Table. Potential Alternatives to Folinic Acid Products in Selected Clinical Situations[7-13]

Indication	Laboratory Values	Dosage Regimen	Comments
Rescue therapy after high-dose methotrexate	<u>Normal methotrexate elimination</u> Methotrexate level after methotrexate dose: • 24 hours after dose: 10 micromolar, • 48 hours after dose: 1 micromolar, or • 72 hours after dose: less than 0.2 micromolar	Leucovorin* 15 mg (or 10 mg/m^2) oral, IM, or IV every 6 hours X 10 doses. Fusilev 7.5 mg (or 5 mg/m^2) IV every 6 hours X 10 doses.	Begin folinic acid therapy 24 hours after starting methotrexate therapy. Continue folinic acid therapy until methotrexate level is less than 0.05 micromolar (5 x 10^{-8} M).
	<u>Delayed early methotrexate elimination or acute renal injury</u> Methotrexate level after methotrexate dose: • 24 hours after dose: 50 micromolar or higher, or • 48 hours after dose: 5 micromolar or higher Serum creatinine after methotrexate dose: • 24 hours after dose: increased 100% or more from baseline	Leucovorin* 150 mg (or 100 mg/m^2) IV every 3 hours until methotrexate level is less than 1 micromolar, then 15 mg IV every 3 hours until methotrexate level is less than 0.05 micromolar. Fusilev 75 mg (or 50 mg/m^2) IV every 3 hours until methotrexate level is less than 1 micromolar, then 7.5 mg IV every 3 hours until methotrexate level is less than 0.05 micromolar.	
	<u>Delayed late methotrexate elimination</u> Methotrexate level after methotrexate dose: • 72 hours after dose: greater than 0.2 micromolar, or • 96 hours after dose: greater than 0.05 micromolar	Leucovorin* 15 mg (or 10 mg/m^2) oral, IM, or IV every 6 hours until methotrexate level is less than 0.05 micromolar. Fusilev 7.5 mg (or 5 mg/m^2) IV every 6 hours until methotrexate level is less than 0.05 micromolar.	
	<u>Significant methotrexate toxicity</u> Any methotrexate or serum creatinine level, including those that do not match the above. All patients with significant methotrexate toxicity receive the same folinic acid dose, regardless of lab values.	Leucovorin* 15 mg (or 10 mg/m^2) oral, IM, IV every 6 hours X 14 doses for subsequent cycles. Fusilev 7.5 mg (or 5 mg/m^2) IV every 6 hours X 14 doses for subsequent cycles.	
	<u>Delayed methotrexate elimination in a patient with fluid third spacing, renal dysfunction, or poor hydration</u> Any methotrexate or serum creatinine level, including those that do not match the above.	Consider increasing the folinic acid dose or prolonging therapy.	

Indication	Laboratory Values	Dosage Regimen	Comments
Rescue therapy after inadvertent overdose with folic acid antagonist (eg, methotrexate, pemetrexed, pyrimethamine, trimethoprim)	Initial dose Not applicable. All patients with inadvertent overdose receive the same initial folinic acid dose.	Leucovorin* 15 mg (or 10 mg/m^2) oral, IM, or IV every 6 hours. Fusilev 7.5 mg (or 5 mg/m^2) IV every 6 hours.	Start folinic acid therapy as soon as possible after overdose. After 24 hours of therapy, adjust subsequent doses based on lab results. Continue folinic acid therapy until methotrexate level is less than 0.01 micromolar (1 x 10^{-8}).
	Dosage adjustments based on lab values Methotrexate level after methotrexate dose: • 24 hours after dose: greater than 5 micromolar, or • 48 hours after dose: greater than 0.9 micromolar Serum creatinine level after folic acid antagonist dose: • 24 hours after dose: increased 50% or more from baseline	Leucovorin* 150 mg IV (or 100 mg/m^2) every 3 hours. Fusilev 75 mg IV (or 50 mg/m^2) every 3 hours.	
Advanced colorectal cancer[14-17]	Not applicable	Low-dose folinic acid regimen: Leucovorin* 20 mg/m^2 IV followed by fluorouracil 370 to 425 mg/m^2 IV, given daily X 5 days each cycle. Fusilev 10 mg/m^2 IV followed by fluorouracil 370 to 425 mg/m^2 IV, given daily X 5 days each cycle.	Repeat cycles every 4 – 5 weeks as tolerated. Continue therapy until disease progression or unacceptable toxicity. Note: multiple regimens exist. These recommendations are not inclusive.
		High-dose folinic acid regimen: Leucovorin* 200 mg/m^2 IV followed by fluorouracil 370 mg/m^2 IV, given daily X 5 days each cycle. Leucovorin 125 mg/m^2/dose orally given in 4 divided doses (at hours 0, 1, 2, and 3) for a total dose of 500 mg/m^2; then followed by fluorouracil 370 mg/m^2 IV at hour 4; both given daily X 5 days each cycle.[14] Fusilev 100 mg/m^2 IV followed by fluorouracil 370 mg/m^2 IV, given daily X 5 days each cycle	
Megaloblastic anemia due to folic acid deficiency	Not applicable	Leucovorin* $\leq$ 1 mg/day IM. Folic acid 400 mcg/day oral, IM, IV, or subcutaneously. Increase dose to 800 mcg/day in pregnant or lactating women.	Racemic leucovorin offers no advantage over folic acid in these patients. Folic acid injection may be used in patients who are unable to take oral folic acid. Fusilev has not been evaluated for this use.

*Most presentations of leucovorin injection are on back order.[1,2]