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

Reference Number: PA.CP.PHAR.310
Effective Date: 01/2018
Last Review Date: 07/2023

Coding Implications
Revision Log

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
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory MM who have received one to three prior lines of therapy

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

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

- MM in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a PI.
- Light chain (AL) amyloidosis in combination with bortezomib, cyclophosphamide, and dexamethasone in newly diagnosed adult 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).

Limitations of Use: Darzalex Faspro is not indicated and is not recommended for the treatment of patients with (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.

It is the policy of PA Health & Wellness ® 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 multiple myeloma;
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 and in combination with one of the following (a or b):
         a) lenalidomide* and dexamethasone;
         b) bortezomib*, melphalan, and prednisone;
      ii. Eligible for ASCT in combination with one of the following (a, b, c, or d):
         a) bortezomib*, thalidomide*, and dexamethasone;
         b) bortezomib*, lenalidomide*, and dexamethasone;
         c) bortezomib*, cyclophosphamide, dexamethasone;
         d) carfilzomib*, lenalidomide*, and dexamethasone;
   b. Subsequent therapy (i, ii or iii):
      i. In combination with dexamethasone and either lenalidomide*, bortezomib* (with or without cyclophosphamide), carfilzomib*, or Xpovio* after ≥ 1 prior therapy;
      ii. 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*);
      iii. As monotherapy after ≥ 3 prior lines of therapy including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent;
      c. Maintenance therapy for symptomatic MM as a single agent for transplant candidates (off-label);

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

Approval duration: 6 months

B. Systemic Light Chain Amyloidosis (off-label) (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*).

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53.

II. Continued Approval

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met initial approval criteria, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
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 IV;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*); or
2. Refer to PA.CP.PMN.53

III. 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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Agents with FDA-approved dosing for MM.		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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^2 SC or IV; frequency of administration varies based on specific use	
Kyprolis® (carfilzomib)	20 mg/m^2, 27 mg/m^2, and/or 56 mg/m^2 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): For multiple myeloma, may be used as a single agent or in combination with other systemic therapies where intravenous daratumumab is recommended.

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Darzalex	MM in combination with lenalidomide or pomalidomide (4-week cycle dosing regimens) and low-dose dexamethasone and for monotherapy	Weeks 1 to 8: 16 mg/kg IV weekly Weeks 9 to 24: 16 mg/kg IV every 2 weeks Weeks 25 onwards until disease progression: 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	Weeks 1 to 6: 16 mg/kg IV weekly Weeks 7 to 54: 16 mg/kg IV every 3 weeks Weeks 55 onwards until disease progression:	See dosing regimen - Package Insert, Table 2

Drug Name	Indication	Dosing Regimen	Maximum Dose
		16 mg/kg IV every 4 weeks	
	MM in combination with bortezomib, thalidomide and dexamethasone ([VTd]; 4-week cycle dosing regimen)	Induction Weeks 1 to 8: 16 mg/kg IV weekly Weeks 9 to 16: 16 mg/kg IV every 2 weeks Consolidation Weeks 1 to 8: 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)	Weeks 1 to 9: 16 mg/kg IV weekly Weeks 10 to 24: 16 mg/kg IV every 3 weeks Weeks 25 onwards until disease progression: 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)	Week 1: 8 mg/kg IV days 1 and 2 Weeks 2 to 8: 16 mg/kg IV weekly Weeks 9 to 24: 16 mg/kg IV every 2 weeks Weeks 25 onwards until disease progression: 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 SC into the abdomen over approximately 3 to 5 minutes Weeks 1 to 8: weekly Weeks 9 to 24: every 2 weeks Weeks 25 onwards until disease progression: 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 SC into the abdomen over approximately 3 to 5 minutes Weeks 1 to 6: weekly Weeks 7 to 54: every 3 weeks Weeks 55 onwards until disease progression: every 4 weeks	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 SC into the abdomen over approximately 3 to 5 minutes Induction: Weeks 1 to 8: weekly (total of 8 doses) Weeks 9 to 16: every 2 weeks (total of 4 doses) Consolidation: Weeks 1 to 8 (following ASCT): every 2 weeks (total of 4 doses)	See dosing regimen - Package Insert, Table 3
	MM in combination with bortezomib and dexamethasone ([D-Vd]; 3-week cycle)	1,800 mg daratumumab -30,000 units hyaluronidase SC into the abdomen over approximately 3 to 5 minutes Weeks 1 to 9: weekly Weeks 10 to 24: every 3 weeks Weeks 25 onwards until disease progression: every 4 weeks	See dosing regimen - Package Insert, Table 3
	Light Chain Amyloidosis – in combination with bortezomib,	1,800 mg daratumumab -30,000 units hyaluronidase SC into the abdomen over	See dosing regimen - Package Insert, Table 5

Drug Name	Indication	Dosing Regimen	Maximum Dose
	cyclophosphamide, and dexamethasone (D-VCd)	approximately 3 to 5 minutes Weeks 1 to 8: weekly (total of 8 doses) Weeks 9 to 24: every 2 weeks (total of 8 doses) Weeks 25 onwards until disease progression or a maximum of 2 years: every 4 weeks	

V. Product Availability

Drug Name	Availability
Daratumumab (Darazel)	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

VI. References

1. Darzalex Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; January 2023. Available at https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf. Accessed April 14, 2023.
2. Darzalex FasPro Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; November 2022. Available at https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX+Faspro-pi.pdf. Accessed April 20, 2023.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed April 20, 2023.
4. National Comprehensive Cancer Network. Multiple Myeloma Version 3.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed April 20, 2023.
5. National Comprehensive Cancer Network Systemic Light Chain Amyloidosis Version 2.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed April 20, 2023.
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.
7. Palladini G, Kastritis E, Maurer MS, et al. Daratumumab plus CyBorD for patients with newly diagnosed AL amyloidosis: safety run-in results of ANDROMEDA. *Blood*. 2020;136(1):71-80. doi: 10.1182/blood.2019004460.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9144	Injection, daratumumab, 10 mg and hyaluronidase-fihj
J9145	Injection, daratumumab, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date
Criteria added for new FDA indication: combination use with bortezomib, mephalan, and prednisone for the treatment of newly diagnosed MM patients ineligible for autologous stem cell transplant; prescriber requirement added; references reviewed and updated.	05/2018	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/2019	
Criteria added for new FDA indication: in combination with lenalidomide and dexamethasone in newly diagnosed MM patients who are ineligible for autologous stem cell transplant; Criteria added for new FDA MM indication: in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed MM 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.	04/2020	
3Q 2020 annual review: Darzalex Faspro added; references reviewed and updated.	07/2020	
3Q 2021 annual review: new FDA approved combination added: Darzalex plus carfilzomib and dexamethasone; 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; references reviewed and updated.	07/2021	
3Q 2022 annual review: per NCCN added additional combination regimens for MM primary therapy in those eligible for ASCT, for MM subsequent therapy added combination use with Xpovio and clarified use as monotherapy is allowable only after at least 3 prior lines of therapy or if double-refractory to PI and immunomodulatory agent; references reviewed and updated.	07/2022	
3Q 2023 annual review: per NCCN added off-label use for maintenance therapy for symptomatic MM as a single agent for transplant candidates; clarified for systemic light chain amyloidosis use is as a single agent for relapsed or refractory disease; references reviewed and updated.	07/2023	