

**2 out of 3 patients
will need more
than a single
antidepressant¹**



deplin[®] 
L-METHYLFOLATE 
Achieve and Maintain

Deplin[®] is a medical food, dispensed by prescription, for the clinical dietary management of the metabolic imbalances associated with depression. Use under medical supervision.

A single antidepressant **MAY NOT BE ENOUGH** to get well.¹



2/3 Achieve Less Than Full Response with a Single Antidepressant

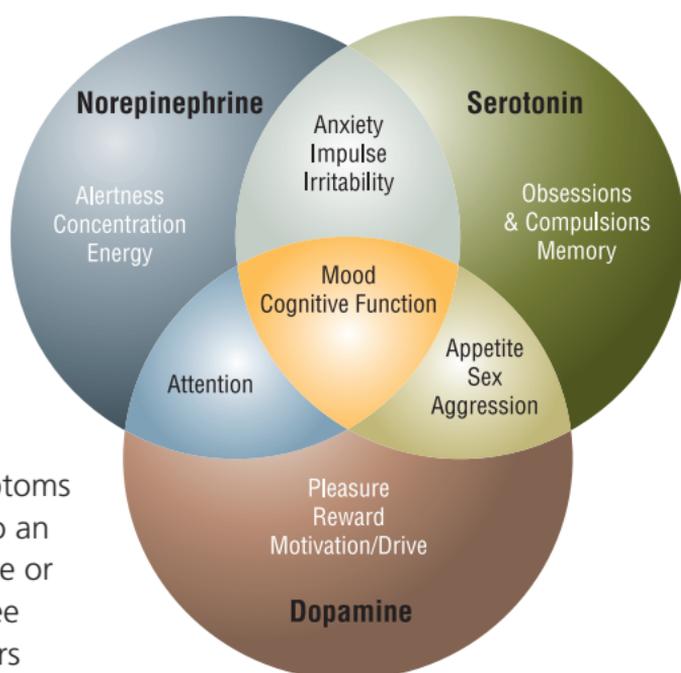
1/3 Achieve Full Remission with a Single Antidepressant

Trivedi M et al. Am J Psych. 2006;163(1):28-40.

People suffering from depression who do not experience a full resolution of all their symptoms are more likely to relapse and each additional episode becomes increasingly more difficult to treat.²

Visit www.deplin.com for more information.

Current therapies **MAY NOT ADDRESS** all three neurotransmitters.



Depressive symptoms may be linked to an imbalance of one or more of the three neurotransmitters believed to be associated with depression.³

Your doctor may choose a therapy that targets one or more of these neurotransmitters. It is important to share all your symptoms so your doctor can choose the best therapy.

Some depressive symptoms you may experience and should tell your doctor about include:

- Sadness, hopelessness or the inability to feel pleasure
- Feeling tired, tearful or discouraged
- Irritability, anxiousness or low energy levels
- Lack of concentration or motivation

Why do so many people **NOT FULLY RESPOND** to antidepressants?

Insufficient Amounts of Neurotransmitters

One theory of depression is that the brain is not developing enough neurotransmitters. This may be due to insufficient amounts of L-methylfolate in the brain.³ L-methylfolate is needed to regulate serotonin, norepinephrine and dopamine production. Without enough L-methylfolate, it may be difficult to produce enough neurotransmitters for your antidepressant to work fully.⁴



7 out of 10 depressed individuals may have a genetic problem that could affect neurotransmitter production.⁵



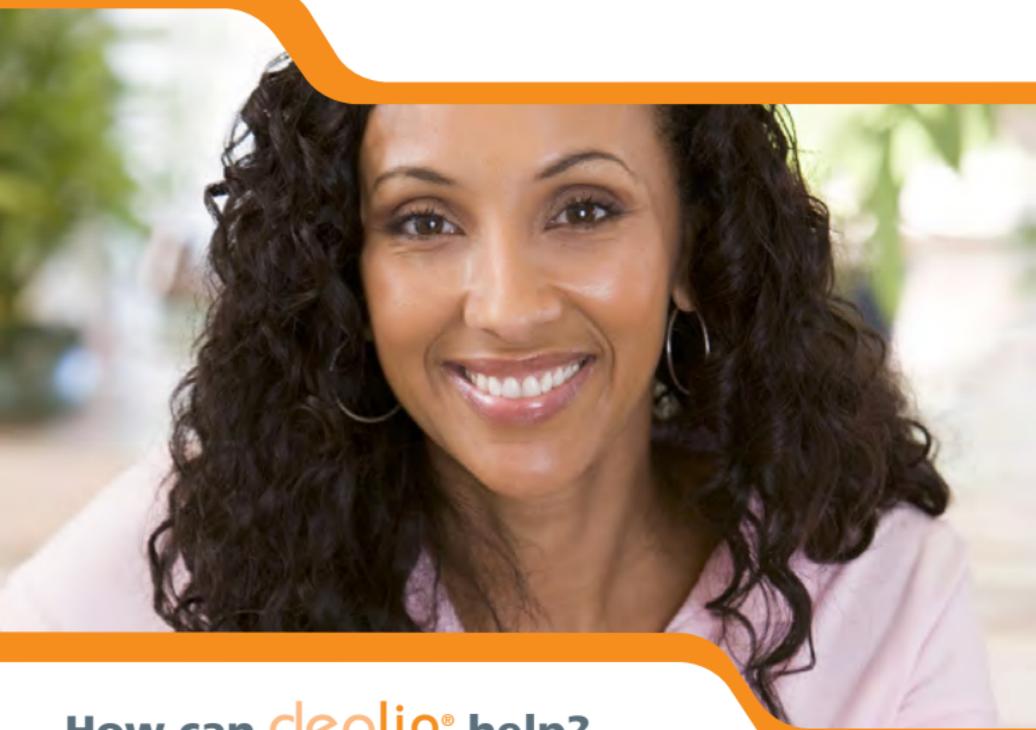
What are the **RISK FACTORS** for low L-methylfolate⁶⁻¹⁰ and neurotransmitter deficiency?¹¹

In individuals who suffer from depression, 70% may have a specific genetic factor that limits their ability to convert folic acid or folate from food to L-methylfolate. This is important because L-methylfolate provides the distinct nutritional requirements and dietary management needed to regulate neurotransmitter production.⁵

Individuals of Hispanic or Mediterranean descent have twice the risk of this genetic problem.¹²

OTHER RISK FACTORS ^{6,12,13}

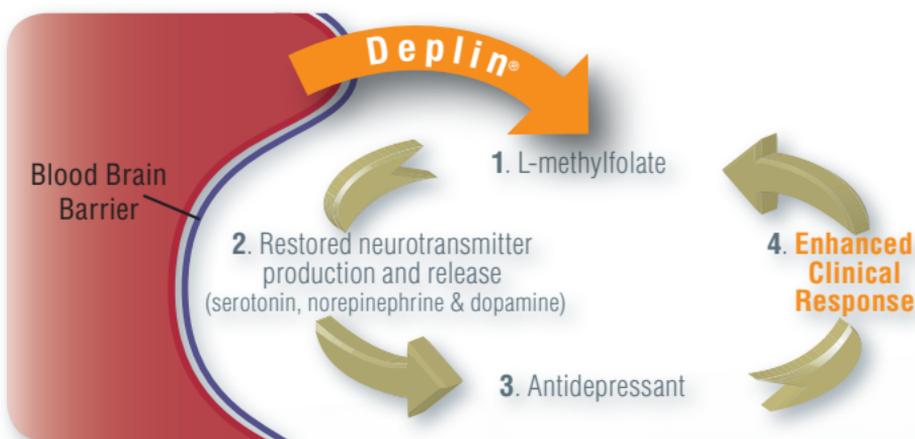
Drugs	Anticonvulsants such as lamotrigine and valproate, methotrexate, sulphasalazine, oral contraceptives, metformin, fluoxetine, niacin, fenofibrates and warfarin
Disease	Diabetes, atrophic gastritis, Crohn's, colitis, renal failure and hypothyroidism
Lifestyle	Excessive alcohol, smoking, and poor nutrition
Aging	L-methylfolate in the brain decreases with age



How can **deplin**® help?

What is deplin®?

Deplin® contains 7.5mg or 15mg of L-methylfolate, the only active form of folate that can cross the blood brain barrier to provide the distinct nutritional requirements to manage brain folate deficiency and help the brain regulate important neurotransmitters associated with mood.



How does deplin® work?

Deplin® works by providing for the higher metabolic requirement of L-methylfolate needed by some depressed individuals to regulate serotonin, norepinephrine, and dopamine.³

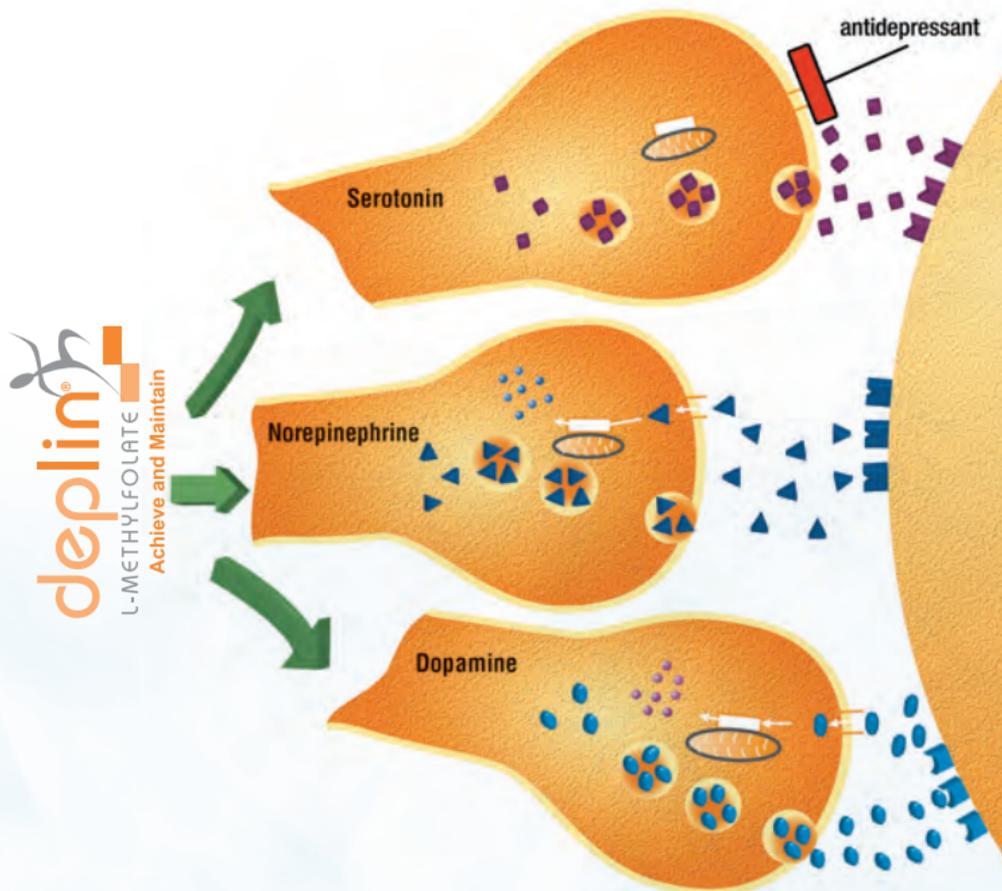
Deplin® is not an antidepressant, but provides necessary dietary support to make your brain a better partner to the antidepressant your doctor prescribes.

deplin® plus an antidepressant

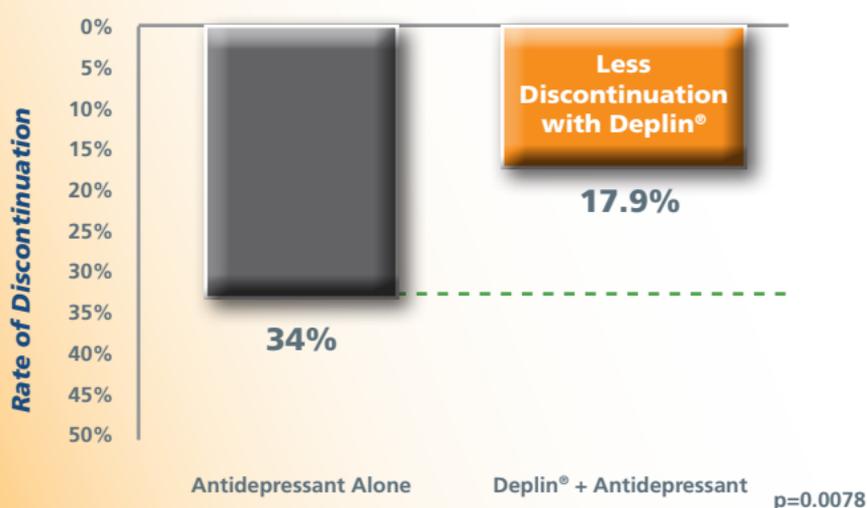
Dietary management of low brain folate levels with L-methylfolate (deplin®): in addition to antidepressant therapy can help support the management of depression.¹⁵

Neurotransmitters (serotonin, norepinephrine and dopamine) are important to maintain your mood. Antidepressants such as SSRIs (selective serotonin reuptake inhibitors) and SNRIs (serotonin norepinephrine reuptake inhibitors) block reabsorption allowing the brain to have greater use of available neurotransmitters.

Sufficient amounts of these neurotransmitters are needed. Combining a medical food such as Deplin®, with an antidepressant in individuals with low folate levels, helps the antidepressant regulate these neurotransmitters.



Better Tolerance with Deplin®



Discontinuation due to side effects was at a lower rate in the Deplin® plus an antidepressant group than discontinuation due to side effects in the antidepressant alone group. No significant difference in side effects were reported between the two groups.¹⁵

What patients say about deplin®

Deplin® Patient Survey



96% of patients find Deplin® very tolerable.



88% of patients report they are very likely to continue

Deplin Clinical Evaluation Response Survey. Aug. 2009. Data on file.

What to expect when taking deplin®

Are there side effects with deplin®?

Methylfolate was well tolerated in both short-term and long-term trials. Side effects did not differ from a sugar pill (placebo).^{6,11,15-17} Deplin® is not associated with weight gain, insomnia, or sexual dysfunction.^{14,17-19}

How do I take deplin®?

For best results, you should take Deplin® 7.5mg or 15mg as directed by your doctor or medical professional. For most people, Deplin® is taken daily, with or without food. You should fill your prescriptions ahead of time to avoid missing a dose.

When will I feel an effect?

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 may take 4 to 6 weeks.¹⁹⁻²¹

How long will I need to take deplin®?

For some, depression can be an ongoing condition that may require long-term treatment. Your healthcare provider will track your progress and work with you to determine the right length of treatment. Do not stop taking Deplin® without first talking to your doctor or medical professional.

What can I expect?

You may feel benefit in one or more of the following:*

- Motivation
- Alertness
- Initiative
- Concentration
- Mood
- Sociability

** 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.*

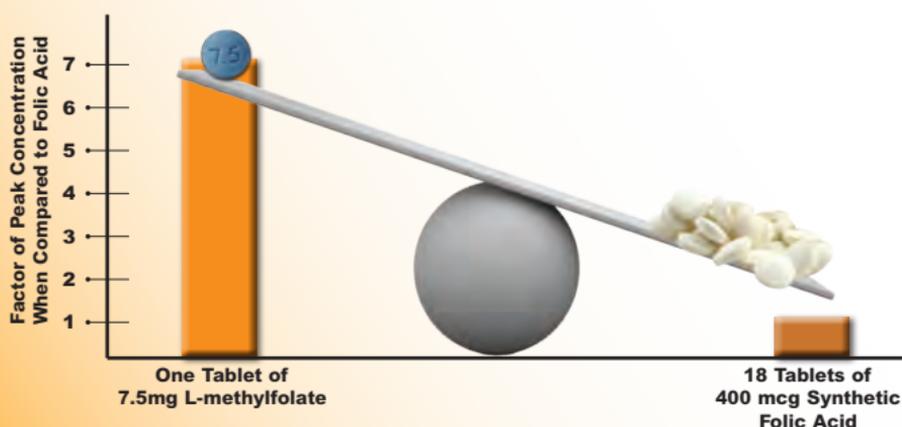
COULD I CORRECT THIS PROBLEM with my diet or folic acid?

- The brain needs L-methylfolate to regulate neurotransmitters associated with depression.
- L-methylfolate is the only form of folate that the brain can use.^{3,16}

Synthetic folic acid and dietary folate must be broken down by a lengthy process into L-methylfolate in order to be used by the brain.

Up to 70% of those with depression may have a compromised ability to break down folic acid from supplements or food into L-methylfolate.⁵

L-methylfolate Is 7X More Bioavailable Than Synthetic Folic Acid



Willems FF et al. Br J Pharmacol.2004;141(5):825-30.

Visit www.deplin.com to get more information and view a series of patient videos.

DEPLIN® 7.5mg Tablets DEPLIN® 15mg Caplets

DESCRIPTION

DEPLIN® is a medical food dispensed by prescription for the clinical dietary management of the metabolic imbalances associated with depression and schizophrenia. Use under medical supervision.

Each DEPLIN® 7.5mg tablet contains 7.5 mg of L-methylfolate (Metafolin®)*. *CAS#151533-22-1
Each DEPLIN® 15mg caplet contains 15mg of L-methylfolate (Metafolin®)*. *CAS#151533-22-1

DEPLIN® 7.5mg Dietary Ingredients:

Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Cellulose 90, Silicified Microcrystalline Cellulose HD 90, Opadry II Blue 85F90748 (Polyvinyl Alcohol, Titanium Dioxide [color], PEG 3350, Talc and FD&C Blue #2[color]), L-methylfolate Calcium, Magnesium Stearate (Vegetable Source), and Carnauba Wax. DEPLIN® 7.5mg tablets do not contain sugar, lactose, yeast or gluten.

DEPLIN® 15mg Dietary Ingredients:

Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Cellulose 90, Opadry II Orange 85F43102, (Polyvinyl Alcohol, Titanium Dioxide [color], PEG 3350, Talc, FD&C Yellow #6[color], FD&C Yellow #5[color], FD&C Red #40[color] and FD&C Blue #2[color]), L-methylfolate Calcium, Magnesium Stearate (Vegetable Source), and Carnauba Wax.

DEPLIN® 15mg caplets do not contain sugar, lactose, yeast or gluten.

Medical foods are intended for a patient who has a limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone.¹ This product is not an Orange Book product.

DEPLIN® is a medical food dispensed by prescription.

CLINICAL PHARMACOLOGY

DEPLIN® is a medical food, which consists of a proprietary biologically active folate, derived from food sources.

INDICATIONS AND USAGE

ADJUNCTIVE USE IN MAJOR DEPRESSIVE DISORDER

DEPLIN® is indicated for the distinct nutritional requirements of individuals who have suboptimal L-methylfolate levels in the cerebrospinal fluid, plasma, and/or red blood cells and have major depressive disorder (MDD) with particular emphasis as adjunctive support for individuals who are on an antidepressant.²⁻⁵

ADJUNCTIVE USE IN

DEPLIN® is indicated for the distinct nutritional requirements of individuals who have or are at risk for hyperhomocysteinemia and have schizophrenia who present with negative symptoms and/or cognitive impairment, with particular emphasis as an adjunctive support for individuals who have stabilized on antipsychotics.²

DEPLIN® is indicated regardless of MTHFR C677T polymorphism genotype.⁶

CONTRAINDICATIONS

DEPLIN® is contraindicated in patients with known hypersensitivity to any of the components contained in this product.

PRECAUTIONS

General:

Folic acid, when administered in daily doses above 0.1mg, may obscure the detection of B₁₂ deficiency (specifically, the administration of folic acid may reverse the hematological manifestations of B₁₂ deficiency, including pernicious anemia, while not addressing the neurological manifestations). L-methylfolate may be less likely than folic acid to mask vitamin B₁₂ deficiency.^{7,8} Folate therapy alone is inadequate for the treatment of a B₁₂ deficiency.

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed, (although not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of a precipitation of a mixed/manic episode in patients at risk for bipolar disorder. DEPLIN® is not an antidepressant; however, 5-MTHF has been shown to enhance antidepressant effects of known antidepressants.² Caution is recommended in patients with a history of bipolar illness. Patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder since mood elevation in this population is possible.

Patient Information:

DEPLIN® is a medical food¹ for use under medical supervision and direction.

DEPLIN® is a medical food dispensed by prescription.

Interaction with Drugs:

Before using this product, tell your doctor or pharmacist of all the products you use. Keep a list of all your medications with you, and share the list with your doctor and pharmacist. No decrease in effectiveness of drugs has been reported with the use of DEPLIN®.

DEPLIN® contains folate, which may have interactions the following:

- Antiepileptic drugs (AED): The AED class including, but not limited to, phenytoin, carbamazepine, primidone, valproic acid, phenobarbital and lamotrigine have been shown to impair folate absorption and increase the metabolism of circulating folate. Additionally, concurrent use of folic acid has been associated with enhanced phenytoin metabolism, lowering the level of this AED in the blood and allowing breakthrough seizures to occur.^{9,10,12,15}
- Capecitabine: Folinic acid (5-formyltetrahydrofolate) may increase the toxicity of Capecitabine.¹¹
- Dihydrofolate Reductase Inhibitors (DHFRi): DHFRi block the conversion of folic acid to its active forms, and lower plasma and red blood cell folate levels. DHFRi include aminopterin, methotrexate, pyrimethamine, triamterene, and trimethoprim.¹²
- Fluoxetine: Fluoxetine exerts a noncompetitive inhibition of the 5-methyltetrahydrofolate active transport in the intestine.¹³
- Isotretinoin: Reduced folate levels have occurred in some patients taking isotretinoin.¹⁴
- Nonsteroidal Anti-inflammatory Drugs (NSAIDs): NSAIDs have been shown to inhibit some folate dependent enzymes in laboratory experiments. NSAIDs include ibuprofen, naproxen, indomethacin and sulindac.¹²
- Oral Contraceptives: Serum folate levels may be depressed by oral contraceptive therapy.¹²
- Methylprednisolone: Reduced serum folate levels have been noted after treatment with methylprednisolone.¹²
- Pancreatic Enzymes: Reduced folate levels have occurred in some patients taking pancreatic extracts.¹²
- Pentamidine: Reduced folate levels have been seen with prolonged intravenous pentamidine.¹²
- Metformin treatment in patients with type 2 diabetes decreases serum folate.^{16,17}
- Warfarin can produce significant impairment in folate status after a 6-month therapy.¹⁸

ADVERSE REACTIONS

Allergic reactions have been reported following the use of oral L-methylfolate.

DOSAGE AND ADMINISTRATION

The usual adult dose is 7.5mg to 15mg given daily with or without food or as directed under medical supervision.

HOW SUPPLIED

DEPLIN® is a medical food dispensed by prescription

7.5mg
Bottle of 30 Product Code # 0525-0410-30* Use under medical/physician supervision.
Bottle of 90 Product Code # 0525-0410-90* Use under medical/physician supervision.
Bottle of 7 Product Code # 0525-0410-07* Professional samples. Not for sale.

A light blue, round, coated, tablet imprinted on one side with "PAL" and imprinted on the other side with "7.5".

15mg
Bottle of 90 Product Code # 0525-0450-90* Use under medical/physician supervision.
Bottle of 7 Product Code # 0525-0450-07* Professional samples. Not for sale.

An orange, scored, oval, coated, caplet imprinted on one side with "deplin" and imprinted on the other side with "15".

*Pamlab LLC does not represent these product codes to be National Drug Codes (NDC). Product codes are formatted according to standard industry practice, to meet the formatting requirements of pharmacy and health insurance computer systems.

Storage:

Store at controlled room temperature 15°C to 30°C (59°F to 86°F) (See USP). Protect from heat, light and moisture.

PATENTS

Some or all of the following patents may apply:

U.S. Patent No. 6,011,040

U.S. Patent No. 6,441,168B1

and other pending patent applications

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Revised 05/11

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Be a step ahead...



**ask your doctor if
deplin[®] is right for you.**