

Market Applicability						
Market	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X

Khapzory (levoleucovorin)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Khapzory (levoleucovorin) 175 mg, 300 mg vial

APPROVAL CRITERIA

Requests for Khapzory (levoleucovorin) may be approved when the following criteria are met:

- I. As a component of high-dose methotrexate therapy in osteosarcoma; **OR**
- II. As a treatment of impaired methotrexate elimination; **OR**
- III. As a treatment of inadvertent over-dosage of folic acid antagonists; **OR**
- IV. In combination chemotherapy with fluorouracil-based regimens to treat colorectal adenocarcinoma; **OR**
- V. When used in combination chemotherapy for any of the following cancers (NCCN 2A):
 - A. Acute lymphoblastic leukemia (ALL); **OR**
 - B. Anal Carcinoma; **OR**
 - C. B-Cell Lymphoma - Mantle Cell Lymphoma, AIDS-Related B-Cell Lymphomas or Burkitt Lymphoma; **OR**
 - D. Bladder Cancer; **OR**
 - E. Bone Cancer; **OR**
 - F. Central nervous system (CNS) Cancers-Primary CNS Lymphoma, Limited Brain Metastases, Extensive Brain Metastases or Leptomeningeal Metastases; **OR**
 - G. Cervical Cancer; **OR**
 - H. Colon Cancer; **OR**
 - I. Esophageal and Esophagogastric Junction Cancers; **OR**
 - J. Gastric Cancer; **OR**
 - K. Gestational Trophoblastic Neoplasia; **OR**
 - L. Hepatobiliary Cancers, Biliary Tract Cancers; **OR**
 - M. Neuroendocrine and Adrenal Tumors-Poorly Differentiated (High Grade)/Large or Small Cell; **OR**
 - N. Occult Primary; **OR**
 - O. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer - Mucinous Carcinoma; **OR**
 - P. Pancreatic Adenocarcinoma; **OR**
 - Q. Rectal Cancer; **OR**

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- R. Small Bowel Adenocarcinoma; **OR**
- S. T-Cell Lymphomas, including Hepatosplenic Gamma-Delta, Peripheral T-Cell Lymphomas, Adult T-Cell Leukemia/Lymphoma or Extranodal NK/T-Cell Lymphoma, nasal type; **OR**
- T. Thymomas and Thymic Carcinomas.

Requests for levoleucovorin agents (Khapzory) may not be approved when the above criteria are not met and for all other indications.

Key References:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2020. 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: July 25, 2020.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2019; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2019 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed on July 25, 2020.
 - a. Acute Lymphoblastic Leukemia. V1.2020. Revised January 15, 2020.
 - b. Anal Carcinoma. V2.2020. Revised July 16, 2020.
 - c. B-Cell Lymphomas. V2.2020. Revised July 9, 2020.
 - d. Bladder Cancer. V6.2020. Revised July 16, 2020.
 - e. Bone Cancer. V1.2020. Revised August 12, 2019.
 - f. Central Nervous System Cancers. V2.2020. Revised April 30, 2020.
 - g. Cervical Cancer. V1.2020. Revised January 14, 2020.
 - h. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. V4.2020. Revised December 20, 2019.
 - i. Colon Cancer. V4.2020. Revised June 15, 2020.
 - j. Esophageal and Esophagogastric Junction Cancers. V3.2020. Revised July 7, 2020.
 - k. Gastric Cancer. V2.2020. Revised May 13, 2020.
 - l. Gestational Trophoblastic Neoplasia. V2.2020. Revised May 19, 2020.
 - m. Hepatobiliary Cancers. V4.2020. Revised June 19, 2020.
 - n. Neuroendocrine and Adrenal Tumors. V1.2020. Revised July 10, 2020.
 - o. Occult Primary. V3.2020. Revised May 12, 2020.
 - p. Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V1.2020. Revised March 11, 2020.
 - q. Pancreatic Adenocarcinoma. V1.2020. Revised November 16, 2019.
 - r. Rectal Cancer. V6.2020. Revised June 25, 2020.
 - s. T-Cell Lymphomas. V1.2020. Revised January 6, 2020.
 - t. Thymomas and Thymic Carcinomas. V1.2020. Revised November 27, 2019.
6. Tsimberidou AM, Kantarjian HM, et al. Fractionated cyclophosphamide, vincristine, liposomal daunorubicin, and dexamethasone plus rituximab and granulocyte-macrophage-colony stimulating factor (GM-CSF) alternating with methotrexate and cytarabine plus rituximab and GM-CSF in patients with Richter syndrome or fludarabine-refractory chronic lymphocytic leukemia. *Cancer* 2003; 97:1711-20.
7. Pappo AS, Bowman LC, et al. A phase II trial of high-dose methotrexate in previously untreated children and adolescents with high-risk unresectable or metastatic rhabdomyosarcoma. *J Pediatr Hematol Oncol* 1997;19:438-42.

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

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

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