Clinical Policy Title:	daratumumab and hyaluronidase-fihj, daratumumab
Policy Number:	RxA.638
Drug(s) Applied:	Darzalex Faspro®, Darzalex®
Original Policy Date:	07/09/2020
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Daratumumab (Darzalex®) is a CD38-directed cytolytic antibody. Daratumumab and hyaluronidase-fihj (Darzalex Faspro®) is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase, Darzalex® and Darzalex Faspro® are 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.
- 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.
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of 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.

Darzalex Faspro® is indicated for the treatment of adult patients with MM additionally:

- In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor.

Darzalex® is indicated for the treatment of adult patients with MM additionally:

- In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

Darzalex Faspro® is also indicated for the treatment of **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
		In combination with lenalidomide, pomalidomide or carfilzomib 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)	
		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)	
		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	

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		dose of the every-4-week dosing schedule is given at Week 25)	
		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 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 (Darzalex®)	Multiple Myeloma	In combination with lenalidomide or pomalidomide (4-Week Cycle) and Low-Dose dexamethasone and for Monotherapy: • Week 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)	16 mg/kg/dose (actual body weight) intravenously
		In combination with bortezomib, melphalan and prednisone ([VMP], 6-Week Cycle): • Week 1 to 6 - weekly (total of 6 doses) • Weeks 7 to 54 - every three weeks (total of 6 doses) (First dose of the every-3-week dosing schedule is given at Week 7) • Week 25 onwards until disease progression - every four weeks (First dose of the every-4-week dosing schedule is given at Week 55)	

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		In combination with dortezomib, thalidomide and dexamethasone ([VTd]; 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 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	
		With bortezomib and dexamethasone (3-Week Cycle) • Weeks 1 to 9 weekly (total of 9 doses) • Weeks 10 to 24 every two weeks (total of 5 doses) • Week 25 onwards until disease progression every four weeks First dose of the every-3-week dosing schedule is given at Week 10 First dose of the every-4-week dosing schedule is given at Week 25	
		With carfilzomib and dexamethasone (4-Week Cycle) • Week 1: 8 mg/kg every 1 and 2 (total of 2 dose) • Weeks 2 to 8 16 mg/kg weekly (total of 7 doses) • Weeks 9 to 24 16 mg/kg every two weeks (total of 8 doses) • Week 25 onwards until disease progression 16 mg/kg every four weeks First dose of the every-3-week dosing schedule is given at Week 9 First dose of the every-4-week dosing schedule is given at Week 25 Based on actual body weight	
daratumumab and	Systemic Light	In Combination with bortezomib,	1,800 mg

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
hyaluronidase (Darzalex Faspro®)	Chain Amyloidosis	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	daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly

Dosage Forms

- Darzalex Faspro®: 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.
- Darzalex®: Injection: 100 mg/5 mL solution, 400 mg/20 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® and Darzalex® are 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 or iii):
      i. For Darzalex Faspro®: In combination with dexamethasone and either lenalidomide*, bortezomib*, carfilzomib* or pomalidomide* after ≥ 1 prior therapy;
      ii. For Darzalex®: In combination with dexamethasone and either lenalidomide*, bortezomib*, carfilzomib* after ≥ 1 prior therapy or with dexamethasone and pomalidomide* after ≥ 2 prior therapy;
      iii. For Darzalex Faspro®; Darzalex®: 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 any one of the following (a, b or c):
   a. Darzalex Faspro®: 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly;
   b. Darzalex®: 16 mg/kg/dose (actual body weight) intravenously.
   c. 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
Commercial: 6 months
Medicaid: 6 months

B. Systemic Light Chain Amyloidosis (Off label for Darzalex®) (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;
6. Dose does not exceed any one of the following (a or b):
   a. Darzalex Faspro®: 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly;
   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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication 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. If request is for dose increase, dose does not exceed (a, b or c):
   a. Darzalex Faspro®: 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly.
   b. Darzalex®: 16 mg/kg/dose (actual body weight) intravenously.
   c. 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
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
AL: amyloidosis

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®	Multiple Myeloma 4 mg orally on days 1, 8, and 15 of every 28-day treatment cycle	4 mg/dose orally
bortezomib (Velcade®)	Multiple Myeloma 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®	Multiple Myeloma 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®	Multiple Myeloma 10 mg or 25 mg orally once daily; dose and frequency of administration vary based on specific use	25 mg/day orally
Thalomid®	Multiple Myeloma 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.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines

- 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® or Darzalex®:
- 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® or Darzalex®.
- 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® or Darzalex®.

References

1. Darzalex Faspro® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; January 2022. Available at: https://www.darzalex.com/. Accessed February 23, 2022.
2. Darzalex® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; January 2022. Available at: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf . Accessed February 23, 2022
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/ . Accessed February 23, 2022.
4. National Comprehensive Cancer Network. Multiple Myeloma. Version 4.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed February 23, 2022.
5. National Comprehensive Cancer Network. Systemic Light Chain Amyloidosis. Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed February 23, 2022.

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	06/29/2021	09/14/2021

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hyaluronidase indication multiple myeloma, “In combination with bortezomib, thalidomide, and dexamethasone…”. 5. Dosing Information was updated to include new indication and its respective 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.		
Policy was reviewed: 1. Clinical Policy Title, Drug(s) Applied: Updated to include generic daratumumab. 2. Clinical Policy Title, Drug(s) Applied: Updated to	2/24/2022	04/18/2022

Review/Revision History	Review/Revision Date	P&T Approval Date
include new drug Darzalex®. 3. Background: Updated to include details(s) regarding multiple myeloma for Darzalex®: • 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. • In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of 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. • In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor. 4. Background: Updated to include detail(s) regarding indication multiple myeloma 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		

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proteasome inhibitor. • In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy. 5. Dosing Information, Dosing Regimen, Darzalex Faspro®: Updated dosing information from 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 to In combination with lenalidomide, pomalidomide or carfilzomib 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 for indication Multiple myeloma 6. Dosing Information, Dosing Regimen, Darzalex®: Updated to include dosing information for indication multiple myeloma. 7. Dosing Information, Maximum Dose, Darzalex®: Updated to include maximum dosing information for indication multiple myeloma. 8. Dosage Forms, Darzalex®: Updated to include intravenous solution. 9. Initial Approval Criteria I.A.4: updated combination/monotherapy criteria from Darzalex Faspro® is prescribed in one of the		

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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*, 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*); to Darzalex Faspro® and Darzalex® are 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 or iii): i. For Darzalex Faspro®: In combination with dexamethasone and either lenalidomide*, bortezomib*, carfilzomib* or pomalidomide* after ≥ 1 prior therapy; ii. For Darzalex®: In combination with dexamethasone and either lenalidomide*, bortezomib*, carfilzomib* after ≥ 1 prior therapy or		

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with dexamethasone and pomalidomide* after ≥ 2 prior therapy; iii. For Darzalex Faspro®; Darzalex®: 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.* 10. Initial Approval Criteria I.A.5: Updated dosing criteria from Dose does not exceed 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly to Dose does not exceed any one of the following (a, b or c): a. Darzalex Faspro®: 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly. b. Darzalex®: 16 mg/kg/dose (actual body weight) intravenously. c. 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 11. Initial Approval Criteria I.B: Updated from Systemic Light Chain Amyloidosis (must meet all) to Systemic Light Chain Amyloidosis (Off label for Darzalex®) (must meet all). 12. Initial Approval Criteria I.B.6: Updated dosing criteria from Dose does not exceed 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly to Dose does not exceed any one of the following (a or b): a. Darzalex Faspro®: 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly; b. Dose is supported by practice		

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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 13. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 14. Continued Therapy Approval Criteria II.A.3: Updated dosing criteria from Dose does not exceed 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly to If request is for dose increase, dose does not exceed (a, b or c): a. Darzalex Faspro®: 1,800 mg daratumumab and 30,000 units hyaluronidase (15 mL) subcutaneously once weekly. b. Darzalex®: 16 mg/kg/dose (actual body weight) intravenously. c. 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 15. Appendix A: Updated to include abbreviations for amyloidosis. 16. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 17. Appendix D, General Information: Updated information available from 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		

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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®. • to Recommended concomitant medications: ○ Pre-medication: Administer the following pre-medications 1-3 hours before each dose of Darzalex Faspro® or Darzalex®: • 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® or Darzalex® • 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		

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corticosteroid) beginning the day after administration of Darzalex Faspro® or Darzalex®. 18. References were reviewed and updated.		