Clinical Policy: Romidepsin (Istodax)

Reference Number: CP.PHAR.314
Effective Date: 01.01.17
Last Review Date: 11.17
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description
Olaratumab (Lartruvo®) is a histone deacetylase (HDAC) inhibitor.

FDA approved indication
Istodax is 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.

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
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® 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 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 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).

3. Request meets one of the following (a or b):
a. Dose does not exceed maximum indicated in section V;
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 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);
3. Request meets one of the following (a or b):
a. Dose does not exceed maximum indicated in section V;
b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
4.

Approval duration: 3 months

C. Other diagnoses/indications
1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Cutaneous and Peripheral T-Cell Lymphomas (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., no disease progression, no significant toxicity);
3. If request is for a dose increase, meets one of the following (a or b):

a. Dose does not exceed maximum indicated in section V;
b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

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

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 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 – CP.PHAR.57 evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALCL: Anaplastic large cell lymphoma	FDA: Food and Drug Administration
CTCL: Cutaneous T-cell lymphoma	MF: Mycosis fungoides

Appendix B: 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 C: Examples of systemic antineoplastic agents for cutaneous T-cell lymphomas (CTCL)

- 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*

- 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]

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

VI. Product Availability

Kit, single-dose vial: 11 mg romidepsin and22 mg bulking agent providone, USP; sterile diluent 2.4 mL of 80% propylene glycol, USP and 20% dehydrated alcohol, USP

VII. References

1. Istodax prescribing information. Summit, NJ: Celgene Corporation; July 2016. Available at http://www.celgene.com/content/uploads/istodax-pi.pdf. Accessed August 30, 2017.
2. Romidepsin. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed August 30, 2017.

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.

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	P&T Approval Date
Policy split from CP.PHAR.182.Excellus Oncology.	01.17	02.17
Policy converted to new template. Annual Review. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Authorization limits extended from 3 and 6 months to 6 and 12 months for initial and continued approval, respectively. Removed Stage I-IIA from Cutaneous T-Cell Lymphoma NCCN criteria due to NCCN 2B rating for stage I-IIA with blood involvement.	08.17	11.17

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the

coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.