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| **Clinical Policy Title:** | elotuzumab |
| **Policy Number:** | RxA.365 |
| **Drug(s) Applied:** | Empliciti® |
| **Original Policy Date:** | 03/06/2020 |
| **Last Review Date:** | 09/14/2021 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

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

It 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.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| elotuzumab (Empliciti®) | MM | Cycles one and two:<br>• Empliciti®: 10 mg/kg intravenously once weekly on cycles 1 and 2 (on days 1, 8, 15, and 22),<br>• Lenalidomide: 25 mg orally once daily x 21 days of a 28-day cycle<br>OR<br>• Pomalidomide: 4 mg orally once daily x 21 days of a 28-day cycle<br>Cycles three and beyond:<br>• Empliciti®:<br>  • With lenalidomide: 10 mg/kg intravenously once every 2 weeks (on days 1 and 15)<br>  • With pomalidomide: 20 mg/kg intravenously once every 4 weeks<br>• Lenalidomide: 25 mg orally once daily x 21 days of a 28-day cycle<br>OR<br>• Pomalidomide: 4 mg orally once daily x 21 days of a 28-day cycle<br>• **Dexamethasone+ lenalidomide+ Empliciti®-**<br>On days that Empliciti® is administered, give dexamethasone 28 mg orally between 3 and 24 hours before Empliciti® plus 8 mg intravenously between 45 | 20 mg/kg |

| Dosing Information | | | |
|---|---|---|---|
| **Drug Name** | **Indication** | **Dosing Regimen** | **Maximum Dose** |
| | | and 90 minutes before Empliciti®.<br>On days that Empliciti® is not administered but a dose of dexamethasone is scheduled (Days 8 and 22 of cycle 3 and all subsequent cycles), give 40 mg orally<br>• **Dexamethasone+ pomalidomide+ Empliciti®-**<br>**Patients ≤75 years**- On days that Empliciti® is administered, give dexamethasone 28 mg orally between 3 and 24 hours before Empliciti® plus 8 mg intravenously between 45 and 90 minutes before Empliciti®. On days that Empliciti® is not administered but dexamethasone is due (Days 8, 15 and 22 of cycle 3 and all subsequent cycles) administer dexamethasone 40 mg orally.<br>**Patients >75 years-** On days that Empliciti® is administered, give dexamethasone 8 mg orally between 3and 24 hours before infusion plus dexamethasone 8 mg intravenously between 45 and 90 minutes prior to infusion. On days that Empliciti® is not administered but dexamethasone is due (Days 8, 15 and 22 of cycle 3 and all subsequent cycles) administer dexamethasone 20 mg orally. | |

## Dosage Forms

- Single-dose vial: 300 mg, 400 mg

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

**I. Initial Approval Criteria**

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

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has received at least one prior therapy (see Appendix B for examples);
5. Empliciti® is prescribed in combination with dexamethasone, and either Pomalyst®, Revlimid®, or Velcade®;*
   *Prior authorization may be required for Pomalyst, Revlimid, and Velcade.
6. Request meets one of the following (a or b):*
   a. Dose does not exceed (i or ii):

i. With lenalidomide: 10 mg/kg per week for the first two cycles (4 doses per 28-day cycle) and 10 mg/kg per 2 weeks (2 doses per 28-day cycle) for subsequent cycles;
ii. With pomalidomide: 10 mg/kg every week for the first 2 cycles (4 doses per 28-day cycle) and 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).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration**
**Commercial:** 6 months
**Medicaid:** 6 months

## II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications and has received this medication for at least 30 days;
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: 10 mg/kg per week for the first two cycles (4 doses per 28-day cycle) and 10 mg/kg per 2 weeks (2 doses per 28-day cycle) for subsequent cycles;
      ii. With pomalidomide: 10 mg/kg every week for the first 2 cycles (4 doses per 28-day cycle) and 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).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration**
**Commercial:** 12 months
**Medicaid**: 12 months

## III. Appendices

**APPENDIX A: Abbreviation/Acronym Key**
FDA: Food and Drug Administration
MM: Multiple myeloma
NCCN: National Comprehensive Cancer Network

**APPENDIX B: Therapeutic Alternatives**
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Velcade® (bortezomib) | Empliciti® in combination with Velcade and dexamethasone:<br>• Regimens vary.<br>• Per NCCN, the subcutaneous rather than intravenous bortezomib formulation is preferred. A subcutaneous generic formulation is not available. | Varies |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Revlimid® (lenalidomide) | Empliciti® in combination with Revlimid and dexamethasone:<br>• Regimens vary. | |
| Pomalyst® (pomalidomide) | Empliciti® in combination with Pomalyst and dexamethasone:<br>• Regimens vary. | |
| Darzalex® (daratumumab)<br>Empliciti® (elotuzumab)<br>Kyprolis® (carfilzomib)<br>Ninlaro® (ixazomib)<br>Revlimid® (lenalidomide)<br>Thalomid® (thalidomide)<br>Velcade® (bortezomib) | Examples of primary and subsequent therapy regimens:<br>• Bendamustine<br>• Bortezomib/doxorubicin/dexamethasone<br>• Bortezomib/thalidomide/dexamethasone<br>• Bortezomib/lenalidomide/dexamethasone<br>• Bortezomib/cyclophosphamide/dexamethasone<br>• Carfilzomib/lenalidomide/dexamethasone<br>• Carfilzomib/cyclophosphamide/dexamethasone<br>• Daratumumab/lenalidomide/dexamethasone<br>• Dexamethasone/thalidomide/cisplatin/ doxorubicin/cyclophosphamide/bortezomib<br>• Elotuzumab/lenalidomide/dexamethasone<br>• Ixazomib/lenalidomide/dexamethasone<br>• Lenalidomide/dexamethasone | Varies |

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

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - None reported.

- Boxed warning(s):
  - None reported.

**APPENDIX D: General Information**

- Infusion reactions: Premedication is required. Interrupt Empliciti® (elotuzumab) for Grade 2 or higher and permanently discontinue for severe infusion reaction.
- Empliciti® can interfere with assays used to monitor M-protein. This interference can impact the determination of complete response.

**References**


1. Empliciti® Prescribing Information. Princeton, NJ: Bristol-Myers Squibb; October 2019. Available at https://www.empliciti.com/ . Accessed May 29, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/ . Accessed May 29, 2021.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 7.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf . Accessed May 29, 2021.

| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 01/2020 | 03/06/2020 |
| Policy was reviewed<br>1. Policy title table was updated.<br>2. Line of business 'Policy Applies to' was updated to all lines of business.<br>3. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..."<br>Reference reviewed and updated | 07/15/2020 | 09/14/2020 |
| Policy was reviewed<br>1. Dosing Information dosing regimen was updated to remove "Dexamethasone: 28 mg PO between 3 and 24 hours before Empliciti®…"<br>2. Dosing Information dosing regimen was updated to include "Dexamethasone+ lenalidomide+ Empliciti®…" and "Dexamethasone+ pomalidomide+ Empliciti®…".<br>3. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy.<br>4. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration.<br>5. Therapeutic Alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance..".<br>6. Appendix B footnote was updated to, "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only".<br>7. Appendix D was updated to include"Infusion reactions. Premedication is required….".<br>8. References were reviewed and updated. | 05/29/2021 | 09/14/2021 |