Clinical Policy: Elotuzumab (Empliciti)

Reference Number: PA.CP.PHAR.308
Effective Date: 01/2018
Last Review Date: 10/2024

Description
Elotuzumab (Empliciti®) is a SLAMF7-directed immunostimulatory antibody.

FDA Approved Indication(s)
Empliciti is indicated in combination with:

- Lenalidomide and dexamethasone for the treatment of patients with multiple myeloma (MM) who have received one to three prior therapies
- Pomalidomide and dexamethasone for the treatment of adult patients with MM who have received at least two prior therapies including lenalidomide and a proteasome inhibitor

Policy/Criteria
It is the policy of PA Health & Wellness ® that Empliciti is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is relapsed or refractory;
5. One of the following (a or b):
   a. Member has measurable disease as evidenced by one of the following assessed within the last 30 days (i, ii, or iii):
      i. Serum M-protein ≥ 0.5 g/dL;
      ii. Urine M-protein ≥ 200 mg/24 h;
      iii. Serum free light chain (FLC) assay: involved FLC level ≥ 10 mg/dL (100 mg/L) provided serum FLC ratio is abnormal;
   b. Member has progressive disease, as defined by the IMWG response criteria (see *Appendix D*), assessed within 60 days following the last dose of the last anti-myeloma drug regimen received;
6. Member has received ≥ 1 prior therapy *(see Appendix B for examples)*;
7. Empliciti is prescribed in combination with dexamethasone, and either Pomalyst®, lenalidomide, or bortezomib;
   **Prior authorization may be required for Pomalyst, Revlimid, and bortezomib.*
8. Request meets one of the following (a or b):
   a. Dose does not exceed (i or ii):
      i. With lenalidomide, both of the following (1 and 2):
         1) 10 mg/kg per week for the first two cycles (4 doses per 28-day cycle);
         2) 10 mg/kg per 2 weeks (2 doses per 28-day cycle) for subsequent cycles;
      ii. With pomalidomide, both of the following (1 and 2):
         1) 10 mg/kg every week for the first 2 cycles (4 doses per 28-day cycle);

2) 20 mg/kg every 4 weeks (1 dose per 28-day cycle) for subsequent cycles;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Multiple Myeloma (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed (i or ii):
      i. With lenalidomide, both of the following (1 and 2):
         1) 10 mg/kg per week for the first two cycles (4 doses per 28-day cycle);
         1. 2) 10 mg/kg per 2 weeks (2 doses per 28-day cycle) for subsequent cycles;
      ii. With pomalidomide, both of the following (1 and 2):
         1) 10 mg/kg every week for the first 2 cycles (4 doses per 28-day cycle);
         2) 20 mg/kg every 4 weeks (1 dose per 28-day cycle) for subsequent cycles;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
FLC: free light clain
IMWG: International Myeloma Working Group
MM: multiple myeloma
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Velcade (bortezomib)	Empliciti in combination with Velcade and dexamethasone: • Regimens vary. • Per NCCN, the SC rather than IV bortezomib formulation is preferred. *An SC generic formulation is not available.*	
Revlimid (lenalidomide)	Empliciti in combination with Revlimid and dexamethasone: Regimens vary.	
Pomalyst (pomalidomide)	Empliciti in combination with Pomalyst and dexamethasone: Regimens vary.	
Kyprolis (carfilzomib), Velcade® (bortezomib), Revlimid (lenalidomide), cyclophosphamide, dexamethasone	Examples of primary therapy • Bortezomib/dexamethasone • Bortezomib/lenalidomide/dexamethasone • Bortezomib/cyclophosphamide/dexamethasone • Bortezomib/doxorubicin/dexamethasone • Bortezomib/thalidomide/dexamethasone • Carfilzomib/cyclophosphamide/dexamethasone • Carfilzomib/lenalidomide/dexamethasone • Cyclophosphamide/lenalidomide/dexamethasone • Daratumumab/lenalidomide/dexamethasone • Daratumumab/lenalidomide/bortezomib/ dexamethasone • Daratumumab/carfilzomib/lenalidomide/ dexamethasone • Daratumumab/cyclophosphamide/bortezomib/ dexamethasone • Daratumumab/bortezomib/thalidomide/ dexamethasone • Daratumumab/bortezomib/melphalan/prednisone • Dexamethasone/thalidomide/cisplatin/doxorubicin/ cyclophosphamide/etoposide/bortezomib (VTD-PACE) • Ixazomib/cyclophosphamide/dexamethasone • Ixazomib/lenalidomide/dexamethasone Lenalidomide/low-dose dexamethasone	Varies
Kyprolis (carfilzomib), Velcade® (bortezomib), Revlimid (lenalidomide), Darzalex® (daratumumab), Ninlaro® (ixazomib),	Examples of therapy for previously treated for relapsed or refractory disease: • Bendamustine • Bendamustine/bortezomib/dexamethasone • Bendamustine/lenalidomide/dexamethasone • Bendamustine/carfilzomib/dexamethasone • Bortezomib/dexamethasone • Bortezomib/lenalidomide/dexamethasone • Bortezomib/liposomal doxorubicin/dexamethasone • Bortezomib/cyclophosphamide/dexamethasone	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Pomalyst (pomalidomide), Empliciti® (elotuzumab), Thalomid® (thalidomide), bendamustine, cyclophosphamide, dexamethasone, Sarclisa® (istatuximab-irfc), Xpovio® (selinexor)	• Carfilzomib/cyclophosphamide/dexamethasone • Carfilzomib/dexamethasone • Carfilzomib/lenalidomide/dexamethasone • Carfilzomib/cyclophosphamide/dexamethasone • Carfilzomib/cyclophosphamide/thalidomide/ dexamethasone • Cyclophosphamide/lenalidomide/dexamethasone • Cyclophosphamide • Daratumumab • Daratumumab/bortezomib/dexamethasone • Daratumumab/carfilzomib/dexamethasone • Daratumumab/cyclophosphamide/bortezomib/ dexamethasone • Daratumumab/lenalidomide/dexamethasone • Daratumumab/pomalidomide/dexamethasone • Dexamethasone/cyclophosphamide/etoposide/cisplatin • Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide/ +/- bortezomib • Elotuzumab/lenalidomide/dexamethasone • Elotuzumab/bortezomib/dexamethasone • Elotuzumab/pomalidomide/dexamethasone • Istatuximab-irfc/carfilzomib/dexamethasone • Ixazomib/cyclophosphamide/dexamethasone • Ixazomib/lenalidomide/dexamethasone • Ixazomib/pomalidomide/desamethasone • Isatuximab-irfc/pomalidomide/dexamethasone • Lenalidomide/dexamethasone • Pomalidomide/bortezomib/dexamethasone • Pomalidomide/carfilzomib/dexamethasone • Pomalidomide/cyclophosphamide/dexamethasone • Pomalidomide/dexamethasone • Selinexor/bortezomib/dexamethasoneSelinexor/carfilzomib/dexamethasone • Selinexor/daratumumab/dexamethasone • Selinexor/opomalidomide/dexamthasone • Venetoclax/dexamethasone • Ideocabtagene vicleucel • Ciltacabtagene autoleucel • Teclistamab-cqyv • Benlantamab mafodotin-blmf	

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Black Box Warnings
None reported

Appendix D: General Information
- The IMWG response criteria for multiple myeloma definition of progressive disease requires only one of the following:
  - Increase of 25% from lowest response value in any of the following:
    - Serum M-component (absolute increase must be ≥ 0.5 g/dL), and/or
    - Urine M-component (absolute increase must be ≥ 200 mg/24 h), and/or
  - Only in patients without measurable serum and urine M-protein levels: the difference between involved and uninvolved FLC levels (absolute increase must be > 10 mg/dL)
  - Only in patients without measurable serum and urine M protein levels and without measurable disease by FLC levels, bone marrow plasma cell percentage irrespective of baseline status (absolute increase must be ≥ 10%)
  - Appearance of a new lesion(s), ≥ 50% increase from nadir in SPD (sum of the products of the maximal perpendicular diameters of measured lesions) of > 1 lesion, or ≥ 50% increase in the longest diameter of a previous lesion >1 cm in short axis;
  - ≥ 50% increase in circulating plasma cells (minimum of 200 cells per µL) if this is the only measure of disease

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	<u>Cycles one and two:</u> • Empliciti: 10 mg/kg IV once weekly on cycles 1 and 2 (on days 1, 8, 15, and 22), • Dexamethasone: 28 mg PO between 3 and 24 hours before Empliciti plus 8 mg IV between 45 and 90 minutes before Empliciti • Lenalidomide: 25 mg PO QD x 21 days of a 28-day cycle OR • Pomalidomide: 4 mg PO QD x 21 days of a 28-day cycle <u>Cycles three and beyond:</u> • Empliciti: o With lenalidomide: 10 mg/kg IV once every 2 weeks (on days 1 and 15)	With lenalidomide: 10 mg/kg With pomalidomide: 20 mg/kg

Indication	Dosing Regimen	Maximum Dose
	o With pomalidomide: 20 mg/kg IV once every 4 weeks • Dexamethasone: Administer as for cycles one and two and on the days Empliciti is not given (days 8 and 22), give 40 mg PO QD if 75 years or younger OR 20 mg PO QD if older than 75 years • Lenalidomide: 25 mg PO QD x 21 days of a 28-day cycle OR • Pomalidomide: 4 mg PO QD x 21 days of a 28-day	

V. Product Availability

Single-dose vials: 300 mg, 400 mg

VI. References

1. Empliciti Prescribing Information. Princeton, NJ: Bristol-Myers Squibb; March 2022. Available at: https://packageinserts.bms.com/pi/pi_empliciti.pdf.. Accessed July 15, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 1, 2024.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed August 1, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9176	Injection, elotuzumab, 1 mg

Reviews, Revisions, and Approvals	Date
4Q 2018 annual review: no significant changes; NCCN and FDA-approved uses summarized for improved clarity; specialist involvement in care and continuation of care added; references reviewed and updated.	08/2018
2Q 2019: added newly FDA-approved use with pomalidomide for MM; references reviewed and updated.	04/2019
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: added age limit; references reviewed and updated.	10/2020
4Q 2021 annual review: updated Appendix B Therapeutic Alternatives; references reviewed and updated.	10/2021

Reviews, Revisions, and Approvals	Date
4Q 2022 annual review: no significant changes; updated Appendix B per NCCN MM guidelines for primary therapy and therapy for previously treated MM; references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; updated Appendix B with examples of previously treated regimens per current NCCN Multiple Myeloma guidelines; references reviewed and updated.	10/2023
4Q 2024 annual review: added hematologist as prescriber option; added criterion disease is relapsed or refractory per NCCN; added IMWG criterion defining progressive MM disease as MM class alignment; references reviewed and updated.	10/2024