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Medication Policy Manual | **Policy No:** dru453

Topic: Empliciti®, elotuzumab | **Date of Origin:** March 11, 2016

Committee Approval Date: November 10, 2017 | **Next Review Date:** October 2018

Effective Date: November 10, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Elotuzumab (Empliciti) is an intravenously administered SLAMF7-directed immunostimulatory monoclonal antibody used in the treatment of relapsed and/or refractory multiple myeloma (MM). Elotuzumab (Empliciti) is administered in combination with lenalidomide (Revlimid) and dexamethasone.

Policy/Criteria

I. Most contracts require prior authorization approval of elotuzumab (Empliciti) prior to coverage. Elotuzumab (Empliciti) may be considered medically necessary when criteria A, B, and C below are met.

A. A diagnosis of relapsed and/or refractory multiple myeloma.

AND

B. At least one prior therapy for multiple myeloma has been ineffective or not tolerated *(see Appendix 1 and 2).*

AND

C. Elotuzumab (Empliciti) will be administered in combination with lenalidomide (Revlimid) and dexamethasone.

II. Administration, Quantity Limitations, and Authorization Period

A. Regence Pharmacy Services does not consider elotuzumab (Empliciti) to be a self-administered medication.

B. When prior authorization is approved, elotuzumab (Empliciti) may be authorized in quantities of 10 mg/kg once weekly for the first two 28-day cycles (i.e. 8 doses), followed by 10 mg/kg every two weeks thereafter until disease progression.

C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Elotuzumab (Empliciti) is considered investigational when used in any other MM treatment setting, and for all other conditions, including but not limited to:

A. Front-line treatment of MM

B. In combination with a proteosome inhibitor (PI) plus an immunomodulator (see *Appendix 1*)

C. In combination with panobinostat (Farydak)

D. In combination with daratumumab (Darzalex)

E. Smoldering multiple myeloma

Position Statement

Summary

- Elotuzumab (Empliciti) is an intravenously administered SLAMF7-directed immunostimulatory monoclonal antibody for the treatment of relapsed and/or refractory multiple myeloma.
- The evidence for efficacy for elotuzumab (Empliciti) comes from a single randomized, open-label trial that demonstrated improvements in progression-free survival (PFS) in patients who had received one to three prior lines of therapy for multiple myeloma. [1]
- PFS is considered a surrogate endpoint in multiple myeloma. It has not been correlated with a clinical benefit, such as improved overall survival.

- The safety and effectiveness of elotuzumab (Empliciti) has only been established when given in combination with lenalidomide (Revlimid) and dexamethasone. There is a smaller, preliminary (phase 2) trial evaluating elotuzumab (Empliciti) as an add-on to bortezomib plus dexamethasone; however, the potential for benefit from this combination regimen has not yet been established. The National Comprehensive Cancer Network (NCCN) Multiple Myeloma guideline lists elotuzumab (Empliciti) in combination with lenalidomide (Revlimid) and dexamethasone among several category 1 recommendations for previously treated multiple myeloma (i.e. patients who have received one to three prior therapies). [2] It is listed as a category 2A recommendation (lower quality) when administered in combination with bortezomib (Velcade) plus dexamethasone.
- The safety and effectiveness of elotuzumab (Empliciti) as an add-on to front-line MM regimens has not been established. [3]
- There is no evidence to support the use of elotuzumab (Empliciti) as an add on to multi-drug regimens that combine an immunomodulator with a proteasome inhibitor [e.g. lenalidomide (Revlimid)/bortezomib (Velcade)/dexamethasone].
- The safety and effectiveness of elotuzumab (Empliciti) in doses exceeding those described in package labeling have not been evaluated.

Clinical Efficacy

- The efficacy of elotuzumab (Empliciti) is based on a single, phase 3, randomized, open-label trial in patients who had received one to three prior therapies for multiple myeloma. The median number of prior treatments was two. Bortezomib (Velcade) was the most common prior therapy (70%), followed by melphalan (65%), thalidomide (48%), and lenalidomide (6%). [1]
- Elotuzumab (Empliciti) plus the combination of lenalidomide (Revlimid) and dexamethasone was compared to lenalidomide (Revlimid) and dexamethasone alone.
- Efficacy was evaluated based on progression-free survival (PFS), a surrogate endpoint. Treatment with elotuzumab (Empliciti) resulted in a 4.5 month PFS advantage compared to lenalidomide (Revlimid) and dexamethasone alone (19.4 months vs 14.9 months, respectively). The effect of elotuzumab (Empliciti) on clinically relevant outcomes such as overall survival or quality of life is not known.
- A small, preliminary (phase 2) trial evaluated elotuzumab (Empliciti) as an add-on to bortezomib (Velcade) plus dexamethasone. [4] A 2.8-month PFS advantage was reported. A larger confirmatory trial is needed to confirm the potential benefit of this combination.

Investigational Uses

Although elotuzumab (Empliciti) is being studied in the front-line multiple myeloma setting and in combination with other multiple myeloma medications, there is not sufficient evidence supporting its safety or efficacy in these settings. [3]

Regence Pharmacy Services performs independent analyses of oncology medications. The Regence Pharmacy Services analysis and coverage policy may differ from NCCN clinical practice guidelines.

Safety [5]

- Elotuzumab (Empliciti) can cause severe infusion reactions. Infusions reactions were reported in approximately 10% of patients treated with elotuzumab (Empliciti) in the randomized trial.
- Of the patients who experienced an infusion reaction, 70% occurred during the first dose.
- Premedication with dexamethasone, antihistamines, and acetaminophen is recommended.

Dosing Schedule [5]

Cycle	**28-Day Cycles 1 and 2**				**28-Day Cycles 3+**			
Day of Cycle	**1**	**8**	**15**	**22**	**1**	**8**	**15**	**22**
elotuzumab (Empliciti) (mg/kg) intravenously	10	10	10	10	10		10	
lenalidomide (Revlimid) (25 mg) orally	Days 1-21				Days 1-21			
dexamethasone (mg) orally	28	28	28	28	28	40	28	40

Appendix 1: Classification of Medications used for Multiple Myeloma				
Chemotherapy	**Histone Deacetylase (HDAC) Inhibitors**	**Immunomodulators**	**Monoclonal Antibodies**	**Proteosome Inhibitors**
• bendamustine • cyclophosphamide • doxorubicin • liposomal doxo-rubicin (Doxil)	panobinostat (Farydak)	• lenalidomide (Revlimid) • pomalidomide (Pomalyst) • thalidomide (Thalomid)	• daratumumab (Darzalex) • elotuzumab (Empliciti)	• bortezomib (Velcade) • carfilzomib (Kyprolis) • ixazomib (Ninlaro)

Appendix 2: NCCN Category 1 Treatment Options for Multiple Myeloma[a] *(Note: A therapy may consist of a multi-drug regimen)*	
Primary Therapy	
Transplant Candidates	Non-Transplant Candidates
bortezomib/lenalidomide/dexamethasone (preferred)	bortezomib/lenalidomide/dexamethasone (preferred)
bortezomib/doxorubicin/dexamethasone	lenalidomide/low-dose dexamethasone (preferred)
bortezomib/dexamethasone	
bortezomib/thalidomide/dexamethasone	
lenalidomide/dexamethasone	

[a] Category 1 recommendations listed only. A complete list of treatment options can be found at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

Appendix 2: NCCN Category 1 Treatment Options for Multiple Myeloma [a] *(continued)* *(Note: A therapy may consist of a multi-drug regimen)*
Maintenance Therapy
lenalidomide (preferred)
Therapy for Previously Treated Multiple Myeloma
carfilzomib (twice weekly)/dexamethasone (preferred)
carfilzomib/lenalidomide/dexamethasone (preferred)
daratumumab/bortezomib/dexamethasone (preferred)
daratumumab/lenalidomide/dexamethasone (preferred)
elotuzumab/lenalidomide/dexamethasone (preferred)
ixazomib/lenalidomide/dexamethasone (preferred)
bortezomib/liposomal doxorubicin/dexamethasone
bortezomib/dexamethasone
lenalidomide/dexamethasone
panobinostat/bortezomib/dexamethasone
pomalidomide/dexamethasone

[a] Category 1 recommendations listed only. A complete list of treatment options can be found at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

Cross References
Darzalex®, daratumumab, Medication Policy Manual, Policy No. 452
Farydak®, panobinostat, Medication Policy Manual, Policy No. 397
Kyprolis®, carfilzomib, Medication Policy Manual, Policy No. 282
Ninlaro®, ixazomib, Medication Policy Manual, Policy No. 455
Pomalyst®, pomalidomide, Medication Policy Manual, Policy No. 293
Revlimid®, lenalidomide, Medication Policy Manual, Policy No. 127
Velcade®, bortezomib, Medication Policy Manual, Policy No. 190

Codes	**Number**	**Description**
HCPCS	J9176	Injection, elotuzumab, 1 mg

References

1. 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. PMID: 26035255
2. NCCN Clinical Practice Guidelines in Oncology™. Multiple Myeloma v.2.2018. [cited 10/9/2017]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf
3. National Institutes of Health, Clinicaltrials.gov [website]. [cited periodically]; Available from: www.clinicaltrials.gov
4. Jakubowiak, A, Offidani, M, Pegourie, B, et al. Randomized phase 2 study: elotuzumab plus bortezomib/dexamethasone vs bortezomib/dexamethasone for relapsed/refractory MM. *Blood*. 2016 Jun 09;127(23):2833-40. PMID: 27091875
5. Empliciti™ (elotuzumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2017.

Revision History

Revision Date	Revision Summary
11/10/2017	Several treatment settings were specifically listed as investigational in section III.
7/11/2016	No changes to coverage criteria with this update
3/11/2016	New policy