Clinical Policy: Moxetumomab pasudotox-tdfk (Lumoxiti)

Reference Number: CP.PHAR.398
Effective Date: 10.16.18
Last Review Date: 11.18
Line of Business: Commercial, Medicaid, HIM-Medical Benefit Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 Centene Corporation® 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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):
   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:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   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): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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 policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit or 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 until a complete response (CR) has been achieved.	4 mg/m^2 IV as a single dose once every other week
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.
3. Kreitman R, Dearden C, Zinzani P, et al. Moxetumomab pasudotox in relapsed/refractory hairy cell leukemia. Leukemia. 2018 Aug;32(8):1768-1777.
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
Policy created	10.16.18	11.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.