Clinical Policy Title:	daratumumab and hyaluronidase-fihj
Policy Number:	RxA.638
Drug(s) Applied:	Darzalex Faspro®
Original Policy Date:	07/09/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Darzalex Faspro® is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase, for the treatment of adult patients with multiple myeloma:

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
daratumumab and hyaluronidase (Darzalex Faspro®)	Multiple myeloma	Recommended dose of Darzalex Faspro® is 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously over approximately 3-5 minutes. See below for the recommended dosing schedule when Darzalex Faspro® is administered as monotherapy or as part of a combination therapy.	1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		In combination with lenalidomide and dexamethasone (4-week cycle) and for monotherapy: Weeks - Schedule • Weeks 1 to 8 - weekly (total of 8 doses) • Weeks 9 to 24 - every two weeks (total of 8 doses) (First dose of the every-2-week dosing schedule is given at Week 9) Week 25 onwards until disease progression - every four weeks (First dose of the every-4-week dosing schedule is given at Week 25)	1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly
		In combination with bortezomib, melphalan and prednisone (6-week cycle): Weeks - Schedule • Weeks 1 to 6 weekly (total of 6 doses) • Weeks 7 to 54 every three weeks (total of 16 doses) (First dose of the every-3-week dosing schedule is given at Week 7) Week 55 onwards until disease progression every four weeks (First dose of the every-4-week dosing schedule is given at Week 55)	1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly
		In combination with bortezomib and dexamethasone (3-week cycle): Weeks - Schedule • Weeks 1 to 9 weekly (total of 9 doses) • Weeks 10 to 24 every three weeks (total of 5 doses) (First dose of the every-3-week dosing schedule is given at Week 10) Week 25 onwards until disease progression every four weeks (First dose of the every-4-week dosing schedule is given at Week 25)	1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly
		In combination with bortezomib, thalidomide, and dexamethasone (4-week cycle): Weeks - Schedule Induction: • Weeks 1 to 8 weekly (total of 8 doses). • Weeks 9 to 16 every two weeks (total of 4 doses) First dose of the every-2-week dosing schedule is given at Week 9 Stop for high dose chemotherapy and ASCT	1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		Consolidation: • Weeks 1 to 8 every two weeks (total of 4 doses) First dose of the every-2-week dosing schedule is given at Week 1 upon re-initiation of treatment following ASCT	
daratumumab and hyaluronidase (Darzalex Faspro®)	Systemic Light Chain Amyloidosis	In Combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd) (4-week cycle): • Weeks 1 to 8 weekly (total of 8 doses) • Weeks 9 to 24 every two weeks (total of 8 doses) • Week 25 onwards until disease progression or a maximum of 2 years First dose of the every-2-week dosing schedule is given at Week 9 First dose of the every-4-week dosing schedule is given at Week 25	1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly

Dosage Forms

- Injection: 1,800 mg daratumumab and 30,000 units hyaluronidase per 15 mL (120 mg and 2,000 units/mL) solution in a single-dose vial.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 Faspro® is prescribed in one of the following ways (a or b):
   a. Primary therapy (i or ii):
      i. Ineligible for autologous stem cell transplant (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;

ii. As monotherapy in patients who have received at least three prior line therapies, including (a and b):
   a. An immunomodulatory agent (e.g., thalidomide*, lenalidomide*);
   b. Proteasome inhibitor (PI) (e.g., ixazomib*, bortezomib*, carfilzomib*);

Prior authorization may be required.

5. Dose does not exceed the 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly.

Approval Duration
Commercial: 6 months
Medicaid: 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. The requested agent will be used as a preferred treatment for newly diagnosed disease or considered for relapse/refractory disease as a repeat of initial therapy if relapse-free for several years in combination with bortezomib*, cyclophosphamide, and dexamethasone;
5. Dose does not exceed the 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving Darzalex Faspro® that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Dose does not exceed the 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug name	Dosing Regimen	Dose Limit/Maximum Dose
Ninlaro®	4 mg orally on days 1, 8, and 15 of every 28-day treatment cycle	4 mg/dose orally
bortezomib (Velcade®)	1.3 mg/m^2 subcutaneously or intravenously; frequency of administration varies based on specific use	1.3 mg/m^2 per dose intravenously or subcutaneously; 1.6 mg/m^2 per dose intravenously
Kyprolis®	20 mg/m^2, 27 mg/ m^2, and/or 56 mg/ m^2 intravenously; frequency of administration varies based on specific use	70 mg/m^2 per dose intravenously; doses capped at a BSA of 2.2 m^2 (154 mg intravenously)
Revlimid®	10 mg or 25 mg orally once daily; dose and frequency of administration vary based on specific use	25 mg/day orally
Thalomid®	100 mg, 200 mg, or 400 mg orally once daily; dose and frequency of administration vary based on specific use	Multiple myeloma: 200 mg/day orally. Erythema nodosum leprosum: 400 mg/day orally

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - History of severe hypersensitivity to daratumumab or any of the components of the formulation.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Recommended concomitant medications:
  - Pre-medication: Administer the following pre-medications 1-3 hours before each dose of Darzalex Faspro®:
    - Acetaminophen: 650 to 1,000 mg orally
    - Diphenhydramine: 25 to 50 mg (or equivalent) orally or intravenously
    - Corticosteroid (long- or intermediate-acting)
  - Post-medication: Administer the following post-medications:
    - Monotherapy: Methylprednisone 20 mg (or an equivalent dose of an intermediate- or long-acting corticosteroid) orally for 2 days starting the day after the administration of Darzalex Faspro®
    - Combination therapy: Consider administering oral methylprednisolone at a dose of less than or equal to 20 mg (or an equivalent dose of an intermediate- or long-acting corticosteroid) beginning the day after administration of Darzalex Faspro®

References

1. Darzalex Faspro® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; March 2021.Available at: https://www.darzalex.com/. Accessed June 29, 2021.

2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/ . Accessed June 29, 2021.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 7.2021 April 26, 2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed June 29, 2021.
4. National Comprehensive Cancer Network. Systemic Light Chain Amyloidosis 1.2022 June 29, 2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed June 29, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	07/09/2020	09/14/2020
Policy was reviewed: 1. Background was updated to include new indications, "In combination with bortezomib, thalidomide, and dexamethasone…" and "Light chain (AL) amyloidosis in combination with bortezomib, cyclophosphamide and dexamethasone…". 2. Background was updated to include Limitations of Use, "Darzalex Faspro® is not indicated and is not recommended for the treatment of patients…". 3. Dosing Information updated to include maximum dose for daratumumab and hyaluronidase, "1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly." 4. Dosing Information was updated to include new dosing regimen for daratumumab and hyaluronidase indication multiple myeloma, "In combination with bortezomib, thalidomide, and dexamethasone…". 5. Dosing Information was updated to include new indication and its respective	06/29/2021	09/14/2021

dosing regimen/maximum dose, “Systemic Light Chain Amyloidosis…”. 6. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 7. Initial Approval Criteria I.A.4.b.ii was updated from “As monotherapy or in combination with pomalidomide and dexamethasone after ≥ 2 prior therapies” to “As monotherapy in patients who have received at least three prior line therapies.” 8. Initial Approval Criteria I.B was updated to include new indication “Systemic Light Chain Amyloidosis...”. 9. Continued Therapy Approval Criteria II.A was updated from “Multiple Myeloma” to “All Indications in Section I.” 10. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 11. Appendix B: Therapeutic Alternatives all dose limits in the table were updated from “See full product information for details” to their respective specific dose limits (ie/1.3 mg/m^2 per dose intravenously or subcutaneously; 1.6 mg/m^2 per dose intravenously…”). 12. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both		

generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 13. References were reviewed and updated.		