Lumoxiti™ (moxetumomab pasudotox-tdfk)
(Intravenous)

-E-

Document Number: IC-0474

Last Review Date: 12/01/2020
Date of Origin: 07/01/2019
Dates Reviewed: 07/2019, 12/2019, 12/2020

I. Length of Authorization

Coverage is provided for six months (6 cycles) and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

– Lumoxiti 1 mg SDV: 15 vials per 28 day cycle

B. Max Units (per dose and over time) [HCPCS Unit]:

- 500 billable units on days 1, 3 and 5 of a 28-day cycle

III. Initial Approval Criteria [1-3]

Coverage is provided in the following conditions:

- Patient is at least 18 years or older; **AND**
- Patient does not have severe renal impairment defined as CrCl ≤ 29 mL/min; **AND**
- Patient does not have prior history of severe thrombotic microangiopathy (TMA) or hemolytic uremic syndrome (HUS); **AND**
- Must be used as a single agent; **AND**

Hairy Cell Leukemia (HCL) † Φ [1-4]

- Patient has a confirmed diagnosis of Hairy Cell Leukemia or a HCL variant; **AND**
- Patient must have relapsed or refractory disease; **AND**
- Patient has previously failed at least TWO prior systemic therapies consisting of one of the following:
  - Failure to two courses of purine analog therapy (e.g., cladribine, pentostatin, etc.); **OR**
  - Failure to at least one purine analog therapy AND one course of rituximab or a BRAF-inhibitor (e.g., vemurafenib, etc.)

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

IV. Renewal Criteria

Coverage cannot be renewed.

V. Dosage/Administration

Indication	Dose
Hairy Cell Leukemia	0.04 mg/kg intravenously on days 1, 3, and 5 of a 28-day cycle. Continue for a maximum of 6 cycles or until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J9313 – Injection, moxetumomab pasudotox-tdfk, 0.01 mg; 1 billable unit = 0.01 mg

NDC:

- Lumoxiti 1 mg single-dose vial: 00310-4700-xx
    - IV solution stabilizer for use during administration: 00310-4715-xx

VII. References (STANDARD)

1. Lumoxiti [package insert]. Wilmington, DE; Astra Zeneca Pharmaceuticals; April 2020. Accessed October 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for moxetumomab pasudotox. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2020.
3. Kreitman RJ, Dearden C, Zingani PL, et al. Moxetumomab pasudotox in relapsed/refractory hairy cell leukemia. Leukemia. 2018; 32(8): 1768–1777.
4. Robbins BA, Ellison DJ, Spinosa JC, et al. Diagnostic application of two-color flow cytometry in 161 cases of hairy cell leukemia. Blood 1993;82:1277-1287.
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Hairy Cell Leukemia, Version 1.2021. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer

Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2020.

VIII. References (ENHANCED)

1e. Chihara D, Kantarjian H, O'Brien S, et al. Long-term durable remission by cladribine followed by rituximab in patients with hairy cell leukaemia: update of a phase II trial. Br J Haematol. 2016;174(5):760–766.

2e. Else M, Dearden CE, Matutes E, et al. Rituximab with pentostatin or cladribine: an effective combination treatment for hairy cell leukemia after disease recurrence. Leuk Lymphoma. 2011 Jun;52 Suppl 2:75-8.

3e. Nieva J, Bethel K, Saven A. Phase 2 study of rituximab in the treatment of cladribine-failed patients with hairy cell leukemia. Blood. 2003 Aug 1;102(3):810-3.

4e. Zenhäusern R, Simcock M, Gratwohl A, et al. Rituximab in patients with hairy cell leukemia relapsing after treatment with 2-chlorodeoxyadenosine (SAKK 31/98). Haematologica. 2008 Sep;93(9):1426-8.

5e. Goodman GR, Burian C, Koziol JA, Saven A. Extended follow-up of patients with hairy cell leukemia after treatment with cladribine. J Clin Oncol. 2003 Mar 1;21(5):891-6.

6e. Jones J, Andritsos L, Kreitman RJ, et al. Efficacy and Safety of the Bruton Tyrosine Kinase Inhibitor Ibrutinib in Patients with Hairy Cell Leukemia: Stage 1 Results of a Phase 2 Study. Blood. 2016;128:1215.

7e. Park JH, Lee JO, Stone RM, et al. Acquired Resistance to BRAF Inhibition in Hcl Is Rare and Retreatment with Vemurafenib at Relapse Can Induce High Response Rates: Final Results of a Phase II Trial of Vemurafenib in Relapsed Hcl. Blood. 2018;132:392.

8e. Tiacci E, De Carolis L, Zaja F, et al. The Chemotherapy-Free Combination of Vemurafenib and Rituximab Produces Deep and Durable Responses in Relapsed or Refractory Hairy Cell Leukemia (HCL) Patients. Blood. 2017;130:409.

9e. Magellan Health, Magellan Rx Management. Lumoxiti Clinical Literature Review Analysis. Last updated October 2020. Accessed October 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C91.40	Hairy cell leukemia not having achieved remission
C91.42	Hairy cell leukemia, in relapse

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; DLBCL = diffuse large B-cell lymphoma; MRD = minimal residual disease; TLS = tumor lysis syndrome; IPI = International Prognostic Index; ASCT = autologous stem-cell transplantation; TTF = time to treatment failure; DFS = disease free survival

Hairy Cell Leukemia

Relapsed or Refractory Disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Moxetumomab pasudotox	2A preferred	Yes (after at least 2 prior therapies, including a purine analog)	Phase 3, multi-center, single-arm, open-label	N/A	CR	Relapsed or refractory HCL after at least 2 prior therapies (including 2 courses of a purine nucleoside analog or one course of rituximab or a BRAF inhibitor following a single prior purine nucleoside analog course)	• Moxetumomab pasudotox treatment achieved a high response rate of 75% and MRD eradication in heavily pretreated patients with HCL.
Cladribine followed by rituximab	2A	No	Phase 2	N/A	-----	Untreated and relapsed HCL	• Cladribine followed by rituximab is highly effective even in patients with relapsed HCL with a CR rate of 100%.
Rituximab + pentostatin or cladribine	2A	No	Retrospective study	N/A	-----	Relapsed HCL	• The combination of a purine analog with rituximab was effective for patients with recurrent HCL with a CR rate of 89%.

Rituximab	2A (if unable to receive purine analogs)	No	Phase 2	N/A	-----	Refractory disease after prior cladribine	• Rituximab has only modest single-agent activity in cladribine-failed HCL with an ORR of 25% and CR of 13%.
Rituximab	2A (if unable to receive purine analogs)	No	Phase 2	N/A	-----	Refractory disease after prior cladribine	• Rituximab demonstrated clinical activity in refractory HCL with an ORR of 80% and CR of 32%.
Cladribine re-treatment	2A	Yes	Extended follow-up	N/A	-----	Relapsed disease	• Retreatment with cladribine is an effective treatment for relapsed HCL with a CR rate of 75% after first relapse and 60% after subsequent relapse.
Ibrutinib	2A	No	Phase 2	N/A	-----	Treatment naïve and relapsed disease	• Ibrutinib can induce remission in HCL including heavily pre-treated patients with an ORR of 46%.
Vemurafenib	2A	No	Phase 2	N/A	ORR	Relapsed or refractory disease after purine analogs	• High response rates with vemurafenib monotherapy in patients with relapsed or refractory HCL was confirmed with an ORR of 86% at a median 24-month follow up.
Vemurafenib + rituximab	2A (after therapy for relapsed or refractory disease)	No	Phase 2	N/A	-----	Relapsed or refractory HCL	• Vemurafenib plus rituximab represents a regimen that produces deep and durable responses in heavily pre-treated relapsed/refractory HCL patients with a CR rate and 14-mon PFS rate of 100%.