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

Reference Number: LA.PHAR.310
Effective Date: 07.01.22
Last Review Date: 10.03.24 ~~05.20.24~~ Coding Implications
Line of Business: Medicaid Revision Log

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

****Please note: This policy is for medical benefit****

**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 bortezomib, lenalidomide, and dexamethasone for induction and consolidation in newly diagnosed patients who are eligible for autologous stem cell transplant.
- 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~~Limitation(s) of ~~Use~~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 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,b, or ~~b~~c):
   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*, Venclexta®*, or Xpovio~~*~~®* after ≥ 1 prior therapy;
      ii. 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*);
      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 or in combination with lenalidomide for transplant candidates (off-label);

**Prior authorization may be required.*

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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, b, or ~~b~~c):
   a. Darzalex Faspro is prescribed in combination with bortezomib*, cyclophosphamide, and dexamethasone;
   b. Darzalex or Darzalex Faspro is prescribed as a single agent for relapsed or refractory disease after ≥ 1 prior therapy (e.g., bortezomib*, lenalidomide*) (*off-label***);
   c. Darzalex or Darzalex Faspro is prescribed as a single agent for newly diagnosed disease if member has significant neuropathy or has Mayo stage IIIb disease (*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 in Section V 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. Acute Lymphoblastic Leukemia (off-label)** (must meet all)**:**

1. Diagnosis of T-cell acute lymphoblastic leukemia (T-ALL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member has relapsed or refractory disease;
4. Prescribed as part of a daratumumab containing regimen (e.g., daratumumab, vincristine, pegaspargase or calaspargase, doxorubicin, and prednisone or dexamethasone);
5. Dose is within FDA maximum limit for any FDA-approved indication in Section V 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.~~**D. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255

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2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

**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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. ~~2.~~ If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1~~2~~ above does not apply, refer to the off-label use policy LA.PMN.53

**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

**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 |

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| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| 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

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| 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 |
| | 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, | Induction<br>Weeks 1 to 8: | See dosing regimen - |

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| | thalidomide and dexamethasone ([VTd]; 4-week cycle dosing regimen) | 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 | 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><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 or pomalidomide 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<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 |
| | MM in combination with bortezomib, melphalan and | 1,800 mg daratumumab -30,000 units hyaluronidase SC into the | See dosing regimen - |

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| | prednisone ([VMP]; 6-week cycle) | 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 | 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<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 SC 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 45 |
| | MM in combination with bortezomib, lenalidomide, and dexamethasone ([D-VRd]; 4-week cycle) | 1,800 mg daratumumab -30,000 units hyaluronidase SC into the abdomen over approximately 3 to 5 minutes<br>Induction: | See dosing regimen - Package Insert, Table 4 |

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| | | 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) | |
| Darzalex Faspro | Light Chain Amyloidosis – in combination with bortezomib, cyclophosphamide, and dexamethasone (D-VCd) | 1,800 mg daratumumab -30,000 units hyaluronidase SC 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~~6 |

## 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.; ~~January 2023~~July 2024. Available at https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf. Accessed ~~April 14, 2023~~August 12, 2024.
2. Darzalex FasPro Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; ~~November 2022~~July 2024. Available at https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX+Faspro-pi.pdf. Accessed ~~April 20, 2023~~August 12, 2024.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed ~~April 20, 2023~~August 12, 2024.
4. National Comprehensive Cancer Network. Multiple Myeloma Version ~~3.2023~~4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed ~~April 20, 2023~~August 15, 2024.
5. National Comprehensive Cancer Network Systemic Light Chain Amyloidosis Version 2.~~2023~~2024. Available at

https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed ~~April 20, 2023~~May 15, 2024.
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.
8. National Comprehensive Cancer Network Pediatric Acute Lymphoblastic Leukemia Version 5.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed May 15, 2024.

**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 | LDH Approval Date |
|---|---|---|
| Converted corporate to local policy | 04.22 | 07.01.22 |
| 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.<br>References reviewed and updated.<br>Template changes applied to other diagnoses/indications and continued therapy section.<br>Updated applicable HCPCS Codes. | 06.02.23 | 10.05.23 |
| 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 | 05.20.24 | 08.20.24 |
| For Darzalex Faspro added to FDA approved indications new use for MM in combination with bortezomib, lenalidomide, and dexamethasone for induction and consolidation in newly diagnosed patients who are eligible for autologous stem cell transplant. | 10.03.24 | |

**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.

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