CALCIUM FOLINATE:

Class: Chemotherapy Modulating Agent; Rescue Agent (Chemotherapy)

Indications: - Treatment of weak folic acid antagonist overdosage
- Folate-deficient megaloblastic anemia - High-dose methotrexate-rescue dose
-Colorectal cancer -Methotrexate overdose - Pemetrexed toxicity
- Prevention of pyrimethamine hematologic toxicity in HIV-positive patients

Available dosage form in the hospital: 15MG TAB || 30MG AMP || 50MG VIAL

Trade Names: Leucovorin ,Acido Folinico/Leucovorina (CN); Antrex (FI, PL, TW); Asovorin (AR); Cafona (TW); Cafonate (PH); Calcium Folinate (NZ), Leucocalcin (PY); Leuconolver (VE

Dosage:

-Treatment of weak folic acid antagonist overdosage (eg, trimethoprim, pyrimethamine): Oral: 5-15 mg/day

-Folate-deficient megaloblastic anemia: I.M.: ≤1 mg/day

-High-dose methotrexate-rescue dose: Initial: Oral, I.M., I.V.: 15 mg (~10 mg/m^2); start 24 hours after beginning methotrexate infusion; continue every 6 hours for 10 doses, until methotrexate level is <0.05 micromole/L. Adjust dose as follows:

-*Normal methotrexate elimination:* Oral, I.M., I.V.: 15 mg every 6 hours

-*Delayed early methotrexate elimination:* I.V.: 150 mg every 3 hours until methotrexate level is <1 micromole/L, then 15 mg every 3 hours until methotrexate level is <0.05 micromole/L

-Colorectal cancer (also refer to Combination Regimens):

-I.V.: 200 mg/m^2 over at least 3 minutes (used in combination with fluorouracil 370 mg/m^2)

-I.V.: 20 mg/m^2 (used in combination with fluorouracil 425 mg/m^2)

-Methotrexate overdose: Note: The amount of leucovorin administered should equal the amount of methotrexate inadvertently administered.

-I.V.: 1 mg per mg of methotrexate inadvertently administered; 100-1000 mg/m^2 every 3-6 hours has been used; administer until methotrexate levels decrease to goal level or longer if methotrexate levels are unavailable or if patient has renal dysfunction or third-space storage (ascites, pleural effusion)

-A nomogram for leucovorin rescue in cancer patients receiving high-dose methotrexate based upon a 48-hour methotrexate level may be helpful (Widemann, 2006). Methotrexate level:

- ≥80 micromole/L: 1000 mg/m^2 every 6 hours
- ≥8 to <80 micromole/L: 100 mg/m^2 every 3 hours
- ≥2 to <8 micromole/L: 10 mg/m^2 every 3 hours
- ≥0.1 to <2 micromole/L: 10 mg/m^2 every 6 hours

Use of I.T. leucovorin is not advised (Jardine, 1996; Smith, 2008).

-Pemetrexed toxicity (unlabeled dose): I.V.: 100 mg/m^2 once, followed by 50 mg/m^2 every 6 hours for 8 days (used in clinical trial for CTC grade 4 leukopenia ≥3 days; CTC grade 4 neutropenia ≥3 days; immediately for CTC grade 4 thrombocytopenia, bleeding associated with grade 3 thrombocytopenia, or grade 3 or 4 mucositis)

-Cofactor therapy in methanol toxicity (unlabeled use): I.V.: 1 mg/kg (maximum dose: 50 mg) over 30-60 minutes every 4-6 hours. Therapy should continue until methanol and formic acid have been completely eliminated (Barceloux, 2002)

-Prevention of pyrimethamine hematologic toxicity in HIV-positive patients (unlabeled uses; CDC, 2009): Oral:

-Isosporiasis (*Isospora belli*):

- Treatment: 10-25 mg once daily (in combination with pyrimethamine)
- Chronic maintenance (secondary prophylaxis): 5-10 mg once daily (in combination with pyrimethamine)

-*Pneumocystis jirovecii* pneumonia (PCP): Prophylaxis (primary and secondary): 25 mg once weekly (in combination with pyrimethamine [with dapsone]) or 10 mg once daily (in combination with pyrimethamine [with atovaquone])

-Toxoplasmosis (*Toxoplasma gondii*):

- Primary prophylaxis: 25 mg once weekly (in combination with pyrimethamine [with dapsone]) or 10 mg once daily (in combination with pyrimethamine [with atovaquone])
- Treatment: 10-25 mg once daily (in combination with pyrimethamine [with either sulfadiazine, clindamycin, atovaquone, or azithromycin]). Note: May increase leucovorin to 50-100 mg/day in divided doses in cases of pyrimethamine toxicity (rash, nausea, bone marrow suppression).
- Chronic maintenance (secondary prophylaxis): 10-25 mg once daily (in combination with pyrimethamine [with either sulfadiazine or clindamycin]) or 10 mg once daily (in combination with pyrimethamine [with atovaquone])

Geriatric

Refer to adult dosing

Renal Impairment:

No dosage adjustment provided in manufacturer's labeling.

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling.

Common side effect:

Dermatologic: Rash, pruritus, erythema, urticaria

Hematologic: Thrombocytosis

Respiratory: Wheezing

Miscellaneous: Allergic reactions, anaphylactoid reactions

Pregnancy Risk Factor: C