

# Medical Drug Clinical Criteria

**Subject:** Istodax (Romidepsin)

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## Overview

This document addresses the use of romidepsin, an intravenously administered histone deacetylase (HDAC) inhibitor. HDAC inhibitors are useful as antineoplastic agents as they cause accumulation of acetylated histones, inducing cell cycle arrest and/or apoptosis of some transformed cells. It is used to treat a certain subset of non-hodgkin lymphoma (NHL) known as T-Cell lymphomas. T-cell lymphomas account for approximately 15% of all non-Hodgkin lymphoma in the United States.

NHLs are a broad and diverse group of malignancies affecting both B- and T-lymphocytes. T-Cell Lymphomas can broadly be classified as cutaneous or non-cutaneous. Romidepsin is currently FDA approved for cutaneous T-cell lymphoma in patients that have received at least one prior therapy. The FDA recently revoked an additional indication for relapsed peripheral t-cell lymphoma which was under accelerated approval. The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of romidepsin as primary treatment for Mycosis Fungoides/Sézary Syndrome and for the cutaneous form of anaplastic large cell lymphoma (ALCL), known as primary cutaneous ALCL.

While NCCN includes romidepsin as a treatment option for other types of T-cell lymphomas, such as peripheral t-cell lymphoma (PTCL), extranodal NK/T-Cell lymphoma, nasal type (NKTL), and hepatosplenic gamma-delta T-Cell Lymphoma (HGTL), the accelerated approval for romidepsin in PTCL was removed in 2021. The accelerated approval status for romidepsin for the treatment of relapsed/refractory PTCL was withdrawn following the results of the confirmatory phase III trial, which failed to meet the primary endpoint of improved PFS for romidepsin + CHOP in patients with previously untreated PTCL (421 patients randomized to receive romidepsin + CHOP or CHOP). After a median follow-up of 28 months the addition of romidepsin to CHOP did not result in any statistically significant improvement in ORR, PFS, or OS but increased the frequency of grade ≥3 adverse events. While the panel acknowledged the change in the regulatory status of romidepsin, the consensus of the panel was to continue the listing of romidepsin as an important option for relapsed or refractory PTCL based on the results of the earlier phase II study and subsequent studies in which romidepsin resulted in durable responses across all three subtypes of PTCL (Anaplastic large cell lymphoma (ALCL), Anaplastic lymphoma kinase (ALK)-negative, PTCL-not otherwise specified (NOS), and Angioimmunoblastic T-cell lymphoma (AITL)).

## Definitions and Measures

Mycosis fungoides/ Sézary Syndrome (MF/SS): Cutaneous T-cell Lymphomas (CTCLs) are a group of NHLs of mature T-cells that primarily present in the skin, and at times progress to involve lymph nodes, blood, and visceral organs. MF is the most common subtype with primary cutaneous involvement and SS is an erythrodermic, leukemic variant of CTCL that is characterized by significant blood involvement and lymphadenopathy.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

## Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

**Istodax (Romidepsin)**

Requests for **Istodax (romidepsin)** may be approved if the following criteria are met:

- I. Individual has a diagnosis of cutaneous T-cell lymphoma; **AND**
  - A. Individual is using for relapsed or refractory disease following at least one prior systemic therapy;
- OR**
- II. Individual has a diagnosis of Primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions; **AND**
  - A. Individual has relapsed or refractory disease; **AND**
  - B. Using romidepsin as monotherapy;
- OR**
- III. Individual has a diagnosis of cutaneous ALCL with regional node (N1); **AND**
  - A. Individual has relapsed or refractory disease; **AND**
  - B. Using romidepsin as monotherapy;
- OR**
- IV. Individual has a diagnosis of Mycosis Fungoides or Sézary Syndrome (NCCN 2A);

Requests for **Istodax (romidepsin)** may not be approved when the above criteria are not met and for all other indications.

**Coding**

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

**HCPCS**

J9318	Injection, romidepsin, nonlyophilized, 0.1 mg
J9319	Injection, romidepsin, lyophilized, 0.1 mg

**ICD-10 Diagnosis**

C84.00	Mycosis fungoides, unspecified site
C84.01	Mycosis fungoides, lymph nodes of head, face, and neck
C84.02	Mycosis fungoides, intrathoracic lymph nodes
C84.03	Mycosis fungoides, intra-abdominal lymph nodes
C84.04	Mycosis fungoides, lymph nodes of axilla and upper limb
C84.05	Mycosis fungoides, lymph nodes of inguinal region and lower limb
C84.06	Mycosis fungoides, intrapelvic lymph nodes
C84.07	Mycosis fungoides, spleen
C84.08	Mycosis fungoides, lymph nodes of multiple sites
C84.09	Mycosis fungoides, extranodal and solid organ sites
C84.10	Sézary disease, unspecified site
C84.11	Sézary disease, lymph nodes of head, face, and neck

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C84.12	Sezary disease, intrathoracic lymph nodes
C84.13	Sezary disease, intra-abdominal lymph nodes
C84.14	Sezary disease, lymph nodes of axilla and upper limb
C84.15	Sezary disease, lymph nodes of inguinal region and lower limb
C84.16	Sezary disease, intrapelvic lymph nodes
C84.17	Sezary disease, spleen
C84.18	Sezary disease, lymph nodes of multiple sites
C84.19	Sezary disease, extranodal and solid organ sites
C84.40	Peripheral T-cell lymphoma, not elsewhere classified, unspecified site
C84.41	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of head, face, and neck
C84.42	Peripheral T-cell lymphoma, not elsewhere classified, intrathoracic lymph nodes
C84.43	Peripheral T-cell lymphoma, not elsewhere classified, intra-abdominal lymph nodes
C84.44	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of axilla and upper limb
C84.45	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of inguinal region and lower limb
C84.46	Peripheral T-cell lymphoma, not elsewhere classified, intrapelvic lymph nodes
C84.47	Peripheral T-cell lymphoma, not elsewhere classified, spleen
C84.48	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of multiple sites
C84.49	Peripheral T-cell lymphoma, not elsewhere classified, extranodal and solid organ sites
C84.60	Anaplastic large cell lymphoma, ALK-positive, unspecified site
C84.61	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of head, face, and neck
C84.62	Anaplastic large cell lymphoma, ALK-positive, intrathoracic lymph nodes
C84.63	Anaplastic large cell lymphoma, ALK-positive, intra-abdominal lymph nodes
C84.64	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of axilla and upper limb
C84.65	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of inguinal region and lower limb
C84.66	Anaplastic large cell lymphoma, ALK-positive, intrapelvic lymph nodes
C84.67	Anaplastic large cell lymphoma, ALK-positive, spleen
C84.68	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of multiple sites
C84.69	Anaplastic large cell lymphoma, ALK-positive, extranodal and solid organ sites
C84.70	Anaplastic large cell lymphoma, ALK-negative, unspecified site
C84.71	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of head, face, and neck
C84.72	Anaplastic large cell lymphoma, ALK-negative, intrathoracic lymph nodes
C84.73	Anaplastic large cell lymphoma, ALK-negative, intra-abdominal lymph nodes
C84.74	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of axilla and upper limb
C84.75	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of inguinal region and lower limb
C84.76	Anaplastic large cell lymphoma, ALK-negative, intrapelvic lymph nodes
C84.77	Anaplastic large cell lymphoma, ALK-negative, spleen
C84.78	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of multiple sites
C84.79	Anaplastic large cell lymphoma, ALK-negative, extranodal and solid organ sites

<a href="#">C84.90</a>	<a href="#">Mature T/NK-cell lymphomas, unspecified site</a>
<a href="#">C84.91</a>	<a href="#">Mature T/NK-cell lymphomas, lymph nodes of head, face, and neck</a>
<a href="#">C84.92</a>	<a href="#">Mature T/NK-cell lymphomas, intrathoracic lymph nodes</a>
<a href="#">C84.93</a>	<a href="#">Mature T/NK-cell lymphomas, intra-abdominal lymph nodes</a>
<a href="#">C84.94</a>	<a href="#">Mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb</a>
<a href="#">C84.95</a>	<a href="#">Mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb</a>
<a href="#">C84.96</a>	<a href="#">Mature T/NK-cell lymphomas, intrapelvic lymph nodes</a>
<a href="#">C84.97</a>	<a href="#">Mature T/NK-cell lymphomas, spleen</a>
<a href="#">C84.98</a>	<a href="#">Mature T/NK-cell lymphomas, lymph nodes of multiple sites</a>
<a href="#">C84.99</a>	<a href="#">Mature T/NK-cell lymphomas, extranodal and solid organ sites</a>
C84.7A	Anaplastic large cell lymphoma, ALK-negative, breast
C84.A0-C84.A9	Cutaneous T-cell lymphoma, unspecified
<a href="#">C84.Z0</a>	<a href="#">Other mature T/NK-cell lymphomas, unspecified site</a>
<a href="#">C84.Z1</a>	<a href="#">Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck</a>
<a href="#">C84.Z2</a>	<a href="#">Other mature T/NK-cell lymphomas, intrathoracic lymph nodes</a>
<a href="#">C84.Z3</a>	<a href="#">Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes</a>
<a href="#">C84.Z4</a>	<a href="#">Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb</a>
<a href="#">C84.Z5</a>	<a href="#">Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb</a>
<a href="#">C84.Z6</a>	<a href="#">Other mature T/NK-cell lymphomas, intrapelvic lymph nodes</a>
<a href="#">C84.Z7</a>	<a href="#">Other mature T/NK-cell lymphomas, spleen</a>
<a href="#">C84.Z8</a>	<a href="#">Other mature T/NK-cell lymphomas, lymph nodes of multiple sites</a>
<a href="#">C84.Z9</a>	<a href="#">Other mature T/NK-cell lymphomas, extranodal and solid organ sites</a>
C86.0	Extranodal NK/T-cell lymphoma, nasal type
C86.1	Hepatosplenic T-cell lymphoma
C86.2	Enteropathy-type (intestinal) T-cell lymphoma
C86.3	Subcutaneous panniculitis-like T-cell lymphoma
C86.5	Angioimmunoblastic T-cell lymphoma
C86.6	Primary cutaneous CD30-positive T-cell proliferations
Z85.72	Personal history of non-Hodgkin lymphomas

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## Document History

Revised: 08/16/2024

Document History:

- 08/16/2024 – Annual Review: Wording and formatting; include brand name. Coding Reviewed: Add ICD-10-CM C84.90, C84.91, C84.92, C84.93, C84.94, C84.95, C84.96, C84.97, C84.98, C84.99, C84.Z0, C84.Z1, C84.Z2, C84.Z3, C84.Z4, C84.Z5, C84.Z6, C84.Z7, C84.Z8, C84.Z9.
- 08/16/2024 – Annual Review: Wording and formatting; include brand name. Coding Reviewed: Add ICD-10-CM C84.90, C84.91, C84.92, C84.93, C84.94, C84.95, C84.96, C84.97, C84.98, C84.99, C84.Z0, C84.Z1, C84.Z2, C84.Z3, C84.Z4, C84.Z5, C84.Z6, C84.Z7, C84.Z8, C84.Z9.

- 08/18/2023 – Annual Review: Add NCCN 2A recommendation for use in primary cutaneous ALCL or cutaneous ALCL with regional node disease. Wording and formatting. Romidepsin is generically available. Coding Reviewed: Removed the name Istodax from HCPCS J9318, J9319.
- 11/18/2022 – Select Review: Update criteria to only include cutaneous T-cell lymphomas per label. Coding Reviewed: No changes.
- 08/19/2022 – Annual Review: Remove requirement for “cutaneous” T-cell lymphoma to allow other types per NCCN. Coding Reviewed: Removed ICD-10-CM C84.A0-C84.A9., C84.00-C84.09, C84.10-C84.19, C84.40-C84.49, C84.60-C84.79. Added ICD-10-CM C84.00, C84.01, C84.02, C84.03, C84.04, C84.05, C84.06, C84.07, C84.08, C84.09, C84.10, C84.11, C84.12, C84.13, C84.14, C84.15, C84.16, C84.17, C84.18, C84.19, C84.40, C84.41, C84.42, C84.43, C84.44, C84.45, C84.46, C84.47, C84.48, C84.49, C84.60, C84.61, C84.62, C84.63, C84.64, C84.65, C84.66, C84.67, C84.68, C84.69, C84.70, C84.71, C84.72, C84.73, C84.74, C84.75, C84.76, C84.77, C84.78, C84.79. Effective 10/1/2022 Added ICD-10-CM C84.A0-C84.A9, C86.0, C86.1, C86.3.
- 09/13/2021 – Select Review: Update criteria to specify cutaneous T-cell lymphomas to align with updated FDA indication. Coding reviewed: Added HCPCS J9318, J9319. Removed HCPCS J9315, C9065.
- 08/20/2021 – Annual Review: No Changes. Coding reviewed: No changes.
- 08/21/2020 – Annual Review: No Changes. Coding reviewed: Added HCPCS C9065. Effective 6/9/2021 Do not terminate C9065. Removed HCPCS J9314 per Medicare update 7/1/2021.
- 11/15/2019 – Annual Review: No Changes. Coding reviewed: No changes.
- 05/17/2019 – Annual Review: First review of Istodax clinical criteria. Add reference for off-label criteria. Coding reviewed: No changes.

## References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>. Accessed: June 30, 2024.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
4. Coiffier B, Pro B, Prince HM, et al. Results from a Pivotal, Open-Label, Phase II Study of Romidepsin in Relapsed or Refractory Peripheral T-Cell Lymphoma after Prior Systemic Therapy. *J Clin Oncol* 2012; 30: 631-636.
5. Bachy E, Camus V, Thieblemont C, et al. Romidepsin Plus CHOP Versus CHOP in Patients with Previously Untreated Peripheral T-Cell Lymphoma: Results of the Ro-CHOP Phase III Study (Conducted by LYSA). *J Clin Oncol* 2022; 40:242-251.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed on June 30, 2024.
  - a. Primary Cutaneous Lymphomas. V2.2024. Revised May 6, 2024.
  - b. T-Cell Lymphomas. V4.2024. Revised May 28, 2024.

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