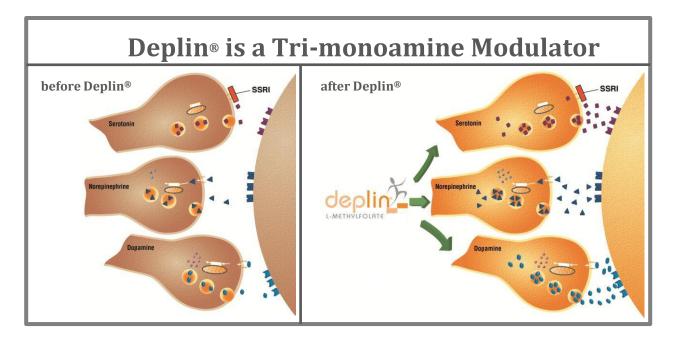


What Is Deplin[®] (L-methylfolate)?

Deplin[®] (L-methylfolate) is an orally administered medical food for use only under medical supervision for the metabolic management of suboptimal L-methylfolate levels in depressed patients.

L-methylfolate, which is a trimonoamine modulator (TMM), is needed to help the body regulate the synthesis or production of monoamines neurotransmitters— serotonin, norepinephrine and dopamine— three important chemicals found in the brain. Low levels of these chemicals have been associated with depression. Patients suffering from major depressive disorder may have a genetic abnormality that reduces their ability to convert folate into the

centrally active compound, L-methylfolate.¹



L-methylfolate, or Deplin[®] works through a natural process in the brain by supplying the distinct nutritional requirements needed by the brain to regulate the neurotransmitters associated with mood.

How is Deplin[®] Different from Folic Acid?

All folate is not the same.

Deplin[®] significantly differs from synthetic forms of folic acid available overthe-counter that do not need to be used under medical supervision. Lmethylfolate is the only form of folate that can cross the blood brain barrier and regulate serotonin, norepinephrine and dopamine, the neurotransmitters associated with mood.³

Synthetic folic acid and dietary folate, found in foods and vitamins must be broken down in the body by a lengthy process into L-methylfolate in order to be used by the brain. Unlike L-methylfolate, synthetic folic acid and dietary folate cannot cross the blood-brain barrier.³

 $\mathsf{Deplin}^{\texttt{®}}$ offers a type of folate used by the body to regulate the body's metabolic functions.

Up to 70 percent of people who suffer from depression may have a specific genetic error (the most common of which is called the MTHFR $C \rightarrow T$ polymorphism) that compromises their ability to convert folic acid and dietary folate into L-methylfolate.¹ Deplin[®], L-methylfolate, is not affected by this common impairment or other genetic impairments of folate metabolism that occur in psychiatric illness.

What are the Benefits of Deplin[®]?

A patient may begin to notice a difference after taking Deplin[®] for one to two weeks, but the full effect may take four to six weeks. Metabolic management of the distinct nutritional requirements of brain L-methylfolate deficiency with Deplin[®], in addition to an antidepressant may result in one or more of the following benefits:^{*}

- □ Motivation
- Initiative

□ Mood

Alertness

 \Box Sociability²

□ Concentration

*These benefits are representative of individual's experiences with Deplin® in Major Depressive Disorder (MDD). Their experiences may not relate to everyone with MDD. You or those who you interact with the most may begin to notice a difference after taking Deplin® for 1 to 2 weeks, but the full effect usually takes 4 to 6 weeks.

What is the Difference Between Medical Foods and Other Therapies?

As defined by the FDA, a medical food is a specially formulated food product that must be used under medical supervision. All components of a medical food must have GRAS status (Generally Recognized as Safe) as designated by the FDA or independent review. A medical food is intended to provide specific dietary management of a disease or condition for which distinct nutritional requirements, based on recognized scientific principles, have been established by medical evaluation.⁴

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Medical foods differ from both dietary supplements and drugs. Pharmaceutical drugs are used to treat, prevent or mitigate a disease or condition and must be prescribed by a licensed healthcare professional. Unlike drugs and medical foods, dietary supplements are generally intended to be used by otherwise healthy individuals, not those with a specific disease or medical condition.⁴

A supplement can be a vitamin, mineral or some other substance obtained over-the-counter without prescription and without physician oversight.⁴

For additional information, including possible side effects, visit www.Deplin.com or see full prescribing information.

¹ Kelly CB et al. The MTHFR C677T Polymorphism is Associated with Depressive Episodes in Patients from Northern Ireland. J Psychopharmacol. 2004;18(4):567-71.

 ² Ginsberg LD, Oubre A, Daoud Y. L-methylfolate Plus SSRI or SNRI from Treatment Initiation Compared to SSRI or SNRI Monotherapy in a Major Depressive Episode. Innov Clin Neurosci. 2011;8(1):19-28.
³ Stahl SM. Novel Therapeutics for Depression: L-methylfolate as a Trimonoamine Modulator and Antidepressant Augmenting Agent. CNS Spectrums. 2007;12(10):739-44.

⁴ Section 5(b) of the Orphan Drug Amendments (21 U.S.C. 360ee (b).