Empliciti® (elotuzumab)
(Intravenous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed

II. Dosing Limits

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

- 300 mg vials: 16 vials per 28 days for 2 cycles; subsequent cycles are 8 vials per 28 days
- 400 mg vials: 12 vials per 28 days for 2 cycles; subsequent cycles are 6 vials per 28 days

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

Multiple Myeloma – Given in combination with Lenalidomide/Dexamethasone:

- 1200 billable units weekly for the first two 28-day cycles (8 doses), then every two weeks thereafter beginning day 1 of cycle 3

Multiple Myeloma – Given in combination with Pomalidomide/Dexamethasone:

- 1200 billable units weekly for the first two 28-day cycles (8 doses), then 2300 billable units every four weeks thereafter beginning D1 of cycle 3

Multiple Myeloma – Given in combination with Bortezomib/Dexamethasone:

- 1200 billable units weekly for the first two 21-day cycles (6 doses), then every 10 days for the next six 21-day cycles (cycles 3 to 8 [12 doses]), then every 2 weeks per 28-day cycle thereafter beginning day 1 of cycle 9

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

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

Multiple Myeloma † Φ [1-5]

- Used in combination with lenalidomide and dexamethasone after failure of one to three prior therapies; **OR**

- Used in combination with pomalidomide and dexamethasone after failure of at least two prior therapies, including an immunomodulatory agent (i.e., lenalidomide, pomalidomide, etc.) and a proteasome inhibitor (i.e. bortezomib, carfilzomib, etc.); **OR**
- Used in combination with bortezomib and dexamethasone for the treatment of relapsed or progressive disease after failure of one to three prior therapies ‡

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

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

IV. Renewal Criteria [1,2]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet 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 or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion reactions, infections, second primary malignancies, hepatotoxicity, etc.

V. Dosage/Administration[1,3]

Indication	Dose
Multiple Myeloma in combination with lenalidomide and dexamethasone	10 mg/kg intravenously every week (Days 1, 8, 15, & 22) for the first two 28-day cycles (8 doses); then every 2 weeks thereafter (Days 1 & 15) beginning with cycle 3. Continue treatment until disease progression or unacceptable toxicity.
Multiple Myeloma in combination with pomalidomide and dexamethasone	10 mg/kg intravenously every week (Days 1, 8, 15, & 22) for the first two 28-day cycles (8 doses); then 20 mg/kg every 4 weeks thereafter (Day 1) beginning with cycle 3. Continue treatment until disease progression or unacceptable toxicity.
Multiple myeloma in combination with	10 mg/kg intravenously every week (Days 1, 8 & 15) for the first two 21-day cycles (6 doses); then on Days 1 & 11 for the next six 21-day cycles (cycles 3 to 8 [12 doses]); then every 2 weeks per 28-day cycle thereafter (Days 1 & 15)

bortezomib and dexamethasone	beginning with cycle 9. Continue treatment until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J9176 – Injection, elotuzumab, 1 mg; 1 billing unit = 1 mg

NDC(s):

- Empliciti 300 mg single-dose vial: 00003-2291-xx
- Empliciti 400 mg single-dose vial: 00003-4522-xx

VII. References (STANDARD)

1. Empliciti [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; October 2019. Accessed March 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for elotuzumab. National Comprehensive Cancer Network, 2021. 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 March 2021.
3. Jakubowiak A, Offidani M, Pégourie B, et al. Randomized phase 2 study: elotuzumab plus bortezomib/dexamethasone vs bortezomib/dexamethasone for relapsed/refractory MM. Blood. 2016 Jun 9;127(23):2833-40.
4. Lonial S, Dimopoulos M, Palumbo A, et al. Elotuzumab Therapy for Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2015 Aug 13;373(7):621-31. doi: 10.1056/NEJMoa1505654. Epub 2015 Jun 2.
5. Dimopoulos MA, Dytfeld D, Grosicki S, et al. Elotuzumab plus Pomalidomide and Dexamethasone for Multiple Myeloma. N Engl J Med. 2018 Nov 8;379(19):1811-1822. doi: 10.1056/NEJMoa1805762.

VIII. References (ENHANCED)

1e. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Multiple Myeloma Version 5.2021. National Comprehensive Cancer Network, 2021. 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 NCCN Guidelines, go online to NCCN.org. Accessed March 2021.

2e. Lonial S, Richardson PG, Mateos MV, et al. ELOQUENT-2 update: Phase III study of elotuzumab plus lenalidomide/dexamethasone (ELd) vs Ld in relapsed/refractory multiple myeloma (RRMM)—Identifying responders by subset analysis. Journal of Clinical Oncology 34, no. 15_suppl (May 2016) 8037-8037.

3e. Richardson PG, Jagannath S, Jakubowiak AJ, et al. Phase II Trial of Lenalidomide, Bortezomib, and Dexamethasone In Patients (pts) with Relapsed and Relapsed/Refractory Multiple Myeloma (MM): Updated Efficacy and Safety Data After >2 Years of Follow-up. Blood, 116(21), 3049.
4e. Stewart AK, Rajkumar SV, Dimopoulos MA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. N Engl J Med. 2015 Jan 8;372(2):142-52
5e. Siegel DS, Dimopoulos MA, Ludwig H, et al. Improvement in Overall Survival With Carfilzomib, Lenalidomide, and Dexamethasone in Patients With Relapsed or Refractory Multiple Myeloma. Journal of Clinical Oncology 2018 36:8, 728-734.
6e. Dimopoulos MA1, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. Lancet Oncol. 2016 Jan;17(1):27-38.
7e. Dimopoulos MA, Goldschmidt H, Niesvizky R, et al. Carfilzomib or bortezomib in relapsed or refractory multiple myeloma (ENDEAVOR): an interim overall survival analysis of an open-label, randomised, phase 3 trial. Lancet Oncol. 2017 Oct;18(10):1327-1337.
8e. Palumbo A, Chanan-Khan A, Weisel K, et al. Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med 2016; 375:754-766.
9e. Dimopoulos MA, Oriol A, Nahi H, et al. Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med 2016; 375:1319-1331.
10e. Moreau P, Masszi T, Grzasko N, et al. Oral Ixazomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med 2016; 374:1621-1634.
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13e. Offidani M, Corvatta L, Maracci L, et al. Efficacy and tolerability of bendamustine, bortezomib and dexamethasone in patients with relapsed-refractory multiple myeloma: a phase II study. Blood Cancer J. 2013;3(11):e162. Published 2013 Nov 22. doi:10.1038/bcj.2013.58.
14e. Baz RC, Martin TG 3rd, Lin HY, et al. Randomized multicenter phase 2 study of pomalidomide, cyclophosphamide, and dexamethasone in relapsed refractory myeloma. Blood. 2016 May 26;127(21):2561-8.
15e. Magellan Health, Magellan Rx Management. Empliciti Clinical Literature Review Analysis. Last updated March 2021. Accessed March 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C90.00	Multiple myeloma not having achieved remission

ICD-10	ICD-10 Description
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 Local Coverage Articles (LCAs) 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/LCA): 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

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; IMiD = immunomodulatory agent

Multiple Myeloma

Relapsed or Progressive Disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Elotuzumab + lenalidomide + dexamethasone (ELd)	1 other	Yes in adults who have received 1-3 prior treatments	Phase 3 (ELOQUENT-2), randomized 3-year follow-up	Lenalidomide + dexamethasone (Ld)	PFS ORR	After 1-3 prior therapies	• Patients with relapsed or refractory multiple myeloma who received a combination of elotuzumab, lenalidomide, and dexamethasone had a significant relative reduction of 30% in the risk of disease progression or death
Carfilzomib + lenalidomide + dexamethasone (CLd)	1 preferred	Yes in patients who have received 1-3 prior treatments	Phase 3 (ASPIRE), randomized, multicenter Final analysis of OS	Lenalidomide + dexamethasone (Ld)	PFS	After 1-3 prior therapies	• CLd combination resulted in a significantly improved PFS and OS (improved survival by 7.9 months)
Carfilzomib (twice weekly) +	1 other	Yes in patients who have	Phase 3 (ENDEAVOR),	Bortezomib + dexamethasone (Bd)	PFS	After 1-3 prior therapies	• Carfilzomib with dexamethasone demonstrated a 2-fold improvement in PFS and a significant increase in OS compared to bortezomib with dexamethasone.

dexamethasone (Cd)		received 1-3 prior treatments	randomized, open-label, multicenter Interim overall survival analysis				
Daratumumab + bortezomib + dexamethasone (DVd)	1 preferred	Yes after at least one prior therapy	Phase 3 (CASTOR), randomized	Bortezomib + dexamethasone (Vd)	PFS	Second-line and later	• Addition of daratumumab to Vd significantly improved PFS and ORR compared to Vd alone
Daratumumab + lenalidomide + dexamethasone (DRd)	1 preferred	Yes after at least one prior therapy	Phase 3 (POLLUX), randomized	Lenalidomide + dexamethasone (Rd)	PFS	After 1 or more prior therapies	• Addition of daratumumab to Rd significantly lengthened PFS
Ixazomib + lenalidomide + dexamethasone	1 preferred	Yes after at least one prior therapy	Phase 3 (TOURMALINE MM1), double-blind, randomized, placebo-controlled	Lenalidomide + dexamethasone (Rd)	PFS	After 1-3 prior therapies	• Addition of ixazomib to Rd significantly increased PFS
Panobinostat (PAN) + bortezomib (BTZ) +	1 other	Yes after at least 2 prior therapies with	Phase 3 (PANORAMA-1), randomized,	Bortezomib + dexamethasone + placebo	PFS	After 1-3 prior therapies	• Benefit from PAN-BTZ-Dex was greatest (7.8 month improvement) in patients who received ≥2 prior regimens including bortezomib and an IMiD agent

dexamethasone (Dex)		regimens including bortezomib and an IMiD agent	placebo-controlled, double-blind Subgroup analysis				
Lenalidomide + bortezomib + dexamethasone (RVD)	2A preferred	Yes	Phase 2, prospective, multicenter	N/A	PFS	After 1-3 prior therapies	• RVD combination therapy is active with durable responses in heavily pretreated patients
Elotuzumab + pomalidomide + dexamethasone (EPd)	2A other after at least 2 prior therapies including an IMiD and proteasome inhibitor	Yes in adults who have received at least 2 prior treatments	Phase 2 (ELOQUENT-3), randomized, open-label	Pomalidomide + dexamethasone (Pd)	PFS	After at least 2 prior lines of therapy which must have included lenalidomide and a proteasome inhibitor	• EPd significantly lowered the risk of progression or death among patients who had received at least 2 prior lines of therapy including lenalidomide and a proteasome 2inhibitor
Elotuzumab + bortezomib + dexamethasone (EBd)	2A other	No	Phase 2, open-label, randomized, proof-of-concept	Bortezomib + dexamethasone (Bd)	PFS	After 1-3 prior therapies	• EBd combination demonstrated a 28% reduction in risk of disease progression or death however did not reach statistical significance

Bendamustine + bortezomib + dexamethasone (BVd)	2A other	No	Phase 2, prospective, single-arm, open-label	N/A	ORR	After 1-3 prior therapies	• BVd regimen demonstrated a high response rate of 71.5%
Pomalidomide + cyclophosphamide + dexamethasone (PCd)	2A other after at least 2 prior therapies including an IMiD and proteasome inhibitor	No	Phase 2, randomized	Pomalidomide + dexamethasone (Pd)	ORR	After more than 2 prior therapies, including lenalidomide	• PCd resulted in a superior ORR and PFS compared to Pd