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

Reference Number: LA.PHAR.310
Effective Date:
Last Review Date: 04.22
Line of Business: 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:

- 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
*Prior authorization is required. 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 Louisiana Healthcare Connections 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 the off-label use policy for if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

**II.** Continued Therapy

**A.** All Indications in Section I (must meet all):
1. Currently receiving medication via Louisiana Healthcare Connections 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 Louisiana Healthcare Connections 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 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.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 policy – LA.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 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:<br>16 mg/kg IV weekly<br>Weeks 9 to 24:<br>16 mg/kg IV every 2 weeks<br>Weeks 25 onwards until disease progression:<br>16 mg/kg IV 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 dosing regimen | Weeks 1 to 6:<br>16 mg/kg IV weekly<br>Weeks 7 to 54:<br>16 mg/kg IV every 3 weeks<br>Weeks 55 onwards until disease progression:<br>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) | Induction<br>Weeks 1 to 8:<br>16 mg/kg IV weekly<br>Weeks 9 to 16:<br>16 mg/kg IV every 2 weeks<br>Consolidation<br>Weeks 1 to 8:<br>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:<br>16 mg/kg IV weekly<br>Weeks 10 to 24:<br>16 mg/kg IV every 3 weeks<br>Weeks 25 onwards until disease progression:<br>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:<br>8 mg/kg IV days 1 and 2<br>Weeks 2 to 8:<br>16 mg/kg IV weekly<br>Weeks 9 to 24:<br>16 mg/kg IV every 2 weeks<br>Weeks 25 onwards until disease progression:<br>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<br>Weeks 1 to 8: weekly<br>Weeks 9 to 24: every 2 weeks<br>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 SQ into the abdomen over approximately 3 to 5 minutes<br>Weeks 1 to 6: weekly<br>Weeks 7 to 54: every 3 weeks<br>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<br><br>Induction:<br>Weeks 1 to 8: weekly (total of 8 doses)<br>Weeks 9 to 16: every 2 weeks (total of 4 doses)<br>Consolidation:<br>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<br>Weeks 1 to 9: weekly<br>Weeks 10 to 24: every 3 weeks<br>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<br>Weeks 1 to 8: weekly (total of 8 doses)<br>Weeks 9 to 24: every 2 weeks (total of 8 doses)<br>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.; March 2021. Available at https://www.darzalex.com. Accessed March 19, 2021.
2. Darzalex FasPro Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; March 2021. Available at https://darzalexhcp.com. Accessed March 19, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed March 19, 2021.
4. National Comprehensive Cancer Network. Multiple Myeloma Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed March 19, 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 |
|---|---|
| J9145 | Injection, daratumumab, 10 mg |

| Reviews, Revisions, and Approvals | Date | LDH Approval Date |
|---|---|---|
| Converted corporate to local policy | 04.22 | |

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. 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.

©2020 Louisiana Healthcare Connections. All rights reserved. All materials are exclusively owned by Louisiana Healthcare Connections and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Louisiana Healthcare Connections. You may not alter or remove any trademark, copyright or other notice contained herein. Louisiana Healthcare Connections is a registered trademark exclusively owned by Louisiana Healthcare Connections.