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

Reference Number: CP.PHAR.310
Effective Date: 07.01.17
Last Review Date: 08.21
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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:

- 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 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 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.

It is the policy of health plans affiliated with Centene Corporation® 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 ≥ 1 prior therapies 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.*
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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Darzalex of 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 health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid 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 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.		
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.

V. 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	Weeks 1 to 6: 16 mg/kg IV weekly Weeks 7 to 54:	See dosing regimen -

Drug Name	Indication	Dosing Regimen	Maximum Dose
	prednisone ([VMP], 6-week cycle dosing regimen	16 mg/kg IV every 3 weeks Weeks 55 onwards until disease progression: 16 mg/kg IV every 4 weeks	Package Insert, Table 2
	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 or pomalidomide 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 Weeks 1 to 8: weekly	See dosing regimen - Package Insert, Table 1

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Weeks 9 to 24: every 2 weeks Weeks 25 onwards until disease progression: every 4 weeks	
	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 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 SQ 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 SQ 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 4

Drug Name	Indication	Dosing Regimen	Maximum Dose
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 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	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

1. Darzalex Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; July 2021. Available at https://www.darzalex.com. Accessed July 22, 2021.
2. Darzalex FasPro Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; July 2021. Available at https://darzalexhcp.com. Accessed July 22, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed July 22, 2021.
4. National Comprehensive Cancer Network. Multiple Myeloma Version 7.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed July 22, 2021.
5. National Comprehensive Cancer Network Systemic Light Chain Amyloidosis Version 2.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed March 19, 2021.
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	P&T Approval Date
Policy split from CP.PHAR.182 Excellus Oncology.	01.17	02.17
Policy converted to new template. Re-organized appropriately prescribed regimen in initial criteria; defined double-refractory in footnote Added new indication: In combination with pomalidomide and dexamethasone for the treatment of patients with MM who have received at least two prior therapies including lenalidomide and a PI.	07.17	11.17
Policy converted to new template. Annual review: no clinical changes.	08.17	11.17
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; HIM-Medical benefit added; prescriber requirement added; references reviewed and updated.	05.29.18	08.18
3Q 2019 annual review: continuity of care added; references reviewed and updated.	05.14.19	08.19
RT4: 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; references reviewed and updated.	06.27.19	
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; HIM line of business added; 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
Added Commercial line of business; 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; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21).	01.21.21	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: no significant changes; updated HCPCS code; references reviewed and updated. RT4: updated MM criteria to reflect new FDA indication for Darzalex Faspro in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a PI.	07.22.21	08.21

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.