Treatment for Neuropathic Pain in Patients with Cancer: Comparative Analysis of Recommendations in National Clinical Practice Guidelines from European Countries

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Abstract

Introduction: Neuropathic pain is a common symptom, present in 39% of the patients with cancer pain. Treating this type of pain is challenging, as this patient group is often frail and has comorbidities which increase the risk of side events and hence influences their quality of life. Clinical practice guidelines (CPGs) can be helpful for clinicians, especially when scientific evidence is uncertain or weak. In this study, we focused on the quality of the review of the literature used in treatment recommendations in the selected European CPGs.

Methods: In a previous study, 9 CPGs from European countries that contained at least one paragraph on treatment for neuropathic pain in cancer were included. Recommendations with their grade (according SIGN 55 classification) and supporting literature (first author, patients’ population, year and type of publication) were compared between CPGs.

Results: In all CPGs, amitriptylin was mentioned as the drug of first choice. Six guidelines proposed also gabapentinoids. Only 30 of the 163 citations (18%) were based on studies in patients with cancer. Seven CPGs did not argue the indirect evidence due to extrapolation of study results from non-cancer to patients with cancer.

Conclusion: The majority of guideline development groups extrapolated their results from non-cancer publications to
formulate recommendations. Consequently, these guidelines fail to address important issues such as altered kinetics and side effect profiles in these patients. We recommend creating specific recommendations by an international expert group for the treatment for neuropathic pain in patients with cancer supported by targeted research in patients with cancer.

Key Words: neuralgia, cancer, neuropathic pain, evidence-based medicine, clinical practice guidelines

INTRODUCTION

In Europe, the prevalence of moderate to severe pain in patients with cancer is about 56%. Pain in patients with cancer is often related to a combination of nociceptive and neuropathic mechanisms. In a systematic review of Bennett, the prevalence of neuropathic pain in patients with cancer was found to be 19%. The combination of mixed pain (nociceptive pain) was found to be 39.7%. Using the World Health Organization (WHO), analgesic ladder for cancer pain relief resolves the nociceptive component in 80% of the treated patients. However, the neuropathic pain component is often more difficult to treat. Not all drugs are specifically registered for the treatment for neuropathic pain in patients with cancer in European countries. This implies that most specific drugs used for the treatment for neuropathic pain in patients with cancer are used off-label. Most clinical research concerning neuropathic pain treatment is performed in patients with diabetic painful neuropathy (DPN) or post-herpetic neuropathy (PHN) and infrequently in patients with neuropathic cancer pain. Patients with cancer suffering from neuropathic pain should be considered different from patients with neuropathic pain in other context for several reasons. Firstly, approximately 50% of the patients with cancer suffering from neuropathic pain also have nociceptive or visceral pain, in contrast to patients suffering from neuropathic pain in another context. Secondly, they are more fragile with a potential life-threatening disease. Thirdly, in patients with cancer, the effect size of antiepileptic or antidepressant drug, used in addition to the opioids, is less than that seen in patients with non-cancer neuropathic pain.

Clinical practice guidelines (CPGs) were created to improve the treatment for a specific condition and are supposed to be based on the latest evidence. Concerning neuropathic pain in patients with cancer, a recent statement of the International Association for the Study of the Pain (IASP) emphasized that the extrapolation of data from studies of other neuropathic conditions to patients with cancer-induced neuropathic pain is far from straightforward. In parallel of the evaluation of recommendations on neuropathic pain diagnosis and assessment in patients with cancer, the aim of this study is to compare recommendations proposed in national CPGs from Europe concerning the treatment for neuropathic pain in patients with cancer and their evidence grading.

METHODS

Study Design

The relation between chosen references, their level of evidence, and the recommendations given in CPGs was systematically studied.

Selection of Guidelines

A European inventory of CPGs was performed with the support of the European Federation of the IASP Chapters (EFIC). Nine CPGs were included, and this material was used for this study. All CPGs were published between 2006 and 2009 from France (1), Italy (2), the Netherlands (2), Norway (2), Spain (1), and the United Kingdom (1). Four were developed under responsibility of a national organization specialized in guideline development. Five were developed by professional societies (oncology, palliative care, or pain societies). One was developed by an Italian regional health organization (Italy 2). None of the guidelines were developed solely or specifically for the treatment for neuropathic pain in patients with cancer.

Collection of the Data and Analysis

We developed a procedure to extract recommendations about how to treat neuropathic pain in patients with cancer. Recommendations were defined as “statements that promote or advocate a particular course of action in clinical care”. These treatment recommendations were extracted together with the related references and used as evidence in each CPG. The references were categorized by study design (meta-analysis and systematic review; randomized controlled trial [RCT] with ≥ 60 patients; RCT with < 60 patients; CPG; other) and topic (neuropathic pain, cancer neuropathic pain, cancer pain, acute and chronic pain, and other). Each reference was also considered according to the country of the first author and/or of the work group, journal, and year of publication.
publication. A reference used in at least two CPGs was a shared reference.

Recommendations were analyzed considering drugs proposed to treat neuropathic pain in patients with cancer in each CPG. We focused our analysis on three main drugs: amitriptyline; gabapentin; and pregabalin. For each of these three drugs, we collected positioning in therapeutic strategy (first or second line), start and maximum doses, titration scheme, mentioned side effects and contra-indications, the level of evidence, and the grade of the recommendation, according to the Scottish intercollegiate guidelines network (SIGN) 50 criteria.13

Statistical Analysis

Analysis was performed with SPSS 16.0 (IBM, Somers, NY, U.S.A.) using descriptives and frequencies.

RESULTS

Pages Specifically Dedicated to the Treatment for Neuropathic Pain in Patients with Cancer

The nine included CPGs represented 1,480 pages with only 53.5 (4%) pages focusing on the treatment for neuropathic pain in patients with cancer. The sections about the treatment for neuropathic pain in patients with cancer ranged between half a page (Spain) to 37 pages (France) (0.2% to 22%, mostly below 5%).

Characteristics of the References Related to Recommendations Selected in the “Neuropathic Pain in Patients with Cancer” Treatment Section of CPG

Our work collected a total of 163 references related to recommendations selected in the “neuropathic pain in patients with cancer” treatment section of CPGs.

Among these, a majority (116/163: 71%) were about neuropathic pain in non-cancer context. Eighteen (11%) references concerned specifically neuropathic pain treatment in patients with cancer (Table 1). A large majority (80%) of references were related to RCTs and meta-analysis, systematic review, or review. According to SIGN-50, 50 references (31%) could be classified as top evidence level (15 systematic reviews and 35 RCTs with a high number of patients).

Only 30 (18%) of the 163 references were shared between at least two guidelines: 21 shared by two guidelines; four by three guidelines; four by four guidelines; and only one by five guidelines.

References specifically related to neuropathic pain in patients with cancer are presented in Table 2. Among these references specifically related to neuropathic pain in patients with cancer, only four were shared by at least two references.

Table 1. Description of CPGs and Characteristics of the References Mentioned in the Section Treatment for Neuropathic Pain in Patients with Cancer

<table>
<thead>
<tr>
<th>Reference Topic</th>
<th>Number of References</th>
<th>Publication Year</th>
<th>Publication Type</th>
<th>Shared References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathic pain</td>
<td>116</td>
<td>1969–2007</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>Cancer neuropathic pain</td>
<td>18</td>
<td>1992–2008</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Cancer pain</td>
<td>14</td>
<td>1980–2007</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Acute and chronic pain</td>
<td>11</td>
<td>1999–2007</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>2000–2004</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>163</td>
<td>1969–2008</td>
<td>34</td>
<td>30</td>
</tr>
</tbody>
</table>

SR:R, Systematic Review, meta-analysis and review; RCT ≥ 60, randomized Controlled Trial with 60 or more patients; RCT < 60, Randomised Controlled Trial with < 60 patients; CPG, Clinical Practice Guideline; Other, cohort study, observational study, case report, local statement; shared references, number of references which are mentioned in at least two guidelines.
and not mentioned in the others. Lidocaine 5% plaster was recommended in three guidelines (France 2010, the Netherlands 2008-I, and Spain) not recommended in two guidelines (Norway 2007 and U.K.) and not mentioned in others. Regarding more invasive therapeutic approaches, only ketamine was recommended after indication confirmation by a pain specialist in four CPGs: Italy 2006, the Netherlands 2008-I, Spain, and U.K. Ketamine was not mentioned by the other CPGs, whereas systemic lidocaine was not recommended in four CPGs (France 2010, Italy 2006 and 2009, the Netherlands 2008-I) or not mentioned in other CPGs.

Focused analysis on amitriptyline, pregabalin, and gabapentin is presented in Table 4. For amitriptyline, evidence level for its recommendation varied from 1++ to four according the SIGN 50 criteria. For pregabalin, evidence level for its recommendation varied also from 1++ to 4. For gabapentin, this level varied from 1++ to 2.

In accordance level of grading varied in the same way for the three drugs. A large majority of CPGs indicated the use rules of drugs but only three CPGs (France 2010, the Netherlands 2008-II and Norway 2009) detailed systematically the side effects and contra-indications of these drugs.

**DISCUSSION**

In the nine included CPGs on cancer pain or neuropathic pain with at least one chapter on neuropathic pain in patients with cancer, all developed in European countries, 163 references were used to support the given recommendations on neuropathic pain treatment in patients with cancer. Although the proportion of population-specific references was low (11%), it was higher than our previous study on diagnosis and assessment of neuropathic pain in patients with cancer (3%). Moreover, the mean level of

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### Table 2. Neuropathic Pain Treatment in Cancer References in Nine National CPGs from European Countries

<table>
<thead>
<tr>
<th>Year</th>
<th>Publication Type</th>
<th>Title of the Reference</th>
<th>First Author</th>
<th>Publication</th>
<th>Shared References</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Clinical trial, 65</td>
<td>Gabapentin and an opioid combination vs. opioid alone for the management of neuropathic cancer pain: a randomized open trial.</td>
<td>Keskinbo</td>
<td>J Pain Symptom Manage</td>
<td>+ (2 CPGs)</td>
</tr>
<tr>
<td>2006</td>
<td>Review</td>
<td>How to use antidepressants and anticonvulsants as adjuvant analgesics in the treatment for neuropathic cancer pain.</td>
<td>McDonald</td>
<td>J Support Oncol</td>
<td>–</td>
</tr>
<tr>
<td>2005</td>
<td>Clinical trial, 62</td>
<td>Gabapentin is effective in the treatment for cancer-related neuropathic pain: a prospective, open-label study.</td>
<td>Ross</td>
<td>J Palliat Med</td>
<td>–</td>
</tr>
<tr>
<td>2004</td>
<td>RCT, 121</td>
<td>Gabapentin for neuropathic cancer pain: a randomized controlled trial from the Gabapentin Cancer Pain Study Group.</td>
<td>Caraceni</td>
<td>J Clin Oncol</td>
<td>+ (4 CPGs)</td>
</tr>
<tr>
<td>2004</td>
<td>Review</td>
<td>Adjuvant analgesics in cancer pain management.</td>
<td>Lussier</td>
<td>Oncologist</td>
<td>–</td>
</tr>
<tr>
<td>2003</td>
<td>Systematic review</td>
<td>Ketamine as an adjuvant to opioids for cancer pain.</td>
<td>Bell</td>
<td>J Pain Symptom Manage</td>
<td>–</td>
</tr>
<tr>
<td>2002</td>
<td>RCT, 16</td>
<td>Amitriptyline in neuropathic cancer pain in patients on morphine therapy: a randomized placebo-controlled, double-blind crossover study.</td>
<td>Mercadente</td>
<td>Tumori</td>
<td>+ (2 CPGs)</td>
</tr>
<tr>
<td>2002</td>
<td>RCT, 51</td>
<td>Phase III evaluation of nortriptyline for alleviation of symptoms of cis-platinum induced peripheral neuropathy</td>
<td>Hammack</td>
<td>Pain</td>
<td>–</td>
</tr>
<tr>
<td>2001</td>
<td>Case report</td>
<td>Gabapentine for pain control in patients with cancer wound dressing care</td>
<td>Devulder</td>
<td>J Pain Symptom Manage</td>
<td>–</td>
</tr>
<tr>
<td>1999</td>
<td>Clinical trial, 593</td>
<td>Assessment and treatment for neuropathic cancer pain following WHO guidelines.</td>
<td>Grond</td>
<td>Pain</td>
<td>–</td>
</tr>
<tr>
<td>1999</td>
<td>Clinical trial, 22</td>
<td>Gabapentin as an adjuvant to opioid analgesia for neuropathic cancer pain.</td>
<td>Caraceni</td>
<td>J Pain Symptom Manage</td>
<td>+ (2 CPGs)</td>
</tr>
</tbody>
</table>

**RCT**, randomized controlled trial; **CPGs**, clinical practice guidelines.

*Number of patients included in the trial.
evidence of used references was high (44%). Nevertheless, few references were used in at least two CPGs (18%), and no reference was shared by all the CPGs.

All CPGs recommended the use of antidepressant drugs, α2δ agonists and others anticonvulsant drugs. Proposal of these drugs in first line treatment is not supported by high evidence level. For example, amitriptyline is the oldest anti-neuropathic drug and well investigated in non-cancer populations, but Mercadante et al. demonstrated the analgesic effects on neuropathic pain of 50 mg of amitriptyline were small and associated with side events in patients with cancer.  

We also found diversity in recommendations concerning strong opioids and more invasive approaches such as ketamine. Such second line therapeutic approaches were proposed by some CPGs, whereas they were not mentioned at all in others. This shows a gap between daily practice (wide utilization of ketamine or lidocaine in cancer pain, not only in case of neuropathic pain) and recommendations in part of the CPGs.  

Ideally, high quality CPGs should describe adverse events and risks of treatments. In the studied CPGs, these were well described for strong opioids. However, in the majority of the CPGs, adverse events of antidepressants or anticonvulsants as treatment for neuropathic pain were not mentioned. Up to now, the benefit-risk ratio of these drugs in patients with cancer is unknown. Consequently, we recommend that CPGs mention restrictions when study findings in non-cancer populations are extrapolated to patients with cancer.

Clinical practice guidelines differ in terms of used references, extrapolation techniques, and assigned levels of evidence. The origin and the composition of the guideline development groups seem to have influenced the clinical recommendations, which are based on their clinical experiment and their choice of evidence-based references.  

Our results should be interpreted with caution. They are merely based on available information in the CPGs. Only one chapter per CPG concerned neuropathic pain in patients with cancer. These results emphasize the lack of robust references on the treatment for neuropathic pain in cancer conditions. As we limited ourselves to Europe, we were able to develop a detailed study including all European countries. In the future, it would be interesting to include CPGs from other continents.

### Recommendations and Perspective

The majority of guideline development groups extrapolated results of studies on non-cancer neuropathic pain to recommendations for patients with cancer. Consequently, these CPGs fail to address important

<table>
<thead>
<tr>
<th>Treatment for Neuropathic Pain in Patients with Cancer</th>
<th>France 2009</th>
<th>Italy 2006</th>
<th>The Netherlands 2008-I</th>
<th>The Netherlands 2008-II</th>
<th>Norway 2009</th>
<th>Norway 2007*</th>
<th>Spain</th>
<th>U.K.*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol, NSAIDs,</td>
<td>–</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Weak opioids (ie, dextropropoxyphene, tramadol)</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tricyclic Antidepressant drugs (ie, amitriptiline, imipramine)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SNRI Antidepressant drugs (ie, venlafaxine, duloxetine)</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>α2δ agonists (ie, gabapentine, pregabaline)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Others Anticonvulsant drugs (ie, carbamazepine, valproate of sodium, phenitoine)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>–</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>–</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Opioids (ie, morphine, oxycodone) in combination with coanalgesics</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lidocaine 5% plaster (only in case of local neuropathic pain)</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Capsaicin plaster (only in case of local neuropathic pain)</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ketamine</td>
<td>0</td>
<td>0</td>
<td>‡</td>
<td>‡</td>
<td>0</td>
<td>0</td>
<td>+R</td>
<td>‡</td>
</tr>
<tr>
<td>Lidocaine, mexiletine</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>–</td>
</tr>
</tbody>
</table>

*The topic of the guideline concerned specifically the treatment for pain in cancer.

†No marketing in Norway.

‡Consultation with a pain or palliative care specialist (+): should be proposed, (–): should not be proposed, (0): no information. R: refractory neuropathic pain.
## Table 4. Comparison of Grade of Recommendations and Level of Evidence Proposed for Treating Neuropathic Pain in Cancer Guidelines

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence literature</td>
<td>1</td>
<td>“low”</td>
<td>nm</td>
<td>4</td>
<td>4</td>
<td>1*</td>
<td>nm</td>
<td>1</td>
<td>1 + +</td>
</tr>
<tr>
<td>Evidence recommendations</td>
<td>“weak”</td>
<td>A</td>
<td>nm</td>
<td>nm</td>
<td>nm</td>
<td>B</td>
<td>B</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Start dose</td>
<td>10–25 mg</td>
<td>10–25 mg</td>
<td>10 mg</td>
<td>10–25 mg</td>
<td>10–25 mg</td>
<td>10 mg 2–4 hours before sleep</td>
<td>nm</td>
<td>10–25 mg</td>
<td>nm</td>
</tr>
<tr>
<td>Titration scheme</td>
<td>5–25 mg†</td>
<td>nm</td>
<td>10 mg/3 days</td>
<td>25 mg/week</td>
<td>25 mg/3–7 days</td>
<td>10 mg/3 days up to 30 mg then 3 weeks stable dose</td>
<td>nm</td>
<td>Slow titration†</td>
<td>nm</td>
</tr>
<tr>
<td>Maximum dose</td>
<td>75–150 mg</td>
<td>50–75 mg</td>
<td>75 mg</td>
<td>50–150 mg</td>
<td>75 mg</td>
<td>40–50 mg</td>
<td>nm</td>
<td>150 mg</td>
<td>nm</td>
</tr>
<tr>
<td>Contra-indications</td>
<td>+</td>
<td>nm</td>
<td>nm</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>nm</td>
<td>nm</td>
<td>nm</td>
</tr>
<tr>
<td>Side effects</td>
<td>+</td>
<td>nm</td>
<td>nm</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>nm</td>
<td>nm</td>
<td>nm</td>
</tr>
<tr>
<td>Pregabalin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence literature</td>
<td>1</td>
<td>“low”</td>
<td>No treatment</td>
<td>4</td>
<td>?</td>
<td>1*</td>
<td>nm</td>
<td>1</td>
<td>1 + +</td>
</tr>
<tr>
<td>Evidence recommendations</td>
<td>“weak”</td>
<td>“positive”</td>
<td>option</td>
<td>nm</td>
<td>nm</td>
<td>B</td>
<td>B</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Start dose</td>
<td>75–150 mg</td>
<td>2 × 25 mg</td>
<td>2 × 75 mg</td>
<td>2 × 75 mg</td>
<td>2 × 25 mg</td>
<td>2 × 25 mg</td>
<td>nm</td>
<td>2 × 25–75 mg</td>
<td>nm</td>
</tr>
<tr>
<td>Titration scheme</td>
<td>75 mg†</td>
<td>nm</td>
<td>150 mg/2 days</td>
<td>150 mg/2 days</td>
<td>Slowly†</td>
<td>nm</td>
<td>50–150 mg/time</td>
<td>nm</td>
<td></td>
</tr>
<tr>
<td>Maximum dose</td>
<td>300–600 mg</td>
<td>600 mg</td>
<td>2 × 300 mg</td>
<td>2 × 300 mg</td>
<td>2 × 300 mg</td>
<td>nm</td>
<td>nm</td>
<td>nm</td>
<td>nm</td>
</tr>
<tr>
<td>Contra-indications</td>
<td>+</td>
<td>nm</td>
<td>nm</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>nm</td>
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<tr>
<td>Side effects</td>
<td>+</td>
<td>nm</td>
<td>nm</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>nm</td>
<td>nm</td>
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</tr>
<tr>
<td>Gabapentin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Evidence literature</td>
<td>2</td>
<td>“low”</td>
<td>nm</td>
<td>2</td>
<td>2</td>
<td>1*</td>
<td>nm</td>
<td>1+</td>
<td>1 + +</td>
</tr>
<tr>
<td>Evidence recommendations</td>
<td>“weak”</td>
<td>A</td>
<td>nm</td>
<td>nm</td>
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<td>B</td>
<td>A</td>
<td></td>
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</tr>
<tr>
<td>Start dose</td>
<td>1 × 100–300 mg</td>
<td>2 × 100 mg</td>
<td>1 × 300 mg</td>
<td>1 × 100–300 mg</td>
<td>1 × 100–300 mg</td>
<td>1 × 300 mg</td>
<td>nm</td>
<td>1 × 300 mg</td>
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</tr>
<tr>
<td>Titration scheme</td>
<td>100–300 mg†</td>
<td>nm</td>
<td>300 mg/day</td>
<td>100–300 mg/day</td>
<td>100–300 mg/day</td>
<td>1 × 300 mg/3 days</td>
<td>nm</td>
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<tr>
<td>Maximum dose</td>
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<td>Contra-indications</td>
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<tr>
<td>Side effects</td>
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</table>

*Non-cancer neuropathy.
†No further information is given.
‡+= mentioned in the CPG, nm = not mentioned in the CPG.
issues such as altered kinetics and side effect profiles in these patients. We recommend creating specific recommendations by an international expert group for the treatment for neuropathic pain in patients with cancer supported by targeted research in patients with cancer. For this purpose, there is a need for research protocols with prospective multicenter and multinational studies in clinical practice comparing different treatment strategies and to publish all studies whether the results reported are positive or negative.

REFERENCES