Clinical Policy: Romidepsin (Istodax)

Reference Number: PA.CP.PHAR.314
Effective Date: 01/2018
Last Review Date: 10/2024

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
- 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 ® 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-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-d):
   a. Mycosis fungoides;
   b. Sezary syndrome;
   c. Peripheral T-cell lymphoma and request is for palliative therapy;
   d. Subcutaneous panniculitis-like T-cell lymphoma with one of the following (i-iii):
      i. Hemophagocytic lymphohistiocytosis;
      ii. Systemic disease;
      iii. High tumor burden (widespread subcutaneous disease);
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 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.PHARM.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^2 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.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
ICC: International Consensus Classification
MF: mycosis fungoides
EBV: Epstein-Barr virus
NCCN: National Comprehensive Cancer Center
PTCL: peripheral T-cell lymphoma
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
  - Lymphomatoid papulosis
- 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
- 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 peripheral T-cell lymphoma with TFH phenotype (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)
- Anaplastic large cell lymphoma (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, PTCL	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.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 19, 2024.
3. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed August 19, 2024.
4. National Comprehensive Cancer Network. T-Cell Lymphomas Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. August 19, 2024.
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.

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

Reviews, Revisions, and Approvals	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 Appendin 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
4Q 2024 annual review: 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.	10/2024