
L-METHYLFOLATE (Deplin) Fact Sheet [G]

Bottom Line:

L-methylfolate is a metabolite of dietary folic acid, and is necessary for the synthesis of the main neurotransmitters relevant to psychiatric disorders. Though the data are not robust, folate supplementation *might* be effective for some patients with depression, but we recommend that patients try the cheap stuff (folic acid) before springing for Deplin (L-methylfolate).

FDA Indications:

None.

Off-Label Uses:

Adjunctive treatment for depression (considered a “medical food product” by the FDA, not an FDA-approved drug product, although available as prescription only).

Dosage Forms:

- **Capsules (Deplin):** 7.5 mg, 15 mg.
- **Tablets and capsules (various other L-methylfolate products, [G]):** 0.4 mg, 0.8 mg, 1 mg, 3 mg, 5 mg.

Dosage Guidance:

Depression (Deplin only): Start 7.5 mg QD; target and max dose 15 mg/day.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: (G): \$\$; Deplin: \$\$\$

Side Effects:

- Most common: Not well known; likely well tolerated.
- Serious but rare: Folic acid supplementation may mask symptoms of vitamin B12 deficiency (administration of folic acid may reverse the hematological signs of B12 deficiency, including megaloblastic anemia, while not addressing neurological manifestations). L-methylfolate may be less likely than folic acid to mask B12 deficiency, though the possibility should be considered.
- Pregnancy/breastfeeding: Considered safe.

Mechanism, Pharmacokinetics, and Drug Interactions:

- May enhance synthesis of monoamine neurotransmitters.
- No typical drug metabolism pathway as it is naturally stored and used by body; $t_{1/2}$: 3 hours.
- Drug interactions generally unlikely, although L-methylfolate may decrease anticonvulsant levels (including carbamazepine and valproic acid). Drugs that lower folate, such as anticonvulsants (including carbamazepine, valproic acid, and lamotrigine), may necessitate higher doses of L-methylfolate.

Clinical Pearls:

- Dietary folic acid is normally transformed to L-methylfolate by the enzyme MTHFR, and L-methylfolate is necessary for the synthesis of monoamines (serotonin, norepinephrine, dopamine). The marketing pitch for prescribing Deplin is that in about 50% of the population, genetic variations impair the function of MTHFR, leading to low levels of methylfolate. A recent review of the data on one of these genetic polymorphisms (called C677T) found that overall, it did not put people at any higher risk of depression (in fact, schizophrenia was more common).
- A few small studies over the years have shown that both folate (over the counter) and L-methylfolate may be somewhat helpful as adjunctive agents in the treatment of depression, particularly in those with low baseline folate levels.

Fun Fact:

“Medical foods” are foods that are specially formulated and intended for the dietary management of a disease with distinctive nutritional needs that cannot be met by normal diet alone. These include total parenteral nutrition as well as nasogastric tube feeds and oral rehydration products. Depression has no accepted distinctive nutritional needs.