



Meeting the Unmet Needs of Patients with Diabetic Neuropathy

What is the Difference Between a Medical Food and Other Therapies?

As defined by the FDA, a medical food is a specially formulated product that must be used under the guidance of a physician. All components of a medical food must have GRAS status (Generally Recognized as Safe) as designated by the FDA or independent review. It is intended to manage a specific disease or condition for which medical evaluation, based on recognized scientific principles, has established distinctive nutritional requirements.

A medical food differs from both dietary supplements and pharmaceuticals. A pharmaceutical is a drug used to treat, prevent or mitigate a disease or condition that must be prescribed by a licensed healthcare professional. Unlike pharmaceuticals and medical foods, dietary supplements are intended to be used by otherwise healthy individuals, not those with a specific disease or medical condition.

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

For complete prescribing information and a list of references, visit www.metanx.com.

Despite the availability of numerous therapies, neuropathy remains a poorly managed diabetes complication. Current pharmacological options for diabetic neuropathy merely mask the painful symptoms but do not address the underlying disease.

The first priority for patients with diabetes is to work with their doctor to control their blood sugar. If complications continue, there are options available to manage the pain associated with diabetic neuropathy. However, it's the loss of protective sensation and not the pain that is the real problem. Sensory loss associated with diabetic neuropathy is the major contributor and predictor of ulcers and amputations of the lower legs and feet.

A Neurotrophic Agent Provides a Novel MOA

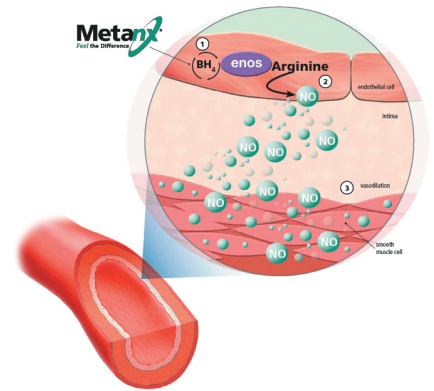
Neurotrophic refers to nutrition for the nerves. Metanx® provides nutritional management of endothelial dysfunction associated with numbness, tingling and burning sensations in diabetes patients with neuropathy. Metanx® offers a neurotrophic benefit by improving endothelial dysfunction and maintaining blood flow in the vessels that carry important nutrients and oxygen to the peripheral nerves.

Metanx® is composed of the bioactive forms of three essential B vitamins that are critical for peripheral nerve health:

- | INGREDIENT | BENEFIT |
|-------------------------------------|----------------------------|
| L-methylfolate (folate) | nitric oxide synthesis |
| Methylcobalamin (vitamin B12) | myelin synthesis |
| Pyridoxal 5' phosphate (vitamin B6) | neurotransmitter synthesis |

The endothelium (the thin layer of cells that line the interior surface of blood vessels) helps maintain blood flow by producing a substance called nitric oxide. Nitric oxide signals the blood vessels to relax corresponding with improved blood flow to peripheral nerves. Studies have shown that endothelial cells produce twice as much nitric oxide in the presence of L-methylfolate.

Maintaining blood flow in the small blood vessels is critical for peripheral nerves to maintain their normal functions, such as peripheral nerve repair and regeneration. This includes production of the myelin sheath, a fatty substance that protects the nerve fibers. Research has demonstrated a significant increase in epidermal nerve fiber density after 6 months of Metanx® compared to baseline; further research is ongoing.



- 1 Metanx regenerates BH₄, a cofactor for eNOS to convert L-arginine into nitric oxide
- 2 Nitric oxide is diffused into the smooth muscle cells
- 3 Smooth muscle cells dilate and blood flow is increased

