Clinical Policy Title:	romidepsin
Policy Number:	RxA.175
Drug(s) Applied:	Istodax®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Istodax® is a histone deacetylase (HDAC) inhibitor. It 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
romidepsin (Istodax®)	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

Dosage Forms

- romidepsin (Istodax®)- Kit, lyophilized powder in a 10 mg single-dose vial for injection: 11 mg romidepsin and 22 mg bulking agent povidone, USP; sterile diluent 2.4 mL of 80% propylene glycol, USP and 20% dehydrated alcohol, USP.
- romidepsin - Injection solution in a single-dose vial: 10 mg/2 mL, 27.5 mg/5.5 mL.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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):

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

   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
Commercial: 6 months
Medicaid: 6 months

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

1. Diagnosis of peripheral T-cell lymphoma (PTCL) (see Appendix E for examples of PTCL subtypes);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member has received at least one prior therapy (e.g., chemotherapy/biologic therapy, radiation therapy, hematopoietic stem cell transplantation);
5. Request meets one of the following (a or b):
   *Prescribed regimen must be FDA-approved or recommended by NCCN.
   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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance, 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, meets one of the following (a or b):

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

   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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CTCL: Cutaneous T-cell Lymphoma
MF: Mycosis Fungoides
NCCN: National Comprehensive Cancer Network
FDA: Food and Drug Administration

PTCL: Peripheral T-cell Lymphoma
HDAC: Histone Deacetylase

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information
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
  - Primary 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, unspecified
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma
  - Cutaneous delta/gamma T-cell lymphoma
  - Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma

*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: PTCL* Subtypes
PTCL, not otherwise specified
Angioimmunoblastic T-cell lymphoma
Anaplastic large cell lymphoma, ALK positive or negative
Enteropathy-associated T-cell lymphoma
Monomorphic epitheliotropic intestinal T-cell lymphoma

*PTLC is classified as a non-Hodgkin T-cell lymphoma. PTCL 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 PTCL.

References

1. Istodax® Prescribing Information. Summit, NJ: Celgene Corporation; October 2020. Available at https://dailymed.nlm.nih.gov/dailymed/. Accessed February 22, 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 February 22, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 22, 2021.
4. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed February 22, 2021.
5. National Comprehensive Cancer Network. T-Cell Lymphomas Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed February 22, 2021.
6. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. May 2005; 105(10): 3768-85.
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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Added term "adult" to background section to be more specific to patient population. 3. Updated dosage form section to include generic romidepsin information since now available. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance". 5. References were updated.	06/26/2020	09/14/2020
Policy was reviewed: 1. Last Review Date was updated.	02/22/2021	06/10/2021

2. Clinical policy verbiage was updated to “The provision of provider samples does not guarantee….”. 3. APPENDIX A: Abbreviation/Acronym Key was updated for HDAC: Histone Deacetylase. 4. References were updated.		