STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Darzalex and Darzalex Faspro
(daratumumab; daratumumab and hyaluronidase-fihj)
PAM–061

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	01/01/2021
Revision Number:	2	**Last Rev Date:**	07/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	07/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	10/20/2023

Overview

Medication:	daratumumab [1]	daratumumab and hyaluronidase-fihj [2]
Brand Name:	Darzalex®	Darzalex Faspro®
Pharmacologic Category: CD38-directed cytolytic antibody		
FDA-Approved Indications **Darzalex® and Darzalex Faspro®** are indicated for the treatment of adult patients with multiple myeloma (MM): 1. in combination with lenalidomide and dexamethasone in newly diagnosed patients NOT eligible for autologous stem cell transplant (ASCT) and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy; 2. in combination with bortezomib, melphalan and prednisone in newly diagnosed patients NOT eligible for ASCT; 3. in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients eligible for ASCT; 4. in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy; 5. in combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy; 6. as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD) or who are double-refractory to a PI and an IMiD.		
Darzalex® is additionally indicated: 1. in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and a PI.		
Darzalex Faspro® is additionally indicated: 1. in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior line of therapy including lenalidomide and a PI. 2. in combination with bortezomib, cyclophosphamide, and dexamethasone for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis. ➢ Accelerated Approval: 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.		
How Supplied:	Single-dose vial containing either 100 mg/5 mL or 400 mg/20 mL	
Dosage and Administration: see Appendix A for Darzalex® and Appendix B for Darzalex Faspro® information		
Benefit Category:	Medical	

Descriptive Narrative

Multiple myeloma (MM) is a malignant hematological disorder characterized by the clonal proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and can result in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures. Most patients with MM present with signs or symptoms related to the infiltration of plasma cells into the bone or other organs or to kidney damage from immunoglobulin deposition. While the clinical presentation is usually subacute, a small percentage of patients present acutely with findings that require rapid attention and intervention (e.g., spinal cord compression, kidney failure, hyperviscosity).

The acronym "CRAB" is sometimes used to remember myeloma-defining events that are used in the diagnosis of MM: **c**alcium elevation; **r**enal insufficiency (kidney impairment); **a**nemia; and **b**one disease. It is important to distinguish MM both from other causes of the clinical presentations above and from other plasma cell dyscrasias for the purposes of prognosis and treatment.

MM primarily affects older individuals, the median age at diagnosis is 65 to 74 years. It is slightly more frequent in men than in women (approximately 1.4:1), and while MM occurs in all races and all geographic locations, the incidence varies by ethnicity. The incidence in African Americans and Black populations is two to three times that in White populations in studies from the United States and United Kingdom. In contrast, the risk is lower in the Japanese and Mexican populations.[3]

Data from the US Surveillance, Epidemiology, and End Results (SEER) registry estimates 35,780 new cases of MM and 12,540 deaths from MM in the United States in 2024 (representing 1.8 percent of all new cancer cases and 2.0 percent of all cancer deaths). This correlates with an annual incidence of approximately 7 per 100,000 men and women per year. [4]

Treatment alleviates symptoms, reverses cytopenias, and decreases end-organ damage, and it aims to achieve a sustained response, improve quality of life, and prolong overall survival (OS). While most patients with multiple myeloma will have an initial response to treatment, conventional therapy is not curative, and MM will ultimately relapse. In addition, a minority will have primary refractory disease that does not respond to initial treatment.[5]

Amyloidosis is a generic term that refers to the extracellular tissue deposition of fibrils composed of subunits in a variety of normal serum proteins. One of the four most common causes of systemic amyloid deposition is immunoglobulin light chain (AL) amyloidosis, a monoclonal plasma cell proliferative disorder characterized by tissue deposits of fibrils composed of monoclonal light chain fragments, leading to organ dysfunction. Affected patients may have amyloidosis alone or in association with other plasma cell dyscrasias (such as multiple myeloma or Waldenström macroglobulinemia).

AL amyloidosis is an uncommon disorder, and while the exact incidence is unknown, in the United States, the incidence appears to be stable at approximately 9 to 14 cases per million person-years. The median age of diagnosis is 64 years, and less than 5 percent of patients are under the age of 40. Males account for 65 to 70 percent of AL amyloidosis patients.

Because systemic light chain (AL) amyloidosis is a clonal plasma cell disorder, it is treated with chemotherapy to eradicate the underlying clone. Patients with systemic AL amyloidosis are not cured with conventional treatment (while remissions can be attained, relapses are common). However, early mortality rates have decreased and survival has improved as there has been a shift toward earlier diagnosis and therapy aimed at achieving deep remissions.[6,7]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[8]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Multiple Myeloma (Version 4.2024 – April 26, 2024)[9]
- NCCN Guidelines® for Systemic Light Chain Amyloidosis (Version 2.2024 – December 12, 2023)[10]

NCCN Guidelines® Recommendation(s) for daratumumab [a] in multiple myeloma – **primary therapy**
(1) Primary therapy for patients who ARE ELIGIBLE candidates for transplant A. Other recommended regimens i. Daratumumab/ lenalidomide/ bortezomib/dexamethasone: Category 2A B. Useful in certain circumstance i. Daratumumab/bortezomib/thalidomide/dexamethasone: Category 2A ii. Daratumumab/bortezomib/cyclophosphamide/dexamethasone: Category 2A iii. Daratumumab/carfilzomib/lenalidomide/dexamethasone: Category 2A [b] (2) Maintenance therapy A. Useful in certain circumstances i. Daratumumab ± lenalidomide: Category 2A [c] (3) Primary therapy for patients who ARE NOT ELIGIBLE candidates for transplant A. Preferred regimens i. Daratumumab/lenalidomide/dexamethasone: Category 1 B. Other recommended regimens i. Daratumumab/bortezomib/melphalan/prednisone: Category 1 ii. Daratumumab/cyclophosphamide/bortezomib/dexamethasone: Category 2A [a] For any regimen that includes daratumumab, this could be daratumumab for intravenous infusion or daratumumab and hyaluronidase-fihj for subcutaneous injection. Darzalex® and Darzalex Faspro® have different dosing and administration instructions. [b] Ixazomib may be substituted for carfilzomib in select patients [c] Two drug maintenance recommended for high-risk MM.

NCCN Guidelines® Recommendation(s) for daratumumab [d] in **previously treated** multiple myeloma [e, f, g]

(1) Preferred regimens for early relapses (1 – 3 prior therapies)
  A. Bortezomib-refractory [h]
    i. Daratumumab/carfilzomib/dexamethasone: Category 1
    ii. Daratumumab/lenalidomide/dexamethasone: Category 1
    iii. Daratumumab/pomalidomide/dexamethasone: Category 1 [*after one prior therapy including lenalidomide and a proteosome inhibitor (PI)]*
  B. Lenalidomide-refractory [h]
    i. Daratumumab/bortezomib/dexamethasone: Category 1
    ii. Daratumumab/carfilzomib/dexamethasone: Category 1
    iii. Daratumumab/pomalidomide/dexamethasone: Category 1 (*after one prior therapy including lenalidomide and a PI)*
(2) Other recommended regimens for early relapses (1 – 3 prior therapies)
  A. Daratumumab/cyclophosphamide/bortezomib/dexamethasone: Category 2A
(3) Useful in certain circumstances for early relapses (1 – 3 prior therapies)
  A. Selinexor/daratumumab/dexamethasone: Category 2A
  B. Venetoclax/dexamethasone ± daratumumab or PI only for t(11;14) patients: Category 2A
  C. Daratumumab: Category 2A *[after at least 3 prior therapies including a PI and an immunomodulatory agent (IMiD) or are double-refractory to a PI and an IMiD]*

[d] For any regimen that includes daratumumab, this could be daratumumab for intravenous infusion or daratumumab and hyaluronidase-fihj for subcutaneous injection. Darzalex® and Darzalex Faspro® have different dosing and administration instructions.
[e] Regimens included under 1–3 prior therapies can also be used later in the disease course. Attempt should be made to use drugs/drug classes the patients have not been exposed to or exposed to > 1 line prior.
[f] Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.
[g] If relapse occurs > 6 months after stopping treatment, the primary regimen could be considered.
[h] Regimens without anti-CD38 should be considered for those refractory to anti-CD38 antibody as long as they have not received or are refractory to other agents in the regimen.

NCCN Guidelines® Recommendation(s) for daratumumab [i] in systemic light chain amyloidosis

(1) Primary therapy for HCT-eligible and non-eligible candidates
  A. Patient characteristics: no significant neuropathy
    i. Mayo 2004 Stage I-IIIa: Daratumumab and hyaluronidase-fihj/cyclophosphamide/ bortezomib/ dexamethasone [j, k] (Category 1, preferred)
    ii. Mayo 2004 Stage IIIb [l]
      a. Dose-modified daratumumab and hyaluronidase-fijh/cyclophosphamide/bortezomib/ dexamethasone [j, k] (Category 2A, preferred)
      b. Single-agent daratumumab [l] (Category 2A, preferred)
  B. Patient characteristics: significant neuropathy
    i. All stages [m]:Single-agent daratumumab [l] (Category 2A, preferred)
(2) Therapy for previously treated disease [n]
  A. Consider repeating initial therapy, especially if relapse-free for several years
    i. Daratumumab [i]: Category 2A
      - No clinical trial data to determine the appropriate regimens for previously treated SCLA. The treatment would depend on prior therapy received, patient preferences, and toxicity profile. The NCCN panel recommends considering repeating the initial therapy, especially if the patient has no relapse of disease for several years.

[i] For any regimen that includes daratumumab, this could be daratumumab for intravenous infusion or daratumumab and hyaluronidase-fihj for subcutaneous injection. Darzalex® and Darzalex Faspro® have different dosing and administration instructions.
[j] Dexamethasone dosing can be considered at the 20 mg weekly dose, per physician discretion, in those who are >70 years of age, were underweight (body mass index < 18.5), or had hypervolemia, poorly controlled diabetes mellitus, or previous unacceptable side effects associated with glucocorticoid therapy. Cyclophosphamide is capped at a 500 mg maximum weekly dose.
[k] Consider neuropathy-sparing regimen if patient has significant baseline neuropathy.
[l] Stage IIIb patients were excluded at screening from the ANDROMEDA trial according to the protocol. Retrospective trials have demonstrated acceptable efficacy and safety profile of daratumumab and hyaluronidase-fihj/cyclophosphamide/bortezomib/dexamethasone in stage IIIb SLCA.
[m] Dose modification and adjustments are mandatory in patients with advanced end organ damage (cardiac or other).
[n] Consider collection of hematopoietic stem cells, if appropriate.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Criteria

Prior authorization is required.

- **ASCT** – autologous stem cell transplant
- **IMiD** – immunomodulatory agent
- **Daratumumab** – Darzalex® or Darzalex Faspro®
- **PI** – proteosome inhibitor

Multiple Myeloma

Daratumumab is considered medically necessary when **ALL** of the following are met:

1. Member is 18 years of age or older; **AND**
2. Prescribed by, or in consultation with, an oncologist or hematologist; **AND**
3. Daratumumab (as Darzalex® *or* Darzalex Faspro® unless otherwise indicated) is prescribed in **ONE** of the following ways (a, b, c, or d):
    a. For treatment of multiple myeloma (MM) in combination with cyclophosphamide, bortezomib, and dexamethasone (NCCN 2A); **OR**
    b. For treatment of MM as primary therapy when either of the following criteria are met [(1) or (2)]:
        1) Member is ineligible for transplant and will be used in combination with (i or ii):
            i. Lenalidomide and dexamethasone (Label; NCCN 1); or
            ii. Bortezomib, melphalan, and prednisone (Label; NCCN 1); or
        2) Member is eligible for transplant and will be used in combination with (i, ii, or iii):
            i. Bortezomib, thalidomide, and dexamethasone for a maximum of 16 doses (Label; NCCN 2A); or
            ii. Bortezomib, lenalidomide, and dexamethasone (NCCN 2A); or
            iii. Carfilzomib, lenalidomide, and dexamethasone (NCCN 2A); **OR**
    c. For treatment of relapsed or refractory MM (**ONE** of the following, 1 – 6):
        1) In combination with lenalidomide and dexamethasone in members who have received at least one prior therapy (Label; NCCN 1); or
        2) In combination with bortezomib and dexamethasone in members who have received at least one prior therapy (Label; NCCN 1); or

3) In combination with carfilzomib and dexamethasone in members who have received one to three prior lines of therapy (Label; NCCN 1); or
4) In combination with selinexor and dexamethasone in members who have received one to three prior therapies (NCCN 2A); or
5) As a single agent in members who have received at least three prior therapies, including a proteosome inhibitor (PI) and an immunomodulatory agent (IMiD), or who are double refractory to a PI and an IMiD (Label; NCCN 2A); or
6) In combination with pomalidomide and dexamethasone in members who have received at least one prior therapy including a PI and an IMiD (Label; NCCN 1); **OR**

d. As maintenance therapy of symptomatic multiple myeloma for transplant candidates, either as a single agent or in combination with lenalidomide (NCCN 2A); **AND**

4. Request meets one of the following (a or b):
   a. Regimen prescribed does not exceed the FDA-approved labeling for dosage, dosing schedule, or duration (reference Appendix A or B); or
   b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Systemic Light Chain Amyloidosis

Daratumumab is considered medically necessary when **ALL** of the following are met:

1. Member is 18 years of age or older; **AND**
2. Member does not have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB (outside of clinical trials); **AND**
3. Prescribed by, or in consultation with, an oncologist or hematologist; **AND**
4. Daratumumab (as Darzalex® *or* Darzalex Faspro® unless otherwise indicated) is prescribed in **ONE** of the following ways (a or b):
   a. As monotherapy for treatment of relapsed or refractory systemic light chain amyloidosis (NCCN 2A); **OR**
   b. Darzalex Faspro® only: as primary therapy for treatment of systemic light chain amyloidosis when used in combination with bortezomib, cyclophosphamide, and dexamethasone (Label; NCCN 1); **AND**
5. Request meets one of the following (a or b):
   a. Regimen prescribed does not exceed the FDA-approved labeling for dosage, dosing schedule, or duration (reference Appendix A or B); or
   b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Continued Therapy – all above indications

Daratumumab (as Darzalex® or Darzalex Faspro®) is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist or hematologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed the FDA-approved labeling for dosage, dosing schedule, or duration (reference Appendix A or B); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

- Multiple myeloma (MM)

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits – Darzalex®	Maximum 16 mg/kg per dose, following recommended dosing schedule*	Maximum 16 mg/kg per dose, following recommended dosing schedule*
Quantity Limits – Darzalex Faspro®	Maximum 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) per dose, following recommended dosing schedule*	Maximum 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) per dose, following recommended dosing schedule*

* see Appendix A (Darzalex®) or Appendix B (Darzalex Faspro®) for recommended dosing schedule and duration

- Systemic light chain amyloidosis (AL)

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months (not to exceed a total of 2 years of treatment)
Quantity Limits	1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) per dose, until disease progression or unacceptable toxicity (not to exceed a total of 2 years of treatment)	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9144	Injection, daratumumab, 10 mg and hyaluronidase-fihj [Darzalex Faspro]
J9145	Injection, daratumumab, 10 mg [Darzalex]

ICD-10	Description
C90.0	Multiple myeloma
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma in relapse
E85.0 – E85.9	Amyloidosis

NDC	Description (SDV = single-dose vial)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
57894-0502-05	Darzalex®: SDV, 100 mg/5 mL	Janssen Biotech, Inc.	10 mg	1	EA	10
57894-0505-05	Darzalex®: SDV, 100 mg/5 mL	Janssen Biotech, Inc.	10 mg	1	EA	10
57894-0502-20	Darzalex®: SDV, 400 mg/20 mL	Janssen Biotech, Inc.	10 mg	1	EA	40
57894-0505-20	Darzalex®: SDV, 400 mg/20 mL	Janssen Biotech, Inc.	10 mg	1	EA	40
57894-0503-01	Darzalex Faspro®: SDV, per 15 mL: 1,800 mg daratumumab and 30,000 units hyaluronidase	Janssen Biotech, Inc.	10 mg	1	EA	180

Appendix A: Darzalex® Dosing and Administration

Dosing & schedule for FDA-approved indications of Darzalex listed below®. For dosing instructions of agents administered in combination with Darzalex®, see manufacturer's prescribing information for each respective agent.

Administration

- Darzalex® should be administered only as an intravenous infusion after dilution in 0.9% sodium chloride injection, USP and only by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur.
- Type and screen patients prior to starting Darzalex®.
  - Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum.
  - Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received Darzalex®.

Table A1: Darzalex® dosing schedule in combination with lenalidomide or pomalidomide (4-week cycle) and low-dose dexamethasone and for monotherapy

Combination therapy (4-week cycle) and monotherapy as follows:

1. Combination therapy with lenalidomide and low-dose dexamethasone for newly diagnosed patients who are NOT eligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma.
2. Combination therapy with pomalidomide and low-dose dexamethasone for patients with relapsed or refractory multiple myeloma.
3. Monotherapy for patients with relapsed or refractory multiple myeloma.

Dosage: 16 mg/kg actual body weight, administered as an intravenous infusion according to the following schedule:

	Weeks	**Schedule**
A1	Weeks 1 to 8	weekly (total of 8 doses)
	Weeks 9 to 24 [a]	every 2 weeks (total of 8 doses)
	Week 25 onwards until disease progression [b]	every 4 weeks

[a] First dose of the every-2-week dosing schedule is given at Week 9 [b] First dose of the every-4-week dosing schedule is given at Week 25

Table A2: Darzalex® dosing schedule in combination with bortezomib, melphalan, and prednisone (6-week cycle)

Combination therapy with bortezomib, melphalan and prednisone (6-week cycle) for patients with newly diagnosed multiple myeloma who are NOT eligible for autologous stem cell transplant (ASCT).

Dosage: 16 mg/kg actual body weight, administered as an intravenous infusion according to the following schedule:

	Weeks	Schedule
A2	Weeks 1 to 6	weekly (total of 6 doses)
	Weeks 7 to 54 [a]	every 3 weeks (total of 16 doses)
	Week 55 onwards until disease progression [b]	every 4 weeks

[a] First dose of the every-3-week dosing schedule is given at Week 7 [b] First dose of the every-4-week dosing schedule is given at Week 55

Table A3: Darzalex® dosing schedule in combination with bortezomib, thalidomide, and dexamethasone (4-week cycle)

Combination therapy with bortezomib, thalidomide, and dexamethasone (4-week cycle) for patients with newly diagnosed multiple myeloma who ARE eligible for autologous stem cell transplant (ASCT).

Dosage: 16 mg/kg actual body weight, administered as an intravenous infusion according to the following schedule:

	Treatment Phase	Weeks	Schedule
A3	Induction	Weeks 1 to 8	weekly (total of 8 doses)
		Weeks 9 to 16 [a]	every 2 weeks (total of 4 doses)
	Stop for high dose chemotherapy and ASCT		
	Consolidation	Weeks 1 to 8 [b]	every 2 weeks (total of 4 doses)

[a] First dose of the every-2-week dosing schedule is given at Week 9

[b] First dose of the every-2-week dosing schedule is given at Week 1 upon re-initiation of treatment following ASCT

Table A4: Darzalex® dosing schedule in combination with bortezomib and dexamethasone (3-week cycle)

Combination therapy with bortezomib and dexamethasone (3-week cycle) for patients with relapsed or refractory multiple myeloma.

Dosage: 16 mg/kg actual body weight, administered as an intravenous infusion according to the following schedule:

	Weeks	Schedule
A4	Weeks 1 to 9	weekly (total of 9 doses)
	Weeks 10 to 24 [a]	every 3 weeks (total of 5 doses)
	Week 25 onwards until disease progression [b]	every 4 weeks

[a] First dose of the every-3-week dosing schedule is given at Week 10 [b] First dose of the every-4-week dosing schedule is given at Week 25

Table A5: Darzalex® dosing schedule in combination with carfilzomib and dexamethasone (4-week cycle)

Combination therapy with carfilzomib and dexamethasone (4-week cycle) for patients with relapsed or refractory multiple myeloma.

Administered as an IV infusion according to the following dose (based on actual body weight) and schedule:

	Weeks	Dose	Schedule
A5	Week 1	8 mg/kg	days 1 and 2 (total of 2 doses)
	Weeks 2 to 8	16 mg/kg	weekly (total of 7 doses)
	Weeks 9 to 24 [a]	16 mg/kg	every 2 weeks (total of 8 doses)
	Week 25 onwards until disease progression [b]	16 mg/kg	every 4 weeks

[a] First dose of the every-2-week dosing schedule is given at Week 9 [b] First dose of the every-4-week dosing schedule is given at Week 25

Appendix B: Darzalex Faspro® Dosing and Administration

Dose of Darzalex Faspro® is 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously. For dosing instructions of agents administered in combination with Darzalex Faspro®, see manufacturer's prescribing information for each agent. Schedules for FDA-approved indications listed below.

Administration

- Darzalex Faspro® should only be administered into the subcutaneous tissue of the abdomen over approximately 3-5 minutes and only by a healthcare provider. Patients should be monitored for systemic administration-related reactions, especially following the first and second injections.
- Type and screen patients prior to starting Darzalex Faspro®.
  - Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum.
  - Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received Darzalex Faspro®.

Table B1: Darzalex Faspro® dosing schedule in combination with lenalidomide, pomalidomide, or carfilzomib and dexamethasone (4-week cycle) and for monotherapy for the treatment of adults with multiple myeloma

Use the dosing schedule in Table B1 when Darzalex Faspro® is administered in combination with dexamethasone and either lenalidomide, pomalidomide, or carfilzomib (4-week cycle) or as monotherapy.

Dosage: 1,800 mg/30,000 units, administered subcutaneously over approximately 3 – 5 minutes:

	Weeks	**Schedule**
B1	Weeks 1 to 8	weekly (total of 8 doses)
	Weeks 9 to 24 [a]	every 2 weeks (total of 8 doses)
	Week 25 onwards until disease progression [b]	every 4 weeks

[a] First dose of the every-2-week dosing schedule is given at Week 9 [b] First dose of the every-4-week dosing schedule is given at Week 25

Table B2: Darzalex Faspro® dosing schedule in combination with bortezomib, melphalan, and prednisone (6-week cycle) for the treatment of adults with multiple myeloma

Use the dosing schedule in Table B2 when Darzalex Faspro® is administered in combination with bortezomib, melphalan, and prednisone (6-week cycle).

Dosage: 1,800 mg/30,000 units, administered subcutaneously over approximately 3 – 5 minutes:

	Weeks	**Schedule**
B2	Weeks 1 to 6	weekly (total of 6 doses)
	Weeks 7 to 54 [a]	every 3 weeks (total of 16 doses)
	Week 55 onwards until disease progression [b]	every 4 weeks

[a] First dose of the every-3-week dosing schedule is given at Week 7 [b] First dose of the every-4-week dosing schedule is given at Week 55

Table B3: Darzalex Faspro® dosing schedule in combination with bortezomib, thalidomide, and dexamethasone (4-week cycle) for the treatment of adults with multiple myeloma

Use the dosing schedule in Table B3 when Darzalex Faspro® is administered in combination with bortezomib, thalidomide, and dexamethasone (4-week cycle).

Dosage: 1,800 mg/30,000 units, administered subcutaneously over approximately 3 – 5 minutes:

	Treatment Phase	**Weeks**	**Schedule**
B3	Induction	Weeks 1 to 8	weekly (total of 8 doses)
		Weeks 9 to 16 [a]	every 2 weeks (total of 4 doses)
	Stop for high dose chemotherapy and autologous stem cell transplant (ASCT)		
	Consolidation	Weeks 1 to 8 [b]	every 2 weeks (total of 4 doses)

[a] First dose of the every-2-week dosing schedule is given at Week 9

[b] First dose of the every-2-week dosing schedule is given at Week 1 upon re-initiation of treatment following ASCT

Table B4: Darzalex Faspro® dosing schedule in combination with bortezomib and dexamethasone (3-week cycle) for the treatment of adults with multiple myeloma		
Use the dosing schedule in Table B4 when Darzalex Faspro® is administered in combination with bortezomib and dexamethasone (3-week cycle).		
Dosage: 1,800 mg/30,000 units, administered subcutaneously over approximately 3 – 5 minutes:		
B4	**Weeks**	**Schedule**
	Weeks 1 to 9	weekly (total of 9 doses)
	Weeks 10 to 24 [a]	every 3 weeks (total of 5 doses)
	Week 25 onwards until disease progression [b]	every 4 weeks
[a] First dose of the every-3-week dosing schedule is given at Week 10 [b] First dose of the every-4-week dosing schedule is given at Week 25		

Table B5: Darzalex Faspro® dosing schedule in combination with bortezomib, cyclophosphamide, and dexamethasone (4-week cycle) for the treatment of adults with light chain amyloidosis		
Use the dosing schedule in Table B5 when Darzalex Faspro® is administered in combination with bortezomib, cyclophosphamide, and dexamethasone (4-week cycle).		
Dosage: 1,800 mg/30,000 units, administered subcutaneously over approximately 3 – 5 minutes:		
B5	**Weeks**	**Schedule**
	Weeks 1 to 8	weekly (total of 8 doses)
	Weeks 9 to 24 [a]	every 2 weeks (total of 8 doses)
	Week 25 onwards until disease progression or a maximum of 2 years [b]	every 4 weeks
[a] First dose of the every-2-week dosing schedule is given at Week 9 [b] First dose of the every-4-week dosing schedule is given at Week 25		

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Darzalex® prescribing information (01/2023). Janssen Biotech, Inc: Horsham, PA. Available online at: www.darzalexhcp.com. Accessed May 28, 2024.

[2] Darzalex Faspro® prescribing information (11/2022). Janssen Biotech, Inc: Horsham, PA. Available online at: www.darzalexhcp.com. Accessed May 28, 2024.

[3] Laubach JP. Multiple myeloma: Clinical features, laboratory manifestations, and diagnosis. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 3, 2024.

[4] SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. Available online at seer.cancer.gov/statfacts/html/mulmy.html. Accessed June 3, 2024.

[5] Laubach JP. Multiple myeloma: Overview of management. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 3, 2024.

[6] Dispenzieri A. Clinical presentation, laboratory manifestations, and diagnosis of immune-globulin light chain (AL) amyloidosis. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 3, 2024.

[7] Dispenzieri A. Treatment and prognosis of immunoglobulin light chain amyloidosis. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 3, 2024.

[8] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

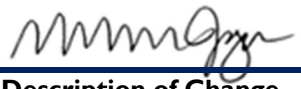
[9] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma (v.4.2024 – April 26, 2024). Accessed June 1, 2024. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

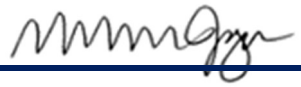
[10] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Systemic Light Chain Amyloidosis (v.2.2024 – December 12, 2023). Accessed June 1, 2024. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Annual review. Updated information on multiple myeloma, including statistics. Reviewed and updated NCCN Guidelines for Multiple Myeloma and Systemic Light Chain Amyloidosis. Updated references.	2
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee