Clinical Policy: Moxetumomab pasudotox-tdfk (Lumoxiti)

Reference Number: PA.CP.PHAR.398
Effective Date: 01.19
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Revision Log

Description
Moxetumomab pasudotox-tdfk (Lumoxiti™) is a CD22-directed cytotoxin.

FDA Approved Indication(s)
Lumoxiti 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).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Lumoxiti is **medically necessary** when the following criteria are met:

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)*, one of which must be a purine nucleoside analog (e.g., cladribine, Nipent®), unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 0.04 mg/kg/dose (actual body weight);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 0.04 mg/kg/dose (actual body weight);
   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: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLS: Capillary Leak Syndrome
CR: complete response
FDA: Food and Drug Administration
HCL: hairy cell leukemia
HUS: Hemolytic Uremic Syndrome
PNA: purine nucleoside analog

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	Adult dose: 0.09 to 0.1 mg/kg/day continuous IV infusion for 7 days or 0.1 mg/kg/day SC for 7 days	0.1 mg/kg/day continuous IV or SC
Nipent® (pentostatin)	Adult dose: 4 mg/m^2 IV as a single dose once every other week. The optimal duration of treatment has not been determined. In the absence of major toxicity and with observed continuing improvement, the patient should be treated	4 mg/m^2 IV as a single dose once every other week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	until a complete response (CR) has been achieved.	
Intron A® (interferon Alfa-2b)	Adult dose: 2 million International Units/m^2 IM or SC 3 times a week for up to 6 months. Administer interferon alfa-2b SC as opposed to IM if the patient's platelet counts is less than 50,000/mm^3.	35 million International Units/m^2 SC or IM as a single dose.
Rituxan® (rituximab)	Off-label adult dose: 375 mg/m^2 IV weekly for 8 weeks	Not applicable
Imbruvica® (ibrutinib)	Off-label adult dose: 420 mg PO once daily in 28-day cycles. Patients experiencing clinical benefit may continue ibrutinib until unacceptable toxicity or progressive disease.	Not applicable
Zelboraf® (vemurafenib)	Off-label adult dose: 960 mg PO twice daily for 12 weeks	Not applicable

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 reported
- Boxed warning(s): capillary leak syndrome (CLS), hemolytic uremic syndrome (HUS)

Appendix D: General Information

- Per the National Comprehensive Cancer Network (NCCN) Hairy Cell Leukemia Treatment Guidelines (Version 2.2019), first line therapy with purine analogs (cladribine or pentostatin) is recommended for patients with indications for treatment. If patients have less than a CR to initial therapy, options include treatment with an alternate purine analog with or without rituximab, interferon alpha, rituximab monotherapy (if unable to receive purine analog), or vemurafenib.
- Second-line therapy for relapse/refractory or progressive disease depends on the quality and duration of remission to initial therapy.
  - Patients with disease relapse after ≥ 2 years after achieving CR to initial therapy with purine analog may benefit from retreatment with the same purine analog with or without rituximab. Other options include treatment with alternative purine analog with or without rituximab or rituximab monotherapy (if unable to receive purine analog).
  - For patients with disease relapse < 2 years after achieving CR to initial therapy, treatment options include alternate purine analog with or without rituximab, interferon alpha, rituximab monotherapy (if unable to receive purine analog), or vemurafenib.
- Vemurafenib with or without rituximab, ibrutinib, or Lumoxiti are appropriate options for progressive disease following second-line therapy.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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)

VI. Product Availability

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

VII. References

1. Lumoxiti Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; September 2018. Available at: https://www.lumoxiti.com/. Accessed September 17, 2018.
2. National Comprehensive Cancer Network Guidelines. Hairy Cell Leukemia Version 2.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed October 1, 2018.
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4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed September 17, 2018.
5. 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 Sep;174(5):760-6. doi: 10.1111/bjh.14129. Epub 2016 Jun 15.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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