Clinical Policy: Romidepsin (Istodax)

Reference Number: LA.PHAR.314
Effective Date: 11.04.23
Last Review Date: 11.20.25~~12.03.24~~
Line of Business: Medicaid

Coding Implications
Revision Log

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

****Please note: This policy is for medical benefit****

Description
Romidepsin (Istodax®) is a histone deacetylase inhibitor.

FDA Approved Indication(s)
Istodax is indicated for the treatment of cutaneous T-cell lymphoma (CTCL) in adult patients who have received at least one prior systemic therapy.

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 Louisiana Healthcare Connections that Istodax and romidepsin injection solution are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. T-Cell Lymphoma (must meet all)**:**

1. Diagnosis of one of the following T-cell lymphomas (a, b, c, d, or e):
   a. CTCL (*see Appendix D for examples of subtypes*);
   b. Hepatosplenic T-cell lymphoma;
   c. Extranodal NK/T-cell lymphoma;
   d. Peripheral T-cell lymphoma (*see Appendix E for examples of subtypes*);
   e. Breast implant-associated anaplastic large cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Failure of at least one prior systemic therapy, unless member has one of the following (a, b, or c):
   a. Mycosis fungoides;
   b. Sezary syndrome;
   c. Peripheral T-cell lymphoma and request is for palliative therapy;
5. For Istodax requests, member must use romidepsin, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 14 mg/m^2 on days 1, 8, and 15 of a 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*).

Formatted: Tab stops: Not at 3.59" + 5.23"

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: ~~6~~12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy ~~for the relevant line of business:~~ LA.PMN.53 ~~for Medicaid~~.

II. Continued Therapy

A. T-Cell Lymphoma (must meet all)**:**

1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Istodax for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Istodax requests, member must use romidepsin, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, meets one of the following (a or b):
   a. New dose does not exceed 14 mg/m^2 on days 1, 8, and 15 of a 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy ~~for the relevant line of business:~~ LA.PMN.53 ~~for Medicaid~~.

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 – LA.PMN.53 ~~for Medicaid or evidence of coverage documents~~.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CTCL: cutaneous T-cell lymphoma
FDA: Food and Drug Administration
ICC: International Consensus Classification
MF: mycosis fungoides
NCCN: National Comprehensive Cancer Center

Formatted: Font: Not Bold
Formatted: Indent: Left: 0", First line: 0.25"
Formatted: Indent: Left: 0", First line: 0.25"
Formatted: Indent: Left: 0.25", Tab stops: 0.38", Left
Formatted: Indent: Left: 0.25", First line: 0"

WHO5: World Health Organization 5th edition

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: WHO-EORTC Classification of CTCL with Primary Cutaneous Manifestations*

- Mycosis fungoides (MF)
  - MF variants and subtypes
    - Folliculotropic MF
    - Pagetoid reticulosis
    - Granulomatous slack skin
- Sezary syndrome
- Adult T-cell leukemia/lymphoma
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Cutaneous anaplastic large cell lymphoma (C-ALCL)
  - Lymphomatoid papulosis (LyP)
- Subcutaneous panniculitis-like T-cell lymphoma
- Primary cutaneous peripheral T-cell lymphoma, rare subtypes
  - Primary cutaneous gamma-delta T-cell lymphoma
  - Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma
  - Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder
  - Primary cutaneous acral CD8+ T-cell lymphoma
  - Primary cutaneous peripheral T-cell lymphoma, not otherwise unspecified
- MF is the most common cutaneous T-cell lymphoma. Sezary syndrome is closely related to MF accounting for less than 5% of cutaneous lymphomas.

**CTCL is classified as a non-Hodgkin T-cell lymphoma. CTCL classification schemes are periodically advanced as new information becomes available; therefore, the above list is provided as general guidance. For additional information, see the 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas.*

Appendix E: Types of Peripheral T-Cell Lymphomas†*

- Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)
- Enteropathy-associated T-cell lymphoma (EATL)
- Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)
- Angioimmunoblastic T-cell lymphoma (AITL)/ (follicular helper T-cell lymphoma [TFH lymphoma], angioimmunoblastic type [ICC]/nodal TFH cell lymphoma, angioimmunoblatic-type [WHO5])
- Nodal PTCL with TFH phenotype (nodal PTCL, TFH)/ TFH lymphoma, NOS (ICC)/nodal TFH cell lymphoma (WHO5)
- Follicular T-cell lymphoma (FTCL)/ TFH lymphoma, follicular type (ICC)/nodal TFH cell lymphoma, follicular-type (WHO5)

Formatted: Indent: Left: 0.25", First line: 0"

- Anaplastic large cell lymphoma (ALCL~~)~~), ALK positive/ALK-positive ALCL
- ALCL, ALK negative/ALK-negative ALCL

**Although the FDA-labeled indication for peripheral T-cell lymphoma was withdrawn in August 2021 following findings from the confirmatory phase 3 trial, the NCCN continues to support use in this indication based on the results of the phase 2 trial and other subsequent trials.*
†ICC: International Consensus Classification; WHO5:5th edition of the World Health Organization

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CTCL	14 mg/m^2 IV over a 4-hour period on days 1, 8, and 15 of a 28-day cycle. Repeat cycles every 28 days provided that the patient continues to benefit from and tolerates the drug.	14 mg/m^2/dose

VI. Product Availability

Single-dose vial: 10 mg

VII. References

1. Istodax Prescribing Information. Summit, NJ: Celgene Corporation; July 2021. Available at https://packageinserts.bms.com/pi/pi_istodax.pdf. Accessed July ~~15, 2024~~10, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August ~~19, 2024~~31, 2025.
3. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version ~~2.2024~~3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed August ~~19, 2024~~31, 2025.
4. National Comprehensive Cancer Network. Peripheral T-Cell Lymphomas Version ~~4.2024~~2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed August ~~19, 2024.~~31, 2025.
5. Willemze R, Cerroni L, Kempf W, et al. The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. *Blood*. May 2019; 133: 1703-1714.
6. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016; 127: 2375-2390.

Formatted: Italian (Italy)

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9319	Injection, romidepsin, lyophilized, 0.1 mg
J9318	Injection, romidepsin, non-lyophilized, 0.1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	06.16.23	10.05.23
Annual review: : no significant changes; updated J code and added "J9318" code; references reviewed and updated.	04.04.24	07.10.24
For initial therapy, added criteria option "unless peripheral T-cell lymphoma and request is for palliative therapy" under criteria "Failure of at least one prior systemic therapy" to align with NCCN compendium and guideline; for Appendix D, updated subtypes for WHO-EORTC Classification of CTCL with Primary Cutaneous Manifestations; for Appendix E, updated subtypes for Peripheral T-Cell Lymphomas; updated description for HCPCS code [J9319]; references reviewed and updated.	12.03.24	3.17.25
Annual review: no significant changes; extended initial approval duration from 6 to 12 months; references reviewed and updated.	11.20.25	

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.