# Darzalex® (daratumumab)
## (Intravenous)

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## I. Length of Authorization [1,16,17,19,21,24,29,30,36]

- Initial: Prior authorization validity will be provided initially for 6 months (180 days).
- Renewal: Prior authorization validity may be renewed every 6 months (180 days) thereafter, unless otherwise specified.
  - Prior authorization validity may NOT be renewed for the following:
    - ❖ Newly diagnosed multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone.
    - ❖ Pediatric Acute Lymphoblastic Leukemia.
    - ❖ HIV-Related B-Cell Lymphomas.
  - Prior authorization validity may be renewed for up to a maximum of 2 years of therapy for the following:
    - ❖ Newly diagnosed multiple myeloma in combination with bortezomib, lenalidomide and dexamethasone as maintenance therapy *(for members eligible for ASCT)*.
    - ❖ Maintenance therapy for multiple myeloma in combination with lenalidomide or as a single agent.
    - ❖ Newly diagnosed OR repeat of initial therapy if relapse-free for several years, systemic light chain amyloidosis in combination with bortezomib, cyclophosphamide, and dexamethasone.
  - Prior authorization validity may be renewed for up to a maximum of 32 weeks of therapy for the following:
    - ❖ Newly diagnosed multiple myeloma in combination with carfilzomib, lenalidomide, and dexamethasone.
  - Prior authorization validity may be renewed for up to a maximum of 80 weeks of therapy for the following:
    - ❖ Newly diagnosed OR relapsed or refractory/progressive multiple myeloma in combination with cyclophosphamide, bortezomib and dexamethasone *(32 weeks of induction therapy and 48 weeks of maintenance therapy).*
  - Prior authorization validity may be renewed for up to a maximum of 36 months of therapy for the following:

- ❖ Monotherapy for primary treatment of high-risk smoldering myeloma (asymptomatic).

## II. Dosing Limits

**Max Units (per dose and over time) [HCPCS Unit]:**

- **Multiple Myeloma:** 180 billable units every 7 days for 12 doses, every 14 days for 8 doses, every 21 days for 16 doses, then every 28 days
- **Systemic Light Chain Amyloidosis:** 180 billable units every 7 days for 8 doses, every 14 days for 8 doses, then every 28 days
- **Pediatric ALL:** 180 billable units every 7 days for 8 doses
- **HIV-Related B-Cell Lymphomas:** 180 billable units every 7 days for 10 doses, then every 21 days for 2 doses

## III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Member is at least 18 years of age (unless otherwise specified); **AND**

**Universal Criteria**

- Therapy will not be used in combination with other anti-CD38 therapies; **AND**

**Multiple Myeloma* † ‡ Φ** [1-11,13,14,16-19,22,23]

- Used in the treatment of newly diagnosed disease in members who are ineligible for autologous stem cell transplant (ASCT) in combination with ONE of the following regimens:
  - Lenalidomide and dexamethasone; **OR**
  - Bortezomib, melphalan, and prednisone; **OR**
  - Cyclophosphamide, bortezomib, and dexamethasone; **OR**
  - Bortezomib, lenalidomide, and dexamethasone; **OR**
- Used in the treatment of newly diagnosed disease in members who are eligible for autologous stem cell transplant (ASCT) in combination with ONE of the following regimens:
  - Bortezomib, lenalidomide, and dexamethasone; **OR**
  - Bortezomib, thalidomide, and dexamethasone (VTd); **OR**
  - Carfilzomib, lenalidomide, and dexamethasone; **OR**
  - Cyclophosphamide, bortezomib, and dexamethasone; **OR**
- Used for disease relapse after 6 months following primary induction therapy with the same regimen in combination with ONE of the following regimens:
  - Lenalidomide and dexamethasone for non-transplant candidates; **OR**
  - Cyclophosphamide, bortezomib, and dexamethasone; **OR**

- Used as subsequent therapy for relapsed or refractory/progressive disease in combination with dexamethasone and ONE of the following:
  - Lenalidomide; **OR**
  - Bortezomib; **OR**
  - Carfilzomib; **OR**
  - Carfilzomib and pomalidomide**; OR**
  - Cyclophosphamide and bortezomib; **OR**
  - Selinexor; **OR**
  - Venetoclax *[for members with t(11:14) ONLY];* **OR**
- Used after prior therapy with lenalidomide and a proteasome inhibitor (bortezomib, carfilzomib, etc.), in combination with ONE of the following regimens:
  - Pomalidomide and dexamethasone; **OR**
  - Teclistamab; **OR**
- Used as single agent therapy; **AND**
  - Member received at least three prior lines of therapy including a proteasome inhibitor (e.g., bortezomib, carfilzomib, etc.) and an immunomodulatory agent (e.g., lenalidomide, pomalidomide, etc.); **OR**
  - Member is double refractory to a proteasome inhibitor and an immunomodulatory agent; **OR**
- Used as maintenance therapy for symptomatic disease in transplant candidates; **AND**
  - Used as a single agent or in combination with lenalidomide; **AND**
    - Used after response to primary myeloma therapy; **OR**
    - Used for response or stable disease following an autologous hematopoietic cell transplant (HCT); **OR**
    - Used for response or stable disease following a tandem autologous or allogeneic HCT for high risk members; **OR**
- Used as primary treatment for high-risk smoldering myeloma (asymptomatic); **OR**
- Used for the management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome; **AND**
  - Used in combination with lenalidomide and dexamethasone

***The regimens listed for treatment of Multiple Myeloma may also be used for the treatment of Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes (POEMS), Monoclonal Immunoglobulin Deposition Disease (MIDD), and plasma cell-related Monoclonal Gammopathy of Renal Significance (MGRS)*

**Systemic Light Chain Amyloidosis ‡** [2,12,15,25-27]

- Used for newly diagnosed disease OR as a repeat of initial therapy if relapse-free for several years; **AND**
  - Used in combination with bortezomib, cyclophosphamide, and dexamethasone (D-VCd); **OR**

- Used as a single agent; **AND**
  - Member has stage IIIb disease with no significant neuropathy; **OR**
- Used for relapsed or refractory disease; **AND**
  - Used in combination with lenalidomide and dexamethasone; **OR**
  - Used in combination with venetoclax for t(11;14); **OR**
  - Used as a single agent

**Pediatric Acute Lymphoblastic Leukemia (ALL) ‡** [2,20,21]

- Member age ≥ 1 and ≤ 30 years; **AND**
- Member has relapsed/refractory T-cell ALL; **AND**
- Used in combination with vincristine, pegaspargase/calaspargase, doxorubicin, and prednisone/dexamethasone

**HIV-Related B-Cell Lymphomas ‡** [2,38,39]

- Used as first-line therapy for HIV-related plasmablastic lymphoma; **AND**
- Used in combination with EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)

**†** FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

## IV. Renewal Criteria [1]

Prior authorization validity can be renewed based upon the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Duration of authorization has not been exceeded (*refer to Section I*); **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions including anaphylactic reactions, neutropenia, thrombocytopenia, etc.

## V. Dosage/Administration [1,12,16-19,21-24,27,29,30-40]

| Indication | Dose |
|---|---|
| Multiple Myeloma | <u>Newly diagnosed disease in members eligible for ASCT in combination with bortezomib, thalidomide and dexamethasone</u><br>▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>▪ Induction –<br>– Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2) |

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| | – Every two weeks Weeks 9 to 16 (four doses; cycles 3 and 4)<br>*Stop for high dose chemotherapy and ASCT.*<br>▪ Consolidation –<br>– Every two weeks Weeks 1 to 8 (four doses; cycles 5 and 6) |
| | <u>Newly diagnosed disease in combination with bortezomib, lenalidomide and dexamethasone</u><br>▪ 16 mg/kg body weight given as an intravenous infusion as follows:<br><u>For members *eligible* for ASCT:</u><br>▪ Induction – **3 week cycle**<br>– Weekly Weeks 1 to 12 (twelve doses; cycles 1 to 4)<br>▪ Consolidation – *(after ASCT)* – **3 week cycle**<br>– Every 3 weeks Weeks 13 to 18 (two doses; cycles 5 and 6)<br>▪ Maintenance – **4 week cycle**<br>– Every 4 or 8 weeks Weeks 1 to 104 for a maximum of 2 years of maintenance treatment<br><u>For members *ineligible* for ASCT:</u><br>▪ Induction – **3 week cycle**<br>– Weekly Weeks 1 to 6 (six doses; cycles 1 and 2)<br>▪ Consolidation – **3 week cycle**<br>– Every 3 weeks Weeks 7 to 24 (six doses; cycles 3 to 8)<br>▪ Maintenance – **4 week cycle**<br>– Every 4 weeks Weeks 25 (cycle 9) and beyond *treat until disease progression or unacceptable toxicity* |
| | <u>Newly diagnosed disease in members eligible for ASCT in combination with carfilzomib, lenalidomide, and dexamethasone</u><br>▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>– Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2)<br>– Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6)<br>– Every four weeks Week 25 to 32 (two doses; cycles 7 and 8) |
| | <u>Newly diagnosed disease in members ineligible for ASCT in combination with bortezomib, melphalan and prednisone</u><br>▪ 16 mg/kg body weight given as an intravenous infusion in a 6 week cycle:<br>– Weekly Weeks 1 to 6 (six doses; cycle 1)<br>– Every three weeks Weeks 7 to 54 (16 doses; cycles 2 to 9)<br>– Every four weeks Week 55 onwards (cycle 10 and beyond)<br>*Treat until disease progression or unacceptable toxicity* |
| | <u>Newly diagnosed OR relapsed or refractory/progressive disease in combination with cyclophosphamide, bortezomib and dexamethasone</u><br>Induction<br>▪ 8 mg/kg body weight given as an intravenous infusion on days 1 and 2 (Week 1; total 2 doses)<br>▪ Followed by 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>– Weekly Weeks 2 to 8 (seven doses; cycles 1 and 2)<br>– Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6) |

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|---|---|
| | – Every four weeks Week 25 to 32 (two doses; cycles 7 and 8)<br>Maintenance *(after ASCT)*<br>▪ 16 mg/kg body weight given as an intravenous infusion every 4 weeks for up to 12 cycles (48 weeks) |
| | <u>Treatment as one of the following:</u><br>• Monotherapy for members with relapsed/refractory multiple myeloma<br>• Combination therapy with lenalidomide and dexamethasone for newly diagnosed members ineligible for ASCT<br>• Combination therapy with lenalidomide, pomalidomide, or selinexor AND dexamethasone in members with relapsed or refractory/progressive disease<br>• Combination therapy with carfilzomib, pomalidomide, and dexamethasone in members with relapsed or refractory/progressive disease<br>• Combination therapy with venetoclax and dexamethasone for relapsed or refractory/progressive t(11;14) disease<br>• Combination therapy with lenalidomide and dexamethasone for the management of POEMS syndrome<br>• Monotherapy as primary treatment for high-risk smoldering myeloma (asymptomatic)^<br>• Combination therapy with teclistamab<br>▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>– Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2)<br>– Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6)<br>– Every four weeks Week 25 onwards (cycle 7 and beyond) *treat until disease progression or unacceptable toxicity*<br><br>*^For high-risk smoldering myeloma (asymptomatic): Treat until disease progression or unacceptable toxicity for a maximum of 36 months* |
| | <u>Combination therapy with carfilzomib and dexamethasone for relapsed or refractory/progressive disease</u><br>▪ 8 mg/kg body weight given as an intravenous infusion on days 1 and 2 (Week 1; total 2 doses) **OR** 16 mg/kg IV on day 1 cycle 1 (Week 1; total 1 dose)<br>▪ Followed by 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>– Weekly Weeks 2 to 8 (seven doses; cycles 1 and 2)<br>– Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6)<br>– Every four weeks Week 25 onwards (cycle 7 and beyond)<br>*Treat until disease progression or unacceptable toxicity* |
| | <u>Combination therapy with bortezomib and dexamethasone for relapsed or refractory/progressive disease</u><br>▪ 16 mg/kg body weight given as an intravenous infusion in a 3 week cycle:<br>– Weekly Weeks 1 to 9 (nine doses; cycles 1 to 3)<br>– Every three weeks Weeks 10 to 24 (five doses; cycles 4 to 8)<br>– Every four weeks Week 25 onwards (cycle 9 and beyond)<br>*Treat until disease progression or unacceptable toxicity* |
| | <u>Maintenance treatment for transplant candidates</u><br>▪ Combination with lenalidomide: 16 mg/kg body weight given as an intravenous infusion |

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| | every 4 or 8 weeks until disease progression or unacceptable toxicity. For a maximum of 2 years of maintenance treatment<br>▪ Single agent: 16 mg/kg body weight given as an intravenous infusion every 8 weeks until disease progression or unacceptable toxicity. For a maximum of 2 years of maintenance treatment. |
| Pediatric ALL | ▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>– Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2) |
| Systemic Light Chain Amyloidosis | <u>Combination with bortezomib, cyclophosphamide, and dexamethasone for newly diagnosed disease OR repeat of initial therapy if relapse-free for several years</u><br>▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>– Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2)<br>– Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6)<br>– Every four weeks Week 25 and onwards (cycle 7 and beyond)<br>*Treat until disease progression or unacceptable toxicity for a maximum of 2 years* |
| | <u>Treatment as one of the following:</u><br>• Single agent therapy for relapsed/refractory disease, OR stage IIIb disease with no significant neuropathy and newly diagnosed OR repeat of initial therapy if relapse-free for several years<br>• Combination with lenalidomide and dexamethasone for relapsed/refractory disease<br>• Combination with venetoclax for relapsed or refractory t(11;14) disease<br>▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:<br>– Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2)<br>– Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6)<br>– Every four weeks Week 25 and onwards (cycle 7 and beyond)<br>*Treat until disease progression or unacceptable toxicity* |
| HIV-Related B-Cell Lymphomas | ▪ 16 mg/kg body weight given as an intravenous infusion in a 3 week cycle:<br>– Weekly Weeks 1 to 9 (nine doses; cycles 1 to 3 on days 1, 8, and 15)<br>– Every three weeks Weeks 10 to 18 (three doses; cycles 4 to 6 on day 1) |
| *To facilitate administration, the first prescribed 16 mg/kg dose at Week 1 may be split over two consecutive days (i.e., 8 mg/kg on Day 1 and Day 2 respectively).* | |
| *Note: Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week after starting Darzalex and continue for 3 months following treatment.* | |

## VI. Billing Code/Availability Information

<u>HCPCS Code</u>:

- J9145 – Injection, daratumumab, 10 mg; 1 billable unit = 10 mg

<u>NDC(s)</u>:

- Darzalex 100 mg/5 mL single-dose vial: 57894-0502-xx
- Darzalex 100 mg/5mL single-dose vial: 57894-0505-xx
- Darzalex 400 mg/20 mL single-dose vial: 57894-0502-xx

- Darzalex 400 mg/20 mL single-dose vial: 57894-0505-xx

## VII. References


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## Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

| Factor | Conclusion |
|---|---|
| Indication | Yes: Consider for PA |
| Safety and efficacy | No: PA not a priority |
| Potential for misuse/abuse | No: PA not a priority |
| Cost of drug | Yes: Consider for PA |

## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|---|---|
| C83.30 | Diffuse large B-cell lymphoma, unspecified site |
| C83.31 | Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck |
| C83.32 | Diffuse large B-cell lymphoma, intrathoracic lymph nodes |
| C83.33 | Diffuse large B-cell lymphoma, intra-abdominal lymph nodes |
| C83.34 | Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb |
| C83.35 | Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb |
| C83.36 | Diffuse large B-cell lymphoma, intrapelvic lymph nodes |

| ICD-10 | ICD-10 Description |
|---|---|
| C83.37 | Diffuse large B-cell lymphoma, spleen |
| C83.38 | Diffuse large B-cell lymphoma, lymph nodes of multiple sites |
| C83.398 | Diffuse large B-cell lymphoma of other extranodal and solid organ sites |
| C90.00 | Multiple myeloma not having achieved remission |
| C90.01 | Multiple myeloma in remission |
| C90.02 | Multiple myeloma, in relapse |
| C90.10 | Plasma cell leukemia not having achieved remission |
| C90.11 | Plasma cell leukemia in remission |
| C90.12 | Plasma cell leukemia in relapse |
| C90.20 | Extramedullary plasmacytoma not having achieved remission |
| C90.21 | Extramedullary plasmacytoma in remission |
| C90.22 | Extramedullary plasmacytoma in relapse |
| C90.30 | Solitary plasmacytoma not having achieved remission |
| C90.31 | Solitary plasmacytoma in remission |
| C90.32 | Solitary plasmacytoma in relapse |
| C91.00 | Acute lymphoblastic leukemia not having achieved remission |
| C91.02 | Acute lymphoblastic leukemia, in relapse |
| D47.9 | Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified |
| D47.Z9 | Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue |
| E31.9 | Polyglandular dysfunction, unspecified |
| E85.3 | Secondary systemic amyloidosis |
| E85.4 | Organ-limited amyloidosis |
| E85.81 | Light chain (AL) amyloidosis |
| E85.89 | Other amyloidosis |
| E85.9 | Amyloidosis, unspecified |
| G62.9 | Polyneuropathy, unspecified |
| G90.9 | Disorder of the autonomic nervous system, unspecified |
| L98.9 | Disorder of the skin and subcutaneous tissue, unspecified |
| Z85.79 | Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues |

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| **Jurisdictio** | **Applicable State/US Territory** | **Contractor** |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |