Clinical Policy: Romidepsin (Istodax)

Reference Number: CP.PHAR.314
Effective Date: 01.01.17
Last Review Date: 11.18
Line of Business: HIM, Medicaid

Coding Implications
Revision Log

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

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 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

Provider must submit documentation (such as office chart notes, lab results or other clinical information) 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 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 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 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):
   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

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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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):
   a. New dose does not exceed maximum indicated in section V;
   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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. 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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 – HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

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]

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	14 mg/m^2

Indication	Dosing Regimen	Maximum Dose
	provided that the patient continues to benefit from and tolerates the drug.	

VI. Product Availability

Kit, lyophilized powder in a 10 mg single-dose vial for injection: 11 mg romidepsin and22 mg bulking agent povidone, 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 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.

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
4Q 2018 annual review: HIM-Medical Benefit added; summarized NCCN and FDA-approved uses for improved clarity; added age requirement and 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.	07.12.18	11.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
No significant changes; modified HIM-Medical Benefit to HIM line of business.	02.25.19	

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.

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.