BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Moxetumomab pasudotox-tdfk (Lumoxiti™)

File Name:	moxetumomab_lumoxiti
Origination:	4/2019
Last CAP Review:	8/2020
Next CAP Review:	8/2021
Last Review:	8/2020

Description of Procedure or Service

Moxetumomab pasudotox-tdfk (Lumoxiti™) is a CD22-directed cytotoxin indicated for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA).

HCL is a rare, slowly progressing cancer affecting B-cells in the blood, and accounts for roughly 2% of all lymphoid leukemias. It is typically characterized by high CD22 expression and presents with pancytopenia, splenomegaly and/or hepatomegaly, and increased risk of infection. Long-term complete remission is achieved in many patients using monotherapy with PNAs (i.e. pentostatin, cladribine); however, approximately half of patients relapse over time and subsequently require further treatment. Following relapse, PNA therapy provides lower and shorter response rates with higher risk of toxicity. Targeted therapies, such as rituximab, as monotherapy or in combination with purine analogs, and more recently, tyrosine kinase inhibitors, such as vemurafenib and ibrutinib, have demonstrated activity in relapsed and refractory HCL in phase 2 and small cohort studies. However, when used as single agents, they rarely eradicate minimal residual disease in patients who demonstrate complete response, and there are often safety and tolerability concerns. Newer therapies are sought that could lead to durable complete response with no minimal residual disease and with fewer associated toxicities.

Moxetumomab pasudotox-tdfk (Lumoxiti) is a CD22-directed cytotoxin that was approved by the U.S. Food and Drug Administration (FDA) in September 2018 for the treatment of relapsed or refractory HCL. It works by binding CD22 on the surface of B-cells and is internalized, which results in ADP-ribosylation of elongation factor 2, inhibition of protein synthesis, and apoptotic cell death.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for moxetumomab pasudotox-tdfk (Lumoxiti™) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Moxetumomab pasudotox-tdfk (Lumoxiti™)

When Moxetumomab pasudotox-tdfk (Lumoxiti) is covered

Moxetumomab pasudotox-tdfk (Lumoxiti) is considered medically necessary for the treatment of adult patients with hairy cell leukemia (HCL) when the following criteria are met:

- The patient has relapsed or refractory disease; **and**
- The patient has received at least two prior systemic therapies, including a purine nucleoside analog (i.e. pentostatin, cladribine); **and**
- The patient does not have severe renal impairment defined as CrCl ≤ 29 ml/min

Authorization: 6 months (maximum of 6 cycles) and may not be renewed.

Use of moxetumomab pasudotox-tdfk (Lumoxiti) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, (see Policy Guidelines); **OR**

- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Moxetumomab pasudotox-tdfk (Lumoxiti) is not covered

Moxetumomab pasudotox-tdfk (Lumoxiti) is considered **investigational** and therefore not covered when the above criteria are not met.

Moxetumomab pasudotox-tdfk (Lumoxiti) is considered investigational when used for:

1. Non-cancer indications; **OR**

2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Moxetumomab pasudotox-tdfk (Lumoxiti) is covered."

Policy Guidelines

The recommended dosing for Lumoxiti is 0.04 mg/kg given as a 30-minute intravenous infusion on days 1, 3, and 5 of every 28-day cycle. Lumoxiti treatment should be continued for a maximum of 6 cycles, or until disease progression or unacceptable toxicity occurs. Lumoxiti is not recommended in patients with severe renal impairment (CrCl ≤ 29 ml/min).

According to the manufacturer's safety information for Lumoxiti, the most common adverse reactions (≥20% incidence) include infusion-related reactions, edema, nausea, fatigue, headache, fever, constipation, anemia, and diarrhea. The most common laboratory abnormalities (≥50%) include increased creatinine, increased ALT and AST, hypoalbuminemia, hypocalcemia, and hypophosphatemia.

The FDA issued black box warnings for Capillary Leak Syndrome (CLS) and Hemolytic Uremic Syndrome (HUS) in patients receiving Lumoxiti.

The efficacy of moxetumomab pasudotox (Lumoxiti) was evaluated in a multicenter, open-label study of 80 patients with relapsed/refractory hairy cell leukemia (HCL). Patients included in the trial were at least 18 years of age and had histologically confirmed HCL with an indication for treatment. Patients must also have received at least two prior systemic therapies, including two courses of a purine nucleoside analog (PNA), or at least one course of a PNA and one course of either rituximab or a *BRAF* inhibitor. Patients received moxetumomab pasudotox 0.04 mg/kg intravenously over 30 minutes on days 1, 3, and 5 every 28 days for a maximum of six cycles or until disease progression, unacceptable toxicity, initiation of alternate therapy, or documented complete response (CR). The median duration of follow-up was 16.7 months (range: 2 to 49). The primary endpoint was durable CR, defined as CR with maintenance of hematologic remission for greater than 180 days as assessed by blinded independent central review and based on no evidence of hairy cells in bone marrow, imaging studies and normalization of hematologic parameters. Additional efficacy endpoints included objective response rate, duration of complete and objective response, progression-free survival, safety/tolerability, immunogenicity, and pharmacokinetics. The durable CR rate was 30% (24/80 patients; 95% CI, 20 to 41), the CR rate was 41% (33/80 patients; 95% CI, 30 to 53), and the objective response rate (CR and partial response) was 75% (60/80 patients; 95% CI, 64 to 84); 64 patients (80%) achieved hematologic remission. Among the 33 complete responders, 85% (n=27) achieved minimal residual disease negativity. Three deaths occurred due to infection or underlying HCL; none were considered treatment related. The most common treatment-related adverse events leading to discontinuation were CLS (n=2), HUS (n=4) and increased blood creatinine (n=2, both associated with HUS). All CLS and HUS events were reversible.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J9313, S0353, S0354*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

AstraZeneca Pharmaceuticals LP. Lumoxiti (moxetumomab pasudotox-tdfk) injection for intravenous use. Highlights of prescribing information. January 2019. Available at: https://www.azpicentral.com/lumoxiti/lumoxiti.pdf#page=1. Accessed March 2019.

U.S. Food and Drug Administration. FDA approves new kind of treatment for hairy cell leukemia. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm620448.htm. Accessed March 2019.

Kreitman RJ, Dearden C, Zinzani PL, et al. Moxetumomab pasudotox in relapsed/refractory hairy cell leukemia. Leukemia. 2018 Aug;32(8):1768-77. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6087717/pdf/41375_2018_Article_210.pdf. Accessed March 2019.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Hairy Cell Leukemia, version 3.2019. Revised January 31, 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed March 2019.

Medical Director review 4/2019

Specialty Matched Consultant Advisory Panel 8/2019

Specialty Matched Consultant Advisory Panel 8/2020

Policy Implementation/Update Information

4/16/19 New policy developed. Lumoxiti is considered medically necessary for the treatment of adult patients with hairy cell leukemia (HCL). Added HCPCS codes C9045, J3490, J3590, J9999, S0353, and S0354 to Billing/Coding section. References added. Medical Director review 4/2019. (krc)

10/1/19 Specialty Matched Consultant Advisory Panel review 8/21/2019. No change to policy intent. Added HCPCS code J9313 to Billing/Coding section and deleted codes C9045, J3490, J3590, and J9999 effective 10/1/19. (krc)

9/22/20 Specialty Matched Consultant Advisory Panel review 8/19/2020. No change to policy intent. (krc)