Medical Policy:

Istodax® (romidepsin) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.152	April 1, 2025	

Definitions

Istodax (romidepsin): is a bicyclic depsipeptide histone deacetylase (HDAC) inhibitor isolated from Chromobacterium violaceum. Histone deacetylases are enzymes that catalyze the removal of acetyl groups from the lysine residues of proteins, including histones and transcription factors. Overexpression of HDACs or an abnormal recruitment of HDACs to oncogenic transcription factors is present in some cancer cells. This causes hypoacetylation of core nucleosomal histones resulting in a condensed chromatin structure and repression of gene transcription. Inhibition of HDAC activity produces an accumulation of acetyl groups on the histone lysine residues resulting in an open chromatin structure and transcriptional activation. In many different malignant cell lines, HDAC inhibitors have been shown to activate differentiation, inhibit the cell cycle, and induce apoptosis.

Istodax (romidepsin) is FDA approved for the treatment of patients with cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy and of peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior therapy.

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

Maintenance Dose:

400 billable units on days 1, 8, and 15 of a 28-day cycle

Guideline

I. Initial Approval Criteria

Istodax *may be considered medically necessary when any of the following selection criteria is met:*

1. **Peripheral T-cell Lymphoma (PTCL)**

   The member has relapsed or refractory PTCL (angioimmunoblastic T-cell lymphoma, peripheral T-cell lymphoma not otherwise specified, anaplastic large cell lymphoma, or enteropathy associated T-cell lymphoma) and:

   A. Failure of at least one prior systemic chemotherapy; **OR**
   B. Used as initial palliative intent therapy

2. **Cutaneous T-cell Lymphoma (CTCL)**

   The member has relapsed, refractory, or advanced CTCL (**mycosis fungoides or Sezary syndrome**) and:

   A. Patient has failed prior systemic therapy; **OR**
   B. Used as primary treatment for Mycosis Fungoides/Sezary Syndrome (excluding use in stage IA disease)

Limitations/Exclusions

Istodax (romidepsin) is not considered medically necessary when any of the following selection criteria is met:

1. Disease progression while taking Istodax (romidepsin).
2. Concurrent use with other chemotherapy for PTCL.
3. Used as initial first line therapy for CTCL or PTCL.
4. Dosing exceeds single dose limit of Istodax (romidepsin) 14mg/m^2.
5. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. Renewal Criteria

1. Patient continues to meet INITIAL APPROVAL CRITERIA; **AND**
2. Tumor response with disease stabilization or reduction of tumor size and spread; **AND**
3. Absence of unacceptable toxicity from the drug including hematological abnormalities such as neutropenia, anemia, leukopenia, thrombocytopenia, as well as severe infections, severe tumor lysis syndrome, and ECG T-Wave changes.

Dosage/Administration

Indication	Dose
All Indications	14 mg/m^2 over 4 hours on days 1, 8, and 15 every 28 days. Cycles should be repeated until disease progression or unacceptable toxicity.

Applicable Procedure Codes

Code	Description
J9319	injection, romidepsin, lyophilized, 0.1 mg
J9318	Injection, romidepsin, non-lyophilized, 0.1 mg; 1 billable unit = 0.1 mg

Applicable NDCs

Code	Description
59572-0984-xx	Istodax Kit (10 mg single-dose vial)
00703-4004-xx	Romidepsin 27.5 mg/5.5 mL solution for injection
00703-3071-xx	Romidepsin 10 mg/2 mL solution for injection

ICD-10 Diagnoses

Code	Description
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
C84.12	Sézary disease, intrathoracic lymph nodes
C84.13	Sézary disease, intra-abdominal lymph nodes
C84.14	Sézary disease, lymph nodes of axilla and upper limb
C84.15	Sézary disease, lymph nodes of inguinal region and lower limb
C84.16	Sézary disease, intrapelvic lymph nodes
C84.17	Sézary disease, spleen
C84.18	Sézary disease, lymph nodes of multiple sites
C84.19	Sézary disease, extranodal and solid organ sites
C84.40	Peripheral T-cell lymphoma, not classified, unspecified site
C84.41	Peripheral T-cell lymphoma, not classified, lymph nodes of head, face, and neck
C84.42	Peripheral T-cell lymphoma, not classified, intrathoracic lymph nodes
C84.43	Peripheral T-cell lymphoma, not classified, intra-abdominal lymph nodes
C84.44	Peripheral T-cell lymphoma, not classified, lymph nodes of axilla and upper limb
C84.45	Peripheral T-cell lymphoma, not classified, lymph nodes of inguinal region and lower limb
C84.46	Peripheral T-cell lymphoma, not classified, intrapelvic lymph nodes
C84.47	Peripheral T-cell lymphoma, not classified, spleen
C84.48	Peripheral T-cell lymphoma, not classified, lymph nodes of multiple sites
C84.49	Peripheral T-cell lymphoma, not 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
C86.2	Enteropathy-type (intestinal) T-cell lymphoma
C86.5	Angioimmunoblastic T-cell lymphoma
C86.6	Primary cutaneous CD30-positive T-cell proliferations

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	04/01/2025	Annual Review: No criteria changes.
EmblemHealth & ConnectiCare	2/16/2024	Annual Review: Updated dosing limits, no criteria changes
EmblemHealth & ConnectiCare	6/22/2023	Annual Review: Removed NDCs: 59572-0962-10 and 59572-0984-01. Added 59572-0984-xx, 00703-4004-xx, 00703-3071-xx. Added J-code J9318 Peripheral T-cell Lymphoma: Initial Criteria: Removed: "a. ECOG performance status 0-2 b. Potassium and magnesium levels are within normal limits" Added "b. Used as initial palliative intent therapy" Cutaneous T-Cell Lymphoma: Initial Criteria: Removed: "a.Failure of at least two prior skin directed therapies including topical corticosteroids, carmustine, mechlorethamine hydrochloride, phototherapy, or total skin electron beamtherapy, unless otherwise contraindicated or intolerance b. Failure of at least one prior systemic therapy including bexarotene or unless otherwise contraindicated or intolerance. c. Potassium and magnesium levels are within normal limits" Added "a. Patient has failed prior systemic therapy; OR b. Used as primary treatment for Mycosis Fungoides/Sezary Syndrome (excluding use in stage IA disease)"
EmblemHealth & ConnectiCare	07/25/2022	Transferred policy to new template, updated billing codes
EmblemHealth & ConnectiCare	7/15/2019	Annual Review

References

1. Istodax [package insert]. Summit, NJ; Celgene, July 2016. Accessed March 2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.