

Policy Title:	Khapzory (levoleucovorin) (Intravenous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	12/18/19		
Revision Date:	12/18/19		

Purpose: To support safe, effective and appropriate use of Khapzory (levoleucovorin).

Scope: Medicaid, Exchange, Medicare-Medicaid (MMP)

Policy Statement:

Khapzory (levoleucovorin) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Khapzory (levoleucovorin) will be reviewed prospectively via the prior authorization process based on criteria below.

Initial Criteria:

- Authorization may be granted for any of the indications listed below when leucovorin is not an available option at this time*:
 - Rescue treatment after high-dose methotrexate therapy
 - Treatment of a folate antagonist overdose
 - Combination therapy with fluorouracil based chemotherapy regimens; AND
- Dose is within FDA guidelines

*The shortage of leucovorin (all strengths) must be confirmed at FDA drug shortage website at: <https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>

Continuation of Therapy Criteria:

- Patient meets all initial criteria; AND
- Patient is tolerating treatment and shows a positive response to treatment

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable.***

Dosage/Administration:

Indication	Dose	Maximum dose (1 billable unit = 0.5 mg)
In combination with high-dose methotrexate	7.5 mg (approximately 5 mg/m ²) IV every 6 hours for 10 doses starting 24 hours after beginning of methotrexate infusion. Dosing is based on a methotrexate dose of 12 grams/m ² administered by intravenous infusion over 4 hours. Continue until methotrexate levels are less than 5 x 10 ⁻⁸ M (0.05 micromolar)	1200 units every 28 days
Reduction of toxicity due to impaired elimination or inadvertent overdose with folic acid antagonists	7.5 mg (approximately 5 mg/m ²) IV every 6 hours until methotrexate levels are less than 5 x 10 ⁻⁸ M (0.05 micromolar).	1200 units every 28 days
In combination with 5-FU for Colorectal Cancer	100 mg/m ² administered by slow intravenous injection over a minimum of 3 minutes, followed by 5-FU at 370 mg/m ² by intravenous injection. OR 10 mg/m ² administered by intravenous injection followed by 5-FU at 425 mg/m ² by intravenous injection. Treatment is repeated daily for five days. This five-day treatment course may be repeated at 4-week (28-day) intervals, for 2 courses and then repeated at 4 to 5 week (28 to 35 day) intervals provided that the patient has completely recovered from the toxic effects of the prior treatment course. <u>Alternate Dosing Regimen</u> 200 mg/m ² administered by intravenous injection DAY 1 followed by 5-FU 400 mg/m ² bolus on DAY 1, then 5-FU 1200 mg/m ² /day x 2 days IV continuous infusion; repeat every 14 days.	2,500 units every 28 days

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:

Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
C9043	Injection, levoleucovorin, 1 mg
J0642	Injection, levoleucovorin, 0.5mg

References:

1. Levoleucovorin injection [package insert]. Princeton, NJ: Sandoz Inc.; November 2013.
2. Khapzory [package insert]. Irvine, CA: Spectrum Pharmaceuticals, Inc.; October 2018.
3. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 22, 2018.
4. The NCCN Clinical Practice Guidelines in Oncology® Colon Cancer (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
5. The NCCN Clinical Practice Guidelines in Oncology® Gastric Cancer (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
6. The NCCN Clinical Practice Guidelines in Oncology® Esophageal and Esophago gastric Junction Cancer (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
7. The NCCN Clinical Practice Guidelines in Oncology® Pancreatic Adenocarcinoma (Version 3.2017). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
8. The NCCN Clinical Practice Guidelines in Oncology® Rectal Cancer (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
9. The NCCN Clinical Practice Guidelines in Oncology® Cervical Cancer (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
10. The NCCN Clinical Practice Guidelines in Oncology® Anal Carcinoma (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
11. The NCCN Clinical Practice Guidelines in Oncology® Thymomas and Thymic Carcinomas (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
12. The NCCN Clinical Practice Guidelines in Oncology® Occult Primary (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.

13. The NCCN Clinical Practice Guidelines in Oncology® Ovarian Cancer (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
14. The NCCN Clinical Practice Guidelines in Oncology® Thymomas and Bladder Cancer (Version 3.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
15. The NCCN Clinical Practice Guidelines in Oncology® Bone Cancer (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
16. The NCCN Clinical Practice Guidelines in Oncology® T-Cell Lymphomas (Version 3.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
17. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphoma (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
18. The NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.
19. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 22, 2018.