



A D A P T E D F O R E U R O P E A N N U R S E S B Y E O N S

# Peripheral Neuropathy

Improving symptom management in cancer care  
through evidence based practice





## Welcome to the Euro PEPs

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The European Oncology Nursing Society is pleased to present its first set of "Putting Evidence into Practice" guidelines to improve the care of cancer patients in Europe.

Improvement in patient care is an ongoing process. There is a gap between the evidence that is available and what is actually implemented. This knowledge gap impacts on patient's in poor or inappropriate care that is detrimental to cancer patients. Results from research studies reveal that nurses insufficiently put evidence into practice. The results indicate that there are multiple reasons for why nurses do not use the latest evidence. Firstly, that research is difficult to understand, overwhelming in the amount published and secondly that they feel they don't have the expertise to interpret the quality of the evidence. If we could put even a little of what we know about symptom management into practice we would improve patient experience.

This Euro PEP has been developed as a partnership with the Oncology Nursing Society and funded by the European Commission as part of the European Action Against Cancer. Many people have contributed to the development and expert review of these documents, both in Europe and in the USA. EONS thanks their dedication and great efforts.

This documentation provides you with a concise summary of the evidence, a synthesis of patient assessments, a summary of evidence based interventions, and expert opinions to help guide you in the interpretation of European standards along with the references and source material. You may wish to adapt the guidance for your own work setting, but the PEPs gives you the confidence that these topics were reviewed in 2012 through a rigorous process by some of the leading experts and practitioners in the field.

On behalf of the review team we are confident that this information, coupled with your efforts and commitment to improve your practice, will help you achieve better, patient-centered outcomes based on scientific evidence.

We wish you great success!





Sara Faithfull  
Anita Marguiles

Chair EPAAC Project  
Chair PEPs

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Putting Evidence into Practice (PEP) resources (evidence syntheses and weight of evidence categorization) are the work of the Oncology Nursing Society (ONS). Because translations from English may not always be accurate or precise, ONS disclaims any responsibility for inaccuracies in words or meaning that may occur as a result of the translation.

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# Introduction to the Sections



## Quick view

The quick view provides very brief summary from the ONS PEP resources. A full copy of this is provided in the course documentation. ONS PEP information for this topic and description of the categories of evidence can be accessed at <http://www.ons.org>.



## Expert opinion

Expert Opinion: low-risk interventions that are (1) consistent with sound clinical practice, (2) suggested by an expert in a peer-reviewed publication (journal or book chapter), and (3) for which limited evidence exists. An expert is an individual with peer-reviewed journal publications in the domain of interest.



## Assessment tools

In general, no single tool measures all of the elements of a symptom. The choice of tool depends on the purpose of the assessment as well as the level of clinician and patient burden. Most symptoms are a subjective experience, thus self-report is the most reliable assessment method.



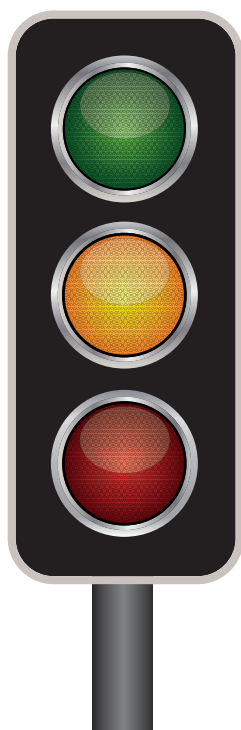
## Definitions

Within the documentation various terms may need further explanation which through better understanding, could improve the outcomes of chosen interventions. The following definitions are tailored to the content of the respective PEP document.

# How to use this guide

- Review the Euro - PEP resources and consider the applicability in your own practice and your patient situation.
- Do a thorough patient assessment of the relevant clinical problem(s). Examples of measurement tools are provided by the evidence-based measurement summaries, located on the individual PEP topic pages.
- Identify interventions with the highest category of evidence and integrate them into the plan of care. Consider the patient's preferences, lifestyle, and the cost and availability of the interventions.
- Evaluate and document the patient's response to the interventions. If indicated, consider implementing other interventions supported by a high level of evidence.
- Educate patients that their care is based on the best available evidence.
- The Weight of Evidence Table (traffic light ) provides information about how the evidence was weighed.

Adapted for Euro PEP Resources from [www.ons.org/Research/PEP](http://www.ons.org/Research/PEP)



### Green = Go!

The evidence supports the consideration of these interventions in practice.

### Yellow = Caution!

There is not sufficient evidence to say whether these interventions are effective or not.

### Red = Stop!

The evidence indicates that these interventions are either ineffective or may cause harm.

### Recommended for practice

Interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, meta-analysis, or systematic reviews, and for which expectation of harm is small compared to the benefits.

### Likely to be Effective

Interventions for which effectiveness has been demonstrated from a single rigorously conducted controlled trial, consistent supportive evidence from well-designed controlled trials using small samples, or guidelines developed from evidence and supported by expert opinion.

### Benefits Balanced with Harm

Interventions for which clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities.

### Effectiveness Not Established

Interventions for which insufficient or conflicting data or data of inadequate quality currently exist, with no clear indication of harm.

### Effectiveness Unlikely

Interventions for which lack of effectiveness has been demonstrated by negative evidence from a single rigorously conducted controlled trial, consistent negative evidence from well-designed controlled trials using small samples, or guidelines developed from evidence and supported by expert opinion.

### Not Recommended for Practice

Interventions for which lack of effectiveness or harmfulness has been demonstrated by strong evidence from rigorously conducted studies, meta-analyses, or systematic reviews, or interventions where the costs, burden, or harm associated with the intervention exceed anticipated benefit.

# Peripheral Neuropathy Quick View

### Definition and Incidence:

*Peripheral neuropathy* is a dysfunction of peripheral, motor, sensory, and autonomic neurons, resulting in peripheral neuropathic signs and symptoms. Depending on agent and dose received, 50–90% of patients who are receiving platinum or taxane containing regimens may be affected. Depending on the dose, patients receiving Vincristin experience up to 50% are affected. Other drugs e.g. Bortezomib, Thalidomide, Ixabepilone are newer agents which can also cause peripheral neuropathy.

### Recommended for practice

There are no evidence based interventions as of September 2012.

### Likely to be Effective

There are no evidence based interventions as of September 2012.

### Benefits Balanced with Harm

There are no evidence based interventions as of September 2012.



**Effectiveness Not Established****Prevention Interventions**

- Amifostine
- Amitriptyline
- Calcium and magnesium Infusion
- Carbamazepine
- Gabapentin (monotherapy)
- Glutamine
- Glutathion
- Pregabalin
- Vitamin

**Treatment Interventions**

- Acetyl-L-Carnitine
- Amitriptyline
- Calcium und Magnesium infusion
- Cannabis (Cannabinoide)\*
- Nortriptylin
- Pregabalin

\* Use of cannabinoids / cannabis is not permitted in many European countries.

**Effectiveness Unlikely**

- Lamotrigine.

**Not Recommended for Practice**

- Recombinant Human Leukemia Inhibitory Factor (RHU LIF)

Literature search completed as of May 2012.

## Expert Opinion

**Low-risk interventions that are:**

- consistent with sound clinical practice
- suggested by an expert in a peer-reviewed publication (journal or book chapter) and
- for which limited evidence exists.

**An expert is an individual who has authored articles published in a peer-reviewed journal in the domain of interest.**

- A dose reduction or drug cessation may be considered medically to reduce and reverse CIPN.
- Important nursing practice includes education and support to preserve patient safety.
- Referral to a physiotherapist or occupational therapies may be recommendable.
- Teach patients the signs and symptoms of peripheral neuropathy, and instruct patients to report them to their healthcare providers as soon as they or their families notice them.
  - tingling, numbness, pain
- Observe patients walking pattern (gait) when entering a room.
- Assess risk of falling, particularly in elderly patients.
- Teach patients strategies for managing personal safety:



- using visual input to compensate for loss of lower-extremity sensation in navigating changing terrain
- removing throw rugs
- clearing walkways or rooms of clutter
- using skid-free shower and bathroom mats
- using a cane or walker if gait is unsteady
- Help patients find solutions to deal with changes/problems in ADL:
  - dressing (buttons, zippers, shoe laces etc.)
  - personal hygiene (toothbrushes, combs, shaving devices etc.)
  - household chores (sewing, dishwashing, food preparation etc.)
- Help patients find solutions to problems at work:
  - finger dexterity for computer operations, safety with tools
- Teach patient the principles of foot care, including inspection of the feet and the importance of wearing properly fitted shoes.
- Teach patients about preventing the risk for ischemic or thermal injury in extremities:
  - lowering water temperature in the home water heater to avoid burns
  - checking settings on a heating pad
  - inspecting the hand and feet for sores or blisters
- Teach patients receiving oxaliplatin about the dysesthesia associated with exposure to cold and how to avoid this.
- Teach strategies to prevent symptoms of autonomic dysfunction such as dangling the legs prior to arising and adequate fluid intake.

For information on neuropathic pain, please refer to the PEP Pain resource.

## Assessment Tools

A baseline assessment for Peripheral Neuropathy is important before beginning chemotherapy with any of the causative drugs. Assessment at regular intervals will allow checking for patient safety and comfort.

Table 15-1. Baseline Assessment for Chemotherapy-Induced Peripheral Neuropathy		
Assessment	Yes	No
History of diabetes		
Arthritis or other connective tissue disease		
Peripheral vascular disease		
Chronic alcohol use		
History of HIV/AIDS		
History of chemical exposures		
History of previous neurotoxic chemotherapy		
Taxanes (paclitaxel, docetaxel, nanoparticle albumin paclitaxel)		
Epothilones (ixebepilone)		
Vinca alkaloids (vincristine, vinblastine, vinorelbine)		
Platinum compounds (cisplatin, carboplatin, oxaliplatin)		
Angiogenesis agents (thalidomide)		
Proteasome inhibitors (bortezomib)		
Current symptoms of neuropathy: Sensory (numbness and tingling, burning or stabbing pain in hands or feet, diminished reflexes)		
Review medication list (prescription, over-the-counter, and vitamins/herbals)		
Pertinent physical examination findings		
Vibration sense with tuning fork		
Proprioception		
Deep tendon reflexes		
Cutaneous sensation		
Muscle strength		
Gait/balance		
Note. Based on information from Visovsky & Daly, 2004; Wickham, 2007; Wilkes, 2004.		

**Figure 15-1. Neurotoxicity Assessment Tool****Instructions for Patients**

By circling one number per line, please indicate how true each statement has been for you during the past seven days using the following scale.

0 = not at all  
1 = a little bit  
2 = somewhat  
3 = quite a bit  
4 = very much

I have numbness or tingling in my hands.	0	1	2	3	4
I have numbness or tingling in my feet.	0	1	2	3	4
I feel discomfort in my hands.	0	1	2	3	4
I feel discomfort in my feet.	0	1	2	3	4
I have joint pain or muscle cramps.	0	1	2	3	4
I feel weak all over.	0	1	2	3	4
I have trouble hearing.	0	1	2	3	4
I get a ringing or buzzing in my ears.	0	1	2	3	4
I have trouble buttoning buttons.	0	1	2	3	4
I have trouble feeling the shape of small objects when they are in my hand.	0	1	2	3	4
I have trouble walking.	0	1	2	3	4

**Along with these tools:**

- Patients should be asked how this side effect changes their daily activities
- Patients receiving Oxaliplatin should be assessed for cold-induced symptoms.

From: Putting Evidence into Practice Oncology Nursing Society Ed. L. Eaton, J. Tipton, 2010

# Peripheral Neuropathy Definition List

### Acetyl-L Carnitine

Acetyl-L-carnitine ( $\gamma$ -trimethyl- $\beta$ -acetylbutyrobetaine, ALC) is the acetyl ester of carnitine and the primary acylcarnitine in human tissues. ALC is present through-out the central and peripheral nervous systems, plays an essential role in the oxidation of free fatty acids, and has displayed neuroprotective properties. (Flatters, Xaio, & Bennett, 2006)

### Acupuncture

Chinese practice of inserting fine needles through the skin at specific points especially to cure disease or relieve pain. The procedure is done by a certified acupuncturist. (US National Library of Medicine, 2003)

### Alpha Lipoic Acid

Intravenous infusion of the trometamol salt solution containing 600 mg of alpha lipoic acid. (Ziegler, Nowak, Kempler, Vargha, & Low, 2004)

### Amifostine

A cytoprotective agent, amifostine is an organic thiophosphate that is dephosphorylated by alkaline phosphate into the active form, therefore neutralizing chemotherapy drugs in normal tissues so that cellular DNA and RNA are not damaged. (Wilkes, & Barton-Burke, 2005)

### Capsaicin

Chemotherapy-induced peripheral neuropathy is hypothesized to occur as the end result of neurotoxic chemotherapy and biotherapy agents directly damaging nerve fibers by inactivating the components required to maintain the metabolic needs of the axon. The longer and larger distal axons are affected first, resulting in interruptions of axonal transport and degeneration of myelinated nerve fibers and unmyelinated axons. (Postma, & Heimans, 2000)

### Epothilones

Epothilones are a new class of antimicrotubule agents derived from mycobacterium *Sorangium cellulosum*. Ixabepilone is a non-taxane microtubule- stabilizing epothilone analog. (Lee et al. 2006)

### Exercise

Physical activity that is planned, structured, and repetitive and results in the improvement or maintenance of one or more facets of physical fitness. (Caspersen, Powell, & Christenson, 1985)

### Glutamine

A crystalline amino acid ( $C_5H_{10}N_2O_3$ ) that is found both free and in proteins of plants and animals and that yields glutamic acid and ammonia on hydrolysis. (US National Library of Medicine, 2003)



### **Glutathione**

A peptide (C<sub>10</sub>H<sub>17</sub>N<sub>3</sub>O<sub>6</sub>S) that contains one amino acid residue each of glutamic acid, cysteine, and glycine that occurs widely in plant and animal tissues and plays an important role in biologic oxidation-reduction processes and as a coenzyme. (US National Library of Medicine, 2003)

### **High Frequency**

Process involving electrodes placed on the skin over muscles with a power device generating pulse widths.

### **External Muscle Stimulation**

of < 350 mA, <70V. The intensity adjusted to level that did not produce pain or uncomfortable paraesthesias. (Reichstein, Labrenz, Ziegler, & Martin, 2005)

### **Lamotrigine**

An antiepileptic that inhibits the function of neuronal sodium channels decreasing the release of excitatory neurotransmitters. (Lees & Leach, 1993)

### **Nortriptyline**

A tricyclic antidepressant that blocks the reuptake of neurotransmitters at neuronal membrane, thus increasing available serotonin and norepinephrine in the central nervous system, potentiating their effects. (Wilkes & Barton-Burke, 2005)

### **Peripheral Neuropathy**

Peripheral neuropathy is a dysfunction of peripheral, motor, sensory, and autonomic neurons, resulting in peripheral neuropathic signs and symptoms. (Postma & Heimans, 2000)

### **Physical Activity**

Any bodily movement produced by skeletal muscles that result in calorie expenditure.

(Caspersen, Powell & Christenson, 1985) Physical activity has three dimensions: duration, frequency, and intensity.

### **Pulsed Infrared Light Therapy (also called Anodyne Therapy)**

Process involving flexible pads placed on the skin of the involved extremity(s) with one pad each placed on the dorsum of the foot, plantar surface of the foot, and lateral and medial aspect of the leg above the ankle. Pads containing near-infrared gallium-arsenide diodes are pulsed to increase circulation by dilating arteries and veins. (Leonard, Farooqi & Myers, 2004; Prendergast, Miranda & Sanchez, 2004)

### **Recombinant Human Leukemia Inhibitory Factor**

Leukemia inhibitory factor (LIF) is a member of the gp130 group of cytokines. Signaling through the LIF receptor leads to changes in gene expression, proliferation, and regeneration of neurons. LIF expression is rapidly up-regulated in response to neural insult and has evidence to suggest that LIF is neuroprotective in models of peripheral neuropathy. (Davis, Kiers, MacGregor, Quinn, Arezo, Green et al 2005)

### **Spinal Cord Stimulation**

Use of pulsed electrical energy that involves implantation of leads in the epidural space to transmit pulsed energy across the spinal cord or near the desired nerve roots. (Cata, Cordella, Burton, Hassenbusch, Weng & Dougherty, 2004)

### **TENS**

Process involving electrodes placed on the skin over muscles or nerves with a power device generating pulse widths of <70 mA. (Forst, Nguyen, Forst, Disselhoff, Pohlmann & Pfutzner, 2004)



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