PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Injectable) – Levoleucovorin Products Prior Authorization Policy
- Fusilev® (levoleucovorin intravenous infusion – Spectrum)
- Khapzory™ (levoleucovorin intravenous infusion – Spectrum)
- Levoleucovorin intravenous infusion – various manufacturers

REVIEW DATE: 06/26/2024

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 National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium recommends levoleucovorin use in combination with methotrexate for the treatment of gestational trophoblastic neoplasia, T-cell lymphomas, central nervous system cancers, B-cell lymphomas, chronic lymphocytic leukemia/small lymphocytic lymphoma, acute lymphoblastic leukemia, pediatric aggressive mature B-cell lymphomas, blastic plasmacytoid dendritic cell neoplasm, osteosarcoma, and Waldenstrom macroglobulinemia.[3] The NCCN Compendium recommends levoleucovorin use in combination with fluorouracil-based chemotherapy for the treatment of occult primary cancer, neuroendocrine and adrenal tumors, biliary tract cancers, ovarian/fallopian tube/primary peritoneal cancer, thymomas and thymic carcinomas, esophageal and esophagogastric junction cancer, anal cancer, colon cancer, appendiceal adenocarcinoma, gastric cancer, small bowel adenocarcinoma, ampullary cancer, cervical cancer, vaginal cancer, rectal cancer, pancreatic adenocarcinoma, and bladder cancer.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of levoleucovorin. 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

1. **Colon or Rectal Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Levoleucovorin is used in combination with fluorouracil-based chemotherapy; AND
   B) Levoleucovorin is prescribed by or in consultation with an oncologist.

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

3. **Osteosarcoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Levoleucovorin is used in combination with high-dose methotrexate; AND
   B) Levoleucovorin is prescribed by or in consultation with an oncologist.

Other Uses with Supportive Evidence

4. **Cancer Diagnosis Currently Being Treated With Methotrexate**. Approve for 1 year if levoleucovorin 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.

5. **Cancer Diagnosis Currently Being Treated With 5-Fluorouracil**. Approve for 1 year if levoleucovorin is prescribed by or in consultation with an oncologist.
   Note: Examples include ovarian cancer, gastric cancer, cervical cancer.

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

1. Fusilev® intravenous infusion [prescribing information]. Irvine, CA: Spectrum Pharmaceuticals; November 2020.
2. Khapzory™ intravenous infusion [prescribing information]. Irvine, CA: Spectrum Pharmaceuticals; March 2020.
3. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 17, 2024. Search term: levoleucovorin.
4. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 3.2024 – May 24, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.
5. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – April 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.