

Drug Policy:

Fusilev™/Khapzory™ (levoleucovorin)

POLICY NUMBER UM ONC_1288	SUBJECT Fusilev™/Khapzory™ (levoleucovorin)	DEPT/PROGRAM UM Dept	PAGE 1 OF 3
DATES COMMITTEE REVIEWED 04/13/16, 02/06/17, 02/01/18, 02/13/19, 12/11/19, 02/12/20, 11/11/20, 10/13/21	APPROVAL DATE October 13, 2021	EFFECTIVE DATE October 29, 2021	COMMITTEE APPROVAL DATES 04/13/16, 02/06/17, 02/01/18, 02/13/19, 12/11/19, 02/12/20, 11/11/20, 10/13/21
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee	
URAC STANDARDS HUM 1	NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS	APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Fusilev/Khapzory (levoleucovorin) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the [Preferred Drug Guidelines OR](#)
2. When health plan Exchange coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the [Preferred Drug Guidelines OR](#)

3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the [Preferred Drug Guidelines shall follow NCH L1 Pathways](#) when applicable, otherwise shall follow NCH drug policies [AND](#)
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision [AND](#)
5. When applicable, generic alternatives are preferred over brand-name drugs.

B. Osteosarcoma

1. [NOTE: Per NCH policy, Fusilev is preferred over Khapzory when Leucovorin is not available at the office and the drug shortage is reported by the FDA. This recommendation is based on the lack of Level 1 evidence \(randomized trials and/or meta-analyses\) to support that Khapzory is superior to Leucovorin/Fusilev.](#)
2. The member has osteosarcoma or dedifferentiated chondrosarcoma and Khapzory is being used only when Leucovorin and Fusilev are not available at the office and the shortage is reported on FDA drug shortage website ^A [AND](#)
3. Fusilev/Khapzory is being used following administration of high-dose methotrexate >500 mg/m² over <4 hours [OR](#) >1 g/m² over >4 hours [AND](#)
4. Is administered 24 hours after start of methotrexate infusion so that it does not interfere with the therapeutic effect of methotrexate.

C. Colorectal Cancer

1. [NOTE: Per NCH policy, Fusilev is preferred over Khapzory when Leucovorin is not available at the office and the drug shortage is reported by the FDA. This recommendation is based on the lack of Level 1 evidence \(randomized trials and/or meta-analyses\) to support that Khapzory is superior to Leucovorin/Fusilev.](#)
2. The member has colorectal cancer and Khapzory is being used only when Leucovorin and Fusilev are not available at the office and the shortage is reported on FDA drug shortage website ^A [AND](#)
3. Fusilev/Khapzory is being used in combination with fluorouracil-based regimens in [ONE](#) of the following conditions:
 - a. For potentiation of fluorouracil therapy in the treatment of colorectal cancer
 - b. For treatment of colorectal cancer in combination regimen consisting of fluorouracil, leucovorin, and either irinotecan and/or oxaliplatin.

D. Overdosages of Folic Acid Antagonists

1. [Note: Per NCH policy, Fusilev is preferred over Khapzory when Leucovorin is not available at the office and the drug shortage is reported by the FDA. This recommendation is based on the lack of Level 1 evidence \(randomized trials and/or meta-analyses\) to support that Khapzory is superior to Leucovorin/Fusilev.](#)
2. Khapzory is being used only when Leucovorin and Fusilev are not available at the office and the shortage is reported on FDA drug shortage website ^A [AND](#)
3. Fusilev/Khapzory is being used to diminish the toxicity and counteract the effects of impaired methotrexate elimination and of inadvertent overdosages of methotrexate in [ONE](#) of the following conditions:
 - a. Used in combination with cerebral spinal fluid (CSF) exchange and dexamethasone for intrathecal methotrexate overdose
 - b. Used in combination with forced diuresis and alkalization of urine to prevent potentially toxic blood levels of methotrexate
 - c. Used as high dose for methotrexate-induced nephrotoxicity.

III. EXCLUSION CRITERIA

- A. Fusilev/Khapzory (levoleucovorin) is being used in member with pernicious or megaloblastic anemia.
- B. Dosing exceeds single dose limit of Fusilev/Khapzory (levoleucovorin) 400 mg/m².
- C. Treatment in colorectal cancer exceeds the maximum 24 weeks duration limit.
- D. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

IV. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

- A. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA:
<http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>
- B. Fusilev prescribing information. Acrotech Biopharma LLC. Irvine, CA. 2020.
- C. Khapzory prescribing information. Acrotech Biopharma LLC. Irvine, CA. 2021.
- D. Clinical Pharmacology Elsevier Gold Standard 2021.
- E. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2021.
- F. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2021.
- G. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2021.