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NeuroRenew™ is a comprehensive formula containing B vitamins, acetyl L-carnitine and R-lipoic acid, designed specifically to address neuropathic pain by promoting a healthy pain response and supporting nerve regeneration.* There is currently no effective pharmacologic treatment protocol for preventing or reversing neuropathic changes or to provide pain relief. Treatment of peripheral diabetic neuropathy is based primarily on intensive glycemic control. Glycemic control may help delay the onset of diabetic neuropathy or slow its progression in patients with type 2 diabetes, but it does not completely prevent the worsening of nerve damage. Complications of diabetic neuropathy typically continue their natural course, resulting in increased pain and discomfort, and loss of sensation.

Pharmaceutical interventions are lacking for this painful, progressive condition, but clinical trials have demonstrated that the use of specific nutrients may help alleviate symptoms of neuropathy and also improve sensation, blood flow and nerve regeneration. The ingredients in NeuroRenew™ help support healthy nerve tissue and may indirectly influence diabetic neuropathy by supporting health blood glucose metabolism and normal insulin sensitivity.*

Vitamin B12 (as methylcobalamin): Vitamin B12 is essential for the synthesis of myelin, the fatty protective substance that insulates axons and facilitates proper neuronal signal transmission. Methylcobalamin facilitates neurite outgrowth and inhibits neural apoptosis¹ while also promoting the regeneration of injured nerves.² Additionally, methylcobalamin has been shown to be effective for improving neuropathic pain. A systematic review of clinical trials concluded that methylcobalamin had beneficial effects on somatic symptoms such as pain and paresthesia, and also improved autonomic symptoms.^{3,4} A study comparing the efficacy of nortriptyline (a tricyclic antidepressant also used for pain relief) and parenteral B12 determined that B12 was more effective than the drug for improving pain, paresthesia and tingling.⁵ A review of methylcobalamin intervention for diabetic neuropathy, neuralgia, and other types of pain concluded that this vitamin has potent analgesic effects and "may be a potential candidate for treating peripheral neuropathy."²

Vitamin B6 (as pyridoxal-5-phosphate, P5P): P5P is the active form of vitamin B6 and is a required cofactor in numerous enzymes, including aromatic L-amino acid decarboxylase, which catalyzes the synthesis of serotonin and dopamine, as well as enzymes that synthesize GABA. Proper levels of these neurotransmitters may influence pain perception, and the nutritional status of B6 has a significant and selective modulatory effect on their production.⁶ Vitamin B6 deficiency has been directly linked to the development of carpal tunnel syndrome and supplementation has typically been shown to be effective for this condition.⁷

Folate (as 5-MTHF): 5-MTHF is the primary biologically active isomer of folate and is seven times more bioavailable than folate.⁶ Polymorphisms in genes that regulate activation of folate or conversion of folic acid to 5-MTHF are associated with diabetic nephropathy, possibly owing to elevated homocysteine, but potentially through other, as yet unidentified mechanisms that may affect nerve tissue as well.⁸⁻¹⁰

B Vitamin Synergies: Looking at things collectively, deficiencies of vitamins B1, B12 and B6 are among the nutritional factors associated with idiopathic neuropathy,¹¹ and supplementation with various combinations of these has proven effective for improving symptoms of neuropathy. In a study of over 500 individuals with diabetic peripheral neuropathy (DPN), after 12 weeks of supplementation with B6, B12 and folate, subjects reported a mean reduction of 35% in Neuropathy Total Symptom Score-6 (NTSS-6). They also reported significant reductions in disruptions to work or school activities, social life, and family life, with a substantial 32% decrease in overall pain rating.¹² Another study using B6, B12 and folate showed that after 6 months of supplementation, subjects with DPN experienced significant increases in epidermal nerve fiber density in the lower extremities. 82% of subjects reported reduced frequency and intensity of paresthesias and/or dysesthesias.¹³ The combination of B6, B12 and folate resulted in significant improvements in cutaneous sensation in the feet in subjects with DPN, with improvement occurring within the first six months and continuing for up to one year.¹⁴

Benfotiamine: Experimental models of diabetes support a protective role for benfotiamine in preventing neuropathy and other diabetic complications.¹⁵ Benfotiamine (S-benzoylthiamine O-monophosphate) is a derivative of thiamine, which is metabolized into lipid-soluble S-benzoylthiamine.¹⁶ Plasma levels of thiamine may be as much as five times higher after oral supplementation with benfotiamine, which has three times higher bioavailability than thiamine HCl,¹⁷ and diabetics are often deficient in thiamine.¹⁸ (The lipid solubility of benfotiamine may account for its better retention compared to water-soluble thiamine.)

May be beneficial for*:

- Supporting the treatment of peripheral neuropathy
- Supporting healthy nerve function

Higher plasma levels of benfotiamine may help reduce the formation of AGEs, which could delay or reduce the progression of diabetic complications, including neuropathy, which may be caused in part by glycation damage to nerve tissue. Rat models of diabetes show that benfotiamine supplementation prevented tissue AGE accumulation and increased urinary excretion of protein glycation precursors.¹⁹ Benfotiamine, but not thiamine, has been shown to produce these results.²⁰ Looking at data in humans, oral benfotiamine supplementation in subjects with type 1 and type 2 diabetes resulted in significant reductions in perceived pain due to polyneuropathy.²¹ Subjects with DPN who were treated with benfotiamine and B6 showed substantial improvements in allodynia and hyperpathy, as well as objective measurements of nerve conduction, with 86% of subjects rating their overall condition as having improved.²²

Acetyl L-Carnitine (ALC): Randomized controlled trials have shown ALC to be effective compared to placebo for decreasing pain and improving nerve fiber regeneration in subjects with diabetic neuropathy.^{23,24} ALC is the product of acetylation of the amino acid derivative carnitine, which is synthesized from other amino acids. Certain conditions may increase demand for carnitine and ALC above that which the body can generate, necessitating supplementation. Suboptimal liver and kidney function, common among those with diabetes, may impair ALC synthesis, and select anticonvulsant medications sometimes used for painful neuropathy may also reduce serum ALC levels.⁶ “ALC is known to produce a strong antinociceptive effect when given after neuropathic pain has been established. ALC can also improve the function of peripheral nerves by increasing nerve conduction velocity, reducing sensory neuronal loss, and promoting nerve regeneration.”²⁵ Beyond facilitating mitochondrial fat oxidation, which may contribute to ALC’s effects on nerve function, the compound also induces select glutamate receptors, a mechanism believed to underlie its analgesic effect.²⁶ Several studies, including double-blind RCTs across a range of neuropathies—stemming from diabetes, chemotherapy, compression/injury, and those induced by HIV and anti-retroviral therapy—have shown efficacy of ALC for reducing pain and improving nerve function and trophism, leading researchers to conclude, “ALC represents a consistent therapeutic option for peripheral neuropathies.”²⁷

R-Lipoic Acid: Considered an “antioxidant of antioxidants” because of its capacity to regenerate or preserve vitamins C and E, glutathione and CoQ10, lipoic acid (LA) may be beneficial for any condition associated with oxidative stress.^{28,29} LA has been shown to be sufficiently effective for improving diabetic neuropathy that both oral and intravenous LA are approved for this purpose in Germany. LA’s multiple antioxidant properties likely underlie its efficacy for delaying or reversing DPN. Several clinical trials support LA improving sensory and motor deficits and electrophysiological tests of nerve conduction.⁶ Among subjects with diabetic polyneuropathy, oral treatment with LA for as little as five weeks resulted in significant improvement in total symptom score, including stabbing and burning pain,³⁰ and improvement may be seen in as little as three weeks (with intravenous administration).³¹ Positive influence on neuropathy was observed in both type 1 and type 2 diabetics, across a range of ages, and in those who’d been diabetic for an average of 10-15 years with neuropathy for 3-5 years.³² A meta-analysis looking at LA for diabetic polyneuropathy determined that this compound not only reduces the symptoms, it influences the underlying pathology,³³ which could potentially slow or possibly even reverse some degree of neuropathy, particularly if supplementation is started early and is combined with dietary and lifestyle changes to manage blood sugar.

Improved glucoregulation and insulin sensitivity are mechanisms by which LA may indirectly affect diabetic neuropathy. Several studies have demonstrated that LA aids in glucoregulation by facilitating proper functioning of the insulin receptor and recruitment of both insulin-sensitive and insulin-independent glucose transporters to muscle and adipose cell membranes.^{34,35} Subjects with type 2 diabetes who took LA for four weeks exhibited insulin sensitivity and glucose disposal that were not significantly different from those of healthy, non-diabetic controls.³⁶

Supplement Facts

Serving Size 4 capsules
Servings Per Container 30

Amount Per Serving		% Daily Value
Vitamin B-6 (as Pyridoxal-5-Phosphate)	25 mg	1471%
Folate (as Quatrefolic® [6S]-5-methyltetrahydrofolate, glucosamine salt 800 mcg)	680 mcg DFE	170%
Vitamin B-12 (as Methylcobalamin)	2000 mcg	83333%
Acetyl L-Carnitine	1 g	*
Benfotiamine	300 mg	*
R-Lipoic Acid	200 mg	*

*Daily Value not established.

Other Ingredients: Cellulose (capsule), stearates (vegetable source), dicalcium phosphate, silicon dioxide.

Recommended Use:

- Take four capsules per day, or as directed by your health care practitioner (divided dosing recommended).

For a list of references cited in this document, please visit:

<http://www.designsforhealth.com/techsheet-references/neurorenew-references.pdf>

Dosing recommendations are given for typical use based on an average 150 pound healthy adult. Healthcare practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.



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

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