, cyclophosphamide, Ninlaro (ixazomib capsules).
    - **b)** The medication is used as maintenance therapy in transplant candidates; AND
- **C)** The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets ALL of the following (A, B, and C):
- **A)** The dose is 1,800 mg/30,000 units; AND
- **B)** During Year 1, Darzalex Faspro is administered no more frequently than once weekly for up to nine subcutaneous injections, followed by injections separated by 2 or more weeks; AND
- **C)** After 1 year of therapy, doses are separated by at least 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Darzalex Faspro 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 Faspro [prescribing information]. Horsham, PA: Janssen; November 2022.
2. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 29, 2025. Search term: daratumumab, Darzalex Faspro.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 2.2025 – April 11, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 24, 2025.
4. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2025 – March 12, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 24, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Multiple Myeloma:** Based on guidelines, changed requirement of combination therapies with Darzalex Faspro to at least "two other therapies". Previously, this was at least one other therapy. Added "dexamethasone or prednisone", Pomalyst, Thalomid, or Kyprolis as examples in Note for this criteria. Added new criterion that "Darzalex Faspro is used as maintenance therapy in transplant candidates." The requirement is either patient meets this new maintenance therapy criterion or has tried at least three different regimens.	06/14/2023
Annual Revision	**Light Chain Amyloidosis:** Added qualifier "Systemic" to the condition name, to match guideline nomenclature. Deleted criteria requiring combination use of Darzalex Faspro or patient has received one other regimen. This is simplified because guidelines recommend Darzalex Faspro use in all scenarios: as a single agent or in combination for primary therapy and it can also be used for previously treated disease.	06/26/2024
Update	04/11/2025: The policy name was changed from "Oncology (Injectable) - Darzalex Faspro UM Medical Policy" to "Oncology (Injectable - CD38-Directed Cytolytic Antibody) - Darzalex Faspro 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 Faspro.	04/30/2025