RXADVANCE
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Clinical Policy Title:	moxetumomab pasudotox-tdfk
Policy Number:	RxA.400
Drug(s) Applied:	Lumoxiti ™
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
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 IV 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.

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
HIM: 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
HIM: 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 Cancer
PNA: Purine nucleoside analog
CLS: Capillary Leak Syndrome
HUS: Hemolytic Uremic Syndrome

APPENDIX B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cladribine (Cladribine Novaplus) *(purine analog)*	Adult dose: 0.09 mg/kg IV QD for 7 days (off-label SC	0.09 mg/kg/day

	dosing has been evaluated).	
Nipent ™ (pentostatin) *(purine analog)*	Adult dose: 4 mg/m^2 IV 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 IM or SC 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 IV weekly up to 10 weeks has been reported. (Micromedex)	Varies
Imbruvica ® (ibrutinib)	Off-label adult dose: 420 mg PO QD in 28day cycles until unacceptable toxicity or progressive disease. (Jones 2016)	Varies
Zelboraf® (vemurafenib)	Off-label adult dose: 960 mg PO BID for up to 24 weeks. (Clinical Pharmacology)	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None

- Boxed Warning(s):
  - Capillary leak syndrome (CLS)
  - Hemolytic uremic syndrome (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 o Disease relapse < 2 years after achieving CR to initial therapy:

- An alternate purine analog ± rituximab
- Interferon alpha
- Rituximab monotherapy if unable to receive purine analog
- Vemurafenib

- Third-line therapy and beyond for progressive disease:
  - Vemurafenib ± rituximab o Ibrutinib
  - Lumoxiti

References

1. Lumoxiti Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; J April 2020. Available at: https://www.lumoxiti.com/. Accessed July 21, 2020.
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3. National Comprehensive Cancer Network Guidelines. Hairy Cell Leukemia Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed July 20, 2020.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed July 21, 2020.
5. Micromedex Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed July 21, 2020.
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