

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Levoleucovorin Products Utilization Management Medical Policy

- Fusilev® (levoleucovorin intravenous infusion – Spectrum)
- Khapzory™ (levoleucovorin intravenous infusion – Spectrum)
- Levoleucovorin intravenous infusion – various manufacturers

REVIEW DATE: 05/20/2026

OVERVIEW

Levoleucovorin (Fusilev, Khapzory, generic) is indicated for the following uses:^{1,2}

- **Colorectal cancer**, in advanced metastatic disease for use in combination chemotherapy with 5-fluorouracil.
- **Impaired methotrexate elimination** or overdosage of folic acid antagonists.
- **Osteosarcoma**, for rescue after high-dose methotrexate therapy.

Levoleucovorin is the pharmacologically active, levo-isomer of racemic *d,l*-leucovorin.^{1,2} Levoleucovorin is a chemically reduced derivative of folic acid, which can counteract the toxic and therapeutic effects of folic acid antagonists, such as methotrexate. In addition, levoleucovorin can enhance the therapeutic and toxic effects of fluoropyrimidines used in oncology.

Guidelines

The use of levoleucovorin is recommended across multiple National Comprehensive Cancer Network (NCCN) guidelines and the NCCN Compendium.³⁻¹⁹ Recommendations with a category of evidence of 2B or higher support the approval criteria outlined below.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of levoleucovorin. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with levoleucovorin as well as the monitoring required for adverse events and long-term efficacy, approval requires levoleucovorin to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of levoleucovorin is recommended in those who meet one of the following:

FDA-Approved Indications

Colon, Rectal, and Appendiceal Cancer. Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) The medication is used in combination with fluorouracil-based chemotherapy; AND
- B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 200 mg/m² administered intravenously before each dose of 5-fluorouracil.

2. **Methotrexate Overdosage, or Impaired Methotrexate Elimination.** Approve for 1 month.

Dosing. Approve ONE of the following dosing regimens (A or B):

- A) Administer up to 7.5 mg intravenously no more frequently than once every 6 hours; OR
- B) Administer up to 75 mg intravenously no more frequently than once every 3 hours.

3. **Osteosarcoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) The medication is used in combination with high-dose methotrexate; AND
- B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):

- A) Administer up to 7.5 mg intravenously no more frequently than once every 6 hours; OR
- B) Administer up to 75 mg intravenously no more frequently than once every 3 hours.

Other Uses with Supportive Evidence

4. **Cancer Diagnosis Currently Being Treated With Methotrexate.** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

Note: Examples include T-cell lymphoma, B-cell lymphoma, gestational trophoblastic neoplasm, central nervous system cancer.

Dosing. Approve ONE of the following dosing regimens (A or B):

- A) Administer up to 7.5 mg intravenously no more frequently than once every 6 hours; OR
- B) Administer up to 75 mg intravenously no more frequently than once every 3 hours.

5. **Cancer Diagnosis Currently Being Treated With 5-Fluorouracil.** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

Note: Examples include ovarian cancer, gastric cancer, cervical cancer.

Dosing. Approve up to 100 mg/m² administered intravenously before each dose of 5-fluorouracil.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of levoleucovorin is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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2. Khapzory[™] intravenous infusion [prescribing information]. Irvine, CA: Spectrum Pharmaceuticals; March 2020.
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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/26/2024
Annual Revision	No criteria changes.	06/18/2025
Annual Revision	Colon, Rectal, and Appendiceal Cancer: Indication was changed to as listed. Previously, listed as Colon or Rectal Carcinoma.	05/20/2026

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