CARECONTINUUM™

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: 11/12/2025

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.
- **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 bortezomib, melphalan, and prednisone in those who are ineligible for autologous stem cell transplant.
  - in newly diagnosed patients, in combination with lenalidomide and dexamethasone in 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, thalidomide, 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 one prior therapy (including lenalidomide and a proteasome inhibitor), in combination with Pomalyst (pomalidomide capsules) 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 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.
  - high risk smoldering multiple myeloma as monotherapy.

The indication for light chain amyloidosis is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). 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.

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 1.2026 – June 11, 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 3.2026 – November 3, 2025) include Darzalex Faspro in the recommendations for all of the daratumumab-containing regimens.[3] NCCN recommend Darzalex or Darzalex Faspro 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).

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

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 (1,800 mg daratumumab and 30,000 units hyaluronidase -fihj); 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,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 Faspro 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 injection), lenalidomide, cyclophosphamide, Ninlaro (ixazomib 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 ALL of the following (A, B, and C):
A) The dose is 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase-fihj); 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® subcutaneous injection [prescribing information]. Horsham, PA: Janssen; November 2025.
2. 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, Darzalex Faspro.
3. 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.
4. 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.

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. 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
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.	11/12/2025