Levoleucovorin products (Fusilev, Khapzory)

Humana

Pharmacy Coverage Policy

Effective Date: April 17, 2019
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Line of Business: Medicare, Commercial, Medicaid - Kentucky, Medicaid - South Carolina, Medicaid - Ohio
Policy Type: Prior Authorization

Products Affected

Fusilev intravenous solution
Khapzory intravenous solution
levoleucovorin calcium intravenous solution
levoleucovorin calcium intravenous powder for solution

Listed Indications

Osteosarcoma
Impaired methotrexate elimination or inadvertent over dosage of folic acid antagonists
Advanced Metastatic Colorectal Cancer

Osteosarcoma

Does the member meet all of the following criteria?	
Criteria #1	The member is being treated with high dose methotrexate for osteosarcoma
Criteria #2	The member has been treated with leucovorin calcium
Criteria #3	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 (For Medicare, this criteria does not apply to medical benefits.)
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	Members with pernicious anemia or megaloblastic anemia secondary to the lack of vitamin B12
Approval Duration	
Initial	Plan year duration

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Impaired methotrexate elimination or inadvertent over dosage of folic acid antagonists

Does the member meet all of the following criteria?	
Criteria #1	The member has been treated with methotrexate or other folic acid antagonist and is currently exhibiting signs of toxicity likely due to aforementioned therapy
Criteria #2	The member has been treated with leucovorin calcium
Criteria #3	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 (For Medicare, this criteria does not apply to medical benefits.)
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	Members with pernicious anemia or megaloblastic anemia secondary to the lack of vitamin B12
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Initial	Plan year duration

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Advanced Metastatic Colorectal Cancer	
Does the member meet all of the following criteria?	
Criteria #1	The member has advanced metastatic colorectal cancer
Criteria #2	The member is receiving palliative treatment with combination chemotherapy with 5-fluorouracil
Criteria #3	The member has been treated with leucovorin calcium
Criteria #4	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 (For Medicare, this criteria does not apply to medical benefits.)
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	Members with pernicious anemia or megaloblastic anemia secondary to the lack of vitamin B12
Approval Duration	
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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 administration, 1 micromolar 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 start of methotrexate infusion)
Delayed late methotrexate elimination	Serum methotrexate level remaining above 0.2 micromolar at 72 hours, and more than 0.05 micromolar at 96 hours after administration	Continue 7.5 mg IV q 6 hours, until methotrexate level is less than 0.05 micromolar
Delayed early methotrexate elimination and/or evidence of acute renal injury	Serum methotrexate level of 50 micromolar or more than 24 hours, or 5 micromolar or more at 48 hours after administration, OR; a 100% or greater increase in serum 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 until methotrexate level is less than 1 micromolar; then 7.5 mg IV q 3 hours until methotrexate level is less than 0.05 micromolar

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.

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.

Provider Claim 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]. Acrotech Biopharma LLC. East Hanover, NJ. March 2020.

Disclaimer	State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, take precedence over clinical policy and must be considered first in determining eligibility for coverage. Coverage may also differ for our Medicare and/or Medicaid members based on any applicable Centers for Medicare & Medicaid Services (CMS) coverage statements including National Coverage Determinations (NCD), Local Medical Review Policies (LMRP) and/or Local Coverage Determinations. See the CMS website at http://www.cms.hhs.gov/. The member's health plan benefits in effect on the date services are rendered must be used. Clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Clinical technology is constantly evolving, and we reserve the right to review and update this policy periodically.