

Clinical Policy: Romidepsin (Istodax)

Reference Number: CP.PHAR.314

Effective Date: 02/17

Last Review Date: 02/17

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

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

Policy/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 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 CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Cutaneous and Peripheral T-Cell Lymphomas (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
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.

**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 Centene benefit and documentation supports positive response to therapy; or
2. Refer to 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

WHO-EORTC: World Health Organization-European Organization for Research and Treatment of Cancer

PTCL-NOS: Peripheral T-cell lymphoma, not otherwise specified

SS: Sezary syndrome

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) subtypes³

- 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 _____

**PTCL 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
Policy split from CP.PHAR.182.Excellus Oncology.	01/17	02/17

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.

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

CLINICAL POLICY

Romidepsin



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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.