# MEDICAL POLICY

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

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|---|---|
| Original Issue Date (Created): | **April 26, 2011** |
| Most Recent Review Date (Revised): | **September 24, 2013** |
| **Effective Date:** | **November 1, 2013** |

## I. POLICY

**Note: Romidepsin (Istodax®) does not require preauthorization.**

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.

## II. PRODUCT VARIATIONS

*[N] = No product variation, policy applies as stated*
*[Y] = Standard product coverage varies from application of this policy, see below*

[N] Capital Cares 4 Kids

[N] Indemnity

[N] PPO

[N] SpecialCare

[N] HMO

[N] POS

[N] SeniorBlue HMO (see note)

[Y] FEP PPO**

[N] SeniorBlue PPO-(see note

Note: "FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice." Refer to Medicare Benefit Policy Manual (100-2, Chapter 15, Section 50.4.2- Unlabeled Use of Drug)." *http://www.cms.gov/manuals/Downloads/bp102c15.pdf*

** The FEP program dictates that all drugs, devices or biological products approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational. Therefore, FDA-approved drugs, devices or biological products may be assessed on the basis of medical necessity,

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## III. DESCRIPTION/BACKGROUND

In November 2009, the 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 Istodax (romidepsin) 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 has not been demonstrated.

Romidepsin (Istodax®) is am antineoplastic agent and 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.

Warnings and precautions for Romidepsin (Istodax®) include the risk of QT prolongation. Therefore, it is important that potassium and magnesium are within normal range before administration of Romidepsin (Istodax®). Treatment with Romidepsin (Istodax®) has been associated with thrombocytopenia, leukopenia (neutropenia and lymphopenia) and anemia, therefore, these hematological parameters should be monitored and the dosage modified as necessary. Based on its mechanism of action, Romidepsin (Istodax®) may cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while taking Romidepsin (Istodax®), the patient should be apprised of the potential hazard to the fetus. Romidepsin (Istodax®). binds to estrogen receptors, therefore women of childbearing potential should be advised that the drug may reduce the effectiveness of estrogen-containing contraceptives.

Romidepsin 14mg/m2 is administered intravenously on days 1, 8, and 15 of a 28-day cycle. Repeat cycles are performed every 28 days provided that the patient continues to benefit from and tolerates the drug.

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## IV. DEFINITIONS

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

## V. BENEFIT VARIATIONS

The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital for benefit information.

## VI. DISCLAIMER

*Capital'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. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.*

## VII. REFERENCES

*Centers for Medicare and Medicaid Services (CMS) Medicare Benefit Policy Manual. Publication 100-02. Chapter 15. Section 50.4.2. Unlabeled Use of Drug. Effective 10/01/03. [Website]: http://www.cms.gov/manuals/Downloads/bp102c15.pdf Accessed July 16, 2013.*

*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 July 16, 2013.*

*Cutaneous Lymphoma Foundation. Treatment Options. Updated August 2010. [Website]: http://www.clfoundation.org/treatment/treatment_options.html Accessed July 16, 2013..*

*Istodax® (romidepsin for injection) prescribing information. Gloucester Pharmaceuticals, Inc.: Cambridge, MA. Revised June 2013. [Website]: http://istodax.com/pdfs/ISTODAX_PackageInsert.pdf Accessed April 23, 2012.*

*National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™: Non-Hodgkin's Lymphomas. v.1.2013. [Website: http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf . Accessed July 16, 2013.*



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*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.*

*Taber's Cyclopedic Medical Dictionary 20th edition.*

## VIII. CODING INFORMATION

**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 |
|---|---|
| J9315 | Injection, romidepsin, 1 mg |

| ICD-9-CM Diagnosis Code* | Description |
|---|---|
| 202.10 | Mycosis fungoides, unspecified site, extranodal and solid organ sites |
| 202.11 | Mycosis fungoides of lymph nodes of head, face, and neck |
| 202.12 | Mycosis fungoides of intrathoracic lymph nodes |
| 202.13 | Mycosis fungoides of intra-abdominal lymph nodes |
| 202.14 | Mycosis fungoides of lymph nodes of axilla and upper limb |
| 202.15 | Mycosis fungoides of lymph nodes of inguinal region and lower limb |
| 202.16 | Mycosis fungoides of intrapelvic lymph nodes |
| 202.17 | Mycosis fungoides of spleen |
| 202.18 | Mycosis fungoides of lymph nodes of multiple sites |
| 202.20 | Sezary's disease, unspecified site, extranodal and solid organ sites |
| 202.21 | Sezary's disease of lymph nodes of head, face, and neck |
| 202.22 | Sezary's disease of intrathoracic lymph nodes |
| 202.23 | Sezary's disease of intra-abdominal lymph nodes |
| 202.24 | Sezary's disease of lymph nodes of axilla and upper limb |
| 202.25 | Sezary's disease of lymph nodes of inguinal region and lower limb |
| 202.26 | Sezary's disease of intrapelvic lymph nodes |
| 202.27 | Sezary's disease of spleen |
| 202.28 | Sezary disease, lymph nodes of multiple sites |
| 202.70 – 202.78 | Peripheral T-cell lymphoma, unspecified site, extranodal and solid organ sites |

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*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

**The following ICD-10 diagnosis codes will be effective October 1, 2014**

| ICD-10-CM Diagnosis Code* | Description |
|---|---|
| C84.00 | Mycosis fungoides, unspecified site |
| C84.09 | Mycosis fungoides, extranodal and solid organ sites |
| 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 |
| C84.10 | Sezary disease, unspecified site |
| C84.19 | Sezary disease, extranodal and solid organ sites |
| C84.11 | Sezary disease, lymph nodes of head, face, and neck |
| 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 |
| C84.40 | Peripheral T-cell lymphoma, not classified, unspecified site |
| C84.49 | Peripheral T-cell lymphoma, not classified, extranodal and solid organ sites |
| C85.20 | Mediastinal (thymic) large B-cell lymphoma, unspecified site |
| C85.29 | Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites |

*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

## IX. POLICY HISTORY

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| **MP-2.156** | **CAC 4/26/11** New policy. |
| | CAC 6/26/12 Minor: Added new FDA indication for treatment of peripheral T- |



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| | cell Lymphoma (PTCL). Added information related to PTCL to description/background. |
| | 7/24/13 Admin coding review complete--rsb |
| | CAC 9/24/13 Consensus. No change to policy statements. Removed Medicare variation and information kept as a note. |





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