Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Romidepsin (Istodax®)	MP-RX-FP-45-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Romidepsin (Istodax®),* a histone deacetylase (HDAC) inhibitor approved by the Food and Drug Administration (FDA) for the treatment of cutaneous T-cell lymphoma (CTCL) in adult patients who have received at least one prior systemic therapy.

Background Information

Romidepsin is 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- hodgkins 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/Sezary 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The accelerated approval status for romidepsin for the treatment of relapsed/refractory PTCL was withdrawn following the results of the confirmatory phase III trial, which failed to meet the primary endpoint of improved PFS for romidepsin + CHOP in patients with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

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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.

Approved Indications

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

Other Uses

i. See the Background section above.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

ICD-10	Description
C84.00- C84.09	Mycosis fungoides
C84.10-C84.19	Sezary disease
C84.40- C84.49	Peripheral T-cell lymphoma, not elsewhere classified
C84.60-C84.69	Anaplastic large cell lymphoma, ALK-positive
C84.70-C84.79	Anaplastic large cell lymphoma, ALK-negative
C84.7A	Anaplastic large cell lymphoma, ALK-negative, breast
C84.A0-C84.A9	Cutaneous T-cell lymphoma, unspecified
C84.90- C84.99	Mature T/NK-cell lymphomas
C84.Z0- C84.Z9	Other mature T/NK-cell lymphomas
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

Medical Necessity Guidelines

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.

Romidepsin (Istodax®)

1. **Criteria For Initial Approval** (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

    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**

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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);

2. Criteria For Continuation of Therapy

i. MMM considers continuation of Romidepsin (Istodax®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:

   A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
   B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

3. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

4. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for romidepsin may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

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B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Romidepsin (Istodax®)	14 mg/m^2 IV on days 1, 8, and 15 of a 28-day cycle. Each cycle is 28-days.
Exceptions	

• Dose is calculated based on Body Surface Area.
• Dose should be adjusted in patients with hepatic impairment:
  ○ Patients with moderate impairment (Bilirubin levels greater than 1.5 x ULN to less than or equal to 3 x ULN): 7 mg/m^2.
  ○ Patients with severe impairment (Bilirubin greater than 3 x ULN): 5 mg/m^2.	

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. 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, 2023.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
5. 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.
6. 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.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on June 30, 2023.
   a. Primary Cutaneous Lymphomas. V1.2023. Revised January 5, 2023.
   b. T-Cell Lymphomas. V1.20223. Revised January 5, 2023.

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review 11/15/2024	Consolidated ICD-10 codes for mycosis fungoides, sezary disease, perypheral T-cell lymphoma, anaplastic large cell lymphoma. Add ICD codes: C84.90- C84.99 and C84.Z0-C84.Z9. Wording and formatting updates.	2/24/2025	3/6/2025
Select Review 2/15/2024	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	3/25/2024	5/9/2024
Policy Inception 11/15/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023