Clinical Policy: Romidepsin (Istodax)

Reference Number: ERX.SPA. 267
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

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

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Istodax and romidepsin injection solution are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of CTCL *(see Appendix D for examples of CTCL subtypes*);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. 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. 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: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. If request is for a dose increase, request 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 guideline 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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
- Extranodal NK*/T-cell lymphoma, nasal type
- *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+ AECTL (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.*

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

- Istodax 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. Accessed August 18, 2021.
2. Romidepsin Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208574Orig2lbl.pdf. Accessed August 18, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 17, 2020.
4. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed August 14, 2021.
5. National Comprehensive Cancer Network. Peripheral T-Cell Lymphomas Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed August 14, 2021.
6. 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.
7. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.12.18	11.18
4Q 2019 annual review: no significant changes; FDA dosing cycle details added; FDA/NCCN labeling requirement added; references reviewed and updated.	08.20.19	11.19
RT4: Added new dose form romidepsin injection solution to the policy.	03.30.20	
4Q 2020 annual review: no significant changes; updated Appendix B; updated Appendix E with additional PTCL subtypes per NCCN; references reviewed and updated.	08.18.20	11.20
RT4: removed PTCL indication per updated labeling as it failed to demonstrate clinical benefit in a phase 3 confirmatory trial.	08.18.21	
4Q 2021 annual review: no significant changes; updated classification/subtypes in Appendix D; references reviewed and updated.	08.19.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.