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:	06/10/2021
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, indicated 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.
- Multiple myeloma 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.
- Multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant.
- Multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy.
- Multiple myeloma 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.
- 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 hyaluronidas (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	See respective dosing regimen

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		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.	
		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)	See dosing regimen
		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)	See dosing regimen
		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	See dosing regimen

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		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)	
daratumumab and hyaluronidas (Darzalex Faspro®)	Light Chain Amyloidosis	Darzalex Faspro® is administered in combination with bortezomib, cyclophosphamide and dexamethasone (4-week cycle). In Combination with Bortezomib, Cyclophosphamide and Dexamethasone: Weeks - Schedule • Weeks 1 to 8 weekly (total of 8 doses) • Weeks 9 to 24 (First dose of the every-2-week dosing schedule is given at Week 9) every two weeks (total of 8 doses) • Week 25 onwards until disease progression or maximum of 2 years: First dose of the every-4-week dosing schedule is given at Week 25 (every four weeks)	See dosing regimen

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 provisions of the pharmacy benefit administer 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 or in combination with pomalidomide* and dexamethasone after ≥ 2 prior 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 maximum indicated regimen in background section;

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Light Chain Amyloidosis (must meet all):
1. Diagnosis of light chain amyloidosis;
2. Member does not have NYHA Class IIIB or Class IV cardiac or Mayo Stage IIIB disease with light chain amyloidosis;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Darzalex Faspro® is prescribed in combination with bortezomib, cyclophosphamide and dexamethasone;
6. Dose does not exceed the maximum indicated regimen in background section;

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 maximum indicated regimen in background section;

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® (ixazomib)	4 mg PO on days 1, 8, and 15 of every 28-day treatment cycle	See full product information for details
bortezomib (Velcade®)	1.3 mg/m^2 SC or IV; frequency of administration varies based on specific use	See full product information for details
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	See full product information for details
Revlimid® (lenalidomide)	10 mg or 25 mg PO once daily; dose and frequency of administration vary based on specific use	See full product information for details
Thalomid® (thalidomide)	100 mg, 200 mg, or 400 mg PO once daily; dose and frequency of administration vary based on specific use	See full product information for details

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):
  - Patients with a history of severe hypersensitivity to daratumumab or any of the components of the formulation.

- Boxed Warning(s):
  - None

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®.
- Monitor patients with cardiac involvement of light chain (AL) amyloidosis more frequently for cardiac adverse reactions and administer supportive care as appropriate.

References

1. Darzalex Faspro® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; February, 2021.Available at: https://www.darzalex.com/. Accessed March 3, 2021.

2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/about/news/ebulletin/ebulletindetail.aspx?ebulletinid=1475. Accessed March 3, 2021.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed March 3, 2021.
4. 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 3, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	07/09/2020	09/14/2020
Policy was reviewed: 1. Background, Dosing information, Initial approval and continued therapy approval criteria updated for new indication “Light chain (AL) amyloidosis”. 2. Clinical policy verbiage added “The provision of provider samples does not guarantee…”. 3. Appendix B: Therapeutic Alternatives verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance...." 4. Appendix C: Contraindication was updated to “Patients with a history of severe hypersensitivity ….”. 5. Appendix D: updated to “Monitor patients with cardiac involvement of light chain (AL)…”. 6. References were reviewed and updated.	03/02/2021	06/10/2021