MANAGING METABOLIC DEFICIENCIES ASSOCIATED WITH DEPRESSION & MOOD DISORDERS, COGNITIVE DISORDERS, & MIGRAINE

A PATIENT'S GUIDE TO A NOVEL APPROACH
What is a medical food?

Medical foods help create a healthy environment to repair injured blood vessels and nerves, improve nerve and vascular function, and to help prevent more damage from occurring.

Medical foods may be beneficial for a variety of conditions, including:

- Mood disorders
- Cognitive disorders
- Migraines
- Peripheral vascular disease
- MTHFR Genetic Variant
- Peripheral neuropathy
- Diabetes complications
- Chronic pain
- Chronic fatigue
- Fractures
- Rheumatoid arthritis
- Fibromyalgia
- Multiple sclerosis
- Heart disease

Medical foods are considered a unique category regulated by the FDA. Medical foods can help manage chronic conditions by addressing the metabolic deficiencies associated with diseases. They are intended for use under medical supervision.)*

*Medical foods are not drugs.
What are mood disorders? 1-3
Mood disorders can disrupt a person’s thinking, feeling, daily functioning, and their ability to relate to others. They are often medical conditions that make it difficult to cope with the ordinary demands of life. The good news is that these conditions are treatable.

Mood disorders can affect people of any age, race, religion, or income. They are not the result of personal weakness, lack of character, or poor upbringing.

If you suffer from mood disorders, remember that you are not alone. Mood disorders are treatable. If you are diagnosed with a mood disorder, your healthcare provider might prescribe treatment plans to help you experience relief.

What is depression? 4-7
Depression is a mood disorder that can affect anyone — even a person who appears to live in relatively ideal circumstances. Major depression is disabling and can prevent a person from functioning normally. Some people might experience only a single episode within their lifetime, but more often a person experiences multiple episodes. Depression can disrupt work, sleep, study, eating, and enjoying once-pleasurable activities.

Neurotransmitters work together for overall mental health
Many commonly prescribed antidepressants work to increase neurotransmitter levels by blocking the reuptake (reabsorption) of neurotransmitters like serotonin in the brain. However, these antidepressants do not provide the essential ingredients or building blocks needed to produce more neurotransmitters.

Traditional mood disorder therapies
Many treatments for mood disorders exist, but not everyone responds to them. Almost two-thirds of people require several different treatments before they feel better.

What causes depression?
Depression is thought to be caused by a combination of genetic, biochemical, environmental, and psychological factors. Neurotransmitter deficiencies are believed to be involved in the development of depression and other mood disorders.

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Examining underlying causes

The underlying causes of several mood disorders have been linked to genetics, and deficiencies in folate and vitamin B12. In fact, low folate and vitamin B12 levels are associated with either a higher prevalence or a longer duration of depression. People with depression also tend to have elevated homocysteine levels, a known risk factor for mood disorders.

The critical role of L-methylfolate and Methyl B12 in mood disorders

Folate and vitamin MethylB12 provide the essential building blocks needed to produce more neurotransmitters associated with mood. SAMe is critical in this process, and is produced as part of a multistep pathway.

The role of genetics in depression

We receive half of our genes from our mother, and the other half from our father. There might be a genetic predisposition to depression — because it often runs in families. One such genetic variant is called MTHFR c677t. MTHFR is an enzyme needed to convert folic acid and dietary folate to its active form, L-methylfolate [see page 13 to learn more]. Up to 70% of people with depression have the MTHFR variant. As a result, they cannot fully complete this activation, and have additional folate needs.

Metabolic management of mood disorders

Low folate and Vitamin B12 levels increase your risk for mood disorders and may result in a partial response to your antidepressant. EB-P1DR contains both cofactors to restore metabolic deficiencies to help produce more neurotransmitters associated with mood. Our products feature Biofolate® — the patented pure crystalline activated form of folic acid — which is unaffected by MTHFR enzyme variant.

EB-P1DR Ingredient Guide

<table>
<thead>
<tr>
<th>ACTIVE INGREDIENT</th>
<th>DESCRIPTION</th>
</tr>
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</table>
| L-methylfolate® Calcium (active folate) | Active ingredients work together to effectively:  
- Homocysteine levels, a known risk factor for mood disorders  
- Natural chemicals in the brain that affects mood |
| Methylcobalamin (active Vitamin B12) | |

L-methylfolate Calcium......................................15 mg  
Methylcobalamin...................................................0.4 mg

Dosage: Adult dose is 1 capsule daily or as directed by physician.

Each delayed-release, vegan capsule is allergen and dye free.
The role of genetics and homocysteine in cognitive impairment

Identification of modifiable risk factors provides a crucial approach to management of cognitive disorders. One such risk factor is an elevated homocysteine level which reflects the functional status of folate, and Vitamins B$_12$, B$_6$.

People with cognitive impairment tend to have the MTHFR c677t genetic variant and are significantly more likely to have folate deficiency, lower acetylcholine levels, and elevated levels of an amino acid in their blood called homocysteine. These elevated levels damage blood vessels and nerves, which may lead to cognitive impairment.

Parallel pathways for cognitive impairment involving homocysteine (Hcy)°

- Raised Hcy may directly cause cognitive impairment (green arrows).
- Nutritional deficiencies may directly cause cognitive impairment (blue arrows) as well as causing cognitive impairment indirectly by raising tHcy.
- Reverse causality (dashed green line) could also explain the association of Hcy with cognitive impairment.

**Mild cognitive impairment (MCI)**

Mild cognitive impairment (MCI) describes problems with memory and thinking beyond what can be explained by age alone, but the decline has not affected daily functions to the extent that it would be classified as dementia.

**Risk factors for MCI°**

The strongest risk factors for MCI are:

- Increasing age
- A gene known as APOE-e4, also linked to Alzheimer’s disease (although having the gene doesn’t always result in cognitive decline)

Other medical conditions and lifestyle factors have been linked to an increased risk of cognitive change, including:

- Diabetes/smoking/high blood pressure
- Elevated cholesterol/obesity
- Depression
- Lack of physical exercise
- Low education level
- Infrequent participation in mentally or socially stimulating activities
- Nutritional deficiencies
- Elevated homocysteine
- MTHFR genetic variant

Most risk factors for cognitive impairment are within your power to control, so it is important to keep your brain and body as healthy as possible.
What is a migraine? A migraine is a neurological condition that is characterized by a severe headache, often affecting only one side of the head. A migraine can occur with or without aura (sensory disturbances). If you have a migraine with aura, you might experience disturbing symptoms before the headache starts. If you experience recurrent, long-lasting headaches, you might be suffering from a headache without migraine aura. This is the most common form of migraine.

What are the symptoms of a migraine? A migraine headache can cause all or some of the following symptoms:

- Intense throbbing or pulsating pain, often on one side of the head
- Nausea, vomiting, or diarrhea
- Increased sensitivity to light, noise, or smell

What Causes Migraines? Researchers aren’t entirely sure what causes migraines, but they know it involves reduced blood flow to the brain.

Metabolic management of cognitive disorders Metabolic deficiencies in the brain reduce the substances that protect the brain, and have been identified as independent risk factors for memory loss. The pharmaceutical-grade active ingredients in EB-C3™ work together to provide the necessary nutrients to help nourish and protect the brain against such impairment.

EB-C3DR Ingredient Guide

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| L-methylfolate Calcium [active folate] | + Acetylcholine, a natural substance in the brain associated with memory
| *The only form of folate that crosses the blood brain barrier |
| Methylcobalamin [active Vitamin B₁₂]  | + Methylation, a process in the brain required for neuroprotection |
| N Acetyl L-Cysteine [active antioxidant] | - Substances harmful to the brain |
| Pyridoxal 5’- Phosphate [active Vitamin B₆] | + Methylation, a process in the brain required for neuroprotection |

Dosage: Adult dose is 1 capsule daily or as directed by physician.

Possible Causes
- Hormonal fluctuations
- Sleep dysfunctions
- Artificial sweeteners
- Caffeine
- Sex
- Alcohol
- Emotional stress
- Certain medications

Possible Solutions
- Identify and avoid triggers
- Regulate stress and sleep
- Nutritional supplements
- Prescription medications
- Surgical procedures

EB-C3DR Developed in compliance with current Good Manufacturing Practices (cGMP) Products feature delayed-release capsules for targeted delivery to promote tolerability.
The role of genetics in migraine

You get half of your genes from mom and the other half from dad. It is thought that there may be a genetic predisposition to migraine as it often runs in families.

One such gene variant is called MTHFR c677t, an enzyme needed for conversion of folic acid and dietary folate to its active form, L-methylfolate.

Up to 50% of people have the MTHFR genetic variant and are unable to fully complete this activation and have additional folate needs.

L-methylfolate Calcium is unaffected by the MTHFR variant and is the only form of folate that crosses the blood brain barrier.

People who suffer from migraines tend to have the MTHFR c677t genetic variant and are significantly more likely to have folate deficiency and elevated levels of an amino acid in their blood called homocysteine. These elevated levels damage blood vessels and nerves and may lead to migraines.

Metabolic management of migraines

Decreased levels of riboflavin, magnesium, and coenzyme Q10 and deficiencies in folate in plasma and in the brain might play a role in the development of migraines. The pharmaceutical grade active ingredients in EB-H4 work together to provide the necessary nutrients to help correct the deficiencies associated with the frequency, duration, and intensity of migraines.

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<td>+ Production of energy in the cells</td>
</tr>
<tr>
<td>Coenzyme Q10 [antioxidant]</td>
<td>+ Production of energy in the cells – Damage to cells</td>
</tr>
<tr>
<td>L-methylfolate Calcium [active folate]</td>
<td>+ Blood flow to the brain</td>
</tr>
<tr>
<td>Magnesium Bisglycinate [mineral]</td>
<td>+ Production of energy in the cells</td>
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DOSAGE: Adult dose is 2 capsules daily or as directed by physician.

The EB-H4 formulation was researched and developed in collaboration with the Diamond Headache Clinic. www.diamondheadache.com

Each capsule is allergen and dye free.
Biofolate®, the patented pure crystalline activated form of folate, is unaffected by the MTHFR genetic variant

Homocysteine and MTHFR

Risk factors for neuropsychiatric conditions include elevated homocysteine levels and the MTHFR genetic variant. Homocysteine is an amino acid that is produced as a byproduct of consuming meat. Homocysteine is normally converted into other amino acids. An abnormal accumulation of homocysteine is believed to damage the cells that line the arteries, and is a marker for the development of many chronic conditions including mood & cognitive disorders and migraine.

How do I lower homocysteine levels?

You can lower your homocysteine levels by eating less meat. You can also take the B vitamins folic acid (folate), B6, B12, and B2. However, it is important that your body be able to break down and utilize these vitamins, and that is where MTHFR becomes important.

MTHFR genetic variant facts:

- Variants of the MTHFR gene are prevalent in up to 50% of the population, and even higher in those with neuropsychiatric conditions
- Reduces folate levels and increases homocysteine levels
- Is an independent pharmacogenetic risk factor for the development and severity of depression, cognitive impairment, and migraine
- Is associated with other conditions including vascular disease, peripheral neuropathy, anxiety, renal disease, and osteoporosis

Visit www.EBMmedical.com or call 844-360-4095 for a requisition form for your doctor.

A simple DNA swab of your saliva can determine whether you have the MTHFR genetic variant.

Drugs that increase homocysteine levels and related vitamin deficiencies include:

- Methotrexate
- Nicotinic acid
- Fenofibrates
- Metformin

How can I lower homocysteine levels?

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Now that I have been prescribed an EBM Medical product, what are the next steps?

1. Your provider will send your prescription to EBM Medical

2. You will receive a text or email to confirm your order —To expedite your order, call us at 1-844-360-4095

3. An EBM representative will contact you to answer your questions and process your payment

4. Within 24 hours, your prescribed formula will be shipped to your door

5. You will receive a confirmation text 10 days before your prescription needs to be refilled

Questions? Contact EBM at 1-844-360-4095, support@EBMmedical.com, or visit our website at www.EBMmedical.com