Levoleucovorin products (Fusilev, Khapzory)

Humana. Pharmacy Coverage Policy

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Line of Business: Medicaid - Louisiana
Policy Type: Prior Authorization

Disclaimer

Description

Levoleucovorin is the pharmacologically active isomer of leucovorin [(6-S)-leucovorin]. Fusilev (levoleucovorin) for injection contains levo-leucovorin calcium; Khapzory (levoleucovorin) contains sodium, chemically reduced derivatives of folic acid. It is useful as antidote to the inhibition of dihydrofolate reductase by methotrexate.

Lvoleucovorin is indicated for rescue after high-dose methotrexate therapy in osteosarcoma, diminishing the toxicity and counteracting the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists, and use in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer. Limitations of use include the treatment of pernicious anemia and megaloblastic anemias secondary to the lack of vitamin B_{12}. Improper use may cause a hematologic remission while neurologic manifestations continue to progress.

Levoleucovorin is available as sterile solution in single-use vials as Fusilev 50 mg, 175 mg, and 250 mg for intravenous (IV) use only or single-dose vial as Khapzory 175 mg and 300 mg lyophilized powder.

Coverage

Please note the following regarding medically accepted indications:

Determination

All reasonable efforts have been made to ensure consideration of medically accepted indications in this policy. Medically accepted indications are defined by CMS as those uses of a covered Part D drug that are approved under the federal Food, Drug and Cosmetic Act, or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in section 1927(g)(1)(B)(i) of the Act. These compendia guide review of off-label and off-evidence prescribing and are subject to minimum evidence standards for each compendium. Currently, this review includes the following references when applicable and may be subject to change per CMS:

- American Hospital Formulary Service-Drug Information (AHFS-DI)
- National Comprehensive Cancer Network (NCCN) Drugs and Biologics
- Compendium
- Truven Health Analytics Micromedex DrugDEX
- Elsevier/Gold Standard Clinical Pharmacology

Wolters Kluwer Lexi-Drugs

Fusilev (levoleucovorin), Khapzory (levoleucovorin) will require prior authorization. This agent may be considered medically necessary when the following criteria are met:

Osteosarcoma

- The member is being treated with high dose methotrexate for osteosarcoma AND
- The member has been treated with leucovorin calcium AND (one of the following applies):
  - member has experienced documented side effects due to lack of
  - leucovorin calcium efficacy OR member has experienced documented side effects due to leucovorin calcium formulation necessitating a change in therapy

- The member has been treated with methotrexate or other folic acid antagonist and is currently exhibiting signs of toxicity likely due to aforementioned therapy AND
- The member has been treated with leucovorin calcium AND (one of the following applies):
  - member has experienced documented side effects due to lack of leucovorin calcium efficacy OR member has experienced documented side effects due to leucovorin calcium formulation necessitating a change in therapy

Advanced Metastatic Colorectal Cancer

- The member has advanced metastatic colorectal cancer AND
- The member is receiving palliative treatment with combination chemotherapy with 5-fluorouracil AND
- The member has been treated with leucovorin calcium AND (one of the following applies):
  - member has experienced documented side effects due to lack of leucovorin calcium efficacy OR member has experienced documented side effects due to leucovorin calcium formulation necessitating a change in therapy

The recommended dosing regimen for Fusilev (levoleucovorin), Khapzory (levoleucovorin):

Levoleucovorin Rescue After High-Dose Methotrexate Therapy:
Levoleucovorin rescue recommendations are based on a methotrexate dose of 12 grams/m^2 administered by intravenous infusion over four hours. Levoleucovorin

rescue at a dose of 7.5 mg (approximately 5 mg/m²) every six hours for ten doses starts 24 hours after the beginning of the methotrexate infusion. Levoleucovorin dose and/or frequency may need to be adjusted.

levoleucovorin aadministration in Combination with 5-Fluorouracil (5-FU): The following regimens have been used historically for the treatment of colorectal cancer:

- levoleucovorin administered at 100 mg/m^2 by slow intravenous injection over a minimum of 3 minutes, followed by 5-FU at 370 mg/m^2 by intravenous injection.
- levoleucovorin is administered at 10 mg/m^2 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 weeks (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.

- 5-FU and levoleucovorin should be administered separately to avoid the formation of a precipitate.
- Alternative dosing: Levoleucovorin, when substituted in place of leucovorin calcium within a chemotherapy regimen, is dosed at one-half the usual dose of leucovorin calcium

Do not administer intrathecally.

levoleucovorin is dosed at one-half the usual dose of the racemic form (leucovorin calcium).

Fusilev (levoleucovorin), Khapzory (levoleucovorin) will be approved for six-month durations or as determined through clinical review.

Coverage Limitations

Fusilev, Khapzory (levoleucovorin) therapy is not considered medically necessary for members with the following concomitant conditions:

- Members with pernicious anemia or megaloblastic anemia secondary to the lack of vitamin B_{12}

- Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

Background

This is a prior authorization policy about Fusilev (levoleucovorin), Khapzory (levoleucovorin).

Dose Adjustments:

Clinical Situation	Laboratory Findings	Fusilev Dosage and Duration
Normal methotrexate elimination	Serum methotrexate level approximately 10 micromolar at 24 hours after start of administration, 1 micromolar methotrexate infusion) at 48 hours, and less than 0.2 micromolar at 72 hours	7.5 mg IV q 6 hours for 60 hours (10 doses starting at 24 hours after methotrexate
Delayed late methotrexate elimination	Serum methotrexate level remaining above 0.2 micromolar at 72 hours, and more than 0.05 micromolar after administration	Continue 7.5 mg IV q 6 hours, until methotrexate level is less than 0.05 micromolar at 96 hours
Delayed early methotrexate until elimination and/or evidence is less of acute renal injury then 7.5	Serum methotrexate level of 50 micromolar or more than 24 hours, or 5 micromolar or more at 48 hours after administration, OR; a 100% is less or greater increase in serum micromolar creatinine level at 24 hours after methotrexate administration (e.g., an increase 0.5 mg/dL to a level of 1 mg/dL or more)	75 mg IV q hours methotrexate level than 1 micromolar; mg IV q 3 hours until methotrexate level than 0.05

levoleucovorin should not be utilized in the following:

- Hypersensitivity to folic acid, folinic acid/leucovorin, or mannitol.
- The safety and efficacy has not been established in pediatric patients less than six years old.

- Patients with pernicious anemia and megaloblastic anemias secondary to the lack of vitamin B_{12}. Improper use may cause a hematologic remission while neurologic manifestations continue to progress.
- Due to Ca^{++} content in Fusilev, no more than 16 mL (160 mg) of levoleucovorin solution should be injected intravenously per minute.
- levoleucovorin may enhance the toxicity of fluorouracil.
- Concomitant use of *d,l*-leucovorin with trimethoprim-sulfamethoxazole for Pneumocystis carinii pneumonia in HIV patients was associated with increased rates of treatment failure in a placebo-controlled study.
- Fusilev (levoleucovorin) may counteract the antiepileptic effect of phenobarbital,phenytoin and primidone, and increase the frequency of seizures in susceptible members.
- Do not administer intrathecally.
- See also Coverage Limitations section of this policy.

Provider Claims Codes

For medically billed requests, please visit www.humana.com/PAL. Select applicable Preauthorization and Notification List(s) for medical and procedural coding information.

Medical Terms

Fusilev; levoleucovorin; prevention of methotrexate toxicity; folic acid antagonist overdose; colorectal cancer; intravenous; pharmacy; Khapzory

References

Fusilev® (levoleucovorin calcium) [prescribing information]. Spectrum Pharmaceuticals, Inc. Irvine, CA. April 2011.
NationalComprehensiveCancerNetwork. Cancer Guidelines and Drugs and Biologics

Compendium. update periodically
Khapzory (levoleucovorin calcium) [prescribing information]. Spectrum Pharmaceuticals, Inc. Irvine, CA. October 2018.