Clinical Policy: Romidepsin (Istodax)

Reference Number: PA.CP.PHAR.314
Effective Date: 01/18
Last Review Date: 11/17

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®).

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 cutaneous T-cell lymphoma (CTCL) (see Appendix B for examples of CTCL subtypes):
2. Meets a or b:
   a. FDA approved use:
      i. Member has received at least one prior *systemic* therapy (see Appendix C for examples of systemic therapies);
   b. Off-label NCCN recommended use prescribed for any of the following CTCL subtypes (*uses are included as off-label if they do not necessarily require a prior systemic therapy*):
      i. Sezary syndrome (SS):
         a) As single-agent therapy;
      ii. Stage IV non-Sezary/visceral (solid organ) disease:
         a) As single-agent therapy for tumors with an aggressive growth rate;
      iii. Mycosis fungoides (MF) (a, b or c):
         a) As adjuvant therapy after total skin electron beam therapy (radiation therapy) for Stage IIB generalized tumor lesions;
         b) As single-agent therapy or in combination with skin-directed therapy for one of the following:
            1) Stage I-IIA/III with blood involvement;
            2) Stage IB-IIB with histologic evidence of folliculotropic or large cell transformation;
            3) Stage IIB with limited or generalized tumor lesions;
         c) As systemic therapy for Stage IA-IIA/IIB which has progressed or is refractory to multiple previous therapies;
      iv. Primary cutaneous CD30+ T-cell lymphoproliferative disorder:
         a) As single-agent therapy for the following types of relapsed or refractory disease (1 or 2):
            1) Primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions;
            2) Cutaneous ALCL with regional nodes (not including systemic ALCL).

Approval duration: 3 months

B. Peripheral T-Cell Lymphoma (must meet all):
1. Diagnosis of peripheral T-cell lymphoma (PTCL) (see Appendix D for examples of PTCL subtypes):
2. Member has received at least one prior therapy (e.g., chemotherapy/biologic therapy, radiation therapy, hematopoietic stem cell transplantation).

Approval duration: 3 months

C. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Cutaneous and Peripheral T-Cell Lymphomas (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;
2. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Nonhematologic toxicities (except alopecia): Recurrence of Grade 3* (severe) or 4* (life-threatening) toxicities after dose reduction.

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**Grading is based on the Common Terminology Criteria for Adverse Events*

Approval duration: 6 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.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy**.**

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.

FDA Approved Indications:
Istodax is a histone deacetylase (HDAC) inhibitor/intravenous formulation indicated for:

- Treatment of cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy.
- Treatment of peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior therapy.

These indications are based on response rate. Clinical benefit such as improvement in overall survival has not been demonstrated.

Appendices

Appendix A: Abbreviation Key

ALCL: Anaplastic large cell lymphoma
CTCL: Cutaneous T-cell lymphoma
HDAC: Histone deacetylase
MF: Mycosis fungoides
PTCL-NOS: Peripheral T-cell lymphoma, not otherwise specified
SS: Sezary syndrome
WHO-EORTC: World Health Organization-European Organization for Research and Treatment of Cancer

Appendix B: WHO-EORTC classification of cutaneous T-cell lymphomas* with primary cutaneous manifestations:[4]

- 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 C: Examples of systemic antineoplastic agents for cutaneous T-cell lymphomas (CTCL)[3]

- Histone deacetylase (HDAC) inhibitors (romidepsin, vorinostat)

- Monoclonal antibodies (brentuximab vedotin)
- Systemic retinoids (bexarotene, all-trans retinoic acid, isotretinoin, acitretin)
- Interferons (IFN-alpha, IFN-gamma)
- Extracorporeal photopheresis
- Other chemotherapeutic agents (bortezomib, chlorambucil, cyclophosphamide, etoposide, gemcitabine, liposomal doxorubicin, methotrexate, pentostatin, pralatrexate, temozolomide)

Appendix D: Peripheral T-cell lymphomas* (PTCL) subtypes[3]

- 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

References

1. Istodax prescribing information. Summit, NJ: Celgene Corporation; July 2016. Available at http://www.celgene.com/content/uploads/istodax-pi.pdf. Accessed January 17, 2017.
2. Romidepsin. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed January 17, 2017.
3. T-cell lymphomas (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 17, 2017.
4. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. May 2005; 105(10): 3768-85.
5. 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.