Darzalex Faspro™ (daratumumab and hyaluronidase-fihj)
(Subcutaneous)

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I. Length of Authorization [1,8]

Coverage will be provided for 6 months and may be renewed.

- Use for newly diagnosed multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Darzalex Faspro 1,800 mg/30,000 unit single-dose vial for injection: 1 vial per dose
  - *Weekly Weeks 1 to 6, then every three weeks Weeks 7-54, then every four weeks Week 55 onwards* ***OR***
  - *Weekly Weeks 1 to 8, then every two weeks Weeks 9-24, then every four weeks Week 25 onwards* ***OR***
  - *Weekly Weeks 1 to 9, then every three weeks Weeks 10-24, then every four weeks Week 25 onwards*
  - *Weekly Weeks 1 to 8, then every two weeks Weeks 9-16 for induction therapy, then every two weeks Weeks 1 to 8 for consolidation therapy*

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

- Bortezomib/Melphalan/Prednisone Regimen
  - 180 billable units per dose
    (Weekly Weeks 1 to 6, then every three weeks Weeks 7-54, then every four weeks Week 55 onwards)
- Lenalidomide or Pomalidomide Regimen
  - 180 billable units per dose
    (Weekly Weeks 1 to 8, then every two weeks Weeks 9-24, then every four weeks Week 25 onwards)
- Bortezomib/Dexamethasone Regimen
  - 180 billable units per dose
    (Weekly Weeks 1 to 9, then every three weeks Weeks 10-24, then every four weeks Week 25 onwards)
- Monotherapy Regimen

- 180 billable units per dose
  (Weekly Weeks 1 to 8, then every two weeks Weeks 9-24, then every four weeks Week 25 onwards)

- Bortezomib/Thalidomide Regimen
  - 180 billable units per dose
    (Weekly Weeks 1 to 8, then every two weeks Weeks 9-16 for induction therapy, then every two weeks Weeks 1 to 8 for consolidation therapy)

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Therapy will not be used in combination with other anti-CD38 therapies (i.e., daratumumab, isatuximab, etc.); **AND**

Multiple Myeloma † Φ [1,2]

- Used in the treatment of newly diagnosed disease in patients 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**
- Used in the treatment of newly diagnosed disease in patients who are eligible for autologous stem cell transplant (ASCT) in combination with bortezomib, thalidomide, and dexamethasone (VTd); **OR**
- Used for disease relapse after 6 months following primary induction therapy with the same regimen in combination with lenalidomide and dexamethasone for non-transplant candidates; **OR**
- Used as subsequent therapy in combination with dexamethasone and either lenalidomide or bortezomib; **OR**
- Used in combination with pomalidomide and dexamethasone after at least two prior therapies including an immunomodulatory agent (e.g., lenalidomide, pomalidomide, etc.) and a proteasome inhibitor (bortezomib, carfilzomib, etc.); **OR**
- Used as single agent therapy; **AND**
  - Patient must have received at least three previous lines of therapy including a proteasome inhibitor (e.g., bortezomib, carfilzomib, etc.) and an immunomodulatory agent (e.g., lenalidomide, pomalidomide, etc.); **OR**
  - Patient is double-refractory to a proteasome inhibitor and an immunomodulatory agent

† FDA Approved Indication(s), ‡ Compendia recommended indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,8]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease and decrease in size of tumor of tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion reactions including anaphylactic reactions, neutropenia, thrombocytopenia, etc.; **AND**
- Use for newly diagnosed disease in combination with bortezomib, thalidomide, and dexamethasone after 24 weeks of induction/consolidation therapy may not be renewed.

V. Dosage/Administration [1,6-14]

Indication	Dose
Multiple Myeloma	Administer 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) as a 15 mL injection subcutaneously into the abdomen. <u>Treatment as one of the following:</u> • Combination therapy with bortezomib, melphalan and prednisone (D-VMP) (6-week cycle) – Weekly Weeks 1 to 6 (six doses; cycle 1) – Every three weeks Weeks 7 to 54 (16 doses; cycles 2 to 9) – Every four weeks Week 55 onwards (cycle 10 and beyond) *Treat until disease progression or unacceptable toxicity.* • Combination therapy with bortezomib, thalidomide, and dexamethasone (4-week cycle) Induction – – Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2) – Every two weeks Weeks 9 to 16 (four doses; cycles 3 and 4) – *Stop for high dose chemotherapy and ASCT.* Condolidation – – Every two weeks Weeks 1 to 8 (four doses; cycles 5 and 6) • Monotherapy **OR** in combination with lenalidomide or pomalidomide and dexamethasone (4-week cycle) – Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2) – Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6) – Every four weeks Week 25 onwards (cycle 7 and beyond) *Treat until disease progression or unacceptable toxicity.* • Combination therapy with bortezomib and dexamethasone (D-Vd) (3-week cycle) – Weekly Weeks 1 to 9 (nine doses; cycles 1 to 3) – Every three weeks Weeks 10 to 24 (five doses; cycles 4 to 8) – Every four weeks Week 25 onwards (cycle 9 and beyond)

	Treat until disease progression or unacceptable toxicity.
**Keep refrigerated. Darzalex Faspro should only be administered subcutaneously by a healthcare professional. Do NOT administer Darzalex Faspro intravenously.*	
Note: Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week after starting Darzalex and continue for 3 months following treatment. Refer to the PI for other pre- and post-medication therapies.	

VI. Billing Code/Availability Information

HCPCS Code:

- J9999 – Not otherwise classified, antineoplastic drugs
- C9399 – Unclassified drugs or biologicals (hospital outpatient use)
- C9062 – Injection, daratumumab 10 mg and hyaluronidase-fihj; 1 billable unit=10 mg *(HOPPS-Hospital Outpatient Prospective Payment System Use Only) (Effective 10/1/20)*

NDC(s):

- Darzalex Faspro 1,800 mg of daratumumab and 30,000 units of hyaluronidase per 15 mL single-dose vial: 57894-0503-xx

VII. References

1. Darzalex Faspro [package insert]. Horsham, PA; Janssen Biotech, Inc; May 2020. Accessed August 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for daratumumab and hyaluronidase-fihj. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed August 2020.
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4. Mateos MV, Nahi H, Legier W, et al. Efficacy and safety of the randomized, open-label, non-inferiority, phase 3 study of subcutaneous (SC) versus intravenous (IV) daratumumab (DARA) administration in patients (pts) with relapsed or refractory multiple myeloma (RRMM): COLUMBA. JCO 2019 37:15_suppl, 8005-8005.
5. Lancman G, Arinsburg S, Jhang J, et al. Blood Transfusion Management for Patients Treated With Anti-CD38 Monoclonal Antibodies. Front. Immunol.9:2616. Doi: 10.3389/fimmu.2018.02616.
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7. Mateos MV, Dimopoulos MA, Cavo M, et al. Daratumumab plus Bortezomib, Melphalan, and Prednisone for Untreated Myeloma. N Engl J Med. 2018 Feb 8;378(6):518-528. doi: 10.1056/NEJMoa1714678. Epub 2017 Dec 12.
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9. Dimopoulos MA, Oriol A, Nahi H, et al. Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2016 Oct 6;375(14):1319-1331.
10. Palumbo A, Chanan-Khan A, Weisel K, et al. Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2016 Aug 25;375(8):754-66. doi: 10.1056/NEJMoa1606038.
11. Chari A, Suvannasankha A, Fay JW, et al. Daratumumab plus pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma. Blood. 2017 Aug 24;130(8):974-981. doi: 10.1182/blood-2017-05-785246. Epub 2017 Jun 21.
12. Lonial S, Weiss BM, Usmani SZ, et al. Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRIUS): an open-label, randomised, phase 2 trial. Lancet. 2016 Apr 9;387(10027):1551-1560. doi: 10.1016/S0140-6736(15)01120-4. Epub 2016 Jan 7.
13. Lokhorst HM, Plesner T, Laubach JP, et al. Targeting CD38 with Daratumumab Monotherapy in Multiple Myeloma. N Engl J Med. 2015 Sep 24;373(13):1207-19. doi: 10.1056/NEJMoa1506348. Epub 2015 Aug 26.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma, in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Articles may exist and compliance with these

policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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