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, 11/15/21, 05/11/22, 10/12/22, 04/12/23, 04/10/24	**APPROVAL DATE** April 10, 2024	**EFFECTIVE DATE** April 26, 2024	**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, 11/15/21, 05/11/22, 10/12/22, 04/12/23, 04/10/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
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.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent 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. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. Colorectal Cancer

1. 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.

C. Osteosarcoma

1. Fusilev/Khapzory is being used following administration of high-dose methotrexate greater than 500 mg/m^2 over less than 4 hours OR greater than 1 g/m^2 over less than 4 hours AND
2. Is administered 24 hours after start of methotrexate infusion so that it does not interfere with the therapeutic effect of methotrexate.

D. Overdosages of Folic Acid Antagonists

1. 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. Dosing exceeds single dose limit of Fusilev/Khapzory (levoleucovorin) 400 mg/m^2.

B. Investigational use of Fusilev/Khapzory (levoleucovorin) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

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. 2023.

C. Khapzory prescribing information. Acrotech Biopharma LLC. Irvine, CA. 2020.

D. Leucovorin prescribing information. Fresenius Kabi USA, LLC Lake Zurich, IL 2018

E. Clinical Pharmacology Elsevier Gold Standard 2023.

F. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.

G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

I. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

J. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.