

## NutriNerve® Soft Gels

### What is in NutriNerve® 2.1?

A patented formulation that supports the body against neuropathy\*

Alpha Lipoic Acid	200 mg
Gamma-Linolenic Acid (GLA) *	130 mg
Benfotiamine	25 mg
Vitamin C	85 mg

\*GLA is the active ingredient derived from Borage Oil

### Physician Support and Involvement

Please tell your doctor as soon as you start taking NutriNerve® as he/she may be aware of unpublished information regarding the use of these ingredients in treating neuropathy.

### Prescription information:

Take 4 capsules per day with meals (2 BID). 4-6 months of uninterrupted use is necessary to see the full benefit.

### Precautions

Some patients may experience an upset stomach and serious diarrhea in doses that equal or exceed 6 capsules in a 24-hour period. There are no known issues with renal insufficiency.

### Statement of Use and Treatment Program

The ingredients in NutriNerve® have been shown to improve neuropathy symptoms by improving underlying physiology\*. This goes beyond simply relieving symptoms, such as pain. Please visit [www.neuroeffex.com](http://www.neuroeffex.com) for a more peer reviewed references.

NutriNerve® is maintained by our scientific advisory board and is available via a continuity program.

### Medical Advisors:

#### Dr. Aaron Vinik, MD, PhD, FCP, FACP

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### Ingredient Summary

**Alpha Lipoic Acid (ALA)** has been shown in placebo controlled randomized studies to improve diabetic neuropathy symptoms. In the SYDNEY 2 trial, there was demonstrated to be a 52% decrease in Total Symptom Score (including stabbing pain, burning pain, paresthesia, and asleep numbness of the feet) after five weeks of 600 mg ALA<sup>i</sup>. ALA is also attributed with a 44% increase in vasodilation of the brachial artery<sup>ii</sup>.

**Gamma Linolenic Acid (GLA)** has been shown to restore nerve conduction velocity in animals that have had a 25% decrease in nerve conduction velocity due to diabetes<sup>iii</sup>.

**Benfotiamine** A statistically significant ( $p = 0.0287$ ) improvement in the neuropathy score was observed in a group given benfotiamine<sup>iv</sup>.

**Vitamin C** is a powerful antioxidant and has been shown to improve endothelial function and nerve perfusion<sup>v</sup>

*\*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.*

## 2007 ADA Scientific Session – Oral Presentation

Effect of 4-Year Antioxidant Treatment with **Alpha-Lipoic Acid** in Diabetic Polyneuropathy: The NATHAN 1 Trial

### Results:

The aim of this study was to evaluate the efficacy and safety of [alpha]-lipoic acid over 4 years in diabetic patients with mild to moderate distal symmetric polyneuropathy (DSP). In this multicenter, randomized, double-masked, parallel-group clinical trial 460 diabetic patients with stage 1 or stage 2a DSP were randomly assigned to oral treatment with **[alpha]-lipoic acid 600 mg qd (ALA; n=233)** or **placebo (n=227)** for 4 years following a 6-week placebo run-in phase. Outcome measures included: Primary outcome measure was a composite score of including the Neuropathy Impairment (NIS) Score of the lower limbs and 7 nerve function tests (NIS[LL]+7 tests; a ). Secondary outcome measures included the **Total Symptom Score (TSS)**; nerve symptom change), Neuropathy Symptoms and Change (NSC), NIS, NIS[LL], individual NIS components, motor and sensory nerve conduction attributes, and quantitative sensory testing (QST). Data analysis was based on the intention to treat. The demographic variables and the outcome measures at baseline were comparable between the groups as were the HbA1c levels during follow-up. The NIS[LL]+7 tests composite score improved after 4 years vs. baseline by  $0.45 \pm [\text{plusmn}]0.37$  (mean $\pm$ [plusmn]SEM) in the ALA group and worsened by  $0.34 \pm [\text{plusmn}]0.35$  points in the placebo group ( $p=0.105$ ). The NIS and NIS[LL] improved by  $0.68 \pm [\text{plusmn}]0.44$  and  $0.34 \pm [\text{plusmn}]0.30$  points on ALA and worsened by  $0.61 \pm [\text{plusmn}]0.46$  and  $0.43 \pm [\text{plusmn}]0.31$  points on placebo, respectively ( $p=0.028$  and  $p=0.051$ ).

**The NIS[LL] muscular weakness subscore improved by  $0.21[\pm]\text{plusmn}]0.11$  on ALA and deteriorated by  $0.17 \pm [\text{plusmn}]0.15$  on placebo ( $p=0.045$ ).** The NSC score for weakness severity improved by  $0.05 \pm [\text{plusmn}]0.03$  points on ALA and worsened by  $0.04 \pm [\text{plusmn}]0.03$  points on placebo ( $p=0.008$ ). No significant differences between both groups after 4 years were noted for the nerve conduction parameters and QST. The rates of adverse events were comparable between the groups during the study. **In conclusion, 4-year treatment with [alpha]-lipoic acid in mild to moderate DSP is well tolerated and improves some neuropathic deficits and symptoms**, but not nerve conduction. Future long-term trials should not anticipate significant progression of DSP in diabetic patients.

<sup>i</sup> Oral treatment with alpha-lipoic acid improves symptomatic diabetic polyneuropathy: the SYDNEY 2 trial. *Diabetes Care*. 2006 Nov;29(11):2365-70

<sup>ii</sup> Irbesartan and lipoic acid improve endothelial function and reduce markers of inflammation in the metabolic syndrome: results of the Irbesartan and Lipoic Acid in Endothelial Dysfunction (ISLAND) study. *Circulation*. 2005 Jan 25;111(3):343-8. Epub 2005 Jan 17.

<sup>iii</sup> Beneficial effects of gamma linolenic acid supplementation on nerve conduction velocity, Na<sup>+</sup>, K<sup>+</sup> ATPase activity, and membrane fatty acid composition in sciatic nerve of diabetic rats. *J Nutr Biochem*. 1999 Jul;10(7):411-20.

<sup>iv</sup> Benfotiamine in the treatment of diabetic polyneuropathy--a three-week randomized, controlled pilot study (BEDIP study). *Int J Clin Pharmacol Ther*. 2005 Feb;43(2):71-7.

<sup>v</sup> Lipid independent effects of statins on endothelial function and bioavailability of nitric oxide in hypercholesterolemic patients *Am Heart Journal* 2005; 149, 471