



Prior Authorization Approval Criteria
Department of Pharmacy Services

Generic Name: Levoleucovorin

Brand Name: Fusilev®

Medication Class: Antimetabolite antidote

FDA Approved Uses:

- Rescue treatment indicated after high-dose methotrexate therapy in osteosarcoma
- Diminish the toxicity and counteract the effects of impaired methotrexate elimination and of inadvertent overdose of folic acid antagonists

Available Dosage Forms:

- 50 mg powder for reconstitution; must be further diluted before infusion

Usual Dose (osteosarcoma):

- 7.5 mg (approximately 5 mg/m²) IV every 6 hours for 10 doses starting 24 hours after beginning of methotrexate infusion. Dosing is based on a methotrexate dose of 12 grams/m² administered by intravenous infusion over 4 hours. Continue until methotrexate levels are <5 × 10⁻⁸ M (0.05 micromolar)
- Hydration and urinary alkalinization (pH of ≥ 7.0) should be continued throughout therapy until target methotrexate levels are achieved

Usual dose (impaired methotrexate elimination or inadvertent overdose):

- 7.5 mg (approximately 5 mg/m²) IV every 6 hours until the serum methotrexate level is less than 10⁻⁸M. Hydration (3L/day) and urinary alkalinization with NaHCO₃ should be employed concomitantly

Duration of Therapy:

- Until methotrexate levels are below 5 × 10⁻⁸ M (0.05 micromolar) for osteosarcoma and 10⁻⁸M for impaired elimination/inadvertent overdose

Approximate monthly cost is unavailable as of 9/2/08

Criteria for Use: (bullet points below are all inclusive unless otherwise noted)

- Patients with osteosarcoma whose regimen includes high-dose methotrexate
- Patients older than 6 years old.

Non-approved disease states

- Pernicious anemia and megaloblastic anemias



- Colorectal cancer in combination with 5-fluorouracil

Criteria for Continuation of Therapy:

- Must be on high dose methotrexate therapy for the treatment of osteosarcoma
- Must have toxic serum levels of methotrexate

Cautions:

- Gastrointestinal complications such as stomatitis (all grades), nausea, vomiting, typhlitis (all grades)
- Immune hypersensitivity reaction

Monitoring:

- Serum methotrexate levels
- Serum creatinine
- Urinary pH to maintain alkalization
- Fluid status
- Renal function
- Serum electrolytes
- Signs of diminishing methotrexate toxicity
- Signs and symptoms of allergic reactions (e.g. dyspnea, pruritis, rash, temperature changes and rigors)

Contraindications:

- Previous allergic reaction to folic acid or folinic acid

Not Approved if:

- Patient does not meet the above listed criteria
- Being used to treat conditions other than FDA indicated uses (such as pernicious and megaloblastic anemias)
- Patient has any contraindications

Special Considerations:

- Fusilev should not be administered intrathecally
- No more than 16 mL (160mg) of levoleucovorin solution should be injected intravenously per minute due to the calcium content.
- Clinical studies did not include patients that were older than 65 years to determine whether they respond differently from younger subjects
- Safety and efficacy have not been studied in pregnant or lactating women. Fusilev should only be administered if clearly needed.
- Fusilev enhances the toxicity of 5-fluorouracil. Deaths from severe enterocolitis, diarrhea and dehydration have been reported among elderly patients.
- Fusilev is dosed at one-half the usual dose of the racemic form
- The concomitant use of *d,l*- leucovorin with trimethoprim/sulfamethoxazole for the acute



treatment of *Pneumocystis jiroveci* pneumonia in patients with HIV was associated with increased rates of treatment failure and morbidity.

P&T Approval: _____ Date: _____