Clinical Policy: Romidepsin (Istodax)

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

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness ® clinical policy for romidepsin for injection (Istodax®).

FDA Approved Indication(s)
Istodax is indicated for the treatment of:

- Cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy
- Peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior therapy

Limitation(s) of use: These indications are based on response rate. Clinical benefit such as improvement in overall survival has not been demonstrated.

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. Request meets one of the following (a or b):
   a. Dose does not exceed maximum indicated in section III;
   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. Member has received at least one prior therapy (e.g., chemotherapy/biologic therapy, radiation therapy, hematopoietic stem cell transplantation);
4. Request meets one of the following (a or b):
   a. Dose does not exceed maximum indicated in section IV;
   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 maximum indicated in section IV;
   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. 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

Background

Description/Mechanism of Action:

Romidepsin is a histone deacetylase (HDAC) inhibitor. HDACs catalyze the removal of acetyl groups from acetylated lysine residues in histones, resulting in the modulation of gene expression. HDACs also deacetylate non-histone proteins, such as transcription factors. In vitro, romidepsin causes the accumulation of acetylated histones, and induces cell cycle arrest and apoptosis of some cancer cell lines with IC50 values in the nanomolar range. The mechanism of

the antineoplastic effect of romidepsin observed in nonclinical and clinical studies has not been fully characterized.

Formulations:
Istodax is supplied as a kit including a sterile, lyophilized powder in a 10 mg single-dose vial containing 11 mg of romidepsin and 22 mg of the bulking agent, povidone, USP. In addition, each kit includes a single-dose sterile diluent vial containing 2.4 mL (2.2 mL deliverable volume) of 80% propylene glycol, USP, and 20% dehydrated alcohol, USP.

Appendices

Appendix A: Abbreviation/Acronym Key

ALCL: anaplastic large cell lymphoma
CTCL: cutaneous T-cell lymphoma
FDA: Food and Drug Administration
MF: mycosis fungoides
PTCL: peripheral T-cell lymphoma

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none
- Boxed warning(s): none

Appendix D: WHO-EORTC classification of cutaneous T-cell lymphomas with primary cutaneous manifestations:*

- Mycosis fungoides (MF)
  - MF variants and subtypes
    - Folliculotropic MF
    - Pagetoid reticulosis
    - Granulomatous slack skin
- Sezary syndrome (SS)
- Adult T-cell leukemia/lymphoma (ATLL)
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma (ALCL)
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK*/T-cell lymphoma, nasal type
- *Primary cutaneous* peripheral T-cell lymphoma, unspecified (PTCL-NOS)
  - 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.*[5]

Appendix E: Peripheral T-cell lymphomas (PTCL) subtypes*

- Peripheral T-cell lymphoma (PTCL), not otherwise specified (NOS)
- Angioimmunoblastic T-cell lymphoma
- Anaplastic large cell lymphoma (ALCL), 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.*[5]

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	

References

1. Istodax Prescribing Information. Summit, NJ: Celgene Corporation; July 2016. Available athttps://dailymed.nlm.nih.gov/dailymed/. Accessed July 12, 2018.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 12, 2018.
3. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. May 2005; 105(10): 3768-85.
4. 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.