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Section:	Prescription Drugs	**Effective Date:**	November 21, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	May 29, 2020
Subject:	Darzalex Faspro	**Page:**	1 of 6

Last Review Date: June 12, 2025

Darzalex Faspro

Description

Darzalex Faspro (daratumumab and hyaluronidase-fihj)

Background
Darzalex Faspro is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase. CD38 is a transmembrane glycoprotein expressed on the surface of hematopoietic cells, including clonal plasma cells in multiple myeloma and light chain (AL) amyloidosis, as well as other cell types. Daratumumab binds to CD38 and inhibits the growth of CD38 expressing tumor cells by inducing apoptosis. Hyaluronidase increases the permeability of the subcutaneous tissue by depolymerizing hyaluronan (1).

Regulatory Status
FDA-approved indications: Darzalex Faspro is indicated for the treatment of adult patients with: (1)

1. Multiple myeloma
    a. In combination with bortezomib, lenalidomide, and dexamethasone for induction and consolidation in newly diagnosed patients who are eligible for autologous stem cell transplant
    b. In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
    c. In combination with lenalidomide and dexamethasone in newly diagnosed patients with multiple myeloma who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
    d. In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant

e. In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
f. In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
g. In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
h. As monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
i. High-risk smoldering multiple myeloma as monotherapy

2. Light chain (AL) amyloidosis
   a. In combination with bortezomib, cyclophosphamide, and dexamethasone in newly diagnosed patients
   b. Limitations of Use: Darzalex Faspro is not indicated and is not recommended for the treatment of patients with light chain (AL) amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials.

Patients being treated for light chain (AL) amyloidosis should be treated with Darzalex Faspro until disease progression, unacceptable toxicity, or a maximum of 2 years (1).

The safety and effectiveness of Darzalex Faspro in pediatric patients less than 18 years of age have not been established (1).

Related Policies
Darzalex, Sarclisa

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Darzalex Faspro may be considered **medically necessary** if the conditions indicated below are met.

Darzalex Faspro may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Multiple myeloma (MM)

   AND ONE of the following:
   a. Newly diagnosed multiple myeloma (MM) **AND ONE** of the following:
      i. Patient is **ineligible** for autologous stem cell transplant
         1. Used in combination with **ONE** of the following:
            a. Bortezomib, melphalan, and prednisone
            b. Lenalidomide and dexamethasone
      ii. Patient is **eligible** for autologous stem cell transplant
         1. Used in combination with **ONE** of the following:
            a. Bortezomib, lenalidomide, and dexamethasone
            b. Bortezomib, thalidomide, and dexamethasone
   b. Used in combination with lenalidomide and dexamethasone
      i. Patient has relapsed or refractory multiple myeloma **AND** patient has received at least one prior therapy
   c. Used in combination with bortezomib and dexamethasone
      i. Patient has received at least one prior therapy
   d. Used in combination with pomalidomide and dexamethasone
      i. Patient has received at least one prior therapy including lenalidomide and a proteasome inhibitor (PI)
   e. Used in combination with carfilzomib and dexamethasone
      i. Patient has relapsed or refractory multiple myeloma **AND** patient has received one to three prior lines of therapy
   f. Used as monotherapy **AND ONE** of the following:
      i. Patient has received at least three prior lines of therapy, including a proteasome inhibitor (PI) and immunomodulatory agent
      ii. Patient has had a double-refractory failure to a proteasome inhibitor (PI) and an immunomodulatory agent
      iii. Patient has high-risk smoldering multiple myeloma

2. Newly diagnosed light chain (AL) amyloidosis

a. Used in combination with bortezomib, cyclophosphamide, and dexamethasone
b. Patient does **NOT** have NYHA Class IIIB or Class IV cardiac disease
c. Patient does **NOT** have Mayo Stage IIIB light chain (AL) amyloidosis

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Multiple myeloma (MM)
   a. **NO** disease progression or unacceptable toxicity
2. Light chain (AL) amyloidosis
   a. **NO** disease progression or unacceptable toxicity
   b. Treatment with Darzalex Faspro has not exceeded 2 years
   c. Patient does **NOT** have NYHA Class IIIB or Class IV cardiac disease
   d. Patient does **NOT** have Mayo Stage IIIB light chain (AL) amyloidosis

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Duration 12 months (**ONE** renewal **ONLY** for light chain amyloidosis)

Rationale

Summary

Darzalex Faspro is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase. CD38 is a transmembrane glycoprotein expressed on the surface of hematopoietic cells. Daratumumab binds to CD38 and inhibits the growth of CD38 expressing tumor cells by inducing apoptosis. Hyaluronidase increases the permeability of the subcutaneous tissue by depolymerizing hyaluronan. The safety and effectiveness of Darzalex Faspro in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Darzalex Faspro while maintaining optimal therapeutic outcomes.

References

1. Darzalex Faspro [package insert]. Horsham, PA: Janssen Biotech, Inc.; November 2025.
2. NCCN Drugs & Biologics Compendium® Daratumumab and hyaluronidase-fihj 2025. National Comprehensive Cancer Network, Inc. Accessed on November 7, 2025.

Policy History

Date	Action
May 2020	Addition to PA
September 2020	Annual review
February 2021	Addition of indication: newly diagnosed MM patients who are eligible for autologous stem cell transplant, in combination with bortezomib, thalidomide, and dexamethasone. Addition of indication: light chain (AL) amyloidosis
March 2021	Annual review and reference update
July 2021	Addition of indication: multiple myeloma in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
September 2021	Annual review and reference update
December 2021	Addition of regimen: used in combination with carfilzomib plus dexamethasone. Revised and rearranged requirements for clarity
March 2022	Annual review and reference update
June 2022	Annual review and reference update
March 2023	Annual review and reference update
December 2023	Annual review and reference update
March 2024	Annual review and reference update
June 2024	Annual review and reference update
August 2024	Per PI update, added indication of newly diagnosed MM who are eligible for autologous stem cell transplant, used in combination with bortezomib, lenalidomide, and dexamethasone

December 2024	Annual review and reference update
March 2025	Annual review and reference update
June 2025	Annual review and reference update
November 2025	Per PI update, added indication of high-risk smoldering multiple myeloma

Keywords

This policy was effective with interim approval on November 21, 2025 and will be reviewed by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026.