IASP 2026
GLOBAL YEAR
Neuropathic Pain

FACT SHEET

An Overview of IASP's Neuropathic Pain Special Interest Group (NeuPSIG) Treatment Recommendations

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High-quality care depends on evidence-based clinical guidelines

High-quality care depends on evidence-based clinical guidelines that reflect the best and most up-to-date research. In 2025, IASP's Neuropathic Pain Special Interest Group (NeuPSIG) published updated treatment guidance in *The Lancet Neurology* (https://doi.org/10.1016/s1474-4422(25)00068-7) based on the most comprehensive review of available evidence to date[1]. The previous NeuPSIG review was published in 2015, so this update includes a decade of new research, covering both established and newer treatments. The updated treatment recommendations help healthcare providers and people with neuropathic pain to choose the safest and most effective available pharmacological and neuromodulation treatment options.

Pharmacological treatments use medicines (drugs) to treat diseases. Neuromodulation uses magnetic or electrical stimulation of nerves. This can be done by surgically implanting devices next to nerves (invasive neuromodulation) or by placing devices on the body (non-invasive) that stimulate the nervous system. Examples of non-invasive neuromodulation include devices placed on the skin (i.e., transcutaneously) or on your head (e.g., repetitive transcranial magnetic stimulation).

Trials included many treatment methods for many different neuropathic pain conditions (e.g., diabetic nerve pain, pain after shingles infection, and pain from infections or chemotherapy), so it was not possible to create a single ranked list of treatments from best to worst. Instead, the guidelines are based on the amount of pain relief (efficacy) and the quality and certainty of the evidence, to group treatments into first-, second-, and third-line options. First-line treatments were those with the most consistent benefits, supported by moderate-certainty evidence; second-line treatments showed smaller or less consistent effects, or lower-certainty evidence; and third-line treatments were supported by limited or low-certainty evidence or had significant safety or tolerability concerns. The recommendations are summarized in Table 1.

First-Line Treatments – what to try first

Based on how well they reduce pain and how safe they are, several medicines are recommended as first-line treatments for neuropathic pain. These include certain antidepressants, like tricyclic antidepressants (e.g., amitriptyline) and serotonin-norepinephrine reuptake inhibitors (e.g., duloxetine). They also include some medicines originally developed for epilepsy, like alpha-2-delta ligands (e.g., pregabalin, gabapentin, and mirogabalin). While these medicines have the strongest evidence for helping relieve pain, their benefits are probably modest, and they are not suitable for everyone. For example, TCAs can cause side effects such as

sleepiness, dry mouth, and dizziness, which may increase the risk of falls in older adults, so extra caution is needed in this group. In addition, pregabalin and gabapentin can have the risk of misuse or dependence in some people, which must be carefully considered and discussed as part of shared decision-making between the person with neuropathic pain and the healthcare provider.

Second-Line Treatments – if the first line is not enough or cannot be used

If first-line options do not provide enough pain relief or cause unwanted side effects, then second-line options may be considered. These treatments may also be especially helpful for localized peripheral neuropathic pain, where pain is limited to a specific area of the body.

Topical treatments such as capsaicin 8% patches, lidocaine patches, and capsaicin cream can be applied directly to painful areas. Because they act mainly where they are applied, these treatments are generally well-tolerated and cause fewer side effects than oral medicines. This makes them particularly suitable for people who may be more sensitive to side effects, such as older adults, people with other medical conditions, or those taking multiple medicines, where the risk of drug-drug interactions is higher. For these more vulnerable individuals, treatments applied directly to the skin may be an appropriate first treatment option.

Third-Line Treatments – for hard-to-treat pain

When other treatments have not helped enough, third-line treatments may be considered. These options are supported by low- and very-low-certainty evidence, meaning there is little confidence in how well they work or who they will help most, and they are usually reserved for people with more difficult-to-treat pain. Third-line options include botulinum toxin A (BTX-A) injections, opioid medicines, and repetitive transcranial magnetic stimulation (rTMS).

Botulinum toxin A may provide meaningful pain relief and has a generally good safety record, but the evidence mainly comes from small studies in people with hard-to-treat pain, which is in a specific, well-defined, and relatively small area. Access to this treatment can be limited due to cost.

Repetitive transcranial magnetic stimulation (rTMS), which uses magnetic pulses applied to the scalp to affect pain-related brain areas, showed greater pain relief than many medicines used earlier in treatment. However, it is recommended as a third-line option because the evidence is still uncertain, the treatment is not widely available, and it can be costly.

Opioid medicines, including tramadol, morphine, and oxycodone, are not routinely recommended for neuropathic pain because of well-known risks such as physical dependence, addiction, misuse, and overdose. Even so, they may still be needed for some people. When used, opioids should be prescribed for the shortest possible time and with careful monitoring to reduce harm.

Why some treatments are not recommended

Some treatments are not currently recommended because existing research does not show clear or reliable overall benefit, or because potential harms outweigh any likely benefits for most people. This does not mean that these treatments will never help anyone, but that the available evidence is too limited, uncertain, or of low quality to support their widespread use.

For example, cannabinoid-based medicines did not show consistent improvement in neuropathic pain and were linked to unwanted side effects, so their routine use is not advised. Similarly, invasive neuromodulation treatments, such as spinal cord stimulation, were not recommended because there is little high-quality evidence showing they work better than a placebo. Currently, there is not enough strong evidence to recommend specific combinations of medicines for neuropathic pain, as studies have not shown a clear added benefit compared with using a single medicine. In some cases, a healthcare provider may still carefully add a second treatment if the first provides only partial relief, aiming to improve the benefit without increasing side effects[2].

The NeuPSIG recommendations focused on medicines and neuromodulation and did not assess other treatment approaches. Psychological treatments, such as cognitive behavioral therapy, can help people manage pain, improve daily functioning, and support well-being, and may be a useful part of an individualized treatment plan[3]. Read more about Non-Medication Approaches to Help Manage Nerve Pain (https://www.iasp-pain.org/resources/fact-sheets/non-medication-approaches-to-help-manage-nerve-pain/).

These recommendations are designed to support choices and involvement of people with neuropathic pain by outlining a range of treatment options and clearly explaining their possible benefits, risks, and uncertainties. Neuropathic pain affects people in different ways, so good care means listening to what matters most to each person, including their values, preferences, and daily life. Shared decision-making helps people with neuropathic pain understand their options, ask questions, and raise concerns, while healthcare providers consider factors such as how well a treatment works, possible side effects, how it is taken, access to care, and effects on mental health and everyday activities. This approach allows treatments to be tailored to the individual.

Table 1.

Treatment Recommendation	Treatment type	How well it helps pain	Side effects	How often it is used
First-line	E.g., amitriptyline, duloxetine, pregabalin, and gabapentin	Help many people	Some side effects	Often tried first
Second-line	Topical treatments (lidocaine plasters, capsaicin patches, and cream)	Help some people, especially those with local pain	Few side effects	Used when pain is in one area
Third-line	Botulinum toxin injections	May help selected people	Usually well tolerated	Specialist use only
	Magnetic brain stimulation (rTMS)	May reduce pain for some	Few side effects	Limited availability
	Opioids	Limited benefit for neuropathic pain	Risk of dependence and overdose	Short-term use only

References

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Declaration of Interests

NS has no interests to declare.

XM has received personal fees from Allergan-Abbvie, Aptis Pharma, Biogen, BMS, Grünenthal, Haute Autorité de Santé, Lilly, Lundbeck, Teva, Merck-Serono, Novartis, Orion, Pfizer, Roche, and Sanofi-Genzyme; grants from APICIL, region Auvergne-Rhone-Alpes, contrat Interface Inserm; and nonfinancial support from SOS Oxygène, not related to the submitted work.

MCF has no interests to declare.

JC served on the Chronic Pain Advisory Board, Vertex Pharmaceuticals Inc.

GEF has no interests to disclose

MZ has no interests to disclose.