Clinical Policy Title:	moxetumomab pasudotox-tdfk
Policy Number:	RxA.400
Drug(s) Applied:	Lumoxiti®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Moxetumomab pasudotox-tdfk (Lumoxiti®) is a CD22-directed cytotoxin. It is 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).

Limitation(s) of use:
Not recommended in patients with severe renal impairment (CrCl ≤ 29 mL/min).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
moxetumomab pasudotox-tdfk (Lumoxiti®)	HCL	0.04 mg/kg intravenously on Days 1, 3, and 5 of each 28-day cycle. Continue treatment for maximum of 6 cycles, disease progression, or unacceptable toxicity.	0.04 mg/kg/dose (actual body weight)

Dosage Forms

- Single-dose vial: 1 mg lyophilized cake or powder for reconstitution

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. Hairy Cell Leukemia (must meet all)**:**

1. Diagnosis of HCL;
2. Prescribed by or in consultation with an oncologist or hematologist;

3. Age ≥ 18 years;
4. Disease is relapsed or refractory;
5. Received at least two prior systemic therapies *(*see Appendix B for examples*)*, one of which must be a purine nucleoside analog (e.g., cladribine, Nipent®), unless contraindicated or clinically significant adverse effects are experienced;*
   *Prior authorization may be required.
6. Request meets one of the following (a or b):
   *Prescribed regimen must be FDA-approved or recommended by NCCN.
   a. Dose does not exceed 0.04 mg/kg/dose (actual body weight) for three days of each 28-day cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Hairy Cell Leukemia (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Lumoxiti® for a covered indication 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):
   *Prescribed regimen must be FDA-approved or recommended by NCCN.
   a. New dose does not exceed 0.04 mg/kg/dose (actual body weight) for three days of each 28-day cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CR: Complete Response
FDA: Food and Drug Administration
HCL: Hairy Cell Leukemia
NCCN: National Comprehensive Cancer Network
PNA: Purine Nucleoside Analog
CLS: Capillary Leak Syndrome
HUS: Hemolytic Uremic Syndrome

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
cladribine (Mavenclad®) *(purine analog)*	Adult dose: 0.09 mg/kg intravenously once dailyfor 7 days (off-label subcutaneous dosing has been evaluated).	0.09 mg/kg/day
pentostatin (Nipent™) *(purine analog)*	Adult dose: 4 mg/m^2 intravenously once every other week up to 6 months if failure to respond.	4 mg/m^2/dose once every other week
Intron A® (interferon alfa-2b)	Adult dose: 2 million units/m^2 intramuscularly or subcutaneously 3 times a week for up to 6 months if failure to respond.	2 million units/m^2/dose
Rituxan® (rituximab)	Off-label adult dose: 375 mg/m^2 intravenously weekly up to 10 weeks has been reported. (Micromedex)	Varies
Imbruvica® (ibrutinib)	Off-label adult dose: 420 mg orally once daily in 28day cycles until unacceptable toxicity or progressive disease. (Jones 2016)	Varies
Zelboraf® (vemurafenib)	Off-label adult dose: 960 mg orally twice daily for up to 24 weeks. (Clinical Pharmacology)	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):
  - Capillary leak syndrome (CLS), including life-threatening cases, occurred in patients receiving Lumoxiti®. Delay dosing or discontinue Lumoxiti® as recommended.
  - Hemolytic uremic syndrome (HUS), including life-threatening cases, occurred in patients receiving Lumoxiti®. Discontinue Lumoxiti® in patient with HUS.

APPENDIX D: General Information

The National Comprehensive Cancer Network (NCCN) HCL treatment recommendations:

- First-line therapy: purine analogs (cladribine, pentostatin).
- Second-line therapy for relapse/refractory or progressive disease:
  - Disease relapse ≥ 2 years after achieving CR to initial therapy:
    - Retreatment with the same purine analog + rituximab;
    - An alternate purine analog + rituximab;
    - Rituximab monotherapy if unable to receive a purine analog.
  - Disease relapse < 2 years after achieving CR to initial therapy:
    - An alternate purine analog + rituximab;
    - Vemurafenib;
    - Interferon alpha;

    - Rituximab monotherapy if unable to receive purine analog.
- Third-line therapy and beyond for progressive disease:
    - Vemurafenib ± rituximab;
    - Ibrutinib;
    - Lumoxiti®.

References

1. Lumoxiti® Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; J April 2020. Available at: https://www.lumoxiti.com/. Accessed June 1, 2021.
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3. National Comprehensive Cancer Network Guidelines. Hairy Cell Leukemia Version 2. March 2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed June 1, 2021.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed June 1, 2021.
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6. Jones J, Andritsos L, Kreitman RJ, et al. (2016). 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, 128(22), 1215.
7. Tiacci E, Park JH, De Carolis L, et al. Targeting Mutant BRAF in Relapsed or Refractory Hairy-Cell Leukemia. N Engl J Med. 2015 Oct 29;373(18):1733-47. doi: 10.1056/NEJMoa1506583. Epub 2015 Sep 9.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy description table was updated 2. Dosage form was updated 3. Continuation therapy criteria II.A.1. rephrased to “Member is currently receiving medication that has been authorized by RxAdvance” 4. Appendix A, Abbreviation/Acronym Key updated to include CLS, HUS 5. References were updated	07/21/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample, ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial Approval Criteria and Continued Therapy Approval Criteriawere updated to remove HIM approval duration.	6/1/2021	09/14/2021

3. Therapeutic Alternatives was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 4. Appendix B was updated to include "Mavenclad" brand. 5. Statement about drug listing format in Appendix B is rephrased 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". 6. Appendix C was updated to include detailed Boxed Warnings for CLS and HUL, “including life-threatening cases, occurred in patients…” 7. References were reviewed and updated.		