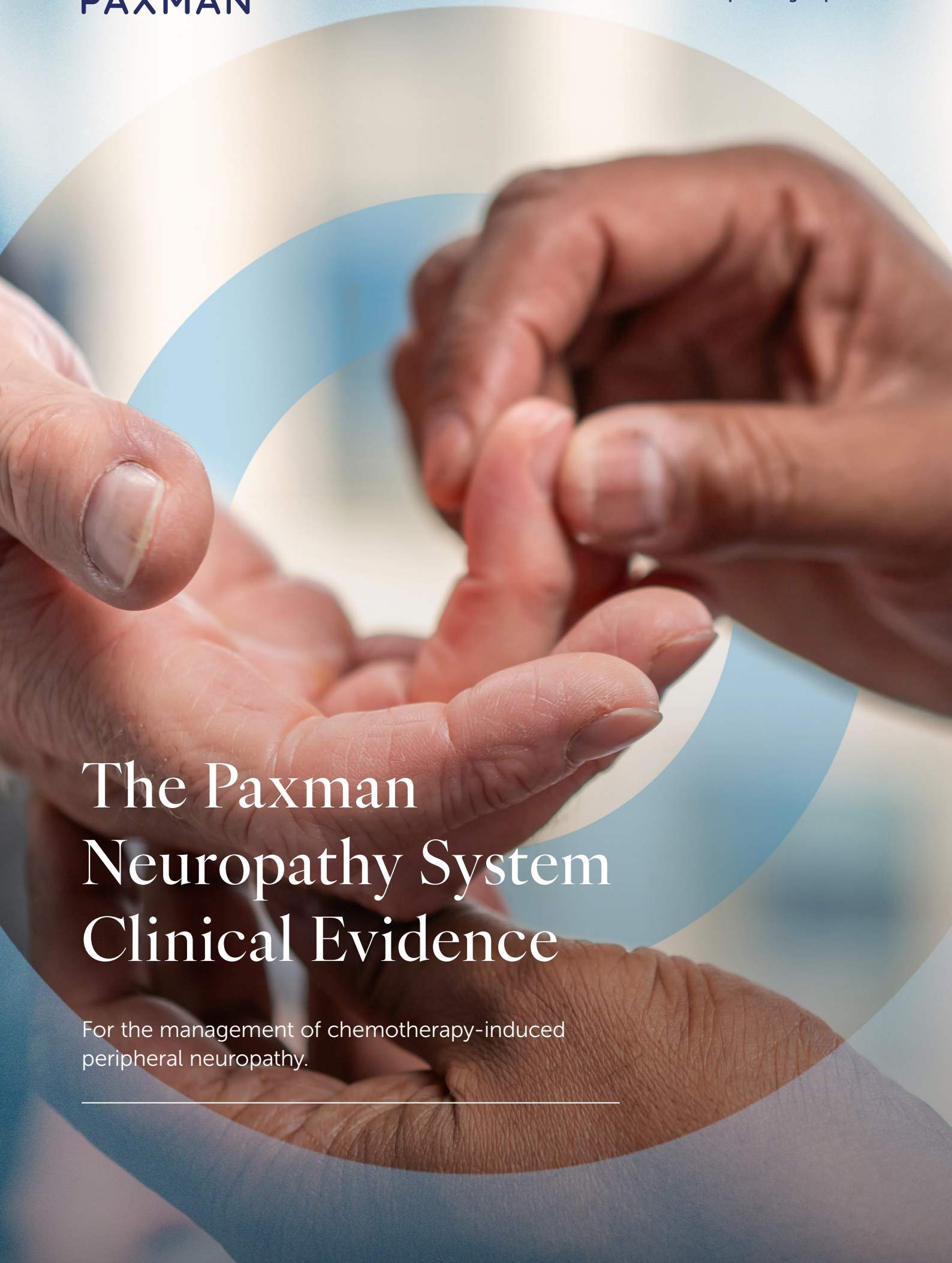
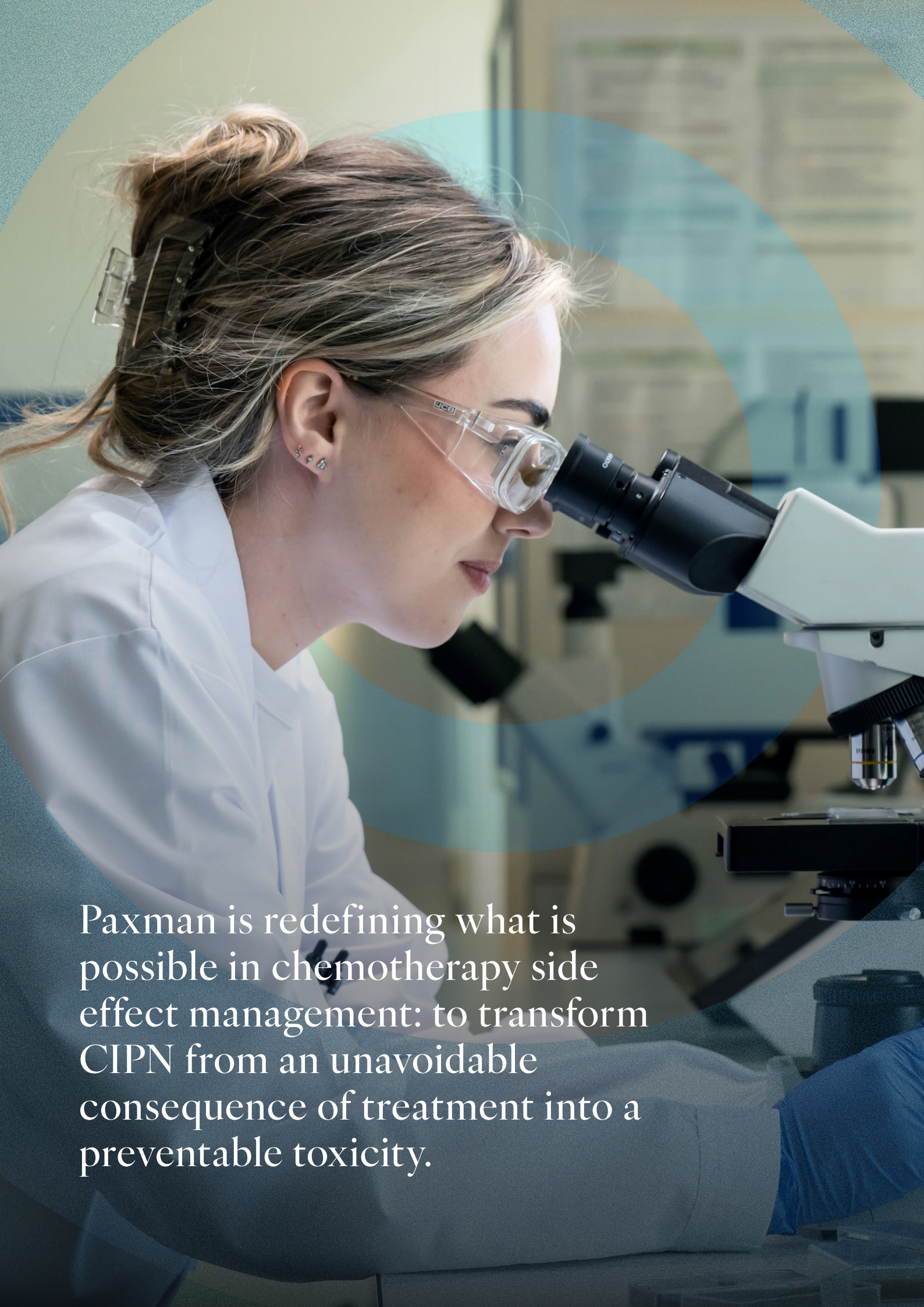
PAXMAN

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# The Paxman Neuropathy System Clinical Evidence

For the management of chemotherapy-induced peripheral neuropathy.



Paxman is redefining what is possible in chemotherapy side effect management: to transform CIPN from an unavoidable consequence of treatment into a preventable toxicity.

# Understanding the biology of CIPN



## What is chemotherapy-induced peripheral neuropathy?

**Chemotherapy-induced peripheral neuropathy (CIPN) is a common and potentially dose-limiting side effect of several chemotherapeutic agents. In studies, it is estimated to affect an average 30% to 90% of patients globally.**[1,2]

CIPN can develop when damage occurs to the peripheral nervous system, particularly to the sensory nerves of the hands and feet, and typically in a glove-and-stocking distribution. This can progress with cumulative treatment exposure and in severe cases, damage can even spread proximally.

CIPN may include sensory symptoms such as numbness, tingling, burning, pain, and cold sensitivity; motor symptoms such as weakness, reduced dexterity, gait disturbance, and balance impairment; and functional consequences affecting writing, dressing, driving, walking, and other instrumental activities of daily living.

Whilst it is predominantly seen as sensory neuropathy, motor and autonomic damage may also occur.

The most recent guidelines from ASCO indicated that, in times when patients exhibit significant neuropathy, physicians must evaluate whether treatment delay, dose modification, substitution or cessation of chemotherapy are required.

**CIPN presents a difficult choice:**
choose a less effective cancer treatment or risk allowing CIPN to progress.

A DEBILITATING AND POTENTIALLY PERMANENT SIDE EFFECT WITH PROFOUND IMPLICATIONS FOR A PERSON'S DAILY LIFE.

## UNDERSTANDING THE BIOLOGY OF CIPN

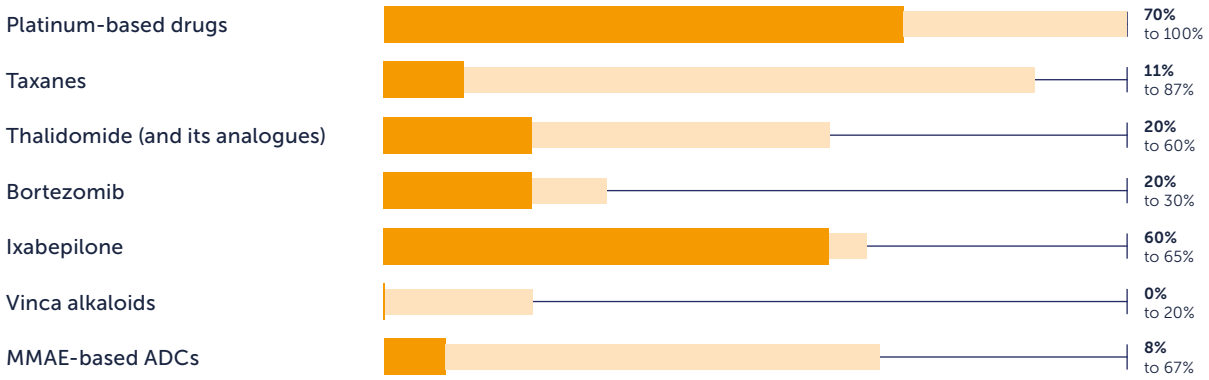
# What causes CIPN?

### Neurotoxic chemotherapy agents

**The most common chemotherapy agents associated with CIPN are those which are neurotoxic, including:**

- Taxanes (e.g. paclitaxel, docetaxel, cabazitaxel)
- Platinum agents (e.g. cisplatin, carboplatin, oxaliplatin)
- Proteasome inhibitors (e.g. bortezomib, ixazomib, carfilzomib)
- Vinca alkaloids (e.g. vincristine, vinblastine, vinorelbine)
- Immunomodulatory agents (e.g. thalidomide, pomalidomide),
- Antibody-drug conjugates (ADCs) with tubulin-binding payloads (e.g. brentuximab vedotin, polatuzumab vedotin, enfortumab vedotin, trastuzumab emtansine)

**CIPN INCIDENCE BY CHEMOTHERAPY DRUG CLASS** [6,7]




Reported incidence varies widely depending on the neurotoxic agent used. Cumulative dose, baseline patient risk, and method of assessment also have an effect. Across the literature, incidence has been reported in the range of **roughly 30% to 90% overall.**[1,2]

### Susceptibility of peripheral nerves

Peripheral nerves are especially susceptible to chemotherapy-induced damage because:

They represent some of the longest and most metabolically demanding cells in the body.

The dorsal root ganglia have relatively poor protection from circulating toxins.



They rely heavily on mitochondrial energy production.

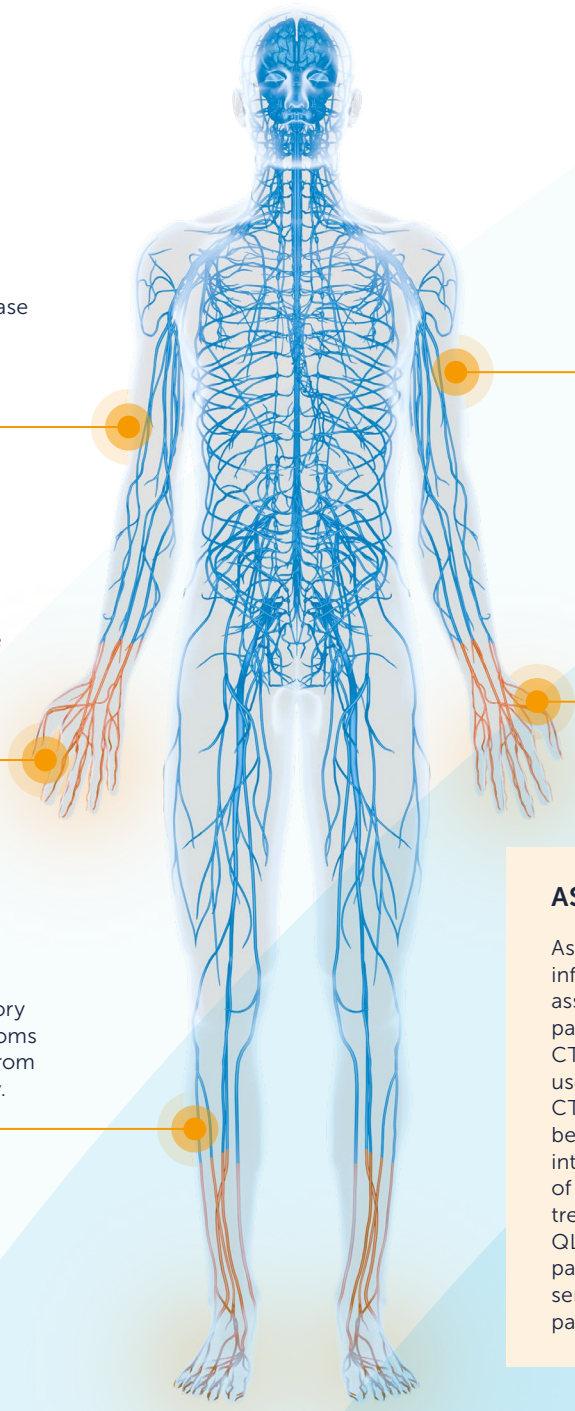
They depend on efficient axonal transport systems.

The blood-nerve barrier is more permeable to chemotherapy.

# Biological mechanisms of CIPN

**The complexity of CIPN means that rather than arising from a single biological pathway, damage occurs through interconnected cellular, metabolic, inflammatory, vascular and electrophysical processes.**

Effective management of CIPN begins with understanding the biology. Paxman is advancing the scientific understanding of CIPN through an ongoing programme of biological research designed to identify how different chemotherapy agents damage peripheral nerves and identify opportunities for effective reduction. Evidence has demonstrated that different chemotherapy drug classes initiate distinct primary molecular 'insults' to cause cellular damage.[7]



### Cell damage

Many chemotherapy agents reduce energy production in cells and increase oxidative stress. This damages the nerve cells and contributes to nerve dysfunction.

### Axon degeneration

Agents such as taxanes and antibody-drug conjugates can cause progressive degeneration of axons, responsible for carrying electrical signals within the body.

### Disruption of normal nerve signalling

Chemotherapy can increase nerve sensitivity and cause abnormal sensory signalling. This contributes to symptoms such as tingling, burning pain, pain from light touch, and cold hypersensitivity.

### Impaired axonal transport

Taxanes and vinca alkaloids disrupt the transport of nutrients and cellular components along the nerve fibres. This weakens nerve function and contributes to damage within cells.

### Neuroinflammation

Chemotherapy activates inflammatory responses that sensitise nerves and may contribute to persistent neuropathic pain.

## ASSESSING CIPN

Assessment of CIPN is most informative when physician-assessed grading is combined with patient-reported outcomes. NCI CTCAE grading remains widely used in clinical practice and trials. CTCAE grade 2 is especially relevant because it reflects symptoms that interfere with instrumental activities of daily living and may influence treatment decisions. The EORTC QLQ-CIPN20 is a commonly used patient-reported tool that captures sensory and motor burden from the patient perspective.

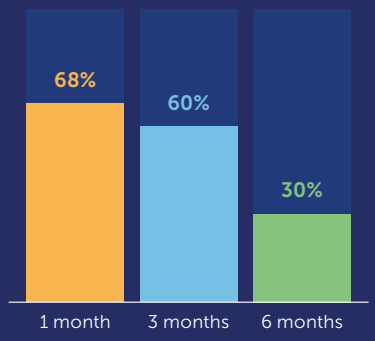
# A growing survivorship challenge

## Positive survival rates can increase CIPN prevalence

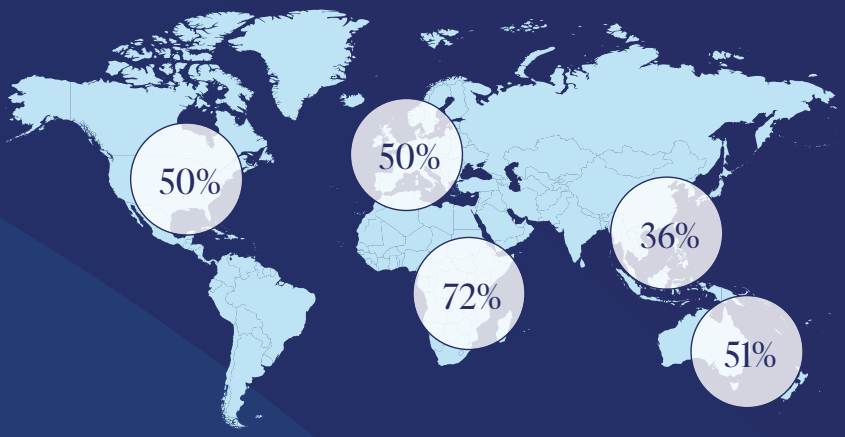
**As cancer incidence rates increase – and positively, survival and cure rates improve – both acute and chronic CIPN prevalence subsequently increases along with it.**

Meta-analysis data was able to find that[1]:

- There was a 68% prevalence of CIPN within the first month after chemotherapy
- 60% prevalence at 3 months
- 30% prevalence at 6 months or longer




**PREVALENCE OF CIPN IN THE MONTHS POST-CHEMOTHERAPY**[1]




A systematic review of 77 studies across 28 countries analysed 24 years' worth of data (from 2000 – 2024), which suggests chronic moderate to severe CIPN has remained highly prevalent worldwide for a long period of time.[9]

High prevalence over 24 years suggests that advancements in prevention and treatment of chronic CIPN have been limited.

## GLOBAL CHRONIC CIPN PREVALENCE IS 41%

**40%**
Prevalence on Taxane-based chemotherapy

**38%**
Prevalence on Platinum-based chemotherapy

This large-scale evidence also suggests the prevalence of chronic CIPN varies depending on geography.

With increasing cancer survival rates and expanding use of neurotoxic therapies, CIPN represents a growing long-term survivorship issue.

# CIPN has multi-faceted, far-reaching consequences

**25%**

of patients responded "always" or "often" to feeling fear most of the day.[11]

**50 DAYS**

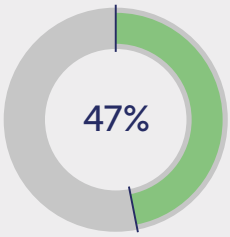
>50 days of work lost per patient due to CIPN.[13]

**30x**

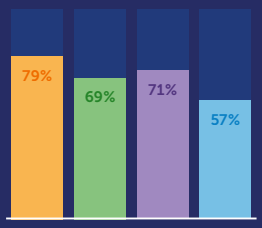
Patients are ~30 times more likely to prefer discontinuing chemotherapy if permanent CIPN symptoms were a risk.[12]

**26%**

of patients reported hostile behaviours at work due to their health conditions.[11]




47% of women still reported CIPN symptoms after an average of 6 years post-chemotherapy.[14]




Impact studies found at least 57% of patients needed to spend a significant amount of time sitting or lying down, with 79% patients changing their habits and 69% experiencing difficulty with daily physical activity and 71% reported difficulty taking long walks.[11]

Up to 1 in 5 patients experience CIPN-related chemotherapy dose modification or discontinuation which can affect treatment outcomes or compromise survival.[15, 16]

**3x**

Patients who develop CIPN are approximately 3 times more likely to fall and suffer from fall related injuries.[10]

Patients with CIPN average 12 more outpatient visits after chemotherapy compared to those without CIPN.[17]

**$17,344**

Healthcare costs are estimated to be $17,344 more in cancer patients with CIPN than those without CIPN.[13]

**30-40%**

of all chemotherapy dose modifications are CIPN related.[15]

**CIPN is linked to:**

- Discontinuation of treatment
- Disruption to a patient's daily life
- Increased healthcare utilisation
- Greater outpatient burden
- Higher overall cost to providers and payers

# The Prevention Gap

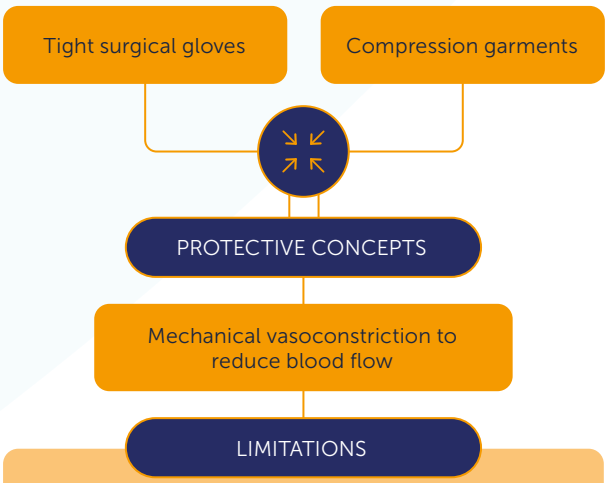
## Traditional methods of CIPN prevention

Whilst early research largely focused on neuroprotective drugs, repeated clinical trials failed to establish a consistently and/or adequately effective pharmacological option. This shifted attention toward physical methods of protection, particularly approaches designed to reduce chemotherapy exposure in the hands and feet during infusion.

Although relatively simple and inexpensive to implement, these methods presented major limitations that reduced patient compliance and/or real-world efficacy.




- Variable and poorly controlled temperature delivery
- Discomfort and pain
- Poor tolerability
- Risk of excessive cold exposure (such as frostbite)
- Difficulty maintaining stable cooling throughout infusion
- Additional nursing burden administering fresh gloves and socks
- Inconsistent adherence
- Lack of standardised cooling protocols




- Fit varies between patients
- Protocols are not yet standardised
- Dose of compression cannot be repeatably measured
- Efficacy may depend on chemotherapy type and treatment duration

# Development of a cryocompression device: The Paxman Neuropathy System




The limitations of frozen gloves, ice bags, and simple compression methods created a need for more controlled technologies. Modern cryotherapy devices aim to deliver prevention strategies that are **tolerable, reproducible, and standardised,** in order to help preserve chemotherapy dose intensity while reducing long-term neuropathy burden.

Compared with frozen gloves and cooling alone, cryocompression has been shown to achieve lower tolerable temperatures over time in a comparative study.[19]

| Frozen gloves | Continuous-flow cooling | Cryocompression |
|---|---|---|
| **Low temperature** | Higher temperature | **Low temperature** |
| Uneven cooling | **Even cooling** | **Even cooling** |
| Low tolerability | Moderate tolerability | **High tolerability** |
| Uncontrolled delivery | **Controlled delivery** | **Controlled delivery** |

Continuous-flow cooling and cryocompression achieved relatively even cooling profiles of the hand whereas frozen gloves tended to cause "cold spots" which could be a reason for intolerance and frostbite over longer exposure times.[19]

Cryocompression as a method of cooling has therefore emerged as a promising neuroprotective intervention, potentially by reducing neurotoxic chemotherapeutic delivery to peripheral nerves through vasoconstriction and decreased metabolism. This is evidenced by several studies and outlined in the clinical guidelines of ASCO,[20] and ESMO,[21] with the National Comprehensive Cancer Network® (NCCN®) guidelines referring to cryotherapy.[22]



# The Paxman Neuropathy Solution

## Redefining CIPN management




### How the Paxman Neuropathy System helps reduce chemotherapy-induced peripheral neuropathy.

Paxman is pioneering research into the biological processes leading to peripheral nerve damage which suggests that controlled cooling could efficiently rescue human neuronal cells from the damage caused by different classes of chemotherapy drugs.

Based on this research, it is believed that cooling can exert direct biological effects, and this neuroprotection is temperature dependent with optimal neuroprotection suggested to be between 20-24°C/68-75°F.

Ongoing laboratory research is focused on further refining the biological understanding of cooling, including optimisation of treatment conditions and evaluation under clinically relevant exposure scenarios.

Together, these efforts support a fundamental shift in perspective: from CIPN as an unavoidable side effect of chemotherapy, to a condition that may be **preventable through biologically informed, cooling-based direct preventative intervention.**

## COOLING FOR PROTECTION. COMPRESSION FOR COMFORT.

### Cooling

Biological Protection

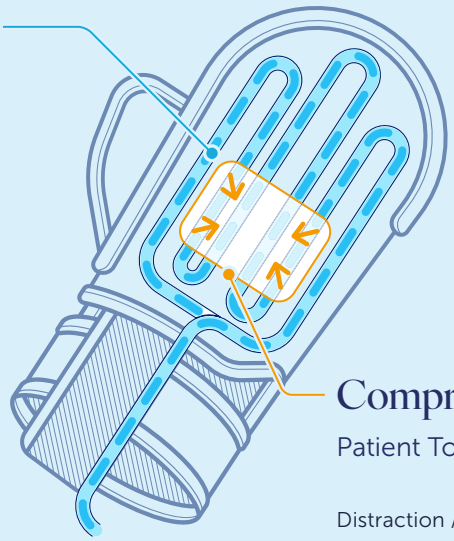
Induces vasoconstriction, to reduce local chemotherapy delivery

Suppresses cellular oxidative stress (by reducing generation of reactive oxygen species, ROS)

Preserves the structural integrity of human neuronal cells (preventing disruption of neurite architecture and loss of cellular connectivity)

Maintains nerve cell signalling and function

Supports cell viability and functional resilience



### Compression

Patient Tolerability

Distraction / counter-pain stimulus

Improves cooling efficiency by increasing contact with the cooling surface[19]

# From biological insight to clinical benefit

With cryocompression suggesting promising results versus continuous-flow cooling or frozen gloves in clinical studies, further trials were initiated to establish efficacy, safety and tolerability.

The Paxman Neuropathy System is supported by the following clinical evidence of efficacy, safety, and tolerability of cryocompression during taxane-based chemotherapy in 150 patients from a single-arm phase II study.

## CLINICAL BENEFIT

**95%**

relative reduction of risk in incidence of NCI CTCAE grade ≥2 CIPN*

**70%**

relative reduction of risk in incidence of any grade CIPN**

*The primary clinical benefit of the Paxman Neuropathy System is a 95% relative reduction of risk in incidence of NCI CTCAE grade ≥2 CIPN versus historical untreated controls, representing reduction of higher grade neuropathy that would otherwise require intervention or chemotherapy dose modification.[+]

**The secondary clinical benefit is a 70% relative reduction of risk in incidence of any grade CIPN, as assessed by NCI CTCAE and EORTC QLQ-CIPN20, versus historical untreated controls, as assessed by the NCI CTCAE and EORTC QLQ-CIPN20.

[+]Data on file as part of the Clinical Evaluation is available upon request.

# Efficacy

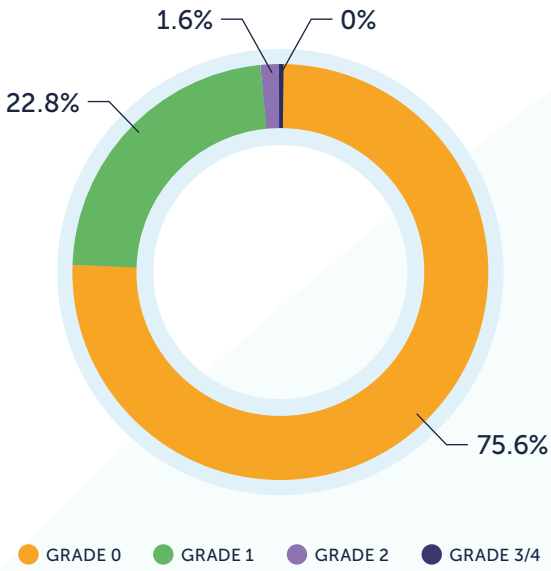
**Efficacy data was both physician-assessed (at 12 weeks) and patient-reported (at 12 and 24 weeks).[24]**

- At 12 weeks, Grade 2 CIPN or higher was reported in 1.6% of patients
- 75.6% of patients were assessed with no CIPN
- Any-grade CIPN was reported in approximately 24.4% of patients
- No Grade 3 or 4 CIPN was reported

**PATIENT-REPORTED CIPN AT 12 AND 24 WEEKS**

| TIMEPOINT | CIPN* | NO CIPN |
|---|---|---|
| 12 Weeks | 13.9% | 86.1% |
| 24 Weeks | 13.1% | 86.9% |

Patient-reported outcomes were available in 115/123 patients (93.5%) at 12 weeks and 107/123 (87.0%) at 24 weeks.




**PHYSICIAN-ASSESSED CIPN AFTER USING THE PAXMAN NEUROPATHY SYSTEM**

## Dose Modification

In the trial cohort:

- Only 5.7% of patients required taxane dose reduction due to CIPN.
- 51.2% (63/123) required taxane dose modifications (reduction or delay) for any reason.

**5.7%**

**Only 5.7% of patients required dose modifications due to CIPN.**

## Safety & Tolerability

The Paxman Neuropathy System was found to be safe and well-tolerated in patients receiving taxane-based chemotherapy. Moreover, it can be safely administered with scalp cooling therapy.

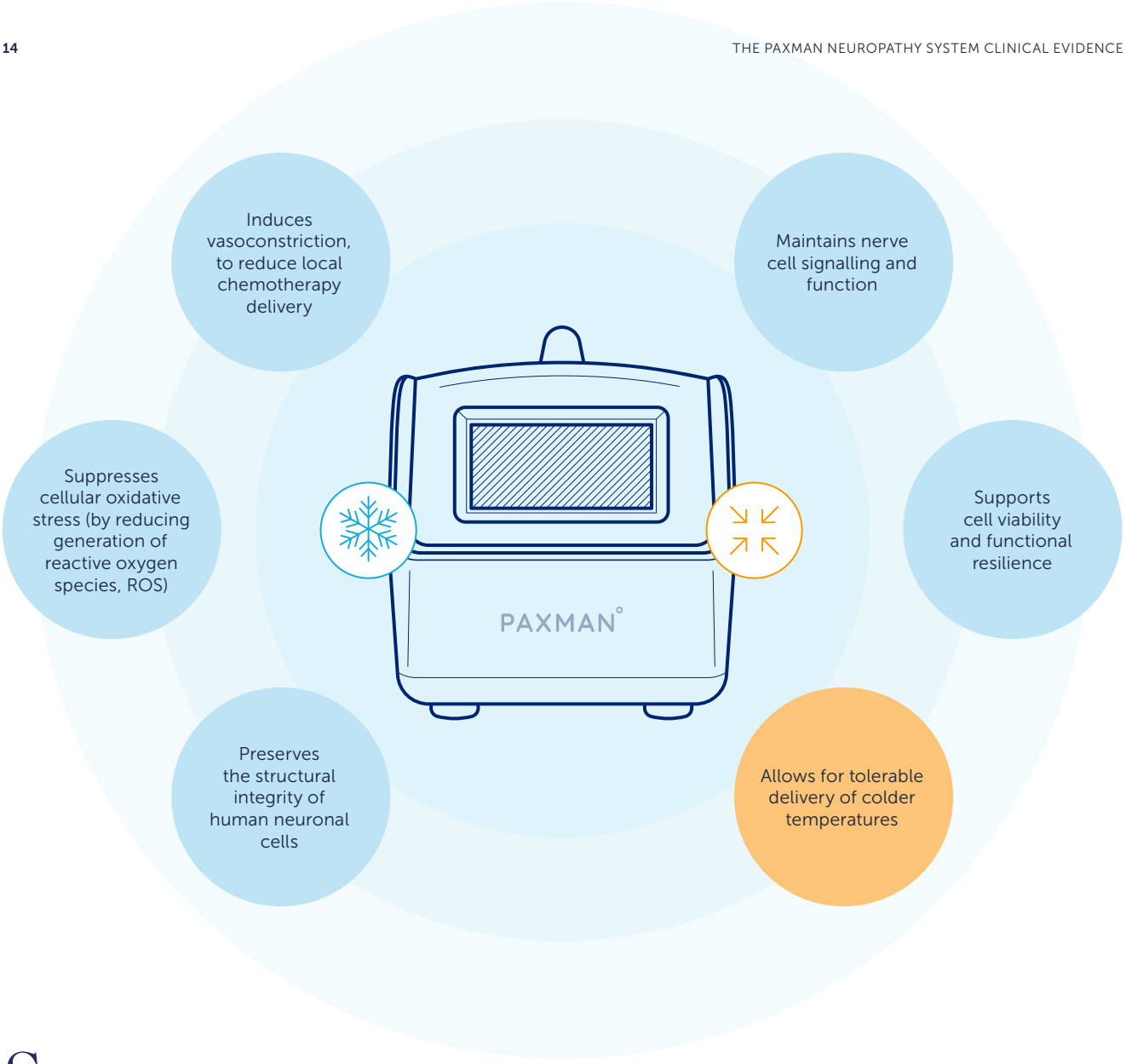
- No incidences of core hypothermia, frostbite or higher grade cold related adverse events.**
- 45% of patients in this study underwent concurrent scalp cooling, which did not affect cryocompression, reinforcing data from a previous safety and feasibility study.

**84%**

**found the Paxman Neuropathy System tolerable.**

*Patient-reported clinically significant CIPN defined as a ≥3-point increase in the EORTC QLQ-CIPN20 sensory subscale assessed at baseline, 12 weeks, and 24 weeks from treatment initiation.

**Barring transient erythema (redness of the skin) that reversed a few minutes after cessation of cooling.




# Summary

The Paxman Neuropathy System brings together controlled cooling and compression to address one of chemotherapy's most persistent side effect management challenges: chemotherapy-induced peripheral neuropathy (CIPN).

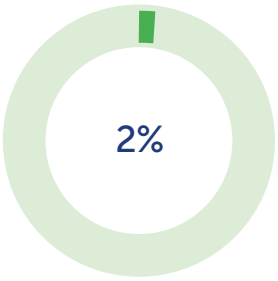
CIPN is both a patient quality-of-life issue and a treatment-delivery challenge, with symptoms that can affect mobility, dexterity, independence, work and long-term survivorship.

As survivorship increases and neurotoxic therapies continue to be widely used, the need for a standardised, tolerable, and evidence-supported prevention approach is clear.

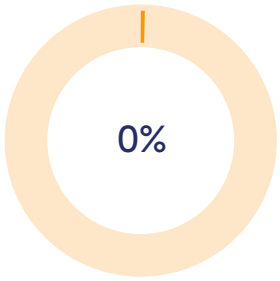
Supported by Paxman's extensive biological research to further understand the mechanisms of CIPN and the effects of controlled cooling, the Paxman Neuropathy System offers a compelling cryocompression solution designed to offer peripheral nerve protection from chemotherapy exposure while supporting patient tolerability.

## KEY CLINICAL DATA: PHASE II TRIAL

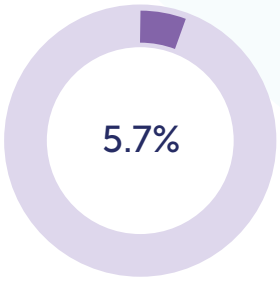
THE PAXMAN NEUROPATHY SYSTEM



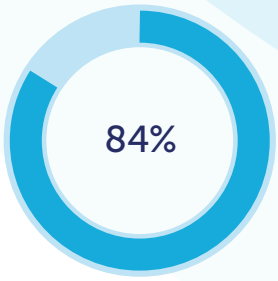

Grade ≥2 CIPN at 12 weeks




Grade 3 or 4 CIPN reported




Required CIPN-related dose modifications




Found cryocompression tolerable

Paxman's phase II clinical data demonstrates that cryocompression and specifically the Paxman Neuropathy System is efficacious, safe, tolerable, and reduced the requirement for dose modification due to CIPN in the trial.

With a strong biological rationale, proven tolerability, and compelling clinical results, the Paxman Neuropathy System is redefining what is possible for patients at risk of chemotherapy-induced peripheral neuropathy, one of the most significant unmet needs in oncology side effect management.

The Paxman Neuropathy System can be used alongside the Paxman Scalp Cooling System for management of chemotherapy-induced alopecia.



# GLOSSARY

**ANTIBODY-DRUG CONJUGATE (ADC)**
A targeted cancer therapy that combines an antibody with a potent anti-cancer drug. Some ADCs can cause peripheral neuropathy as a side effect.

**AXON**
The long fibre of a nerve cell that carries electrical signals throughout the body. Damage to axons is a key feature of CIPN.

**AXONAL TRANSPORT**
The movement of nutrients, proteins and other essential materials along a nerve fibre. Certain chemotherapy drugs can disrupt this process, contributing to nerve damage.

**CELL VIABILITY**
A measure of how healthy and functional living cells remain following exposure to a treatment or environmental stress. Preserving neuronal cell viability means helping nerve cells survive and continue functioning despite chemotherapy exposure.

**CLINICALLY SIGNIFICANT CIPN**
Neuropathy severe enough to meaningfully affect a patient's symptoms, daily functioning, treatment decisions, or quality of life. In clinical studies, specific assessment criteria are often used to define what is considered clinically significant.

**COUNTER-PAIN STIMULUS**
A sensory stimulus used to reduce the perception of pain or discomfort. In cryocompression, intermittent compression may help improve patient tolerability by providing a competing sensory input that distracts from the sensation of cold.

**CTCAE (COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS)**
A standardised grading system used by healthcare professionals to classify and assess the severity of treatment-related side effects, including CIPN.

**CUMULATIVE TREATMENT EXPOSURE**
The total amount of chemotherapy a patient receives over the course of treatment. In many cases, the risk and severity of CIPN increase as exposure to neurotoxic chemotherapy accumulates over time.

**DOSE MODIFICATION**
A reduction, delay, interruption or discontinuation of chemotherapy treatment due to side effects or safety concerns.

**EORTC QLQ-CIPN20**
A validated patient-reported questionnaire used to measure the sensory, motor and autonomic symptoms associated with CIPN.

**FUNCTIONAL RESILIENCE**
The ability of cells or tissues to maintain normal function despite stress or injury. In the context of CIPN, functional resilience refers to the ability of nerve cells to continue operating effectively despite exposure to neurotoxic chemotherapy.

**IMMUNOMODULATORY AGENTS**
A class of anti-cancer drugs that modify the body's immune response. Examples include thalidomide and pomalidomide, both of which are associated with a risk of peripheral neuropathy.

**INCIDENCE**
The proportion of people who develop a condition within a specified period of time. For example, CIPN incidence describes how many patients develop neuropathy during or after chemotherapy treatment.

**META-ANALYSIS**
A statistical research method that combines results from multiple independent studies to produce a more robust overall estimate. Meta-analyses are often considered a high level of clinical evidence because they evaluate findings across large patient populations.

**MMAE-BASED ADCS**
Antibody-drug conjugates (ADCs) that use monomethyl auristatin E (MMAE) as their cytotoxic payload. Because MMAE disrupts microtubules within cells, these drugs can be associated with peripheral neuropathy.

**NERVE SIGNALLING**
The process by which nerves transmit electrical and chemical messages throughout the body. Chemotherapy-induced damage can disrupt normal nerve signalling, leading to symptoms such as tingling, numbness, burning pain and cold sensitivity.

**NEUROINFLAMMATION**
Inflammation affecting the nervous system that may contribute to nerve damage, increased sensitivity and persistent neuropathic symptoms.

**NEURITE**
A projection from a nerve cell, including axons and dendrites, that helps transmit information throughout the nervous system.

**NEUROPROTECTION**
Strategies designed to prevent, reduce or limit damage to nerve cells and preserve nervous system function.

**NEUROTOXIC CHEMOTHERAPY**
Chemotherapy drugs known to cause damage to peripheral nerves. Common examples include taxanes, platinum agents and vinca alkaloids.

**NEUROTOXICITY**
Damage caused to the nervous system by a drug or other substance. CIPN is a form of chemotherapy-induced neurotoxicity affecting peripheral nerves.

**OXIDATIVE STRESS**
Cellular damage caused by an imbalance between harmful reactive molecules and the body's ability to neutralise them. Oxidative stress is a recognised mechanism in CIPN.

**PERIPHERAL NERVOUS SYSTEM**
The network of nerves outside the brain and spinal cord that carries signals between the central nervous system and the rest of the body.

**PERIPHERAL NEUROPATHY**
Damage to the peripheral nerves that can result in numbness, tingling, pain, weakness or loss of sensation.

**PREVALENCE**
The proportion of people living with a condition at a particular point in time. Unlike incidence, prevalence captures both new and existing cases, making it useful for understanding the long-term burden of CIPN.

**PROTEASOME INHIBITORS**
A class of anti-cancer therapies that block proteasomes, cellular structures responsible for breaking down unwanted proteins. Drugs such as bortezomib, ixazomib and carfilzomib are commonly used in haematological cancers and can cause CIPN.

**REACTIVE OXYGEN SPECIES (ROS)**
Highly reactive molecules that can damage cells and tissues when present in excessive amounts. Increased ROS production is associated with chemotherapy-induced nerve damage.

**RELATIVE RISK REDUCTION (RRR)**
A measure used in clinical studies to describe how much an intervention reduces the risk of an outcome compared with a reference or control group.

**VINCA ALKALOIDS**
A class of chemotherapy drugs that interfere with cell division and can cause peripheral neuropathy as a side effect.

# REFERENCES


1. Seretny, Martaa,*; Currie, Gillian L.b; Sena, Emily S.b; Ramnarine, Sabrinaa; Grant, Robinc; MacLeod, Malcolm R.b; Colvin, Leslie A.c; Fallon, Mariea. Incidence, prevalence, and predictors of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis. Pain 155(12):p 2461-2470, December 2014. | DOI: 10.1016/j.pain.2014.09.020
2. Argyriou A., Bruna J., Marmiroli P., Guido Cavaletti G., Chemotherapy-induced peripheral neurotoxicity (CIPN): An update, Critical Reviews in Oncology/Hematology, Volume 82, Issue 1, 2012, Pages 51-77, https://doi.org/10.1016/j.critrevonc.2011.04.012.
3. Charles L. Loprinzi et al. Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update. J Clin Oncol 38, 3325-3348(2020). DOI:10.1200/JCO.20.01399
4. Zhang J, Yang H, Lu Y. Management of neurotoxic reactions induced by antibody-drug conjugates. Asia Pac J Oncol Nurs. 2024 Sep 14;11(11):100595. doi: 10.1016/j.apjon.2024.100595. PMID: 39582554; PMCID: PMC11582371.
5. Fu Z, Gao C, Wu T, Wang L, Li S, Zhang Y, Shi C. Peripheral neuropathy associated with monomethyl auristatin E-based antibody-drug conjugates. iScience. 2023 Aug 29;26(10):107778. doi: 10.1016/j.isci.2023.107778. PMID: 37727735; PMCID: PMC10505985.
6. Banach, Marta & Juranek, Judyta & Zygulska, Aneta. (2016). Chemotherapy-induced neuropathies-a growing problem for patients and health care providers. Brain and Behavior. 7. e00558. 10.1002/brb3.558.
7. Etheridge H, Wong R, Sundar R, Bandla A, Georgopoulos NT. Chemotherapy-induced peripheral neuropathy (CIPN): Disease mechanisms, experimental models and emerging prevention strategies. Therapeutic Advances in Medical Oncology. 2026;18. doi:10.1177/17588359261502344
8. Park, S.B., Goldstein, D., Krishnan, A.V., Lin, C.S.-Y., Friedlander, M.L., Cassidy, J., Koltzenburg, M. and Kiernan, M.C. (2013), Chemotherapy-induced peripheral neurotoxicity: A critical analysis. CAA Cancer Journal for Clinicians, 63: 419-437. https://doi.org/10.3322/caac.21204
9. D'Souza RS, Saini C, Hussain N, et al. Global estimates of prevalence of chronic painful neuropathy among patients with chemotherapy-induced peripheral neuropathy: systematic review and meta-analysis of data from 28 countries, 2000–24. Regional Anesthesia & Pain Medicine Published Online First: 29 January 2025. doi: 10.1136/rapm-2024-106229
10. Kolb NA, Smith AG, Singleton JR, Beck SL, Stoddard GJ, Brown S, Mooney K. The Association of Chemotherapy-Induced Peripheral Neuropathy Symptoms and the Risk of Falling. JAMA Neurol. 2016 Jul 1;73(7):860-6. doi: 10.1001/jamaneurol.2016.0383. PMID: 27183099; PMCID: PMC6715416.
11. Cavaletti, G., D'Acunti, A., Porcu, A., Masiello, G., Del Campo, L., Traclò, G., De Lorenzo, F., & Bernasconi, D. P. (2023). Self-Reported Assessment of the Socio-Economic Impact of Anticancer Chemotherapy-Related Neurotoxicity. Toxics, 11(2), 104. https://doi.org/10.3390/toxics11020104
12. Yerial Jun et al. Effect of Chemotherapy-Induced Peripheral Neuropathy Symptom Permanence on Patient's Preference to Alter or Continue Neurotoxic Chemotherapy Treatment. JCO Oncol Adv 2, e2500136(2025). DOI:10.1200/OA-25-00136
13. Pike, Crystal T., Birnbaum, Howard G., Muehlenbein, Catherine E., Pohl, Gerhardt M., Natale, Ronald B., Healthcare Costs and Workloss Burden of Patients with Chemotherapy-Associated Peripheral Neuropathy in Breast, Ovarian, Head and Neck, and Nonsmall Cell Lung Cancer, Chemotherapy Research and Practice, 2012, 913848, 10 pages, 2012. https://doi.org/10.1155/2012/913848
14. Kerri M. Winters-Stone et al. Falls, Functioning, and Disability Among Women With Persistent Symptoms of Chemotherapy-Induced Peripheral Neuropathy. J Clin Oncol 35, 2604-2612(2017). DOI:10.1200/JCO.2016.71.3552
15. Bao T, Bhatnagar B, Gilmore S, Goloubeva O, Pelser C, Medeiros M, Chumsri S, Tkaczuk K, Edelman M. Chemotherapy dose reduction due to chemotherapy-induced peripheral neuropathy in breast cancer patients receiving chemotherapy in the neoadjuvant or adjuvant setting: A single-center experience. SpringerPlus. 2014;3:366. doi:10.1186/2193-1801-3-366.
16. Iglesias M, Pocobelli G, O'Connell K, et al. Patterns of Chemotherapy Delivery Following Neuropathy in Patients with Stage I–IIIA Breast Cancer. Journal of Clinical Oncology. 2026.
17. Pike CT, Birnbaum HG, Muehlenbein CE, Pohl GM, Natale RB. Healthcare costs and workloss burden of patients with chemotherapy-associated peripheral neuropathy in breast, ovarian, head and neck, and nonsmall cell lung cancer. Chemother Res Pract. 2012;2012:913848. doi: 10.1155/2012/913848. Epub 2012 Mar 14. PMID: 22482054; PMCID: PMC3312207.
18. Accordino MK, Lee S, Leu CS, Levin B, Trivedi MS, Crew KD, Kalinsky K, Raghunathan R, Faheem K, Harden E, Taboada A, de Oliveira BD, Larson E, Franks L, Honan E, Law C, Hershman DL. Randomized adaptive selection trial of cryotherapy, compression therapy, and placebo to prevent taxane-induced peripheral neuropathy in patients with breast cancer. Breast Cancer Res Treat. 2024 Feb;204(1):49-59. doi: 10.1007/s10549-023-07172-y. Epub 2023 Dec 7. PMID: 38060077; PMCID: PMC10840989.
19. A. Bandla et al., "Limb Hypothermia for the Prevention of Chemotherapy-Induced Peripheral Neuropathy – Modality for Optimal Cooling," 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), Montreal, QC, Canada, 2020, pp. 5061-5064, doi: 10.1109/EMBC44109.2020.9175432.
20. Charles L. Loprinzi et al.Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update. J Clin Oncol 38, 3325-3348(2020). DOI:10.1200/JCO.20.01399
21. Jordan B, Margulies A, Cardoso F ...Systemic anticancer therapy-induced peripheral and central neurotoxicity: ESMO–EONS–EANO Clinical Practice Guidelines for diagnosis, prevention, treatment and follow-up. Annals of Oncology, 2020; 31, 1306-1319
22. Gradishar WJ, Moran MS, Abraham J, Abramson V, Aft R, Agnese D, Allison KH, Anderson B, Bailey J, Burstein HJ, Chen N, Chew H, Dang C, Elias AD, Giordano SH, Goetz MP, Jankowitz RC, Javid SH, Krishnamurthy J, Leitch AM, Lyons J, McCloskey S, McShane M, Mortimer J, Patel SA, Rosenberger LH, Rugo HS, Santa-Maria CA, Schneider BP, Smith ML, Soliman H, Stringer-Reasor EM, Telli ML, Wei M, Wisinski KB, Yellala A, Yeung KT, Young JS, Schonfeld R, Kumar R. NCCN Guidelines® Insights: Breast Cancer, Version 5.2025. J Natl Compr Canc Netw. 2025 Nov;23(11):426-436. doi: 10.6004/jnccn.2025.0053. PMID: 41213254.
23. Murgier J, Cassard X. Cryotherapy with dynamic intermittent compression for analgesia after anterior cruciate ligament reconstruction. Preliminary study. Orthop Traumatol Surg Res. 2014 May;100(3):309-12. doi: 10.1016/j.otsr.2013.12.019. Epub 2014 Mar 25. PMID: 24679367.
24. Wong, R., Bandla, A., et al. A Single-Arm Combined Phase I/II Study Evaluating Limb Cryocompression To Prevent Chemotherapy-Induced Peripheral Neuropathy In Patients Receiving Taxane-Based Chemotherapy. Journal of Clinical Oncology Advances. In press. 2026.
25. Bandla A, Wong R, Santhanakrishnan P, Magarajah G, Yee YE, Ng WY, Ow S, Chan G, Choo J, Lim SE, Wong A, Vijayan J, Paxman R, Lee YM, Hui F, Hairom Z, Ang E, Loprinzi C, Thakor N, Lee SC, Kumarakulasinghe N, Lim J, Sundar R. Safety and feasibility of concomitant scalp cooling and limb cryocompression to prevent paclitaxel-induced alopecia and neuropathy. Support Care Cancer. 2025 Feb 12;33(3):180. doi: 10.1007/s00520-024-08982-6. PMID: 39937296; PMCID: PMC11821790.
26. NCCN Task Force Report: Management of Neuropathy in Cancer, Journal of the National Comprehensive Cancer Network 7, (2009)
27. Hanai et al. JNCI J Natl Cancer Inst, 2018, Vol. 110, No. 2
28. Beijers et al. Ann Oncol. 2020 Jan;31(1):131-136
29. Accordino et al. Breast Cancer Research and Treatment (2024) 204:49–59
30. Bandla et al. Support Care Cancer (2020) 28:3691–3699;
31. Sundar et al. JCO 36, 10095-10095 (2018)
32. ClinicalTrials.gov, "Cryocompression for CIPN," ClinicalTrials.gov Identifier: NCT07064798, sponsored by Dana-Farber Cancer Institute, first posted July 15, 2025, last updated April 15, 2026, https://clinicaltrials.gov/study/NCT07064798

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