MEDICAL POLICY

POLICY TITLE	ROMIDEPSIN (ISTODAX®)
POLICY NUMBER	MP-2.156

Original Issue Date (Created):	**9/1/2011**
Most Recent Review Date (Revised):	**5/16/2020**
Effective Date:	**10/1/2020**

I. POLICY

Romidepsin (Istodax®) may be considered **medically necessary** for the treatment of cutaneous T-cell lymphoma (CTCL) and peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior systemic therapy. Prior systemic therapy can include, but is not limited to the following: retinoids, interferons, extracorporeal photophoresis, denileukin diftitox, methotrexate, liposomal doxorubicin or gemcitabine.

Romidepsin (Istodax®) for the treatment of other conditions/diseases is considered **investigational**. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Note: The safety and effectiveness of romidepsin (Istodax®) in pediatric patients has not been established.

Note: For patients with late stage metastatic disease (Stage IV), please refer to **MP 2.373** *Step Therapy Treatment in Cancer, Including Treatments for Stage Four, Advanced Metastatic Cancer and Severe Related Health Conditions* for additional guidance.

***Cross-reference*:**

MP 2.103 Off-Label Use of Medications
MP 2.373 Step Therapy Treatment in Cancer, Including Treatments for Stage Four, Advanced Metastatic Cancer and Severe Related Health Conditions

II. PRODUCT VARIATIONS

TOP

This policy is only applicable to certain programs and products administered by Capital BlueCross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO: Refer to FEP Medical Policy Manual MP-5.21.57 Istodax (romidepsin). The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

POLICY TITLE	ROMIDEPSIN (ISTODAX®)
POLICY NUMBER	MP-2.156

Note for Medicare Advantage:
Off-label use of FDA approved drugs and biologicals used in an anti-cancer chemotherapeutic regimen for medically accepted indications may be covered under Medicare if the indications are supported in either one or more Medicare recognized compendia or in peer-reviewed literature. Refer to Medicare Benefit Policy Manual (100-2, Chapter 15, Section 50.4.5- Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen.
http://www.cms.gov/manuals/Downloads/bp102c15.pdf

III. DESCRIPTION/BACKGROUND

TOP

In November 2009, romidepsin (Istodax®) was FDA-approved for the treatment of cutaneous T-cell lymphomas (CTCL) in patients who have received at least one prior therapy. In June 2011, the FDA granted accelerated approval for an additional indication for romidepsin (Istodax®) for injection for the treatment of peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior therapy. The PTCL approval was based on a priority (6 month) review by the FDA. Priority reviews are reserved for serious and life-threatening conditions that have an unmet medical need. These indications are based on response rate. Clinical benefit such as improvement in overall survival had not been demonstrated.

Romidepsin (Istodax®) is a histone deacetylase (HDAC) inhibitor, resulting in modulation of gene expression and the induction of cell differentiation, cell cycle arrest and apoptosis of some cancer cells. CTCL belongs to a heterogeneous group of T-cell lymphomas with primary manifestations in the skin. CTCL is a slow growing cancer of the infection-fighting white blood cells. The antienoplastic mechanism of romidepsin has not been fully established. Peripheral T-cell lymphoma comprises a heterogeneous group of malignancies of T-cell origin that account for about 10-15% of all cases of non-Hodgkin's lymphoma. PTCL can occur from young adulthood to old age and is slightly more common in men than in women. It is a particularly aggressive form of lymphoma with a short median duration of survival (approximately two years) from diagnosis.

See prescribing information for details of safety and administration considerations.

IV. RATIONALE

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For information on clinical studies for romidepsin (Istodax®), refer to Prescribing Information.

V. DEFINITIONS

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APOPTOSIS refers to programmed cell death; genetic limitation of the lifespan of cells. The process may be important in the limiting growth of tumors.

VI. BENEFIT VARIATIONS

TOP

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital BlueCross. Members and providers should consult the member's health benefit plan for information or contact Capital BlueCross for benefit information.

VII. DISCLAIMER

TOP

Capital BlueCross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital BlueCross' Provider Services or Member Services. Capital BlueCross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

TOP

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

HCPCS Code	Description
C9065	Injection, romidepsin, non-lypohilized (e.g. liquid), 1mg
J9315	Injection, romidepsin, 1 mg

ICD-10-CM Diagnosis Codes	Description
C84.A0	Cutaneous T-cell lymphoma, unspecified, unspecified site
C84.A1	Cutaneous T-cell lymphoma, unspecified lymph nodes of head, face, and neck
C84.A2	Cutaneous T-cell lymphoma, unspecified, intrathoracic lymph nodes
C84.A3	Cutaneous T-cell lymphoma, unspecified, intra-abdominal lymph nodes
C84.A4	Cutaneous T-cell lymphoma, unspecified, lymph nodes of axilla and upper limb

POLICY TITLE	ROMIDEPSIN (ISTODAX®)
POLICY NUMBER	MP-2.156

ICD-10-CM Diagnosis Codes	Description
C84.A5	Cutaneous T-cell lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C84.A6	Cutaneous T-cell lymphoma, unspecified, intrapelvic lymph nodes
C84.A7	Cutaneous T-cell lymphoma, unspecified, spleen
C84.A8	Cutaneous T-cell lymphoma, unspecified, lymph nodes of multiple sites
C84.A9	Cutaneous T-cell lymphoma, unspecified, extranodal and solid organ sites
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
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy

IX. REFERENCES

TOP

1. *Centers for Medicare and Medicaid Services (CMS) Medicare Benefit Policy Manual. Publication 100-02. Chapter 15. Section 50.4.5. Off-Label Use of Anti-Cancer Drugs and Biologicals. [Website]: http://www.cms.gov/manuals/Downloads/bp102c15.pdf . Accessed May 16, 2020.*
2. *Centers for Medicare and Medicaid Services (CMS) Medicare Benefit Policy Manual. Publication 100-02. Chapter 15. Sections 50, 50.4.1, 50.4.3. Drugs and Biologicals. Effective 10/01/03. [Website]: http://www.cms.gov/manuals/Downloads/bp102c15.pdf. Accessed May 16, 2020.*
3. *Coiffier B, Pro B, Prince HM, et al, "Final Results from a Pivotal, Multicenter, International, Open-Label, Phase 2 Study of Romidepsin in Progressive or Relapsed Peripheral T-Cell Lymphoma (PTCL) Following Prior Systemic Therapy," Blood, 2010, 116(21):114 [abstract 114 from 2010 ASH Annual Meeting].*
4. *Cutaneous Lymphoma Foundation. Treatment Basics. [Website]: https://www.clfoundation.org/treatment-basics Accessed May 16, 2020.*
5. *Istodax® (Romidepsin for injection) prescribing information. Summit, NJ: Celgene Corporation; Revised November 2018. [Website]: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=4&ved=2ahUKEwj*

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6. *Accessed May 16, 2020.*
7. *National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™: Non-Hodgkin's Lymphomas. Version 4:2018. [Website]: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Last accessed May 16, 2020.*
8. *National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™: T-Cell Lymphomas. Version 1:202020. [Website]: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed May 16, 2020.*
9. *Piekarz RL, Frye R, Turner M, Wright JJ, Allen SL, et al. Phase II multi-institutional trial of the histone deacetylase inhibitor romidepsin as monotherapy for patients with cutaneous T-cell lymphoma. J Clin Oncol. 2009; 27(32):5410-7.*
10. *Romidepsin: Drug information In: UpToDate Online Journal [serial online]. Waltham, MA: UpToDate. [Website]: www.uptodate.com. Accessed May 16, 2020.*
11. *Taber's Cyclopedic Medical Dictionary 20th edition.*

X. POLICY HISTORY

TOP

MP-2.156	**CAC 4/26/11 New policy**.
	CAC 6/26/12 Minor review. Added new FDA indication for treatment of peripheral T-cell Lymphoma (PTCL). Added information related to PTCL to description/background.
	7/24/13 Administrative update. Coding review complete
	CAC 9/24/13 Consensus review. No change to policy statements. Removed Medicare variation and information kept as a note.
	CAC 9/30/14 Consensus review. No change to policy statements. References updated. Added rationale section. *Deleted notation regarding preauthorization requirement. All users should refer to officially posted preauthorization resources for requirements.*
	CAC 9/29/15 Consensus review. No change to the policy statements. References updated**.** Coding reviewed
	CAC 9/27/16 Consensus review. No change to the policy statements. References updated. FEP variation revised to refer to the FEP medical policy manual. Variations reformatted. Coding reviewed.
	CAC 11/28/17 Consensus review. Policy statements unchanged. Description/Background, Rationale and Reference sections updated. Coding reviewed.
	8/13/18 Consensus review. No change to policy statements. Deleted rationale and added direction to refer to prescribing information. References updated.
	5/28/19 Consensus review. No change to policy statements. References updated.
	4/10/20 Administrative update. Added note for patients with late stage metastatic disease (Stage IV), please refer to MP 2.373 Step Therapy Treatment

POLICY TITLE	ROMIDEPSIN (ISTODAX®)
POLICY NUMBER	MP-2.156

	in Cancer, Including Treatments for Stage Four, Advanced Metastatic Cancer and Severe Related Health Conditions for additional guidance.
	5/16/2020 Consensus review. Policy statement unchanged. References and Coding reviewed.
	9/8/2020 Administrative update. Code C9065 added as medically necessary.

Top