Folinic acid

Newborn use only

2025

Alert	Folinic acid is not the same as folic acid but does have an equivalent vitamin activity. Also known as calcium folinate or Leucovorin.
Indication	Concurrent therapy with dihydrofolate reductase inhibitors, e.g. pyrimethamine. [1, 2] Folinic acid dependent seizures and cerebral folate deficiency.[3, 4]
Action	Folinic acid is the active metabolite of folate that bypasses dihydrofolate reductase.
Drug Type	B Group Vitamin
Trade Name	DBL Leucovorin Calcium Injection, Pfizer Leucovorin Calcium Solution for Injection DBL Leucovorin Calcium Tablets, Folinic Acid Capsules (FIT-Bioceuticals)
Presentation	DBL Leucovorin Calcium injection - 15 mg/2 mL, 50 mg/5 mL, 300 mg/30 mL. Pfizer (Perth) Leucovorin Calcium Injection USP 50 mg (folinic acid) in 5 mL (sterile) and 100 mg (folinic acid) in 10 mL Plastic Vial. Pfizer (Perth) Leucovorin Calcium Injection USP 50 mg (folinic acid) in 5 mL (sterile) and 100 mg (folinic acid) in 10 mL Steriluer ampoule. DBL Leucovorin Calcium tablet 15 mg folinic acid. Folinic Acid Capsules (FIT-Bioceuticals) 500 microg (Not on the NSW State Formulary).
Dose	**Concurrent therapy with dihydrofolate reductase inhibitors[1, 2]** 10 mg three times per **week.** **Folinic acid responsive seizures[3, 5]** 2.5 mg twice a day (doses up to 8 mg/kg/day have been used)
Dose adjustment	Therapeutic hypothermia – Not applicable. ECMO – No information. Hepatic impairment – No dose adjustment. Renal impairment – No dose adjustment.
Maximum Daily Dose	Not established.
Route	Oral
Preparation	**Liquid injection solution:**[16-18] Measure the dose and give undiluted orally. **Folinic acid tablet:** 1. Dispense one tablet into 15 mL of water for injection to make a concentration of 1 mg/mL 2. Shake well to ensure even dispersion 3. Administer required dose immediately, discard any remaining solution
Administration	ORALLY or via gastric tube, ideally administer on an empty stomach (i.e. at least one hour before food or two hours after food).[13]
Monitoring	No specific monitoring required.
Contraindications	Little information. Not effective in methylenetetrahydrofolate reductase deficiency.
Precautions	Avoid use with folic acid antagonists unless under a specialist's advice.[6]
Drug Interactions	Antiepileptics – folinic acid may counteract the antiepileptic effect of phenobarbital (phenobarbitone), phenytoin, primidone, and succinimides and increase the frequency of seizures. Fluorouracil – folinic acid may enhance the toxicity of fluorouracil. Folic acid antagonists – when folinic acid is given in conjunction with a folic acid antagonist (e.g. cotrimoxazole, pyrimethamine) the efficacy of the folic acid antagonist may either be reduced or completely neutralised.[6] Chloramphenicol - Concurrent administration of chloramphenicol and folinic acid in folate deficient patients may result in antagonism of haematopoietic response to folinic acid.
Adverse Reactions	Allergic sensitisation, including anaphylactic reactions, and urticarial rash.[6] Nausea and vomiting with high doses.
Overdose	AUSTRALIA Contact the Poisons Information Centre on **13 11 26** for information on the management of overdose. NEW ZEALAND Contact the National Poisons Centre on **0800 764 766** for information on the management of overdose.
Compatibility	Not applicable.

Incompatibility	Not applicable.
Stability	Use solution prepared from tablets immediately. Discard remaining
Storage	**Solution for injection** Store at 2 to 8°C. (Refrigerate. Do not freeze). Protect from light. **Tablets** Store below 25°C.
Excipients	**Solution for injection.** *DBL Brand*: Sodium chloride and water for injections. Sodium hydroxide and/or hydrochloric acid (used to adjust pH of 300 mg/30 mL only). *Pfizer Brand*: Sodium chloride in water for injections. **Tablets.** Lactose monohydrate, microcrystalline cellulose, magnesium stearate.
Special Comments	
Evidence	**Efficacy** **Concurrent therapy with dihydrofolate reductase inhibitors:** ***Pyrimethamine/sulfadiazine:*** Current guidelines for treatment of the infant with congenital toxoplasmosis are for use of pyrimethamine and sulfadiazine plus folinic acid. [1, 2] Folinic acid 10 mg three times a week is recommended until 1 week following cessation of pyrimethamine treatment. It is advised not to use folic acid as a substitute for folinic acid.[1, 2] Levels of folinic acid in the cerebrospinal fluid (CSF) from folinic acid supplemented infants treated with pyrimethamine for congenital toxoplasmosis are thought to be too low to inhibit the effect of pyrimethamine. [7] However, there are no clinical trials comparing folate or folinic acid versus placebo in infants with toxoplasmosis. ***Methotrexate:*** Folate and folinic acid have a protective and probably similar effect against methotrexate-related adverse effects (including a reduction in gastrointestinal side effects, hepatic dysfunction, and discontinuation of MTX treatment for any reason) in patients with inflammatory disease.[8, 9] ***Trimethoprim/sulfamethoxazole:*** There are no clinical trials comparing folate or folinic acid versus placebo in infants with treated with trimethoprim/sulfamethoxazole. **Folinic acid responsive seizures** Folinic acid responsive epilepsies are caused by low concentrations of 5-methyltetrahydrofolate (MTHF) in the CSF. Genetic or autoimmune mechanisms cause cerebral folate deficiency and delayed treatment may lead to encephalopathy with severe learning disabilities. An EEG may show abnormal background activity with multifocal spike-wave complexes but typically has no diagnostic features. Neuroimaging results are also usually normal. Patients either do not respond to pyridoxine at all or exhibit only a temporary improvement. However, such patients show a marked neurological recovery including cessation of seizures upon folinic acid treatment.[3, 5,10] In infants, folinic acid responsive seizures typically present within days after birth as epileptic spasms – myoclonic, absence, or generalized tonic clonic seizures. Identified gene abnormalities include ALDH7A1, SLC46A1, FOLR1, MTHFR, and MTHFS. Folinic acid 2.5 mg twice a day has been commenced with good effect in many case reports including one report with gradual increase of the dose over 14 months to 45 mg twice a day.[4, 5, 10-15] Recommended treatment includes initial treatment with folinic acid or 5-methyltetrahydrofolate 3–5 mg/kg and long-term treatment with folinic acid or 5-methyltetrahydrofolate 3–5 mg/kg daily. [3] **Safety** No paediatric data are available.
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