



WESTERN NEUROPATHY ASSOCIATION

Celebrating our 26<sup>th</sup> Year!

# Neuropathy Hope

Hope through caring, support, research, education, and empowerment

A newsletter for members of Western Neuropathy Association (WNA)

December 2023

Issue 11  
Volume 21

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## ■ NONPHARMACOLOGIC SUPPLEMENTS ARE RECOMMENDED FOR DIABETIC PERIPHERAL NEUROPATHY

Lisa Kuhns, PhD, Clinical Pain Advisor, October 20, 2023

**Alpha-lipoic acid (ALA), vitamin D, and acetyl-L-carnitine (ALCAR)** show promise for managing diabetic peripheral neuropathy (DPN), but there is no evidence supporting the use of supplements for managing chemotherapy-induced peripheral neuropathy (CIPN), according to a study published in *Pain Practice*.

Researchers conducted a systematic review to evaluate the efficacy of dietary interventions, vitamins, and nutritional supplementation in managing CIPN in adults. Literature published between January 1, 2000, and October 21, 2021, was analyzed. A total of 40 papers were included in the review.

The change in pain scores for Chemotherapy-Induced Peripheral Neuropathy was assessed in 22 studies, including 3367 patients.

- Goshajinkigan\*, vitamin E, and vitamin B had mixed results in decreasing pain scores.
- Guilongtongluofang\* and Ninjin'yoeito\* revealed reductions in peripheral neuropathy.
- Glutamine, N-acetylcysteine, l-carnosine, magnesium or calcium, and crocin improved pain scores.
- Multiple antioxidants were found to increase CIPN compared with nonusers.

Diabetic Peripheral Neuropathy was assessed in 13 studies, which included 2540 patients.

- ALA revealed significant improvements in pain scores.
- In 1 study, vitamin B12 revealed significant improvements.
- ALCAR revealed improvements, and vitamin E, vitamin D, and alpha-lipoic acid significantly improved pain scores.
- Additionally, a low-fat, plant-based diet in combination with vitamin B12 revealed significant improvements.
- The study authors recommend ALA due to a significant reduction in neuropathy total symptom score.

**For DPN, the review supports the use of ALA, vitamin D, and ALCAR in the management of DPN and is equivocal regarding the use of B vitamins, vitamin E, and diet.**

**For CIPN, the review failed to find overwhelming evidence to support the use of any supplement.**

Study limitations included a lack of high-quality studies, small patient populations, and the heterogeneity of the scales measuring neuropathic pain.

### REFERENCE

Frediani JK, Lal AA, Kim E, et al. The Role Of Diet And Non-Pharmacologic Supplements In The Treatment Of Chronic Neuropathic Pain: A Systematic Review. *Pain Practice*. Published online August 31, 2023. doi:10.1111/papr.13291

### \*Definitions

Goshajinkigan is a Japanese herbal medicine that may alleviate neuropathy and general pain.

Guilongtongluofang is a traditional Chinese medicine that may prevent oxaliplatin-induced neurotoxicity.

Ninjin'yoeito is a traditional Japanese (Kampo) medicine that originates from China and may reduce oxaliplatin-induced cumulative peripheral neuropathy in patients with colorectal cancer.

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# PERIPHERAL NEUROPATHY SUPPORT GROUPS DECEMBER 2023 SCHEDULE

*Encourage, inform, share, support, and hope.  
Join a meeting to help others, learn something new, and/or share experiences.  
In-person or virtual – connect to others with peripheral neuropathy*

**December 2 Houston TX Support Group – Quarterly Meeting**

1:00pm-3:00pm Central, Memorial Drive United Methodist Church  
12955 Memorial Drive, Houston, TX 77079, Room DS100, enter at back (south) of building  
Host - Katherine Stenzel, klstenzel@hotmail.com

**December 4 Auburn CA Support Group**

11:00 am PST, Woodside Village Mobile Home Park, 12155 Luther Road, Auburn, CA  
Contact: Sharlene McCord (530) 878-8392, Kathy Clemens (916) 580-9449, kaclemens@earthlink.net

**December 9 2nd Saturday Virtual Support Group**

11:00am-1:00pm Pacific/1:00pm-3:00pm Central, Meeting ID: 856 7106 1474, Passcode: 114963  
Host – Katherine Stenzel, klstenzel@hotmail.com, contact Katherine for Zoom link

**Odd Months Santa Cruz CA Support Group**

Contact: Mary Ann Leer (831) 477-1239

Virtual Support Groups are on a reduced schedule in December.

## TOPICAL AMITRIPTYLINE FOR NEUROPATHIC PAIN - UPDATE

Katherine Stenzel, Editor

The September 2022 issue reported that topical amitriptyline (ATX01), developed by AlgoTx, was being investigated for chemotherapy-induced neuropathic pain. A phase 1 trial was completed that indicated favorable local and systemic tolerance on healthy participants. AlgoTx planned to initiate a phase 2 trial evaluating ATX01 for the treatment of chemotherapy-induced neuropathic pain in late 2022.

ClinicalTrials.gov lists clinical trial (NCT05593614) titled “Efficacy and Safety of ATX01 in Adult Patients with CIPN (Chemotherapy-induced Peripheral Neuropathy)” (ACT). Last information posted October 19, 2023 indicated that Algo Therapeutix is recruiting 240 participants for this 12-week Phase 2 study.

ClinicalTrials.gov also lists a clinical trial (NCT05917912) called EASE – “Efficacy of ATX01 Study in Erythromelalgia”. Erythromelalgia is a rare disease similar to peripheral neuropathy. It is characterized by a triad of redness, warmth and burning pain, most notably affecting the extremities. This Phase 2 6-week trial is recruiting 14 participants.

## MARK YOUR 2024 CALENDAR!

• January 2024 Webinar •

### NEVRO HFX Spinal Cord Stimulator

January 25, 2023, 1pm Pacific | 3pm Central

More information on page 3

No Webinar in December

## FROM THE PRESIDENT Pam Hart, WNA President

Happy Holidays! It is the time of the year for celebrations and at WNA we have many things to celebrate: Our first ever online Gala. Thanks to Katherine Stenzel we were able to host an online gala complete with games and speakers. We were very excited that one of our members, Brian Lockard, stepped up with wonderful handmade cutting boards for prizes. Other members contributed by being our judges. We honored:

- The person who has tried the most treatments: Helaine Greenburg, Reno, NV
- The person who has created the best catch-phrases: Don Tallman, Houston, TX
- The longest running peripheral neuropathy support group in California and WNA: Auburn CA - Kathy Clemens and Sharlene McCord
- For outstanding (medical) service to the WNA: Dr. Bill Donovan, Carmel, CA
- The best neuropathy caregiver/supporter – Geoff Dyott, Houston, TX
- For longest continuous service to neuropathy – Bev Anderson, Colfax, CA

Our online support groups continue to grow and we have started a new one – CIDP/Autoimmune Neuropathy with John Phillips. (See the monthly support schedule for times).

We added a new Board Member – Shana Phelps. Shana is a younger member and will help us with the ‘new’ generation perspective. She also brings her energy to social media sites to get our word out.

We were able to contribute \$10,000 to Dr. Hammock’s research at UC Davis. His research company is in drug trials for pain relief medication that is not opioid-based. The drug is licensed by the university to EicOsis ([www.eicosis.com](http://www.eicosis.com)), a company that is directing its development and is a UC Davis spin-off.

These are only the highlights. We should also mention the monthly webinars, monthly support group meetings and monthly Board meetings that keep us going and focused.

As you can see, we have much to be grateful for and many people to thank for making it all possible.

Thank you to all members and supporters.

*Cheers,  
Pam*

## JANUARY 2024 WEBINAR: NEVRO HFX SPINAL CORD STIMULATOR

**The Nevro’s HFX system involves the surgical implantation of a small electronic device near the spine.** Thin wires to the spinal cord offer “direct neural inhibition,” blocking the passage of pain signals between the extremities and the brain.

A two-year study published in Diabetes Research and Clinical Practice showed that Nevro’s system reduced pain by an average of 80 percent with ninety percent of participants experienced greater than 50 percent pain relief.

The spinal cord stimulation treatment also produced intriguing knock-on effects. In a post-hoc analysis, study participants using the HFX system were found to enjoy both weight loss and better blood sugar control (A1C). The therapy also appeared to improve sensory and neurological function. One hypothesis is that instant pain relief allowed people to perceive sensations that had previously been masked by pain. There is also some preliminary, unpublished evidence that high-frequency spinal stimulation helps to increase nerve fiber density. This unanticipated bonus needs to be evaluated in more-focused trials, but it suggests that high-frequency spinal cord stimulation is not merely masking pain but also addressing peripheral neuropathy in a more profound manner.

**Join us on January 25 to hear more about this treatment for painful peripheral neuropathy.**

**REFERENCE:** Ross Wollen, [Diabetesdaily.com](http://Diabetesdaily.com), August 30, 2023

### Health Care Challenges Websites (updated)

**SHIPs**  
**State Health Insurance Assistance Programs**  
[www.shiphelp.org](http://www.shiphelp.org)  
(877) 839-2675

Help for navigating the complexities of Medicare. Search the website for your specific state program.

**Medicare Rights Center**  
[www.medicarerights.org](http://www.medicarerights.org)  
(800) 333-4114

Non-profit that works to ensure access to affordable health care for older adults and people with disabilities.

**Medicare**  
[www.medicare.org](http://www.medicare.org)  
(800) MEDICARE  
(800) 633-4227

Get started with Medicare, options, news.

**Benefits and Insurance for People with Disabilities**  
[www.usa.gov/disability-benefits-insurance](http://www.usa.gov/disability-benefits-insurance)  
(844) USAGOV1  
(844) 872-4681

For those with a disability, learn how government programs and services can help in your daily life.

# CURRENT PHARMACOTHERAPY OPTIONS FOR NEUROPATHIC PAIN

Clear J, Uebbing E, Hartman K. Emerging Neuropathic Pain Treatments. *Pract Pain Manag.* 2022 May/June;22(3).

More than 20 million people in the United States suffer from peripheral neuropathy. Neuropathic pain can be caused by any damage to the somatosensory nervous system, potentially affecting both the peripheral and central nervous systems. There is no specific diagnostic test that can confirm neuropathic pain with 100% accuracy, making the best diagnostic approach the patient interview, identification of underlying causes, and exclusions.

Clinically, neuropathic pain is characterized by spontaneous ongoing or shooting pain accompanied by patient descriptor words such as “burning,” “tingling,” or “shocking.” Due to the pathological complexity of the disease, treatment is often most successful with multimodal analgesia that is individualized to the patient. The goal of therapy is to optimize pain control and improve functional status. In addition to treatment interventions, identification of realistic treatment expectations is imperative for this patient population.

Current best practice recommendations for the management of neuropathic pain include a stepwise algorithm of therapies. A summary of the recommendations is described as follows (see diagram on the right):

## TREATMENT DESCRIPTIONS

### Topicals

Topical agents such as capsaicin and lidocaine may provide benefit with minimal risk of side effects, however, they should be used only peripherally or at localized areas and must be applied frequently.

### Antidepressants

Antidepressants, notably tricyclic antidepressants (TCAs) and serotonin norepinephrine reuptake inhibitors (SNRIs), provide another therapeutic approach, capitalizing on the role of norepinephrine accumulation in hypoalgesia and analgesia. Antidepressants can be utilized to reduce neuropathic pain that is accompanied by insomnia or depression, both of which are common comorbidities in those living with chronic pain. However, adverse effects such as gastrointestinal distress, sexual dysfunction, and sleep disturbances may be often limiting factors.

### Anticonvulsants

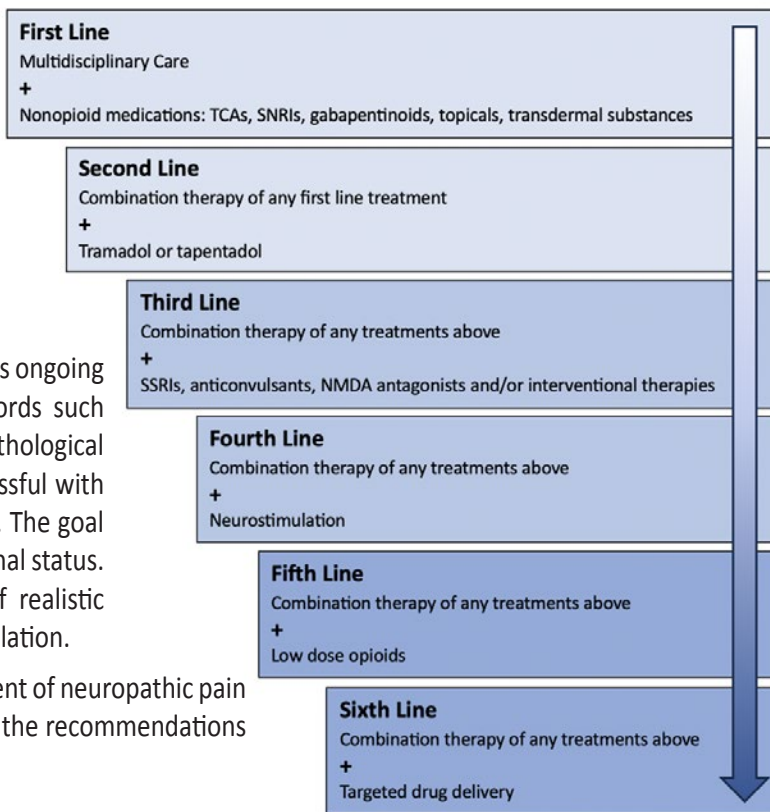
Anticonvulsants, such as gabapentin and pregabalin, may relieve pain by modulating the hyperexcitable state of injured neurons. However, similarly to antidepressants, gabapentinoids may be associated with limiting adverse effects such as nausea, vomiting, constipation, and psychiatric disturbances.

### Opioids

Opioids for the use of neuropathic pain is controversial. Several clinical trials have shown positive results for relief in this patient population; however, there is not a clear duration of time that therapy would be needed, and neuropathic pain is typically a chronic condition. Therefore, it is often argued that the risk for addiction, adverse effects, and organ damage from chronic use outweighs the potential benefit.

## CLOSING REMARKS

Some people with neuropathic pain are fortunate and find that one of these treatment combinations is successful in reducing their neuropathic pain to a functional threshold. Unfortunately, despite the vast number of medications available, others still do not gain relief and the pain remains detrimental to their mental and physical health.



## NOVEL NEUROPATHIC PAIN TREATMENTS IN CLINICAL TRIALS

Clear J, Uebbing E, Hartman K. Emerging Neuropathic Pain Treatments. *Pract Pain Manag*. 2022 May/June;22(3).

The complexity of neuropathic pain calls for numerous treatment options that target a variety of mechanisms. Below is a very simplified description of four emerging treatment options and therapeutic targets that could provide an additional avenue for people who have exhausted the usual protocols with subtherapeutic relief.

Intervention	Potential Mechanism Of Action	Place In Research
<b>Alpha lipoic acid / Thioctic acid</b>	Decrease nerve damage from oxidative stress through antioxidant redox balance	Clinical trials in humans
<b>HCN2 Blockage</b>	Mitigate inflammatory and cellular factors of neuropathic pain stemming from L4-L5 ipsilateral spinal dorsal horns	Preclinical for HCN2 Clinical trial in humans for non-specific HCN
<b>AAK1 Inhibitor</b>	Analgesia through modulation of alpha adrenergic signaling	Phase 1 clinical trials in humans
<b>GABAergic Transplant</b>	Transplanting embryonic cells from the medial ganglionic eminence (MGE) of the forebrain into an adult spinal cord allows for generation of functioning nerve cells to replaced damaged or injured nerves	Preclinical

Each treatment option requires further research before efficacy and safety can be definitely described. Phase 2 and 3 clinical trials of AAK1 inhibitors can be expected to emerge now that Phase 1 trials have indicated safety in healthy adults. In order to determine utility of thioctic acid, higher quality studies compared to placebo are needed. Alternatively, although HCN2 inhibition and GABAergic transplant show significant strides in animal studies, further research is required before human studies can begin. Overall, although the four emerging therapies require additional research, existing data suggest they could have clinically significant utility for neuropathic pain.

## GINGER SUPPLEMENTS MAY BE HELPFUL IN TREATING AUTOIMMUNE DISEASES

Paul Ian Dross, PhD., Medical News Today, September 28, 2023. Suggested by John Phillips, WNA Director

- **New research reveals that ginger supplements may offer a promising approach to managing inflammation in individuals with autoimmune conditions.**
- **The study highlights ginger’s ability to influence neutrophils (a type of white blood cell), making them less susceptible to NETosis—a process linked to inflammation and various autoimmune diseases.**
- **As more patients turn to natural remedies like ginger to alleviate symptoms, researchers are eager to further explore its therapeutic potential, especially for conditions like lupus, antiphospholipid syndrome (APS), rheumatoid arthritis and even COVID-19.**

This research suggests that ginger supplements could revolutionize the management of autoimmune diseases, such as APS and lupus, by changing how specific immune cells function. Combining ginger with existing treatments could potentially improve therapeutic outcomes in chronic inflammatory diseases.

*(Editor – Autoimmune diseases that can cause peripheral neuropathy include Sjogren’s syndrome, lupus, rheumatoid arthritis, vasculitis, Guillain-Barre syndrome (GBS), and chronic inflammatory demyelinating polyneuropathy (CIDP).*



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# THE IMPORTANCE OF EXERCISE ON BALANCE AND PAIN IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY

Summarized by Katherine Stenzel, WNA Editor

This page contains summaries of four articles that reviewed clinical trials testing **how exercise can improve balance, posture and gait, and reduce neuropathic pain.**

## The Application of Exercise Training for Diabetic Peripheral Neuropathy (DPN)<sup>1</sup>

It has been hypothesized that improvement in both balance and stability, as well as strengthening of the lower-body of individuals with DPN, has the potential to enhance gait and physical capacity, while also reducing disability, foot deformity, and the risk of amputation.

Damage to the sensory and motor nerves can severely impair myofiber innervation and perfusion, causing muscle atrophy and balance impairments, which is of even greater concern for older adults already at an elevated risk of developing sarcopenia and falling. For these reasons, practitioners have sought to implement therapeutic strategies focused on improving balance.

Upon reviewing the literature, there is support that exercise-based interventions  $\geq 4$  weeks are beneficial for patients with DPN. This conclusion falls in line with other recently conducted literature reviews investigating the effects of exercise on enhancing gait function [2], decreasing neuropathic pain [3], and improving posture and balance among patients with peripheral neuropathy [4]. (Editor – all described below)

**Mobility and functional movement-based training, specifically weight-bearing exercise, is not only safe for people with DPN to participate in, but can provide significant increases in gait, balance, and strength.** Improvements were thought to be tied to increases in foot and ankle musculature strength, as well as greater coordination of muscle activation, body stability, and joint flexibility. Following weight-bearing exercise training, DPN patients demonstrated greater daily step counts and walking distances, which lend themselves well towards improving daily physical function and quality of life for patients with DPN. The research suggests that exercise sessions should start using “light” intensities and then slowly titrate up over time.

Aerobic exercise is one of the most commonly utilized training modalities in both healthy and special populations. Aerobic exercise training at moderate intensities has shown the ability to improve sensorimotor function, cardiorespiratory endurance, reduce fatigue, and promote increased physical activity. Mechanisms for the observed improvements following aerobic exercise interventions may be tied to enhanced glycemic control and endothelial function. Furthermore, three studies demonstrated improvements in electrophysiological examinations, specifically in greater nerve conduction velocity within the sensory nerves. These significant changes are also thought to be influenced by changes in glycemic status, as well as decreases in lower limb edema and increases in blood supply to meet certain metabolic requirements for neural collateral sprouting. Because NCS are regarded as the standard for measuring peripheral nerve functions, clinicians should look to incorporate aerobic exercise into treatment protocols for patients with DPN, as a non-pharmacological aide to help bolster the effects of prescribed medications and other therapy.

Resistance exercise training has many potential benefits for individuals with DPN and has demonstrated its effectiveness when combined with aerobic exercise. Training programs should be designed utilizing 1–3 sets of 10–15 repetitions at “moderate” intensities of 50–69% 1-RM for either 2–4 lower-body focused exercises or 8–10 exercises targeting the full body to elicit potential favorable changes in glycemic control, microvascular perfusion, and neural drive.

Traditional balance, proprioception-based, yoga, and tai chi-based exercise training interventions have all demonstrated the ability to improve multiple different measures of static and dynamic balance performance, postural control, and strength, and to reduce fall risk. For individuals who are less physically fit, older, or have more severe cases of peripheral neuropathy, these modalities of exercise may be a more efficacious choice.

## Effectiveness Of Exercise Therapy on Gait Function in Diabetic Peripheral Neuropathy Patients: A Systematic Review of Randomized Controlled Trials<sup>2</sup>

The purpose of this study was to review the current evidence on the effectiveness of exercise therapy on gait function in patients

– Continued on page 7

## Drug-free help for diabetic nerve pain

Early in 2023, the FDA approved use of the Abbott's Eterna, Proclaim Plus and Proclaim XR Spinal Cord Stimulation (SCS) Systems to relieve lower-extremity pain caused by diabetic peripheral neuropathy (DPN). The devices send mild electrical signals to the spinal cord, reducing pain by an average of 53 percent in studies.

## Virtual reality for back pain

A virtual reality program called RelieVRx, by AppliedVR, successfully reduced back pain by half for 46 percent of users who followed the program daily for eight weeks. Users of the prescription-only system put on a VR headset to learn cognitive behavioral skills for pain management such as deep relaxation and breathing exercises. Sessions last two to 16 minutes. The program is available in some health systems and through the Department of Veterans Affairs.

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## The Importance Of Exercise On Balance And Pain In Patients With Diabetic Peripheral Neuropathy

– Continued From Page 6

with diabetic peripheral neuropathy. The primary outcome measures of gait functions were the six-minute walk test, 10-meter walk test and Tinetti scale. Nine randomized controlled trials with 370 participants were analyzed. Out of them, eight studies proved its effectiveness on gait function on individuals with diabetic peripheral neuropathy. The finding of this study suggested that multi-component exercise therapy consisted of strength, ROM exercise, balance, flexibility and stretching exercises, circuit exercise training, and gait training found to enhance gait function for individuals suffering with diabetic peripheral neuropathy.

### Exercise And Neuropathic Pain: A General Overview of Preclinical and Clinical Research<sup>3</sup>

The following review includes an overview of the preclinical and clinical literature examining the influence of exercise on neuropathic pain. Preclinical studies support the hypothesis that exercise reduces hyperalgesia and allodynia in animal models of neuropathic pain. In human research, observational studies suggest that those who are more physically active have lower risk of developing neuropathic pain compared to those who are less active. Exercise studies suggest aerobic exercise training (e.g., 16 weeks); a combination of aerobic and resistance exercise training (e.g., 10–12 weeks); or high-intensity interval training (e.g., 15 weeks) reduces aspects of neuropathic pain such as worst pain over the past month, pain over the past 24 h, pain scores, or pain interference.

### A Systematic Review and Meta-Analysis on Efficacy of Exercise on Posture and Balance in Patients Suffering from Diabetic Neuropathy<sup>4</sup>

The aim of this study is to assess the effects of exercises on posture and balance in patients suffering from diabetes mellitus. Sixteen randomized controlled trials met the selection criteria and were included in the study. The primary outcome measures were mean changes in Timed Up and Go test (TUGT), Berg Balance Scale, and Postural Sway with eyes open and eyes closed on Balance System were primary outcome measures. The risk of bias was assessed by the Cochrane collaboration tool of risk of bias. Results of meta-analysis showed that there was a statistically significant improvement in TUGT, a statistically significant difference in Berg Balance Scale scores and significant changes in postural stability (eyes open and eyes closed). **It can be concluded that various exercises like balance training, core stability, Tai-Chi, proprioceptive training, etc. have a significant effect on improving balance and posture in diabetic neuropathy.**

### References

<sup>1</sup>Holmes C., Hastings M. The Application Of Exercise Training For Diabetic Peripheral Neuropathy. *J Clin Med.* 2021;10(21): 5042. doi: 10.3390/jcm10215042

<sup>2</sup>Melese H., Alamer A., Hailu Temesgen M., Kahsay G. Effectiveness Of Exercise Therapy On Gait Function In Diabetic Peripheral Neuropathy Patients: A Systematic Review Of Randomized Controlled Trials. *Diabetes Metab. Syndr. Obes.* 2020;13:2753–2764. doi: 10.2147/DMSO.S261175

<sup>3</sup>Leitzelar B.N., Koltyn K.F. Exercise And Neuropathic Pain: A General Overview Of Preclinical And Clinical Research. *Sport Med.* 2021;7:21.

<sup>4</sup>Thukral N., Kaur J., Malik M. A Systematic Review And Meta-Analysis On Efficacy Of Exercise On Posture And Balance In Patients Suffering From Diabetic Neuropathy. *Curr. Diabetes Rev.* 2021;17:332–344. doi: 10.2174



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# HAPPY HOLIDAYS

From All Of Us At WNA

## IN THIS ISSUE

A common comment I hear is “Who is researching about cures... treatments... for Peripheral Neuropathy?” Believe me, there is a lot of research into the disease, why/how it happens, and what can be done to treat the pain and regenerate nerves. I’ve captured some information in this issue.

**Novel Neuropathic Pain Treatments in Clinical Trials** describes four areas of investigation and their status in clinical trials. I’m so glad the article included this summary table as otherwise I could hardly decipher the science!

**Topical Amitriptyline for Neuropathic Pain – Update** describes how this treatment for chemotherapy-induced peripheral neuropathy is progressing into a 12-week Phase 2 study, and as of press time is still recruiting 240 participants.

And for research that has turned into reality, Abbott’s neuromodulation systems were approved in early 2023 for lower-extremity pain caused by diabetic peripheral neuropathy.

I hope these give you Hope.

..Katherine

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Our mission is to provide support, information and referral to people with neuropathy and to those who care about them, to inform and connect with the health care community, and to support research.

Dues - \$30 a year

All contributions and dues are tax-deductible.

We are supported by dues-paying members, contributions by members and friends, and occasionally, small grants and fundraisers.

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