

## Clinical Policy: Romidepsin (Istodax)

Reference Number: PA.CP.PHAR.314

Effective Date: 01/2018

Last Review Date: 10/2023

[Coding Implications](#)[Revision Log](#)

### Description

Romidepsin (Istodax<sup>®</sup>) 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
- Peripheral T-cell lymphoma (PTCL) in adult patients who have received at least one prior therapy
  - This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

### Policy/Criteria

It is the policy of PA Health & Wellness<sup>®</sup> that Istodax is **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  $\geq$  18 years;
4. Failure of at least one prior systemic therapy, unless member has mycosis fungoides, Sezary syndrome or initial palliative intent therapy for peripheral T-cell lymphoma;
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<sup>2</sup> for three days of a 28-day cycle;
  - b. Requested 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 Approval**

**A. All Indications in Section I (must meet all):**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies, or documentation supports that member is currently receiving Istodax for a covered indication;
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<sup>2</sup> for three days 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*).

**Approval duration: 12 months**

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHARM.01) applies; or
2. Refer to the 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 policies – PA.CP.PMN.53

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CTCL: cutaneous T-cell lymphoma  
FDA: Food and Drug Administration  
MF: mycosis fungoides  
EBV: Epstein-Barr virus

NCCN: National Comprehensive Cancer Center  
PTCL: peripheral T-cell lymphoma

*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
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Primary cutaneous peripheral T-cell lymphoma, not otherwise unspecified
- Primary cutaneous peripheral T-cell lymphoma, rare subtypes
  - Primary cutaneous delta/gamma T-cell lymphoma
  - CD8+ AECTCL (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
- 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 WHO's 2016 updated classification of hematological malignancies for a complete list of lymphoid neoplasms, including CTCL.*

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

- Peripheral T-cell lymphoma, not otherwise specified
- Enteropathy-associated T-cell lymphoma (EATL)
- Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)
- Angioimmunoblastic T-cell lymphoma (AITL), including nodal peripheral T-cell lymphoma with TFH phenotype (PTCL, TFH), and follicular T-cell lymphoma (FTCL)
- Anaplastic large cell lymphoma

*\*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.*

**V. Dosage and Administration**

| Indication    | Dosing Regimen   | Maximum Dose               |
|---------------|--|----------------------------|
| CTCL,<br>PTCL | 14 mg/m <sup>2</sup> 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 <sup>2</sup> /dose |

## **VI. Product Availability**

Single-dose vial: 10 mg

Generic injection solution: 27.5 mg/5.5 mL

## **VII. References**

1. Istodax Prescribing Information. Summit, NJ: Celgene Corporation; July 2021. Available at [https://packageinserts.bms.com/pi/pi\\_istodax.pdf](https://packageinserts.bms.com/pi/pi_istodax.pdf). Accessed August 6, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed August 6, 2023.
3. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 1.2023. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/primary\\_cutaneous.pdf](https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf). Accessed August 6, 2023.
4. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2023. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/t-cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf). August 6, 2023.
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.

## **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.

| <b>HCPCS Codes</b> | <b>Description</b>                             |
|--------------------|--|
| J9319              | Injection, romidepsin, 1 mg                    |
| J9318              | Injection, romidepsin, non-lyophilized, 0.1 mg |

| Reviews, Revisions, and Approvals  | Date    | Approval Date |
|--|---------|---------------|
| 4Q 2018 annual review: summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; PTCL: extended initial approval duration from 3 to 6 months; updated continued therapy section to include language for continuity of care; references reviewed and updated.   | 07/2018 |               |
| 4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020  | 10/2019 |               |
| 4Q 2020 annual review: FDA dosing cycle details added; FDA/NCCN labeling requirement added; added new dose form romidepsin injection solution to the policy; updated Appendix B; updated Appendix E with additional PTCL subtypes per NCCN; references reviewed and updated.   | 10/2020 |               |
| 4Q 2021 annual review: added a trial of 1 systemic therapy in CTCL coverage as per FDA approved indication; updated Appendix B Therapeutic Alternatives for CTCL and classification/subtypes in Appendix D and E; references reviewed and updated.   | 10/2021 |               |
| 4Q 2022 annual review: per NCCN, clarified CTCL vs other coverable T-cell lymphomas; per NCCN and PI, added requirement for failure of at least one prior systemic therapy, unless member has mycosis fungoides or Sezary syndrome; added redirection to generic; updated classification/subtypes in Appendix D and added Appendix E; updated HCPCS code; references reviewed and updated. | 10/2022 |               |
| 4Q 2023 annual review: no significant changes; updated J code and added “J9318” code; references reviewed and updated.   | 10/2023 |               |