CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Darzalex Faspro Utilization Management Medical Policy
- Darzalex Faspro® (daratumumab and hyaluronidase-fihj subcutaneous injection – Janssen)

REVIEW DATE: 06/26/2024

OVERVIEW

Darzalex Faspro, a CD38-directed antibody, 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 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 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:** The NCCN guidelines (version 2.2024 – December 12, 2023) specifically recommended Darzalex Faspro/bortezomib/cyclophosphamide/dexamethasone as a first-line preferred therapy (category 1) for systemic light chain amyloidosis. Dose-modified Darzalex Faspro in combination with other agents and single-agent daratumumab (either Faspro or

intravenous) are also "Preferred Regimens" (category 2A) for primary therapy. Darzalex Faspro or Darzalex intravenous as monotherapy are among the alternatives for previously treated disease (category 2A).[4]

- **Multiple Myeloma:** The NCCN guidelines (version 4.2024 – April 26, 2024) 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. Darzalex/bortezomib/dexamethasone in combination with lenalidomide, Thalomid, or cyclophosphamide and Darzalex/Kyprolis/lenalidomide/dexamethasone are among the regimens recommended as primary therapy for transplant candidates. Darzalex intravenous or Faspro as monotherapy is recommended (category 2A) under "other recommended regimens" as maintenance therapy for transplant candidates. For patients who are non-transplant candidates, Darzalex/lenalidomide/prednisone is a preferred regimen, and Darzalex/bortezomib/melphalan/prednisone and Darzalex/cyclophosphamide/bortezomib/dexamethasone are other recommended regimens for primary treatment. For previously treated multiple myeloma, there are multiple Darzalex-containing regimens in the guidelines, including Darzalex/dexamethasone plus bortezomib, Kyprolis, or lenalidomide (preferred regimens). Darzalex/Pomalyst/dexamethasone is a preferred regimen after two prior therapies, including lenalidomide and a proteasome inhibitor. Darzalex/cyclophosphamide/bortezomib/dexamethasone is an "other recommended regimen", and Darzalex monotherapy (in patients who have received at least three prior therapies) and Xpovio® (selinexor tablets)/Darzalex/dexamethasone are listed as useful in certain circumstances.

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. 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 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.

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, 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 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 the following:
   - **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. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 24, 2024. Search term: daratumumab, Darzalex Faspro.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 4.2024 – April 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 24, 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 June 24, 2024.

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