leucovorin calcium (loo-koe-vor-in)

Classification
Therapeutic: antidotes (for methotrexate), vitamins
Pharmacologic: folic acid analogues

Pregnancy Category: C

Indications
Minimizes hematologic effects of high-dose methotrexate therapy (leucovorin rescue).
Advanced colorectal carcinoma (with 5-fluorouracil).
Management of overdoses/prevention of toxicity from folic acid antagonists (pyrimethamine, trimethoprim, trimetrexate).
Folic acid deficiency (megaloblastic anemia) unresponsive to oral replacement.

Action
The reduced form of folic acid that serves as a cofactor in the synthesis of DNA and RNA.

Therapeutic Effects:
Reversal of toxic effects of folic acid antagonists.
Reversal of folic acid deficiency.

Pharmacokinetics
Absorption: Well absorbed (38%) following PO administration. pBioavailability with larger doses. Oral absorption is saturated at doses >/= 25 mg.
Distribution: Widely distributed. Concentrates in the CNS and liver.
Metabolism and Excretion: Extensively converted to tetrahydrofolic derivatives, including 5-methyltetrahydrofolate, a major storage form.
Half-life: 3.5 hr.

TIME/ACTION PROFILE (serum folate levels)
ROUTE ONSET PEAK DURATION
PO 20–30 min unknown 3–6 hr
IM 10–20 min unknown 3–6 hr
IV 5 min unknown 3–6 hr

Contraindications/Precautions
Contraindicated in: Hypersensitivity; Pedi: Preparations containing benzyl alcohol should not be used in neonates.

Use Cautiously in: Undiagnosed anemia (may mask the progression of pernicious anemia); OB: Lactation: Safety not established but has been used safely to treat megaloblastic anemia in pregnancy.

Adverse Reactions/Side Effects
Hemat: thrombocytosis.
Misc: allergic reactions (rash, urticaria, wheezing).

Interactions
Drug-Drug: May ] anticonvulsant effect of barbiturates, phenytoin, or primidone. High doses of the liquid contain significant alcohol and may cause CNS depression when used with CNS depressants. Concurrent use with trimethoprim/sulfamethoxazole may result in anti-infective efficacy and poor therapeutic outcome when used to treat Pneumocystis jirovecii pneumonia in HIV patients. May ↑ therapeutic effects and toxicity of fluorouracil. Therapy may be combined for this purpose.

Route/Dosage

High-Dose Methotrexate—Leucovorin Rescue. Must start within 24 hr of methotrexate.
PO, IM, IV (Adults and Children): Normal methotrexate elimination—10 mg/m² q 6 hr (1st dose IV/IM, then change to PO) until methotrexate level is 5–10 μg/L. If 0.9 intravenous) Larger doses/longer duration may be required in patients with ascites, acute, dehydration, renal impairment, GI obstruction, portal/pertoneal fistulas. Dose of leucovorin should be determined on the basis of plasma methotrexate levels.

Advanced Colorectal Cancer
IV (Adults): 200 mg/m² followed by 5-fluorouracil 370 mg/m² or leucovorin 20 mg/m² is followed by 5-fluorouracil 425 mg/m². Regimen is given daily for 5 days q 4–5 wk.

Prevention of Hematologic Toxicity from Trimetrexate
PO, IV (Adults and Children): 20 mg/m² q 6 hr continued for 72 hr after last trimetrexate dose (oral doses should be rounded up to the next 25 mg); both trimetrexate and leucovorin doses require adjustment for hematologic toxicity.
Prevention of Hematologic Toxicity from Pyrimethamine
PO, IV (Adults and Children): 5–15 mg/day.

Inadvertent Overdose of Folic Acid Antagonists
IM, IV (Adults and Children): Methotrexate–large doses—75 mg IV followed by 12 mg IV q 5 hr for 4 doses; methotrexate–average doses—6–12 mg IV q 5 hr for 4 doses; other folic acid antagonists—amount equal in mg to folic acid antagonist.

Megaloblastic Anemia
PO, IM, IV (Adults and Children): Up to 1 mg/day (up to 6 mg/day for dihydrofolate reductase deficiency).

NURSING IMPLICATIONS

Assessment
- Assess patient for nausea and vomiting secondary to methotrexate therapy or folic acid antagonists (pyrimethamine and trimethoprim) overdose. Parenteral route may be necessary in severe or persistent nausea.
- Monitor for development of allergic reactions (rash, urticaria, wheezing). Notify health care professional if these occur.
- Megaloblastic Anemia: Assess degree of weakness and fatigue.
- labs: Monitor serum methotrexate levels to determine dose and effectiveness of therapy. Leucovorin calcium levels should be equal to or greater than methotrexate level. Rescue continues until serum methotrexate level is <5 μM.
- Monitor CCr and serum creatinine prior to and every 24 hr during therapy to detect methotrexate toxicity. An increase ≥50% over the pretreatment concentration at 24 hr is associated with severe renal toxicity.
- Monitor urine pH every 6 hr during therapy; pH should be maintained ≥7 to decrease nephrotoxic effects of high-dose methotrexate. Sodium bicarbonate or acetazolamide may be ordered to alkalinize urine.

Potential Nursing Diagnoses
- Risk for injury (Indications)
- Imbalanced nutrition: less than body requirements (Indications)

Implementation
- Do not confuse folic acid (leucovorin calcium) with folic acid. Do not confuse leucovorin with Leukeran (chlorambucil).
- Make sure leucovorin calcium is available before administering high-dose methotrexate therapy.
- Administer as soon as possible after toxic dose of folic acid antagonist (pyrimethamine and trimethoprim). Effectiveness of therapy begins to decrease 1 hr after overdose.
- PO: Parenteral therapy should be used in patients with GI toxicity, with nausea and vomiting, or with doses >25 mg.

IV Administration
- Direct IV: Bacteriostatic water or sterile water. Do not use product containing benzyl alcohol. Use immediately if reconstituted with sterile water for injection. Stable for 7 days when reconstituted with bacteriostatic water. Concentration: reconstitute 50 mg, 100 mg, and 200 mg vials to a concentration of 10 mg/mL; reconstitute 500 mg vial to a concentration of 20 mg/mL. Rate: Administer by slow injection over a minimum of 5 min; not to exceed 160 mg/min.
- Intermittent Infusion: Diluent: May be diluted in 100–500 mL of D5W, D10W, 0.9% NaCl, or LR. Stable for 24 hr.
- Y-Site Compatibility: alemtuzumab, amifostine, amikacin/sulbactam, ampicillin, aztreonam, bivalirudin, bleomycin, carboplatin, carmustine, caspofungin, cisplatin, cladribine, cyclophosphamide, cisplatin, cyclosporine, cyclosporine, dactinomycin, daptomycin, dexamethasone, dexrazoxane, dextran, docetaxel, doxorubicin, doxorubicin liposome, etoposide, etoposide phosphate, fluorouracil, fludarabine, famotidine, fenoldopam, filgrastim, flucytosine, furosemide, gemcitabine, granisetron, heparin, hetastarch, idarubicin, irinotecan, levofloxacin, linezolid, mitomycin, mitoxantrone, nesiritide, octreotide, oxaliplatin, piperacillin/tazobactam, potassium acetate, rituximab, sodium bicarbonate, sodium thiosulfate, sodium valproate, streptokinase, streptodornase, teniposide, ticarcillin, tigecycline, tirofiban, tocilizumab, vinorelbine, vincristine, voriconazole.
- Y-Site Incompatibility: amphotericin B cholesteryl, amphotericin B lipid complex, amphotericin B liposomal; amphotericin B lipid complex, amphotericin B lipid complex, amphotericin B lipid complex.
leucovorin calcium

Patient/Family Teaching
- Explain purpose of medication to patient. Emphasize need to take exactly as or-
dered. Advise patient to contact health care professional if dose is missed.
- Leucovorin Rescue: Instruct patient to drink at least 3 liters of fluid each day
during leucovorin rescue.
- Folic Acid Deficiency: Encourage patient to eat a diet high in folic acid (meat
proteins; beans; dark leafy greens; and green, leafy vegetables).

Evaluation/Desired Outcomes
- Reversal of bone marrow and G1 toxicity in patients receiving methotrexate or in
overdose of folic acid antagonists.
- Increased sense of well-being and increased production of normal cells in pa-
tients with megaloblastic anemia.

Why was this drug prescribed for your patient?