

## Clinical Policy: Daratumumab (Darzalex), Daratumumab/Hyaluronidase-fihj (Darzalex Faspro)

Reference Number: ERX.SPA.330

Effective Date: 09.01.19

Last Review Date: 08.20

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

### Description

Daratumumab (Darzalex®) is a CD38-directed cytolytic antibody. Daratumumab/hyaluronidase-fihj (Darzalex Faspro™) is a combination of daratumumab and hyaluronidase, an endoglycosidase.

### FDA Approved Indication(s)

Darzalex and Darzalex Faspro are indicated for the treatment of adult patients with multiple myeloma (MM):

- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant (ASCT) and in patients with relapsed or refractory MM myeloma who have received at least one prior therapy
- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for ASCT
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- 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

Darzalex is additionally indicated for the treatment of adult patients with MM:

- In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a PI
- In combination with carfilzomib and dexamethasone in patients who have received one to three prior lines of therapy

Darzalex Faspro is additionally indicated for the treatment of adult patients with:

- Light chain (AL) amyloidosis in combination with bortezomib, cyclophosphamide, and dexamethasone in newly diagnosed patients. This indication 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).

Limitation(s) 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.

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Darzalex and Darzalex Faspro are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Multiple Myeloma** (must meet all):

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Darzalex or Darzalex Faspro is prescribed in one of the following ways (a or b):
  - a. Primary therapy (i or ii):
    - i. Ineligible for ASCT (a or b):
      - a) In combination with lenalidomide\* and dexamethasone;
      - b) In combination with bortezomib\*, melphalan, and prednisone;
    - ii. Eligible for ASCT in combination with bortezomib\*, thalidomide\*, and dexamethasone;
  - b. Subsequent therapy (i or ii):
    - i. In combination with dexamethasone and either lenalidomide\*, bortezomib\*, or carfilzomib\* after ≥ 1 prior therapy (*off-label for Darzalex Faspro\*\**);
    - ii. As monotherapy or in combination with pomalidomide\* and dexamethasone after ≥ 2 prior therapies (*off-label for Darzalex Faspro\*\**), including both of the following (a and b):
      - a) An immunomodulatory agent (e.g., thalidomide\*, lenalidomide\*);
      - b) A PI (e.g., ixazomib\*, bortezomib\*, carfilzomib\*);

*\*Prior authorization may be required.*

*\*\*If request is for Darzalex Faspro, refer to NCCN for dosing regimen.*

5. Request meets one of the following (a or b):\*
  - a. Dose does not exceed the maximum indicated regimen in section V;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration: 6 months**

**B. Systemic Light Chain Amyloidosis** (must meet all):

1. Diagnosis of systemic light chain amyloidosis;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
  - a. Darzalex Faspro is prescribed in combination with bortezomib\*, cyclophosphamide, and dexamethasone;
  - b. Darzalex or Darzalex Faspro is prescribed for relapsed or refractory disease after ≥ 1 prior therapy (e.g., bortezomib\*, lenalidomide\*) (*off-label\*\**);

*\*Prior authorization may be required.*

*\*\*If request is for off-label use, refer to NCCN for dosing regimen.*

5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).\*

*\*Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration: 6 months**

**C. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

**A. All Indications in Section I** (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Darzalex or Darzalex Faspro for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):\*
  - a. New dose does not exceed the maximum indicated regimen in section V;
  - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

\*Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration: 12 months**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

ASCT: autologous stem cell transplant

FDA: Food and Drug Administration

MM: multiple myeloma

NCCN: National Comprehensive Cancer Network

PI: proteasome inhibitor

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria.*

*The drugs listed here may not be a formulary agent and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b>Agents with FDA-approved dosing for MM</b>		
Ninlaro® (ixazomib)	4 mg PO on days 1, 8, and 15 of every 28-day treatment cycle	See dosing regimen
bortezomib (Velcade®)	1.3 mg/m <sup>2</sup> SC or IV; frequency of administration varies based on specific use	
Kyprolis® (carfilzomib)	20 mg/m <sup>2</sup> , 27 mg/m <sup>2</sup> , and/or 56 mg/m <sup>2</sup> IV; frequency of administration varies based on specific use	
Revlimid® (lenalidomide)	10 mg or 25 mg PO QD; dose and frequency of administration vary based on specific use	
Thalomid® (thalidomide)	100 mg, 200 mg, or 400 mg PO QD; dose and frequency of administration vary based on specific use	

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): hypersensitivity
- Boxed warning(s): none reported

*Appendix D: General Information*

- The National Comprehensive Cancer Network compendium makes the following recommendation for Darzalex Faspro (category 2A): May be used as a single agent or in combination with other systemic therapies where intravenous daratumumab is recommended.

**V. Dosage and Administration**

<b>Drug Name</b>	<b>Indication</b>	<b>Dosing Regimen</b>	<b>Maximum Dose</b>
Darzalex	MM in combination with lenalidomide or pomalidomide (4-week cycle dosing regimens) and low-dose dexamethasone and for monotherapy	<u>Weeks 1 to 8:</u> 16 mg/kg IV weekly <u>Weeks 9 to 24:</u> 16 mg/kg IV every 2 weeks <u>Weeks 25 onwards until disease progression:</u> 16 mg/kg IV every 4 weeks	See dosing regimen - Package Insert, Table 1
	MM in combination with bortezomib, melphalan and prednisone ([VMP], 6-week cycle dosing regimen)	<u>Weeks 1 to 6:</u> 16 mg/kg IV weekly <u>Weeks 7 to 54:</u> 16 mg/kg IV every 3 weeks <u>Weeks 55 onwards until disease progression:</u> 16 mg/kg IV every 4 weeks	See dosing regimen - Package Insert, Table 2
	MM in combination with bortezomib, thalidomide and dexamethasone ([VTd]; 4-week cycle dosing regimen)	<u>Induction</u> <u>Weeks 1 to 8:</u> 16 mg/kg IV weekly <u>Weeks 9 to 16:</u> 16 mg/kg IV every 2 weeks <u>Consolidation</u> <u>Weeks 1 to 8:</u> 16 mg/kg IV every 2 weeks	See dosing regimen - Package Insert, Table 3
	MM in combination with bortezomib and dexamethasone (3-week cycle dosing regimen)	<u>Weeks 1 to 9:</u> 16 mg/kg IV weekly <u>Weeks 10 to 24:</u> 16 mg/kg IV every 3 weeks <u>Weeks 25 onwards until disease progression:</u> 16 mg/kg IV every 4 weeks	See dosing regimen - Package Insert, Table 4
	MM in combination with carfilzomib and dexamethasone (4-week cycle dosing regimen)	<u>Week 1:</u> 8 mg/kg IV days 1 and 2 <u>Weeks 2 to 8:</u> 16 mg/kg IV weekly <u>Weeks 9 to 24:</u> 16 mg/kg IV every 2 weeks <u>Weeks 25 onwards until disease progression:</u> 16 mg/kg IV every 4 weeks	See dosing regimen - Package Insert, Table 5
Darzalex Faspro	MM in combination with lenalidomide and dexamethasone (4-week cycle) or as monotherapy	1,800 mg daratumumab -30,000 units hyaluronidase SQ into the abdomen over approximately 3 to 5 minutes <u>Weeks 1 to 8:</u> weekly <u>Weeks 9 to 24:</u> every 2 weeks <u>Weeks 25 onwards until disease progression:</u> every 4 weeks	See dosing regimen - Package Insert, Table 1

Drug Name	Indication	Dosing Regimen	Maximum Dose
	MM in combination with bortezomib, melphalan and prednisone ([VMP], (6-week cycle)	1,800 mg daratumumab -30,000 units hyaluronidase SQ into the abdomen over approximately 3 to 5 minutes <u>Weeks 1 to 6: weekly</u> <u>Weeks 7 to 54: every 3 weeks</u> <u>Weeks 55 onwards until disease progression: every 4 weeks</u>	See dosing regimen - Package Insert, Table 2
	MM in combination with bortezomib, thalidomide, and dexamethasone ([D-VTd]; 4-week cycle)	1,800 mg daratumumab -30,000 units hyaluronidase SQ into the abdomen over approximately 3 to 5 minutes  Induction: <u>Weeks 1 to 8: weekly (total of 8 doses)</u> <u>Weeks 9 to 16: every 2 weeks (total of 4 doses)</u> Consolidation: <u>Weeks 1 to 8 (following ASCT): every 2 weeks (total of 4 doses)</u>	See dosing regimen - Package Insert, Table 3
	MM in combination with bortezomib and dexamethasone (3-week cycle)	1,800 mg daratumumab -30,000 units hyaluronidase SQ into the abdomen over approximately 3 to 5 minutes <u>Weeks 1 to 9: weekly</u> <u>Weeks 10 to 24: every 3 weeks</u> <u>Weeks 25 onwards until disease progression: every 4 weeks</u>	See dosing regimen - Package Insert, Table 4
Darzalex Faspro	Light Chain Amyloidosis – in combination with bortezomib, cyclophosphamide, and dexamethasone (D-VCd)	1,800 mg daratumumab -30,000 units hyaluronidase SQ into the abdomen over approximately 3 to 5 minutes <u>Weeks 1 to 8: weekly (total of 8 doses)</u> <u>Weeks 9 to 24: every 2 weeks (total of 8 doses)</u> <u>Weeks 25 onwards until disease progression or a maximum of 2 years: every 4 weeks</u>	See dosing regimen - Package Insert, Table 5

**VI. Product Availability**

Drug Name	Availability
Daratumumab (Darzalex)	Single-dose vial: 100 mg/5 mL, 400 mg/20 mL
Daratumumab/hyaluronidase-fihj (Darzalex Faspro)	Single-dose vial: providing 1,800 mg of daratumumab and 30,000 units of hyaluronidase/15 mL

**VII. References**

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6. 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.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	06.11.19	08.19
Criteria added for new FDA MM indications: in combination with lenalidomide and dexamethasone in newly diagnosed MM patients who are ineligible for ASCT, and in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT; NCCN MM recommendation added for Darzalex as subsequent therapy in combination with dexamethasone and carfilzomib; NCCN recommendation added for relapsed or refractory amyloidosis; references reviewed and updated.	01.28.20	05.20
3Q 2020 annual review: Darzalex Faspro added; references reviewed and updated.	05.12.20	08.20
RT4: New FDA approved combination added: Darzalex plus carfilzomib and dexamethasone.	09.02.20	
RT4: updated MM criteria to reflect new FDA indication for Darzalex Faspro in combination with D-VTd; updated light chain amyloidosis criteria updated to reflect new FDA indication for Darzalex Faspro in combination with D-VCd.	01.21.21	

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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