BlueCross BlueShield of Alabama

Name of Policy:
Empliciti™ (Elotuzumab)

Policy #:	671	Effective Date:	June 30, 2017
Category:	Pharmacology	Latest Review Date:	May 2017

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Empliciti™ (elotuzumab) is a humanized IgG1 monoclonal antibody that targets the signaling lymphocytic active molecule (SLAM) family member F7 (SLAMF7) protein which is expressed on myeloma cells and natural killer cells. Elotuzumab directly activates natural killer cells through both the SLAMF7 pathway and Fc receptors .Elotuzumab also targets SLAMF7 on myeloma cells and facilitates the interaction with natural killer cells to mediate the killing of myeloma cells through antibody-dependent cellular cytotoxicity.

Policy:

Empliciti™ (elotuzumab) meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the treatment of individuals with **multiple myeloma**, including plasma-cell leukemia, when **all** of the following criteria are met:

1. When used in combination with lenalidomide and dexamethasone for relapsed or refractory disease;**and**
2. Prior lines of therapy did not include elotuzumab.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Multiple myeloma is a systemic malignancy of plasma cells that accumulate in the bone marrow, leading to destruction of bone and failure of the bone marrow. Multiple myeloma is highly treatable but rarely curable. However, when it presents as a solitary plasmacytoma of bone or as an extramedullary plasmacytoma it is potentially curable. Multiple myeloma accounts for approximately 10% of all hematologic cancers. The American Cancer Society has estimated 30,280 new cases of multiple myeloma will be diagnosed in the United States in 2017, with an estimated 12,590 deaths. The stage of the disease at presentation is a strong determinant of survival, but has little influence on the choice of therapy since almost all individuals (except for those with solitary bone tumors or extramedullary plasmacytomas) have generalized disease. Multiple myeloma affects mostly older individuals around 62 years of age. The age and general health of the individual, prior therapy and the presence of complications of the disease influence treatment selection. The median survival in the pre-chemotherapy era was about 7 months. Multiple myeloma has demonstrated chemosensitivity to initial treatment or treatment for relapsed disease. Improvements in newer treatments have resulted in an increase in 5-year survival which is currently around 50%.

Richardson and colleagues reported final phase II results of a randomized, multi-center, open-label, dose-escalation study of elotuzumab in combination with lenalidomide and dexamethasone. Between January 2010, and December 2010, a total of 73 participants were recruited and randomly assigned to elotuzumab (36 to 10 mg/kg, 37 to 20 mg/kg). Subjects were at least 18 years of age with relapsed multiple myeloma, Eastern Cooperative Oncology Group (ECOG) performance status of 0-2, and one to three previous therapies, excluding lenalidomide. Treatment consisted of 28 day cycles given until disease progression or unacceptable toxic side effects. At data cutoff in January 2014, 13 subjects continued on treatment (6 subjects on 10 mg/kg and 7 subjects on 20 mg/kg). A total of 61 subjects (84%) achieved an objective response (33 [92%] with 10 mg/kg, 28 [76%] with 20 mg/kg). Thirty-one subjects (42%) had a very good partial response (17 [47%] with 10 mg/kg, 14 [38%] with 20 mg/kg); and 20 (27%) a partial response (10 [28%] with 10 mg/kg, 10 [27%] with 20 mg/kg). Those most common adverse events were diarrhea, muscle spasms and fatigue. Grade 3–4 events occurred in 57 (78%), the most common of which were lymphopenia and neutropenia. Three deaths occurred; however, none were related to the study drugs. The authors concluded that elotuzumab combined with lenalidomide and dexamethasone in subjects with relapsed multiple myeloma showed acceptable safety and efficacy that seemed better than that previously noted with lenalidomide and dexamethasone only.

A single randomized phase III, controlled, open-label, multi-center trial (ELOQUENT-2) evaluated the effectiveness and safety of elotuzumab in individuals with relapsed or refractory multiple myeloma who had disease progression after one to three previous therapies. The median number of prior therapies was two, including stem cell transplant (55%), bortezomib (70%), melphalen (65%), thalidomide (48%), and lenalidomide (6%). Prior lines of therapy did not include elotuzumab. Previous treatment with lenalidomide was allowed, subject to restrictions. All subjects had a creatinine clearance of 30 ml per minute or higher. Coprimary end points were progression-free survival (PFS) and the overall response rate (partial response or better). A total of 646 subjects were randomized to receive elotuzumab (10 mg/kg) in combination with lenalidomide/ dexamethasone (E-Ld) (n=321) or lenalidomide/ dexamethasone alone (Ld) (n=325). The final analysis showed a statistically significant improvement in median PFS time of 4.5 months between Arm E-Ld (19.4 months) and Arm Ld (14.9 months) and overall response rates of 78.5 and 65.5%, respectively. PFS increased with increasing elotuzumab exposure. The most common adverse reactions were fatigue, diarrhea, pyrexia, constipation, cough, peripheral neuropathy, nasopharyngitis, upper respiratory tract infection, decreased appetite, and pneumonia. At the approved dose, 10% of subjects had grade 3 or lower infusion reactions and 1% discontinued elotuzumab due to infusion reactions. Individuals on elotuzumab had increased infections relative to those in the active control group. The rates of grade three or higher adverse events or adverse events leading to discontinuations or deaths did not increase with increasing elotuzumab concentration.

The National Comprehensive Cancer Network (NCCN) Multiple Myeloma Clinical Practice Guideline (V3.2017) and the NCCN Drugs and Biologics Compendium indicate that elotuzumab is recommended in combination with lenalidomide and dexamethasone for the treatment of individuals with multiple myeloma who have received one to three prior therapies (category 1 recommendation).

Key Words:
Empliciti, elotuzumab, multiple myeloma

Approved by Governing Bodies:
On November 30, 2015, the U.S. Food and Drug Administration (FDA) granted approval to elotuzumab (Empliciti™) injection in combination with lenalidomide and dexamethasone for the treatment of individuals with multiple myeloma who have received one to three prior therapies.

Benefit Application:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply.
FEP: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:
CPT Codes:

J9176	Injection, elotuzumab 1 mg

References:

1. EMPLICITI™ (elotuzumab). Highlights of prescribing information. Bristol-Myers Squibb Company, Princeton, NJ. Revised November 2015. Available at: www.packageinserts.bms/pi/pi_empliciti.pdf.
2. Lonial S, Dimopoulos M, Palumbo A, et al. Elotuzumab therapy for relapsed or refractory multiple myeloma. N Engl J Med. 2015; 373(7):621-631.
3. National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium™ (electronic version). Available at: www.nccn.org.
4. NCCN Clinical Practice Guidelines in Oncology®. 2016 National Comprehensive Cancer Network, Inc. Multiple Myeloma (V.3.2017). Available at: www.nccn.org/index.asp.
5. Richardson PG, Jagannath S, Moreau P, et al; 1703 study investigators. Elotuzumab in combination with lenalidomide and dexamethasone in patients with relapsed multiple myeloma: final phase 2 results from the randomised, open-label, phase 1b-2 dose-escalation study. Lancet Haematol. 2015; 2(12):e516-527.

Policy History:
Medical Policy Group, May 2017 (**2**): New policy created
Medical Policy Administration Committee, May 2017
Available for comment May 15, 2017 through June 29, 2017

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.