Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2020**
Policy Number: PA.CP.PHAR.314	**Effective Date: 01/2018** **Revision Date: 10/2020**
Policy Name: Romidepsin (Istodax)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

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.

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Romidepsin (Istodax)

Reference Number: PA.CP.PHAR.314
Effective Date: 01/18
Last Review Date: 10/2020

Coding Implications
Revision Log

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 health plans affiliated with Pennsylvania Health and Wellness ® that Istodax is **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. 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. 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) (*see Appendix B for examples*);
   **Prior authorization may be required for prior therapies*;
5. 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

C. 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 Pennsylvania Health and 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. 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 Pennsylvania Health and 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
NCCN: National Comprehensive Cancer Center
PTCL: peripheral T-cell lymphoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
PTCL - examples of first-line and subsequent therapy: • Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • DHAP (dexamethasone, cisplatin, cytarabine) • ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) • Belinostat, brentuximab vedotin, romidepsin as single agents	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

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
  - 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/Histologies**

- PTCL, not otherwise specified
- Anaplastic large cell lymphoma
- Angioimmunoblastic T-cell lymphoma
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma
- Nodal peripheral T-cell lymphoma with TFH phenotype
- Follicular 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.

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

Drug Name	Availability
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

VII. References

1. Istodax Prescribing Information. Summit, NJ: Celgene Corporation; November 2018. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022393s015lbl.pdf. Accessed August 17, 2020.
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 17, 2020.
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 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed August 17, 2020.

5. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed August 17, 2020.
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.

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
J9315	Injection, romidepsin, 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.	07/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	
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	