Drug Class Review
on
Drugs for Neuropathic Pain

Final Report Evidence Tables

October 2007

The Agency for Healthcare Research and Quality has not yet seen or approved this report

A literature scan of this topic is done periodically

The purpose of this report is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use or approach. Oregon Health & Science University does not recommend or endorse any guideline or recommendation developed by users of these reports.

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Note: A scan of the medical literature relating to the topic is done periodically (see http://www.ohsu.edu/ohsuedu/research/policycenter/DERP/about/methods.cfm for scanning process description). Upon review of the last scan, the Drug Effectiveness Review Project governance group elected not to proceed with another full update of this report. Some portions of the report may not be up to date.

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Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Number of trials/ Number of patients
Finnerup, 2005 (5)	To update existing systematic reviews to include more recent trials, to provide up-to-date calculations of NNT and NNH in neuropathic pain as the basis of a proposal for an evidence-based treatment algorithm	MEDLINE, EMBASE, Cochrane Reviews, Cochrane CENTRAL, 1966 to April 2005 References lists, author queries for dichotomous data.	Randomized double-blind studies in neuropathic pain conditions using chronic dosing and placebo studying at least 10 patients; English language; cancer pain excluded except for well-defined post-mastectomy pain syndromes and postsurgical pain with post-operative pain compatible with a nerve section.	105 trials (31 of drugs included in DERP review)

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Number of trials/ Number of patients
Hempenstall, 2005 (7)	To conduct a systematic review and meta-analysis for both efficacy and adverse events of analgesic therapy in postherpetic neuralgia.	MEDLINE, EMBASE, CINAHL, PubMed, Cochrane CCTR, Cochrane Library 1966 to October 2004; Reference lists	Trials that examined adult patients with zoster-associated pain for greater than 3 months, were blinded, randomized, and had at least one clinically relevant measure of pain outcome. Unpublished, letter, and abstract-only studies were excluded as were studies on prevention of PHN and anecdotes. Studies where data for PHN were not analyzed separately from other neuropathic pain syndromes were also excluded.	35 trials 248 patients in tricyclic antidepressant trials, 559 in gabapentin, 411 in pregabalin, 70 in dextromethorphan, 64 in lidocaine patch

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Author Year (Quality)	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Number of trials/ Number of patients
Saarto, 2005 (Cochrane Review) (4)	To determine the analgesic effectiveness and adverse effects of antidepressant drugs in treatment of neuropathic pain.	1966 to December 2003	RCTs of antidepressants in treatment of neuropathic pain, published and unpublished trials eligible, no language restrictions. Abstracts and reviews excluded. Studies could have taken place in any care setting (inpatient, outpatient, day care, community). Studies with less than 10 patients excluded. Studies in adults over age 18. Migraine and headache studies excluded.	50 trials; 2515 patients
Wiffen, 2005 (Gabapentin, Cochrane Review)	To evaluate the analgesic effectiveness of gabapentin	1966 to November 2004	RCTs of the analgesic effects of gabapentin, with pain assessment as either the primary or a secondary outcome. Full journal publication was required, abstracts not included. Adult patients age 18 and older with neuropathic pains including diabetic neuropathy, post-herpetic neuralgia, phantom limb pain, Guillain Barre, and spinal cord injury.	15 trials; 1468 patients

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Author Year (Quality)	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Number of trials/ Number of patients
Wiffen, 2005 (Carbamazepine, Cochrane Review) (4)	To evaluate the analgesic effectiveness of carbamazepine in acute and chronic pain and to evaluate adverse effects reported in the clinical trials	1966 to November 2004	RCTs which investigated the analgesic effects of carbamazepine in neuropathic pain, with pain assessment as either the primary or secondary outcome, adults ages 18 to 84. Excluded non-randomized studies, studies of experimental pain, case reports, clinical observations, or studies of carbamazepine used to treat pain produced by other drugs.	11 trials in chronic pain (1 acute); 364 patients

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Author Year (Quality)	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Number of trials/ Number of patients
Khaliq, 2007 Topical Lidocaine, Cochrane Review (6)	To review systematically all randomized and quasi-randomized trials of the use of topical lidocaine and examine its efficacy and safety in the treatment of post herpetic neuralgia	Jan 1966-Nov 2006. CPPSCR, Cochrane CCRT, Medline, Embase, Lilacs, SIGLE for conference proceedings, citation index, reference lists, key textbooks, previous systematic reviews for additional studies	All randomized and quasi-randomized trials that compare the use of topical lidocaine in the treatment of post herpetic neuralgia, with placebo or any other active treatment. Patients of any age who fulfil the criteria which approximate to the definition of postherpetic neuralgia posed by McDonald 2000. Included interventions are topical applications of all lidocaine, such as patch and gel preparations. Trials will be included where topical lidocaine is administered in any setting by any person.	3 trials, 314 patients

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Author Year (Quality)	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Number of trials/ Number of patients
Wiffen (lamotrigine), Cochrane review (6)	To assess the analgesic efficacy and adverse effects of anticonvulsant lamotrigine for acute and chronic pain	1966-2006 Medline, Embase, the Cochrane Library, reference lists of retrieved papers, and contacting investigators.	RCTs which investigated the analgesic effects of lamotrigine in patients with pain assessment as either the primary or secondary outcome were included. Full journal publications were required, abstracts not included. Non randomized studies, studies of experimental pain, case reports, clinical observations, or studies of lamotrigine used to treat pain produced by other drugs were not included. Adults aged 18 and over were included. Participants complaining of pain in either the acute pain setting or suffering from a wide range of neuropathic pains including diabetic neuropathy, post-herpetic neuralgia, phantom-limb pain, trigeminal neuralgia, Guillain Barre and spinal cord injury were included. Trials of participants with more than one type of neuropathic pain were also included.	7 trials, 502 patients: 59 patients with diabetic neuropathy, 269 patients with HIV related neuropathy, 100 with intractable neuropathic pain, 30 with spinal cord injury related pain, 14 with trigeminal neuralgia, 30 with central post stroke pain

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Author Year (Quality)	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Number of trials/ Number of patients
Wong, 2007 (5)	To evaluate the effects of treatments for the symptom of painful diabetic neuropathy.	1966-Oct 2006 Medline (R), Embase, EMB reviews-AP journal club, CCRT, reference lists	Adults 18 years and above with diabetic neuropathy. The interventions involved the administration of oral or topical analgesics. Classes of drugs included paracetamol, antidepressants, opioids, NSAIDS, N-methyl-D-aspartate antagonists, tramadol, capsaicin and anticonvulsants. The comparator was a placebo. RCTs that investigated the analgesic effects of pain relieving drugs for patients with diabetic neuropathy. English language publications were included.	A total of 25 trials:1576 patients on anticonvulsants, 94 patients on antidepressants 805 patients on SNRI, 173 patients on Ion channel blockers, 14 patients on NMDA antagonists, 329 patients on opioids, 299 patients on topical agents.

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Data synthesis methods	Main efficacy outcome
Finnerup, 2005 (5)	105 placebo-controlled trials: 59 crossover, 46 parallel design; 5 studies used an active placebo	Patients with central post-stroke pain, spinal cord injury pain, multiple sclerosis, painful polyneuropathy, post-herpetic neuralgia, phantom limb pain, post-mastectomy and post-surgical pain, brachial plexus avulsion, trigeminal neuralgia, HIV-neuropathy, and mixed neuropathic pain	Antidepressants (26 trials), anticonvulsants (39), opioids (11), NMDA antagonists (7), mexiletine (9), topical lidocaine (4), cannabinoids (3), capsaicin (11), glycine antagonist (1).	NNT and NNH calculated if relative risk statistically significant. Data pooled assuming clinically homogenous trials.	More than 50% pain relief.

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Author Year (Quality)	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Data synthesis methods	Main efficacy outcome
Hempenstall, 2005 (7)	35 trials: 18 crossover, 17 parallel group; 31 placebo-controlled (including active placebo). 4 active control studies without a placebo group, not included in meta-analysis	Post-herpetic neuralgia. Definition of PHN was pain persisting for longer than 3 months after the crusting of skin lesions following an acute attack of herpes zoster.	Tricyclic antidepressants (7 trials; 5 with dichotomous data included in meta-analysis), gabapentin (2 trials), pregabalin (2 trials), dextromethorphan (2 trials), topical lidocaine (3 trials, 1 with dichotomous data included in meta-analysis); also memantine, opioids, tramadol, capsaicin, topical NSAIDs, i.v. lidocaine, intrathecal therapies, other therapies.	Quantitative analysis on trials where dichotomous data were available. Calculated relative benefit and NNT for efficacy, relative risk and NNH for safety. If tests of homogeneity were favorable, pooling of data for groups of similar treatments. Qualitative comment on studies from which dichotomous data could not be extracted.	Hierarchy of outcome measures used: 1) top 2 values on a 5-point patient-reported global scale for pain relief or effectiveness or improvement; 2) top 3 values on a 6-point patient-reported global scale for pain relief or effectiveness or improvement; 3) top value on a 3-point patient-reported global scale for pain relief or effectiveness or improvement; 4) top 2 values on a 4-point patient-reported categorical pain-relief scale; 5) 50% or greater reduction on a visual analogue or 11-point numerical rating scale for pain intensity.

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Author Year (Quality)	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Data synthesis methods	Main efficacy outcome
Saarto, 2005 (Cochrane Review) (4)	50 trials: 20 parallel design, 30 crossover.	Diabetic neuropathy (17 studies), postherpetic neuralgia (8), postherpetic and trigeminal neuralgia (1), central pain (4), atypical facial pain (4), burning mouth pain (2), HIV-related neuropathy (2), post-treatment neuropathic pain in breast cancer patients (2), mixed neuropathic pain (10).	Tricyclic antidepressants (amitriptyline, clomipramine, desipramine, dothiepin, doxepin, imipramine, mianserin, maprotiline, nortriptyline); SSRIs (citalopram, fluoxetine, paroxetine, sertraline); other types of antidepressants (bupropion, L-tryptophan, phenelzine, venlafaxine, trazodone), St., John's wort (1 study).	Where appropriate, data from included studies were combined. For dichotomous variables, the Relative Benefit expressed as Relative Risk (RR) with 95% CI. Results were reported as NNT for pain relief and NNH for mild and severe adverse drug reactions.	Number of patients with global improvement or pain relief available in 33 studies; in 17 studies only mean data were available
Wiffen, 2005 (Gabapentin, Cochrane Review)	15 trials	Acute pain (1 trial), chronic post-herpetic neuralgia (2), diabetic neuropathy (7), cancer related pain (1), phantom limb pain (1), Guilland Barre (1), spinal cord injury pain (1), mixed neuropathic pains (1). Participants ages 18-90 years.	Gabapentin only	NNTs were calculated as the reciprocal of the absolute risk reduction. For unwanted effects, the NNT becomes NNH and is calculated the same way.	Hierarchy of outcome measures used: 1) Patient reported pain relief of 50% or greater; 2) patient reported global impression of change; 3) pain on movement; 4) pain on rest; 5) any other pain related measure.

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Author Year (Quality)	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Data synthesis methods	Main efficacy outcome
Wiffen, 2005 (Carbamazepine, Cochrane Review) (4)	Eleven trials in chronic pain: 6 placebo-controlled, 5 active-controlled (carbamazepine vs tizanidine, tocainide, pimozide, nortriptyline/fluphenazine combination, or transcutaneous electronic nerve stimulation)	7 trials in trigeminal neuralgia, 2 in diabetic neuropathy, 1 post-herpetic neuralgia, 1 post-stroke pain.	Carbamazepine	NNTs were calculated as the reciprocal of the absolute risk reduction. For unwanted effects, the NNT becomes NNH and is calculated the same way.	A hierarchy of outcome measures used: 1) patient reported pain relief of 50% or greater; 2) patient reported global impression of clinical change; 3) pain on movement; 4) pain on rest or spontaneous pain; 5) any other pain related outcome 6) adverse events

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Author Year (Quality)	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Data synthesis methods	Main efficacy outcome
Khaliq, 2007 Topical Lidocaine, Cochrane Review (6)	Out of the 3 trials, 2 were cross- over, randomized double blind trials. All trials compared topical lidocaine to placebo. Two trials were single center studies and the remaining one was a multi-center study.	3 trials of patients with postherpetic neuralgia, pain persisting at the site of shingles at least one month after the onset of acute rash). A total of 182 patients were treated with topical lidocaine and 132 control patients.	All included studies compared topical lidocaine to placebo. One trial used lidocaine gel versus a vehicle gel, while others used lidocaine patches. All the lidocaine concentrations that were used, whether gel or patch were 5%.	Relative Risks (RR) with 95% confidence intervals (CI s) and risk differences (RDs) with 95%CI for dichotomous outcome measures, and weighted mean difference with 95% CI for continuous outcomes. If statistical heterogeneity was found, sensitivity analysis was done by repeating calculations after omitting the trials which had low scores on individual quality items. If there were still some unexplained heterogeneity, "random-effects" methods was used to combine studies. Statistical analysis was undertaken to obtain NNT data wherever appropriate.	The primary outcome measure is the mean improvement in the patient's reports of pain relief measured by a categorical scale such as the 6 point pain relief scale. Secondary outcomes were i) mean reduction in VAS scores at any time after randomization, II) highest recorded blood lidocaine level at any time between 4 hours and 30 days, iii) proportion of patients with adverse skin reactions. Two trials provided data on pain relief, while the remaining study provided data on secondary outcome measures.

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Author Year (Quality)	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Data synthesis methods	Main efficacy outcome
Wiffen (lamotrigine), Cochrane review (6)	7 studies are randomized double blind placebo controlled studies. 3 are cross over studies	Central post stroke pain(1 trial), diabetic neuropathy(1 trial), HIV related neuropathy (2 trials), intractable neuropathic pain (1 trial), spinal cord injury related pain (1 trial), and trigeminal neuralgia (1 trial). Participants were aged between 26-77 years.	Administration of lamotrigine, in any dose by any route to achieve analgesia	NNT was calculated as the reciprocal of the absolute risk reduction. For unwanted effects, NNT becomes NNH. Dichotomous data were used to calculate relative risk with 95% confidence intervals using fixed effect models unless significant statistical heterogeneity was found.	a hierarchy of outcome measures used: 1) patient reported pain relief of 50% or greater; 2) patient reported global impression of clinical change; 3) pain on movement; 4) pain on rest ; 5) any other pain related outcome 6) adverse event with a subgroup analysis of elderly if data were available

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Data synthesis methods	Main efficacy outcome
Wong, 2007 (5)	25 RCTs comparing drugs to placebo, 16 parallel studies, 9 cross over studies	Patients were adults with painful diabetic neuropathy	Anticonvulsants (10 trials), antidepressants (4 trials), SNRI (2 trials), Ion channel blockers (3 trials), NMDA antagonists (1 trial), opioids (3 trials), Topical agents (2 trials)	Results were expressed as OR with 95% CI, using a random effect model for studies with sufficient data. Homogeneity with I square statistic was used for studies with sufficient data, and for those without sufficient data, homogeneity was assessed visually. Quorum guidelines were followed for subgroup analysis of different types of drugs.	Primary outcome was dichotomous information for 50% or moderate reduction of pain. Secondary outcomes were 30% reduction of pain and withdrawals related to adverse events

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Main efficacy results	Main safety results	Results in subgroups	Quality assessment method
Finnerup, 2005 (5)	NNT (95% CI) to obtain one patient with more than 50% pain relief in neuropathic pain (all pain conditions combined): All antidepressants: 3.3 (2.9–3.8) TCA: 3.1 (2.7–3.7) SSRI: 6.8 (3.4–4.41) SNRI: 5.5 (3.4–14) DNRI: 1.6 (1.3–2.1) All anticonvulsants: 4.2 (3.8–4.8) carbamazepine: 2.0 (1.6–2.5) phenytoin: 2.1 (1.5–3.6) lamotrigine: 4.9 (3.5–8.1) valproate: 2.8 (2.1–4.2) gape tin, pregabalin: 4.7 (4.0–5.6) topiramate: 7.4 (4.3–28) dextromethorphan: 4.4 (2.7–12) topical lidocaine: 4.4 (2.5–17)	NNH (95% CI) to obtain one withdrawal due to adverse effects (all pain conditions combined): All antidepressants: 16.0 (12–25) TCA: 14.7 (10–25) SSRI: NS SNRI: NS DNRI: NS All anticonvulsants: 10.6 (9–13) carbamazepine: 21.7 (13–79) phenytoin: NS lamotrigine: NS valproate: NS gabapentin, pregabalin: 17.8 (12–30) topiramate: 6.3 (5–8) dextromethorphan: 8.8 (6–21) topical lidocaine: NS	N/A	Jadad score

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Main efficacy results	Main safety results	Results in subgroups	Quality assessment method
Hempenstall, 2005 (7)	NNT (95% CI) from studies with dichotomous data available: Tricyclic antidepressants: 2.64 (2.1–3.54) gabapentin: 4.39 (3.34–6.07) pregabalin: 4.93 (3.66–7.58) dextromethorphan: NS topical lidocaine: 2.00 (1.43–3.31)	NNH (95% CI) for withdrawals due to adverse events, from studies with dichotomous data available: Tricyclic antidepressants: 16.9 (8.85–178) gabapentin: 12.25 (7.69–30.2) pregabalin: NS dextromethorphan: 3.8 (2.09–21.3) topical lidocaine: NS	N/A	Jadad score

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Author Year (Quality)	Main efficacy results	Main safety results	Results in subgroups	Quality assessment method
Saarto, 2005 (Cochrane Review) (4)	Tricyclic antidepressants: NNT (95% CI) vs placebo for global improvement or pain relief, at least moderate improvement: amitriptyline: 2 (1.7—2.5) desipramine: 2.1 (1.5—3.2) imipramine: similar NNT but few participants and result not significant. RR for tricyclic antidepressants combined: 2.37 (95% CI 1.96 to 2.87) SSRIs: Data insufficient to calculate NNT. 4 placebo controlled studies included; all found SSRI superior to placebo (fluoxetine in idiopathic facial pain and in diabetic neuropathy, citalopram in diabetic nephropathy, paroxetine and sertraline in burning mouth syndrome)	NNH (95% CI) for withdrawals due to adverse effects for tri- and tetracyclic antidepressants: 16 (10—45) For other antidepressants, no statistically significant difference compared to placebo.	Where data were available, subgroup analyses were performed by neuropathic disorder, antidepressant, and different classes of antidepressant and individual drugs (tricyclic antidepressants, SSRIs)	Oxford quality scale (Jadad 1996) & 4 point grade scale defined in the Cochrane reviewers handbook for allocation concealment
Wiffen, 2005 (Gabapentin, Cochrane Review)	NNT for improvement, all trials combined: 4.3 (95% CI 3.5 to 5.7); relative risk 2.2 (95% CI 1.8 to 2.7); 42% of participants improved on gabapentin compared to 19% on placebo. NNT for improvement in diabetic nephropathy 2.9 (95% CI 2.2 to 4.3); relative risk 2.2 (95% CI 1.7 to 3.0); 64% of participants improved on gabapentin compared to 28% on placebo. NNT for improvement in post-herpetic neuralgia: 3.9 (95% CI 3.0 to 5.7); relative risk 2.5 (95% CI 1.8 to 3.3); 43% of participants improved on gabapentin compared to 17% on placebo.	NNH for withdrawal due to adverse effects NS. Frequencies: dizziness 24%, somnolence 20%, headache 10%, diarrhea 10%, confusion 7%, nausea 8%.	N/A	Jadad score

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Author Year (Quality)	Main efficacy results	Main safety results	Results in subgroups	Quality assessment method
Wiffen, 2005 (Carbamazepine, Cochrane Review) (4)	NNT for at least moderate pain relief in any neuropathic pain 2.5 (95% CI 1.8 to 3.8) Relative benefit 2.1 (95% CI 1.5 to 2.7) Trigeminal neuralgia NNT for pain relief: 1.9 (95% CI 1.4 to 2.8). Relative benefit NS (based on 3 studies with 47 participants) Diabetic neuropathy Placebo-controlled trial (N=30): 30% to 50% more patients improved on carbamazepine vs placebo. Carbamazepine vs nortriptyline: NSD Post-herpetic neuralgia carbamazepine plus clomipramine superior to transcutaneous electronic nerve stimulation Post-stroke pain NNT vs placebo NS; No difference between carbamazepine and amitriptyline (OR 3.3; 95% CI 0.8 to 13.8).	NNH for withdrawals due to AEs NS. NNH for minor harm 3.7 (95% CI 2.4 to 7.8)	N/A	Jadad score

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Main efficacy results	Main safety results	Results in subgroups	Quality assessment method
Khaliq, 2007 Topical Lidocaine, Cochrane Review (6)	Primary outcome: mean improvement in pain relief as derived from 2 studies indicate that topical lidocaine was better than placebo for pain relief. The combined weighted mean difference from these two trials was 0.42 (95%CI 0.14-0.69, P=0.003).	2 trials reported this outcome. One trial reported 12 adverse reactions in both groups, while the other reported 2 adverse reactions in active group and 1in placebo group. None of the participants dropped out of the study due to adverse reactions. Adverse skin reactions could also be due to the use of patch, as opposed to lidocaine itself. There were no reported cardiovascular, respiratory and neurological adverse reactions.	N/A	Quality assessment took into account 7 criteria. Allocation concealment was graded according to criteria presented in Cochrane's review writing software, RevMan 4.2

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Author Year (Quality)	Main efficacy results	Main safety results	Results in subgroups	Quality assessment method
Wiffen (lamotrigine), Cochrane review (6)	Central post stroke pain (n=30) Statistically significant difference between lamortigine and placebo. RR was 4 (1.3 to 12.6), NNT was 3 (1.8 to 9) Diabetic neuropathy (n=59) NNT for global impression of "highly effective" was not significant. A 50% reduction of pain was achieved by more people taking lamotrigine than placebo (RR not significant), for global impression of moderate or better improvement RR 1.7 (0.97 to 3 (NS), NNT 3 (2 to 59, NS) HIV related neuropathy: Mean difference in pain score Placebo -0.18 (0.09), Lamotrigine -0.55 (0.14). Significantly greater fall in pain scores in the tx group, but over half of this group dropped out. Intractable neuropathic pain (n=100): A calculated NNT was not Statistically significant. Spinal cord injury related pain (n=30): No significant effects on pain intensity. Trigeminal neuralgia: (n=14): Lamotrigine was slightly more effective than placebo (RR not significant)	7% of participants developed a rash. .	HIV related neuropathy: n=227. Subgroups of patients receiving antiretroviral therapy (ART). ART group had an RR of 2.0 (1.1 to 3.6 (SSD); an NNT of 4.3 (2.3 to 37). The non ART RR was 1.3 (0.94 to 1.9 (NS), and NNT was not significant.	Oxford quality scale (Jadad 1996)

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Author Year (Quality)	Main efficacy results	Main safety results	Results in subgroups	Quality assessment method
Wong, 2007 (5)	17 studies were included in the meta analysis for efficacy results. Anticonvulsants: The pooled ratio (a total of 50% reduction of pain and moderate relief of pain) of treatment efficacy with traditional anticonvulsants was 5.33 (95%CI 1.77 to 16.02), with newer anticonvulsants was 3.25 (2.27 to 4.66). The Odds ratio (OR) in terms of 50% pain relief with pregabalin 600 mg daily and 300 mg daily were 3.96 (2.to-5.55) and 3.95 (2.34 to 6.66). Antidepressants: Pooled OR was 22.24 (5.83 to 84.75) SNRI: Pooled OR in terms of 50% pain relief with duloxetine 60mg was 2.55 (1.73 to 3.77), with duloxetine 120mg, OR was 2.10 (1.03-4.27) NMDA agonists: OR in terms of 50% pain relief with 381 mg dextromethorphan was 31.2 (1.5 to 633.1)	21 studies are included in the meta analysis of withdrawals related to adverse effects (AE). Traditional anticonvulsants: pooled OR for withdrawal related to AE was 1.51 (0.33 to 6.96) Newer generation anticonvulsants: Pooled OR for withdrawal related to AE was 2.98 (1.75 to 5.07) Pregabalin: The OR for withdrawal related to AE was 2.81(1.13 to 7.04) for 600 mg daily and 2.23 (0.68 to 7.26) for pregabalin 300 mg daily. Antidepressants: The pooled OR for AE related to withdrawal was 2.32 (0.59 to 9.69) SNRIs: Pooled OR for withdrawal related to AE was 2.36 (1.05-5.35) for 60 mg duloxetine, and 4.65 (2.18-9.94) for 120 mg duloxetine.	N/A	Jadad score

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Limitations of primary studies
Finnerup, 2005 (5)	The major cause of heterogeneity was dose, pain diagnosis, and study design, with small, crossover trials having the greatest treatment effects. There was also a large variation in placebo response among studies.

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Limitations of primary studies
Hempenstall, 2005 (7)	In 14 studies there were no reference to ITT analysis. In these studies, % of non completers varied between 1% and 24%.

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Author Year (Quality)	Limitations of primary studies
Saarto, 2005 (Cochrane Review) (4)	Many reports gave insufficient information, used a variety of different outcome measures and variable dosing. The quality of reporting in recent trials remains disappointing, in particular insufficient details are provided to enable effectiveness to be assessed.
Wiffen, 2005 (Gabapentin, Cochrane Review)	Authors say that the usefulness of primary studies would be increased greatly by improvements in the quality of reporting. Investigators presenting mean data for treatment and control should also consider the presentation of categorical and binary data.

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Author Year (Quality)	Limitations of primary studies
Wiffen, 2005 (Carbamazepine, Cochrane Review) (4)	Poor quality reporting limited the ability to combine data. Many reports gave insufficient information, used a variety of different outcome measures and variable dosing. Although contacted by letter, all the authors did not reply and those who did often did not have data available. No. of participants in trials is small.

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Author Year (Quality)	Limitations of primary studies
Khaliq, 2007 Topical Lidocaine, Cochrane Review (6)	Only a small number of studies on topical lidocaine have been performed. Different outcome measures have been used between the various studies, so there is very little data to combine efficacy. One study was only published as an abstract and the actual paper has not been through a peer review and remains unpublished. All the three studies showed modest efficacy on pain relief. The unpublished trial had no statistical difference between VAS scores. All the trials have been written by the same first author. Shortcomings in trial designs: studies assessed patients' reports of pain using subjective assessments. In one of the trials, allocation concealment was not mentioned, none of the trials stated the effectiveness of blinding

Evidence Table 1. Systematic reviews of drugs for neuropathic pain

Author Year (Quality)	Limitations of primary studies
Wiffen (lamotrigine), Cochrane review (6)	Most of the studies were small and only 1 study had more than 100 participants. This together with the fact that generally there is only one study for each condition means that results show weak evidence to support the effect of lamotrigine. None of the studies used allocation concealment.

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Author Year (Quality)	Limitations of primary studies
Wong, 2007 (5)	Sample size was small and some trials used a cross over design without a washout period resulting in a carry over effect. Treatment period was less than 6 months in all of these studies, so the long term effect of these drugs cannot be judged. Few studies reported treatment efficacy for different types of pain such as allodynia and burning pain.

Evidence Table 2. Quality assessment of included systematic reviews

Study	Searches through	1. Search methods reported?	2. Comprehensive search?	3. Inclusion criteria reported?	4. Selection bias avoided?	5. Validity criteria reported?	6. Validity assessed appropriately?
Finnerup, 2005 Algorithm for neuropathic pain treatment	April 2005	Yes	Yes	Yes	No- only reports numbers meeting selection criteria, no information on exclusion	Yes (Jadad)	Yes
Hempenstall, 2005 Analgesic therapy in postherpetic neuralgia	October 2004	Yes	Yes	Yes	Yes	Yes	Yes (excluded if Jadad score less than 3 or if 10 patients or less)
Khaliq, 2007 Topical lidocaine for postherpetic neuralgia (Cochrane Review)	November 2006	Yes	Yes	Yes	Yes	Yes	Yes; discussion of qualtiy in the text and presented in the Ets
Saarto, 2005 Antidepressants for neuropathic pain (Cochrane Review)	December 2003	Yes	Yes	Yes	Yes	Yes	No- no analysis based on validity assessment
Wiffen, 2005 Carbamazepine for acute and chronic pain (Cochrane Review)	November 2004	Yes	Yes	Yes	Yes	Yes	No: Jadad score reported in evidence table but not discussed

Evidence Table 2. Quality assessment of included systematic reviews

Study	Searches through	1. Search methods reported?	2. Comprehensive search?	3. Inclusion criteria reported?	4. Selection bias avoided?	5. Validity criteria reported?	6. Validity assessed appropriately?
Wiffen, 2005 Gabapentin for acute and chronic pain (Cochrane Review)	November 2004	Yes	Yes	Yes	Yes	Yes	No: Jadad score reported in evidence table but not discussed
Wiffin, 2007 Lamotrigine for acute and chronic pain	Aug 2006	Yes	Yes	Yes	Yes	Yes	Yes, reported in evidence tables although little discussion in text
Wong, 2006 Treatment of painful diabetic neuropathy	October 2006	Yes	Yes	Yes	Yes	Yes (Jadad)	Partial

Evidence Table 2. Quality assessment of included systematic reviews

Study	7. Methods used to combine studies reported?	8. Findings combined appropriately?	9. Conclusions supported by data?	10. Overall scientific quality (score 1-7; higher is better)
Finnerup, 2005 Algorithm for neuropathic pain treatment	Yes	Yes	Yes	5
Hempenstall, 2005 Analgesic therapy in postherpetic neuralgia	Yes	Yes	Yes	7
Khaliq, 2007 Topical lidocaine for postherpetic neuralgia (Cochrane Review)	Used fixed effects model without explaining why	Yes	Yes	6
Saarto, 2005 Antidepressants for neuropathic pain (Cochrane Review)	Yes	Yes, except no sensitivity analysis by validity assessment	Overstated: "antidepressants are effective for a variety of neuropathic pains" although evidence is mainly in tricyclics and limited for SSRIs. Quality assessment of trials not addressed.	4
Wiffen, 2005 Carbamazepine for acute and chronic pain (Cochrane Review)	No- states only "meta-analysis was undertaken when appropriate data were available"	No, I2 very large but still combined without discussion	Yes	4

Evidence Table 2. Quality assessment of included systematic reviews

Study	7. Methods used to combine studies reported?	8. Findings combined appropriately?	9. Conclusions supported by data?	10. Overall scientific quality (score 1-7; higher is better)
Wiffen, 2005 Gabapentin for acute and chronic pain (Cochrane Review)	No- states only "meta-analysis was undertaken when appropriate data were available"	Can't tell	Yes	4
Wiffin, 2007 Lamotrigine for acute and chronic pain	NA as only 1 study identifed for each comparison	NA	Yes	6
Wong, 2006 Treatment of painful diabetic neuropathy	Yes	Partial (combined different outcome measures, for some analyses combined different drugs)	Partial. Combined results for different drugs (newer anticonvulsants). Also draws conclusions about comparative efficacy based on informal indirect comparisons.	5

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
Backonja US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=165 Age Mean (SD): 53.0 Male: 60% Female: 40%	Gabapentin 3600 mg Placebo
Bone 2002 UK and Ireland Efficacy quality: Fair	RCT Crossover Single Center	Phantom limb pain N=19 Age	Gabapentin 2400 mg Placebo
Gilron (A) 2005 Canada Efficacy quality: Fair	RCT Crossover Single Center	Mixed N=57 Age Mean (SD): 60 (pts PDN), 68 (pts PHN) Range: 40-81	Gabapentin 3200 mg Lorazepam 1.6 mg
Gorson 1999 Efficacy quality: Fair	RCT Crossover	Painful diabetic neuropathy N=40 Age Mean (SD): 62 (10.9) Range: 43-82	Gabapentin 900 mg Placebo
Hahn 2004 Germany Efficacy quality: Fair	RCT Parallel Multicenter	HIV-related neuropathic pain N=26 Age	Gabapentin 1200-2400 mg Placebo
Levendoglu	RCT	Spinal cord injury-related pain	Gabapentin

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
2004 Turkey Efficacy quality: Fair	Crossover	 N=20 Age Mean (SD): 35.9 (9.8) Male: 65% Female: 35%	3600 mg Placebo
Rice 2001 UK Efficacy quality: Fair	RCT Parallel Multicenter	Post-herpetic neuralgia N=334 Age Mean (SD): 75.3 Range: 22.5-94.8 Male: 41.32% Female: 58.68%	Gabapentin 1800 mg Gabapentin 2400 mg

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
			Placebo
Rowbotham (D 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Post-herpetic neuralgia N=225 Age Mean (SD): 74 Range: 39-90	Gabapentin 3600 mg Placebo
Serpell 2002 UK and Republic of Ireland Efficacy quality: Fair	RCT Parallel Multicenter	Mixed N=305 Age Mean (SD): 57	Gabapentin Placebo
Simpson (A) Part 1 2001 US Efficacy quality: Fair	RCT Parallel Single Center	Painful diabetic neuropathy N=60 Age Mean (SD): 50.0 Male: 60% Female: 40%	Gabapentin 900-2700 mg Placebo
Tai 2002 US Efficacy quality: Poor	RCT Crossover Single Center	Spinal cord injury-related pain N=7 Age	Gabapentin up to 1800 mg daily

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
		Mean (SD): 35.9 Range: 27-48 Male: 85.71% Female: 14.29%	
			Placebo
Yildirim 2003 Turkey Efficacy quality: Fair	RCT Parallel	Radiculopathy N=50 Age	Gabapentin 900 mg-3600 mg
			Placebo
Simpson (A) Part 1 2001 US Efficacy quality: Fair	RCT Parallel Single Center	Painful diabetic neuropathy N=60 Age Mean (SD): 50.0 Male: 60% Female: 40%	Gabapentin 900-2700 mg
			Placebo
Dworkin 2003 US Efficacy quality: Fair	RCT Parallel Multicenter	Post-herpetic neuralgia N=173 Age	Pregabalin 300-600 mg

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
		Mean (SD): 71.5 (10.9) Male: 46.82% Female: 53.18% White: 94.8% Asian: 1.2%	
			Placebo
Freynhagen 2005 Multiple European Efficacy quality: Fair	RCT Parallel Multicenter	Mixed N=338 Age Mean (SD): 62.2 (11.1) Range: 26-87 Male: 54.14% Female: 45.86% White: 97.6%	Pregabalin 150-600 mg
			Pregabalin 600 mg
			Placebo
Lesser 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=337 Age Mean (SD): 59.9 (10.5)□ Range: 26-85□ Male: 59.94% Female: 40.06% White: 94.4%□ Black: 3.6%□ Other: 2.1%	Pregabalin 75 mg
			Pregabalin 300 mg
			Pregabalin 600 mg

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
			Placebo
Richter 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=246 Age Mean (SD): 57.1 Male: 60.57% Female: 39.43% White: 83.7% Black: 7.7% Hispanic: 7.3% Other: 1.2%	Pregabalin 150 mg
			Pregabalin 600 mg
			Placebo
Rosenstock 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=146 Age Mean (SD): 59.7 (11.4) Male: 56.16% Female: 43.84%	Pregabalin 300 mg
			Placebo
Sabatowski 2004 Multiple European and Australia	RCT Parallel Multicenter	Post-herpetic neuralgia N=238	Pregabalin 150 mg

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
Efficacy quality: Fair		Age Mean (SD): 72.1 Range: 32-96 Male: 44.96% Female: 55.04% Race/ethnicity White: 99.2%	Pregabalin 300 mg Placebo
Siddall 2006 Australia Efficacy quality: Fair	RCT Parallel Multicenter	N=137 Age: Mean 50 (range 21-80) Male: 83% Female: 17% 97.1% white	Pregabalin 150-600 mg (flexible dose) mean dose 460 mg Placebo
van Seventer 2006 US and Multiple European Efficacy quality: Fair	RCT Parallel Multicenter	Post-herpetic neuralgia N=368 Age Mean (SD): 70.7 (10.6) Range: 18-92 Male: 45.65% Female: 54.35% White: 98.9% Black: 0.5%	Pregabalin 150 mg Pregabalin 300 mg Pregabalin 300-600 mg Placebo

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
		Other: 0.5%	
Goldstein 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=457 Age Mean (SD): 60.1 (10.9) Male: 61.49% Female: 38.51% White: 77.2% Black: 8.1% Hispanic: 11.2% Other: 3.5%	Duloxetine 20 mg daily
			Duloxetine 60 mg daily
			Duloxetine 60 mg BID Total daily dose: 120 mg/d
			Placebo
Raskin (B) 2005 and 2006 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=348 Age Mean (SD): 58.8 (10.1) Male: 46.55% Female: 53.45%	Duloxetine 60 mg once daily Total daily dose: 60 mg
			Duloxetine 60 mg twice daily Total daily dose: 120 mg

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
		White: 99.7% Asian: 0.3%	
			Placebo
Wernicke 2006 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=334 Age Mean (SD): 60.7 (10.6) Male: 61.08% Female: 38.92% Race/ethnicity White: 78.1% Black: 3.3% Hispanic: 16.2% Other: 2.4%	Duloxetine 60 mg once daily
			Duloxetine 60 mg twice daily Total daily dose: 120 mg
			Placebo
Rowbotham (C) 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=244 Age Mean (SD): 59.0 Male: 59.43% Female: 40.57%	Venlafaxine 75 mg daily
			Venlafaxine 150-225 mg daily
			Placebo

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
Tasmuth 2002 Finland Efficacy quality: Fair	RCT Crossover Single Center	Cancer-related neuropathic pain N=13 Age Mean (SD): 55 Range: 37-72 Male: 0% Female: 100%	Venlafaxine 37.5 mg Venlafaxine 75 mg Placebo Placebo
Yucel 2005 Turkey Efficacy quality: Fair	RCT Parallel Single Center	Mixed N=55 Age Mean (SD): 50.3 Male: 29.09%	Venlafaxine 75 mg Venlafaxine 150 mg Placebo
Estanislao 2004 US Efficacy quality: Fair	RCT Crossover Multicenter	HIV-related neuropathic pain N=64 Age Mean (SD): 45	Lidocaine gel 5% Placebo
Rowbotham (A) 1995 US	RCT Crossover Single Center	Type of pain studied□ Post-herpetic neuralgia□ □ N=39□	Lidocaine gel 5% Placebo

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size and characteristics	Intervention
Efficacy quality: Fair		□ Age□	
Galer (A) 2002 US Efficacy quality: Poor	RCT Parallel Multicenter	Post-herpetic neuralgia N=96 Age Mean (SD): 74 Male: 37.5%	Lidocaine transdermal patch Placebo
Galer (B) 1999 US	RCT Crossover Multicenter	Post-herpetic neuralgia N=32	Lidocaine transdermal patch Placebo
Meier 2003 Germany and Switzerland	RCT Crossover Multicenter	Mixed N=58 Age	Lidocaine transdermal patch 5% Placebo
Rowbotham (B) 1996 US	RCT Crossover Single Center	Post-herpetic neuralgia N=35	Lidocaine transdermal patch 5%; up to 3 patches to cover area Placebo

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
Backonja US Efficacy quality: Fair	At screening, pain attributed to diabetic neuropathy for 1 to 5 years, a diagnosis of diabetes mellitus (type 1 or 2), and a pain rating score of at least 40 mm on the 100-mm VAS of the Short-Form McGill Pain Questionnaire. Patients with an average pain score of at least 4 on an 11-point Likert scale and at least 4 observations recorded in daily pain diaries over the next week were randomized. Only paitents with a hemoglobin A1c level of 0.11 or less	Presence of other severe pain that could confound assessment or self-evaluaiton of the pain due to diabetic neuropathy, receipt of any investigational drug within 30 days prior to screening, and amputations other than toes. Creatinine clearance of less than 60 mL/min.
Bone 2002 UK and Ireland Efficacy quality: Fair	Patients attending a Disablement Services Clinic, with established phantom limb pain of a minimum of 6 months duration after a previous surgical amputation, between age 18 and 75 years, and had a pain score of at least 40 mm on a 100-mm VAS.	Coexisting epilepsy or a known allergy to gabapentin, significant hepatic or renal insufficiency, severe hematologic disease, a history of illicit drug or alcohol abuse, any serious psychiatric conditon, and other severe pain that could confound the assessment.
Gilron (A) 2005 Canada Efficacy quality: Fair	Diabetic nephropathy or postherpetic neuralgia. Patients with diabetic nephropathy had distal, symmetric, sensory diabetic polyneuropathy as determined on the basis of their medical history and either an unequivocal decrease in response to pinprick, temperature, or vibration in both feet or bilaterally decreased or absent ankle-jerk reflexes. Patients with post-herpetic neuralgia had an	Hypersensitivity to study medications, another painful condition as severe as the diabetic neuropathy or postherpetic neuralgia, recent MI, unstable angina or congestive heart failure, any central neurologic disorder (including seizures), a serious mood disorder, a history of serious drug or alcohol abuse, pregnancy, lactation, and lack of a primary care physician.
Gorson 1999 Efficacy quality: Fair	Painful diabetic neuropathy and 1) diabetes for at least 6 months on a stable dosage of insulin or oral hypoglycemic agent, 2) distal symmetric sensorimotor neuropathy as shown by impaired pin prick, temperature, or vibration sensation in both feet and absent or reduced ankle reflexes, and 3) daily neuropathic palin in the acral extremities, of at least moderate severity, for over 3 months that	Diabetes and chronic renal insufficiency, painful diabetic plexopathy, or lumbosacral polyradiculopathy, peripheral vascular disease, another painful condition, or other cause for neuropathy.
Hahn 2004 Germany Efficacy quality: Fair	Symptoms of painful HIV-associated sensory neuropathy, diagnosed by a neurologist based on history, as well as clinical and neurophysiological examination, gave informed written consent, aged 18 years or over and completed a baseline pain	Pregnant or taking tricyclic or tetracyclic antidepressants, other anticonvulsants, topical capsaicin, mexiletine, alpha-liponic acid, systemic corticosteroids or immune modulators, central analgesics or had received nerve blocks or acupuncture. Alternative causes for neuropathy (i.e.,
Levendoglu	Paraplegic patients with complete traumatic spinal	Severe cognitive impairment, pregnancy, seizure disorder,

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
2004 Turkey Efficacy quality: Fair	cord injury at the thoracic and lumvar level, aged between 20 and 65 years, with neuropathic pain for more than 6 months confirmed by a physician.	use of anticonvulsants and antidepressants, major depression or a score above 16 on the Beck Depression Inventory, and hypersensitivity to gabapentin.
Rice 2001 UK Efficacy quality: Fair	Men and women aged at least 18 years, of any race. Nonpregnant (using barrier or hormonal contraception where appropriate), nonlactating, postmenopausal or surgically sterilized. Pain had to have been present for more than 3 months after the healing of the acute herpes zoster skin rash. Average pain scores of 4 or more, based on an 11-point Likert scale, on the week before commencing study medication.	Failure to respond to previous treatment with gabapentin at >=1200 mg/day, failure to respond to gabapentin at any dose level due to side effects or contraindication to gabapentin treatment.

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
Rowbotham (D 1998 US Efficacy quality: Fair	At least 18 years of age, pain present for more than 3 months after healing of a herpes zoster skin rash; a pain intensity score of at least 40 mm on the 100-mm VAS on the Short-Form McGill Pain Questionnaire at screening and randomization; average daily diary pain score of at least 4 (on a scale of 0-10) during the baseline week, and	Prior treatment with gabapentin or demonstrated hypersensitivity to the drug or its ingredients, neurolytic or neurosurgical therapy for postherpetic neuralgia, immunocompromised state, significant hepatic or renal insufficiency, significant hematological disease, severe pain other than that caused by postherpetic neuralgia, use of experimental drugs or participation in a clinical study within
Serpell 2002 UK and Republic of Ireland Efficacy quality: Fair	Male or female, aged at least 18 years, of any race. Required to have a definite diagnosis of neuropathic pain, made and confirmed by an experienced, practicing chronic pain specialist and based on clinical ground of history, examination, and appropriate investigation of symptoms and	Failure to respond to previous treatment with gabapentin at >=900 mg/day or failure to respond to gabapentin at any dose level due to side effects; known creatinine clearance <=60 ml/min or known renal impairment; clinically significant hepatic, respiratory, hematological illnesses or unstable cardiovascular disease; significant neurological or
Simpson (A) Part 1 2001 US Efficacy quality: Fair	Part 1: Pain attributed to diabetic neuropathy for 3 months to 1.5 years, a diagnosis of diabetes mellitus from 6 months to 17 years, a pain score of at least 40 mm on the 100-mm VAS of the Short-Form McGill Pain Questionnaire, and an average score of 4 on an 11-point Likert scale in daily pain diaries over the next week.□ Part 2: patients from the gabapentin-treated group in Part 1 who had minimal improvement/no change or worse as determined by the Patient Global	Part 1: Severe pain other than that attributed to diabetic neuropathy, amputations other than toes, and renal failure with a creatinine clearance of less than 60 mL/min. The following medications taken within 30 days before screening: tricyclic antidepressants, mexiletine, carbamazepine, phenytoin, valproate, dextromethorphan, opioids, capsaicin, NSAIDs, skeletal muscle relaxants, benzodiazepines, and over the counter centrally acting agents.
Tai 2002 US Efficacy quality: Poor	Traumatic spinal cord injury, age 18 to 85 years, neuropathic pain confirmed by a spinal cord injury physician, and traumatic injury for greater than 30 days. Score of >4 on the 11-point Neuropathic Pain Scale.	Severe cognitive impairment, pregnancy, seizure disorder, major depression or a score >16 on the Beck Depression Inventory, known hypersensitivity to gabapentin, and renal insufficiency with a creatinine clearance less than 60 mL/minute. A score of >16 on Beck Depresion Inventory.

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
Yildirim 2003 Turkey Efficacy quality: Fair	Not reported. Chronic pain and nerve impairment were the main symptoms of the patients under study.	Contraindications to gabapentin treatment, severe depression, severe nephropathy, chronic alcoholism, pregnancy, and spinal surgery; coexistence of another type of pain.
Simpson (A) Part 1 2001 US Efficacy quality: Fair	Part 1: Pain attributed to diabetic neuropathy for 3 months to 1.5 years, a diagnosis of diabetes mellitus from 6 months to 17 years, a pain score of at least 40 mm on the 100-mm VAS of the Short-Form McGill Pain Questionnaire, and an average score of 4 on an 11-point Likert scale in daily pain diaries over the next week.□ Part 2: patients from the gabapentin-treated group in Part 1 who had minimal improvement/no change or worse as determined by the Patient Global	Part 1: Severe pain other than that attributed to diabetic neuropathy, amputations other than toes, and renal failure with a creatinine clearance of less than 60 mL/min. The following medications taken within 30 days before screening: tricyclic antidepressants, mexiletine, carbamazepine, phenytoin, valproate, dextromethorphan, opioids, capsaicin, NSAIDs, skeletal muscle relaxants, benzodiazepines, and over the counter centrally acting agents.
Dworkin 2003 US Efficacy quality: Fair	Men and women of any race who were at least 18 years of age and had postherpetic neuralgia defined as pain present for more than 3 months after healing of a herpes zoster skin rash. Pain at least 40 mm on the 100 mm VAS of the Short-Form	Pregnant or lactating women, serious or unstable medical conditions, other severe pain that might confound assessment or self-evaluation of pain due to post-herpetic neuralgia, or previous neurolytic or neurosurgical therapy for postherpetic neuralgia; patients who had failed to

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
	McGill Pain Questionnaire at baseline and randomization visits, completed at least 4 daily pain diaries and had a minimum mean daily pain rating of 4 on an 11-point numerical pain rating scale during the baseline week preceding randomization; women had to practice an appropriate method of contraception throughout the study, normal chest X-	respond to previous postherpetic neuralgia treatment with gabapentin at dosages >=1200 mg/day; baseline serum creatinine clearance <=30 ml/min, white blood cell count <2500/mm3, neurtrophil count <1500/mm3, or platelet cound <100X103/mm3; participation in any other clinical trial of an investigational drug within 30 days before screening.
Freynhagen 2005 Multiple European Efficacy quality: Fair	Men and non-pregnant, non-lactating women >=18 years of age with a primary diagnosis of painful diabetic peripheral neuropathy (type 1 or 2 diabetes mellitus with HbA1c <=11% and painful, distal, symmetrical, sensorimotor polyneuropathy for >=6 months) or postherpetic neuralgia (pain present for >=3 months after healing of the herpes zoster skin rach). Also required to have a score of >=40 mm (0 mm=no pain, 100 mm=worst possible pain) on the VAS of the Short Form McGill Pain Questionnaire at baseline and randomization.	Any clinically significant or unstable medical or psychiatric condition. Malignancy within the past 2 years (with the exception of basal cell carcinoma) or an anticipated need for surgery during the study; patients with an abnormal ECG, creatinine clearance <60 mL/min, or abnormal hematology; patients who had abused illicit drugs or alcohol within the last 2 years; participated in a previous clinical trial for pregabalin or had taken any investigational drug or agent within 30 days prior to screening. History of hepatitis B or C or HIV infection, neurologic disorders, severe pain unrelated to primary diagnosis of postherpetic neuralgia or diabetic neuropathy, or any potentially sensation-altering skin
Lesser 2004 US Efficacy quality: Fair	Men and women 18 or older with a diagnosis of type 1 or type 2 diabetes mellitus and distal symmetric sensorimotor polyneuropathy for 1 to 5 years. Female patients were required to be nonpregnant, nonlactating, postmenopausal, or surgically sterilized; women at risk of pregnancy were required to be using an appropriate method of contraception. Antidiabetic medication was to be stabilized prior to initiation of the study and held constant throughout the study, provided adequate glucose control was maintained to ensure patient safety. Patients must have completed at least 4 daily pain diaries during the baseline phase, and had to have an average baseline daily pain score of >=4 on a 0 to 10 scale. Score of >=40mm on the VAS of the Short-Form McGill Pain Questionnaire at baseline and randomization visits.	HbA1c levels >11%, clinically significant or unstable hepatic, respiratory, or hematiologic illnesses, unstable cardiovascular disease, or symptomatic peripheral vascular disease. Estimated creatinine clearance of <=60 mL/minute; any conditions that might confound pain assessment (for example, other severe pain or a skin condition in the area affected by neuropathy), patients who had failed to respond to previous treatment with gabapentin at doses >=1200 mg/day for treatment of pain associated with diabetic neuropathy.

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
Richter 2005 US Efficacy quality: Fair	Diabetes and painful distal symmetrical sensorimotor polyneuropathy for 1 to 5 years. Neuropathy was confirmed by history and detailed neurologic examination. Age >=18 years, HbA1c levels <=11%, and the ongoing experience of moderate to severe pain. Poorly controlled pain, including a score of >=40 mm on the VAS of the Short Form-McGill Pain Questionnaire and an average daily pain score of >=4 for 4 or more days during baseline (1 week).	Neurologic disorders unrelated to diabetic neuropathy, any condition that could confound study assesments, recent treatment with any investigational drug, or serious medical problems. Women could not be lactating and were required to have a negative pregnancy test result and to use appropriate contraception if of childbearing potential.
Rosenstock 2004 US Efficacy quality: Fair	Male or female patients of at least 18 years of age with type 1 or 2 diabetes mellitus who reported symmetrical painful symptoms in distal extremities for a period of 1-5 years prior to the study, and whose symptoms were attributable to sensorimotor diabetic peripheral neuropathy; a score of at least 40 mm on the 100-mm VAS of the Short-Form McGill Pain Questionnaire at baseline and randomization visits; completion of daily diaries (a minimum of four) during the week preceding	Pregnancy or lactation; serious or unstable medical conditions, including psychiatric disorders, certain conditions that cold confound evaluation of painful diabetic peripheral neuropathy, in particular, amputations other than toes, non-diabetic neurologic disorders and skin conditions affecting sensation in painful limbs. Baseline serum creatinine clearance <=60 ml.min, or if baseline WBC count was <2500/mm3, neutrophil count was <1500/mm3, or platelet count was <100 x 103/mm3. Failue to respond to previous treatment with gabapentin at doses of >=1200 mg/day for
Sabatowski 2004 Multiple European and Australia	Age 18 years or older, pain present for more than 6 months after healing of herpes zoster rash. Female patients required to be non-pregnant, non-lactating and either postmenopausal, surgically sterilized, or	Active malignancy or any clinically significant respiratory, hematologic, hepatic, or cardiovascular disease. Failure to respond to previous treatment for postherpetic neuralgia with gabapentin at doses >=1200 mg/day or if they had

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
Efficacy quality: Fair	using an appropriate method of contraception. Needed to have completed at least 4 daily pain diaries during the 7 day baseline phase, with an average daily pain score >=4. Score >=40 mm on the 100 mm VAS of the Short-Form McGill Pain Questionnaire at baseline and randomization visits.	undergone neurolytic or neurosurgical therapy for postherpetic neuralgia. Skin condition or severe non-postherpetic neuralgia pain that might compromise evaluation of pain caused by postherpetic neuralgia. Creatinine clearance <=30 ml.min.
Siddall 2006 Australia Efficacy quality: Fair	Men or women at least 18 years of age with a spinal cord injury (paraplegia or tetraplegia) that had been incurred at least 1 year previously, in whom it had been nonprogressive for at least 6 months. Central neuropathic pain as defined by the IASP classification. Pain must have been chronic, having persisted continuously for at least 3 months or with relapses and remission for at least 6 months, and started after sustaining the spinal cord injury. Score of at least 40 mm on the 100 mm VAS of the SF-McGill Pain Questionnaire at both screening and randomization. Inpatients and outpatients eligible.	Severe pain of another origin that could confound the assessment of central neuropathic pain related to spinal cord injury excluded if they were unable to distinguish between neuropathic pain and other pain such as musculoskeletal pain. Creatine clearance <60 mL/minute, breastfeeding or pregnant women.
van Seventer 2006 US and Multiple European Efficacy quality: Fair	Age >=18 years, pain for >3 months after healing of herpes zoster lesions, had a VAS pain score >=40 mm at baseline and at randomization, and had at least 4 daily pain diary entries with a mean daily pain score >=4 prior to randomization.	Malignancy (with the exception of basal cell carcinoma) within the past 2 years, WBC <2500 mm3, neutrophil count <1500 mm3, or platelet count <100 x 103/mm3; clinically significant or unstable hepatic, respiratory, or hematologic illnesses or psychologic conditions; unstable cardiovascular disease; abnormal 12-lead ECG; history of chronic hepatitis B or C, hepatitis B or C within the past 3 months, or HIV infection; immunocompromise, history of alcohol or illicit drug abuse within the last 2 years; or participaton in a clinical trial for an investigational drug or agent within 30 days prior to baseline or participation in a previous trial of pregabalin. Creatinine clearance <=30 mL/min, previous surgical therapy for postherpetic neuralgia, other severe

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
		pain or skin conditions in the affected dermatome that could alter sensation or that might compromise postherpetic neuralgia assessment, or who had used prohibited
Goldstein 2005 US Efficacy quality: Fair	Age 18+; daily pain due to polyneuropathy caused by Type 1 or Type 2 diabetes mellitus which was present for at least 6 months (pain had to begin in the feet with relatively symmetrical onset); minimum score of 4 on the 24-hour Average Pain Score (11-point Likert scale)	DSM-IV criteria for Axis I diagnosis of MDD, depression-partial remission, dysthymic disorder, generalized anxiety disorder, alcohol or eating disorders as determined by the Mini International Neuropsychiatric Interview (MINI); current or historical DSM-IV diagnosis of mania, bipolar disorder, or psychosis as determined by the MINI; pain that could not be clearly differentiated from, or conditions that might interfere with, the assessment of the DPNP, such as peripheral vascular disease (ischemic pain); neurological disroders unrelated to diabetic neuropathy (e.g. phantom limb pain from amputation); skin condition in the area of the neuropathy that could alter sensation; other painful conditions; history of substance abuse or dependence within the past year or had positive urine drug screen, or received treatment within last 30 days; had taken excluded medications within 7 days of baseline; received treatment with a MAOI or fluxetine within 30 days of baseline, or used an opioid within 3 days of baseline
Raskin (B) 2005 and 2006 2005 US Efficacy quality: Fair	Age 18 or older, presented with pain due to bilateral peripheral neuropathy caused by type 1 or type 2 diabetes. Pain had to begin in the feet and with relatively symmetrical onset.; Daily pain must have been present for at least 6 months, and diagnosis was to be confirmed by a score of at least 3 on the Michigan Neuropathy Screening Instrument. Mean score of 4 or greater when assessed for 24-hour average pain severity on the 11-point Likert scale	Pregnant or breastfeeding, prior renal transplant or current renal dialysis, or a serious or unstable illness, symptomatic peripheral vascular disease, or other medical condition or psychological conditions that might compromise participation in the study. Current (within 1 year) DSM-IV Axis I diagnosis of major depressive disorder, dysthymia, generalized anxiety disorder, alcohol, or eating disorders, or diagnosis or previous diagnosis of mania, bipolar disorder, or psychosis. Historical exposure to drugs known to cause

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
	from patient diary prior to randomization, and stable glycemic control.	neuroathy, history of substance abuse or dependence within previous year, positive urine drug screen for any substances of abuse or excluded medication, or history of a medical condition including pernicious anemia and hypothyroidism that could have been responsible for neuropathy, and treatment with a MAO inhibitor or fluoxetine within 30 days of randomization. Severe allergic reactions to multiple medications, and prior participation in a study of duloxetine.
Wernicke 2006 US Efficacy quality: Fair	Age 18 years or older and presented with diabetic peripheral neuropathic pain caused by type 1 or type 2 diabetes. Pain had to begin in the feet and with relatively symmetric onset. Daily pain must have been present for at least 6 months, and the diagnosis was to be confirmed by a score of at least 3 on the Michigan Neuropathy Screening Instrument. Mean score of 4 or greater (between Visit 2 and visit 3 before randomization), when assessed by 24-hour average pain severity on the 11-point Likert scale from the patient diary, stable glycemic control assessed by a physician investigator, and a HbA1c <=12%. Only paitents who were judged to be reliable and had an educational level and degree of understanding that allowed them to communitcate intelligibly were included	Pregnant or breastfeeding, previous renal transplant or current renal dialysis, or serious or unstable cardiovascular, hepatic, renal, respiratory, or hematologic illness, symptomatic peripheral vascular disease, or other medical conditions or psychological conditions that might compromise participation. Current (within 1 year) DSM-IV Axis I diagnosis of major depressive disorder, dysthymia, generalized anxiety disorder, alcohol, or eating disorders, or previous diagnosis or DSM-IV diagnosis of mania, bipolar disorder, or psychosis, historical exposure to drugs knoown to cause neuropathy, history of substance abuse or dependence within the previous year, positive urine drug screen for any substances of abuse or excluded medication, or a history of a medical condition, including pernicious anemia and hypothyroidism or treatment with a MAO inhibitor or fluoxetine within 30 days of randomization; severe allergic reactions to multiple medications and prior participaton in a study of duloxetine.
Rowbotham (C) 2004 US Efficacy quality: Fair	18 years or older with metabolibally stable type 1 or 2 diabetes, with symptomatic peripheral neuropathy due only to diabetes and daily pain consistent with bilateral distal peripheral neuropathy of at least moderate severity for 3 months or longer. At screening and during the baseline period, patients had to have a score of more than 40 mm on the VAS-Pain Intensity (100-mm line scale, 0-100 mm).	Clinically significant psychiatric disorders or a history of recent drug or alcohol abuse, as defined by the DSM-IV; major depressive disorder within 6 months of study initiation; prestudy or baseline score of 13 or greater on the patient-rated Beck Depression Inventory; total score greater than 9 (or greater than 3 on any single item) on the clinician-administered Raskin Depression Scale; history of seizure disorders; clinically significant cardio vascular, renal or hepatic disease; or clinically significant abnormalities in

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
		physical examination results, vital signs, ECG , or laboratory test results at the prestudy evaluations. Use of
Tasmuth 2002 Finland Efficacy quality: Fair	Neuropathic pain after treatment for breast cancer. Pain had to be in the anterior chest wall and/or axilla and/or median upper arm in an area with sensory disturbances. Pain had to be moderate in severity.	Relapses or metastases of the breast cancer, clinically overt cardiac, renal, or hapatic disease, concomitant medication with MAO inhibitors or drugs that are significantly metabolized by the P4502D6 isoenzyme or which inhibit this enzyme.
Yucel 2005 Turkey Efficacy quality: Fair	Aged between 20 and 70 years, having symptoms compatible with neuropathic pain present for a period longer than 6 months, a pain rating of at least 4 on a VAS (0-10) without medical treatment.	Pain other than neuropathic pain, pain presumably of mixed origin, previous hypersensitivity to venlafaxine, myocardial infarction experience in the prior 6 months or currently treated for angina pectoris, alcohol or drug addiction, bipolar depressioin, and psychotic disorder, or receiving major depressive treatment with MAO inhibitors.
Estanislao 2004 US Efficacy quality: Fair	HIV-associated distal symmetric polyneuropathy, with or without exposure to neurotoxic nucleoside analogues. Diagnosis was made by a neurologist based on: presence of pain or paresthesias in both feet for at least 2 weeks, rated on the Gracely pain scale as at least "mild" all the time or "moderate" for	Causes of neuropathy other than HIV, received neurotoxic drugs other than antiretrovirals, had skin lesions within the area of neuropathic pain, or had lidocaine allergy.
Rowbotham (A) 1995 US	Pain present more than 1 month after healing of the zoster skin rash, had a well-defined area of painfully sensitive skin, and were in stable health.	Medical contraindications to topical local anesthetic application, patients who had undergone neurolytic or neurosurgical therapy for postherpetic neuralgia.

Evidence Table 3. Characteristics of RCTs of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Eligibility	Exclusion
Efficacy quality: Fair		
Galer (A) 2002 US Efficacy quality: Poor	Established torso postherpetic neuralgia for at least 1 month and the presence of allodynia on physical examination.	Not reported.
Galer (B) 1999 US	All patients had been successfully treated with lidocaine patches on a regular basis for at least 1 month. Subjects were recruited from postherpetic neuralgia patients who were enrolled in the open-	Patients who reported they did not experience pain before patch application.
Meier 2003 Germany and Switzerland	Outpatients suffering from chronic peripheral focal neuropathic pain syndromes, defined as damage to or dysfunction of the peripheral nervous system with positive spontaneous or evoked sensory signs with mechanical allodynia in the territories of	Another form of pain with greater or similar intensity, previous nerve blockade or neurosurgery, or patients taking topical products for pain relief or with ascertained hypersensitivity to lidocaine or to amide-type anesthetics. Injuries, inflammation, or insufficient wound healing of the
Rowbotham (B) 1996 US	Postherpetic neuralgia, defined as pain present more than 1 month after healing of the skin rash, and had a well-defined area of painfully sensitive (allodynic) skin on the torso or limbs; in stable	Medical contraindications to topical local anesthetic application, neurolytic or neurosurgical therapy for postherpetic neuralgia.

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Backonja 1999 US Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 3600 mg N=84	Average pain, 11-point Likert scale (0-10) Mean score: 3.9 at 8 weeks (p<0.001)
			Average pain, SF-MPQ VAS (0-100) Mean score: 36.9 at 8 weeks (p<0.001)
			Average pain, Total SF McGill Pain Questionnaire (SF-MPQ) Mean score: 10.9 at 8 weeks (p<0.001)
			Pain intensity, SF-MPQ Present Pain Intensity (0-5) Mean score: 1.2 at 8 weeks (p<0.001)
		Placebo N=81	Average pain, 11-point Likert scale (0-10) Mean score: 5.1 at 8 weeks
			Average pain, SF-MPQ VAS (0-100) Mean score: 53.8 at 8 weeks
			Average pain, Total SF McGill Pain Questionnaire (SF-MPQ) Mean score: 16.8 at 8 weeks
			Pain intensity, SF-MPQ Present Pain Intensity (0-5) Mean score: 1.8 at 8 weeks
Bone 2002 UK and Ireland Efficacy quality: Fair	RCT Crossover Single Center	Gabapentin 2400 mg N=10	Pain intensity, Categorical (0-3; none, mild, moderate, severe) Mean score: 1.45 at 6 weeks (p=0.80) 95% CI: 0.83, 2.07
			Pain intensity, VAS (0-100) Mean score: 2.9 at 6 weeks (p=0.025) 95% CI: 1.54, 4.26
		Placebo N=9	Pain intensity, Categorical (0-3; none, mild, moderate, severe) Mean score: 1.6 at 6 weeks 95% CI: 0.82, 2.38
			Pain intensity, VAS (0-100) Mean score: 5.1 at 6 weeks 95% CI: 3.66, 6.54
Gilron (A) 2005 Canada Efficacy quality: FAIR	RCT Crossover Single Center	Gabapentin 3200 mg N=48	Average pain intensity (0-10), 10- cm VAS Mean score: 3.5 at 5 weeks (p=NS) 95% CI: 2.72, 4.28
			Average pain, Short-Form McGill Pain Questionnaire Total (0-45) Mean score: 10.7 at 5 weeks (p<0.05) 95% CI: 8.15, 13.25
			Interference with activities, Brief Pain Inventory (General activity, 0-10) Mean score: 3.0 at 5 weeks (p<0.05) 95% CI: 2.22, 3.78
			Pain intensity, Present pain intensity (0-3) Mean score: 1.64 at 5 weeks (p<0.05) 95% CI: 1.33, 1.95
		Lorazepam 1.6 mg N=44	Average pain intensity (0-10), 10- cm VAS Mean score: 3.9 at 5 weeks 95% CI: 3.12, 4.68
			Average pain, Short-Form McGill Pain Questionnaire Total (0-45) Mean score: 14.4 at 5 weeks 95% CI: 11.85, 16.95
			Interference with activities, Brief Pain Inventory (General activity, 0-10) Mean score: 4.5 at 5 weeks 95% CI: 3.72, 5.28

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain intensity, Present pain intensity (0-3) Mean score: 2.07 at 5 weeks 95% CI: 1.76, 2.38
Gorson 1999 Efficacy quality: FAIR	RCT Crossover	Gabapentin 900 mg N=19	24-hour average pain score, VAS (0-10) Mean score: 1.8 at 6 weeks (p=0.42) 95% CI: 1.58, 2.02
			Pain intensity, Present pain intensity (0-10) Mean score: 1.2 at 6 weeks (p=0.20) 95% CI: 1.02, 1.38
			Pain relief, Moderate or excellent vs none or mild % of patients: 89.5% at 6 weeks (p=0.11)
			Pain, McGill Pain Questionnaire Mean score: 8.9 at 6 weeks (p=0.03) 95% CI: 7.87, 9.93
		Placebo N=21	24-hour average pain score, VAS (0-10) Mean score: 1.4 at 6 weeks 95% CI: 1.27, 1.53
			Pain intensity, Present pain intensity (0-10) Mean score: 0.3 at 6 weeks 95% CI: 0.09, 0.51
			Pain relief, Moderate or excellent vs none or mild % of patients: 42.9% at 6 weeks
			Pain, McGill Pain Questionnaire Mean score: 2.2 at 6 weeks 95% CI: 1.26, 3.14
Hahn 2004 Germany Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 1200-2400 mg N=15	Pain, VAS (0-10) % change from baseline: -44.1% at 4 weeks (p=NS)
			Pain, VAS (0-10) Median score: 2.85 at 4 weeks (pNRvsplacebo)
		Placebo N=11	Pain, VAS (0-10) % change from baseline: -29.8% at 4 weeks
			Pain, VAS (0-10) Median score: 3.3 at 4 weeks
Levendoglu 2004 Turkey Efficacy quality: Fair	RCT Crossover	Gabapentin 3600 mg N=20	Pain intensity, Neuropathic Pain Scale (NPS) Pain intensity (0-10) Mean score: 4.8 at 4 weeks (p=0.000) 95% CI: 4.32, 5.28
			Pain intensity, NPS Pain Intensity (0-10) Mean score: 3.2 at 8 weeks (p=0.000) 95% CI: 2.67, 3.73
			Pain, NPS cold (0-10) Mean score: 0.7 at 4 weeks (p=NS) 95% CI: -0.13, 1.53
			Pain, NPS cold (0-10) Mean score: 0.8 at 8 weeks (p=NS) 95% CI: -0.03, 1.63
			Pain, NPS deep (0-10) Mean score: 3.5 at 8 weeks (p=0.000) 95% CI: 2.80, 4.20
			Pain, NPS deep (0-10) Mean score: 4.5 at 4 weeks (p=0.001) 95% CI: 3.71, 5.29
			Pain, NPS dull (0-10) Mean score: 0.3 at 8 weeks (p=NS) 95% CI: -0.23, 0.83
			Pain, NPS dull (0-10) Mean score: 0.4 at 4 weeks (p=NS) 95% CI: -0.13, 0.93

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain, NPS hot (0-10) Mean score: 2.7 at 8 weeks (p=0.001) 95% CI: 1.82, 3.58
			Pain, NPS hot (0-10) Mean score: 3.9 at 4 weeks (p=0.001) 95% CI: 2.67, 5.13
			Pain, NPS itchy (0-10) Mean score: 0.0 at 4 weeks (p=NS) 95% CI: 0.00, 0.00
			Pain, NPS itchy (0-10) Mean score: 0.0 at 8 weeks (p=NS) 95% CI: 0.00, 0.00
			Pain, NPS sensitive (0-10) Mean score: 0.5 at 8 weeks (p=NS) 95% CI: -0.11, 1.11
			Pain, NPS sensitive (0-10) Mean score: 0.6 at 4 weeks (p=NS) 95% CI: -0.06, 1.26
			Pain, NPS sharp (0-10) Mean score: 3.0 at 8 weeks (p=0.000) 95% CI: 2.34, 3.66
			Pain, NPS sharp (0-10) Mean score: 4.6 at 4 weeks (p=0.000) 95% CI: 3.77, 5.43
			Pain, NPS surface pain (0-10) Mean score: 2.8 at 8 weeks (p=0.001) 95% CI: 2.58, 3.02
			Pain, NPS surface pain (0-10) Mean score: 3.9 at 4 weeks (p=0.001) 95% CI: 2.72, 5.08
			Pain, NPS unpleasantness (0-10) Mean score: 3.6 at 8 weeks (p=0.000) 95% CI: 3.03, 4.17
			Pain, NPS unpleasantness (0-10) Mean score: 4.8 at 4 weeks (p=0.000) 95% CI: 4.36, 5.24
		Placebo N=20	Pain intensity, Neuropathic Pain Scale (NPS) Pain intensity (0-10) Mean score: 7.8 at 4 weeks 95% CI: 7.49, 8.11
			Pain intensity, NPS Pain Intensity (0-10) Mean score: 7.4 at 8 weeks 95% CI: 7.09, 7.71
			Pain, NPS cold (0-10) Mean score: 0.8 at 8 weeks 95% CI: -0.12, 1.72
			Pain, NPS cold (0-10) Mean score: 0.9 at 4 weeks 95% CI: -0.11, 1.91
			Pain, NPS deep (0-10) Mean score: 6.2 at 8 weeks 95% CI: 5.19, 7.21
			Pain, NPS deep (0-10) Mean score: 6.3 at 4 weeks 95% CI: 5.29, 7.31
			Pain, NPS dull (0-10) Mean score: 0.6 at 4 weeks 95% CI: -0.19, 1.39
			Pain, NPS dull (0-10) Mean score: 0.6 at 8 weeks 95% CI: -0.19, 1.39
			Pain, NPS hot (0-10) Mean score: 5.2 at 4 weeks 95% CI: 3.62, 6.78

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain, NPS hot (0-10) Mean score: 5.2 at 8 weeks 95% CI: 3.62, 6.78
			Pain, NPS itchy (0-10) Mean score: 0.0 at 4 weeks 95% CI: 0.00, 0.00
			Pain, NPS itchy (0-10) Mean score: 0.0 at 8 weeks 95% CI: 0.00, 0.00
			Pain, NPS sensitive (0-10) Mean score: 0.8 at 8 weeks 95% CI: -0.08, 1.68
			Pain, NPS sensitive (0-10) Mean score: 0.9 at 4 weeks 95% CI: 0.02, 1.78
			Pain, NPS sharp (0-10) Mean score: 6.2 at 8 weeks 95% CI: 5.10, 7.30
			Pain, NPS sharp (0-10) Mean score: 6.4 at 4 weeks 95% CI: 5.26, 7.54
			Pain, NPS surface pain (0-10) Mean score: 5.3 at 4 weeks 95% CI: 3.77, 6.83
			Pain, NPS surface pain (0-10) Mean score: 5.5 at 8 weeks 95% CI: 3.92, 7.08
			Pain, NPS unpleasantness (0-10) Mean score: 7.3 at 8 weeks 95% CI: 6.77, 7.83
			Pain, NPS unpleasantness (0-10) Mean score: 7.6 at 4 weeks 95% CI: 7.07, 8.13
Rice 2001 UK Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 1800 mg N=115	24-hour average pain score, Likert scale (0-10) Mean score: 4.3 at 7 weeks (p<0.01)
			Improvement, Very much or much improved % of patients: 41% at 7 weeks (p=0.003)
			Pain intensity, SF McGill Pain Present pain intensity (0-5) Mean score: 1.9 at 7 weeks (p=NS) 95% CI: 1.70, 2.10
			Pain relief, 50% or greater reduction in mean pain score % of patients: 32% at 7 weeks (p=0.001)
			Pain, SF McGill Pain Score Total (0-45) Mean score: 11.9 at 7 weeks (p<0.05) 95% CI: 10.29, 13.51
			Pain, SF McGill Pain VAS (0-100) Mean score: 47 at 7 weeks (p=NS) 95% CI: 41.88, 52.12
		Gabapentin 2400 mg N=108	24-hour average pain score, Likert scale (0-10) Mean score: 4.2 at 7 weeks (p<0.01)
			Improvement, Very much or much improved % of patients: 43% at 7 weeks (p=0.005)
			Pain intensity, SF McGill Pain Present pain intensity (0-5) Mean score: 1.9 at 7 weeks (p=NS) 95% CI: 1.67, 2.13
			Pain relief, 50% or greater reduction in mean pain score % of patients: 34% at 7 weeks (p=0.001)

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain, SF McGill Pain Score Total (0-45) Mean score: 12.5 at 7 weeks (p<0.05) 95% CI: 10.93, 14.07
			Pain, SF McGill Pain VAS (0-100) Mean score: 46 at 7 weeks (p<0.05) 95% CI: 41.28, 50.72
		Placebo N=111	24-hour average pain score, Likert scale (0-10) Mean score: 5.3 at 7 weeks
			Improvement, Very much or much improved % of patients: 23% at 7 weeks
			Pain intensity, SF McGill Pain Present pain intensity (0-5) Mean score: 2.0 at 7 weeks 95% CI: 1.76, 2.24
			Pain relief, 50% or greater reduction in mean pain score % of patients: 14% at 7 weeks
			Pain, SF McGill Pain Score Total (0-45) Mean score: 13.7 at 7 weeks 95% CI: 11.93, 15.47
			Pain, SF McGill Pain VAS (0-100) Mean score: 54 at 7 weeks 95% CI: 49.16, 58.84
Rowbotham (D) 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 3600 mg N=113	Average daily pain, Likert scale (0-10) Mean score: 4.2 at 8 weeks (p<0.001) 95% CI: 3.78, 4.62
			Global Impression of Change, Moderately or much improved % of patients: 43.2% at 8 weeks (p=NR)
			Pain, SF McGill Pain Questionnaire Total Mean score: 11.4 at 8 weeks (p<0.001) 95% CI: 9.69, 13.11
		Placebo N=116	Average daily pain, Likert scale (0-10) Mean score: 6.0 at 8 weeks 95% CI: 5.56, 6.44
			Global Impression of Change, Moderately or much improved % of patients: 12.1% at 8 weeks
			Pain, SF McGill Pain Questionnaire Total Mean score: 16.8 at 8 weeks 95% CI: 14.83, 18.77
Serpell 2002 UK and Republic of Ireland Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin N=153	Average daily pain score, Likert scale (0-10) Mean score: 5.6 at 8 weeks (p=0.048)
			Global Impression of Change, Very much or much improved % of patients: 34% at 8 weeks (p=0.03)
			Response, >50% reduction in mean pain score from baseline % of patients: 21% at 8 weeks (p=0.16)
		Placebo N=152	Average daily pain score, Likert scale (0-10) Mean score: 6.3 at 8 weeks
			Global Impression of Change, Very much or much improved % of patients: 16% at 8 weeks
			Response, >50% reduction in mean pain score from baseline % of patients: 14% at 8 weeks

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Simpson (A) Part 1□ 2001□ US□ □ Efficacy quality: FAIR	RCT Parallel Single Center	Gabapentin 900-2700 mg N=30	Average pain intensity, SF-MPQ Present Pain Intensity□ Mean score: data NR at 8 weeks (pNR(significant))
			Average pain, 11-point Likert scale (0-10)□ Mean score: 4.0 at 8 weeks (p<0.01)
			Average pain, SF-MPQ Total□ Mean score: data NR at 8 weeks (pNR(significant))
			Average pain, SF-MPQ VAS (0-100)□ Mean score: data NR at 8 weeks (pNR(significant))
			Global Impression of Change, Much/moderately improved□ % of patients: data NR at 8 weeks (p=NR)
		Placebo N=30	Average pain intensity, SF-MPQ Present Pain Intensity□ Mean score: data NR at 8 weeks
			Average pain, 11-point Likert scale (0-10)□ Mean score: 6.0 at 8 weeks
			Average pain, SF-MPQ Total□ Mean score: data NR at 8 weeks
			Average pain, SF-MPQ VAS (0-100)□ Mean score: data NR at 8 weeks
			Global Impression of Change, Much/moderately improved□ % of patients: data NR at 8 weeks
Tai 2002 US Efficacy quality: Poor	RCT Crossover Single Center	Gabapentin up to 1800 mg daily N=7	Average pain intensity (0-10), 0-10 (NPS cold pain)□ Mean score: 1.59 at 4 weeks (p=NS)
			Average pain intensity (0-10), 0-10 (NPS deep pain)□ Mean score: 4.30 at 4 weeks (p=NS)
			Average pain intensity (0-10), 0-10 (NPS dull pain)□ Mean score: 1.67 at 4 weeks (p=NS)
			Average pain intensity (0-10), 0-10 (NPS hot pain)□ Mean score: 1.11 at 4 weeks (p=0.065)
			Average pain intensity (0-10), 0-10 (NPS itchy pain)□ Mean score: 0.01 at 4 weeks (p=NS)
			Average pain intensity (0-10), 0-10 (NPS sensitive pain)□ Mean score: 1.46 at 4 weeks (p=NS)
			Average pain intensity (0-10), 0-10 (NPS sharp pain)□ Mean score: 1.37 at 4 weeks (p=NS)
			Average pain intensity (0-10), 0-10 (NPS surface pain)□ Mean score: 1.01 at 4 weeks (p=NS)
			Average pain intensity (0-10), 0-10 (NPS unpleasant pain)□ Mean score: 3.60 at 4 weeks (p=0.028)
			Average pain intensity (0-10), Neuropathic Pain Scale (NPS) 0-10 (intense)□ Mean score: 3.7 at 4 weeks (p=0.094)
		Placebo N=7	Average pain intensity (0-10), 0-10 (NPS cold pain)□ Mean score: 1.67 at 4 weeks
			Average pain intensity (0-10), 0-10 (NPS deep pain)□ Mean score: 4.50 at 4 weeks

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Average pain intensity (0-10), 0-10 (NPS dull pain) Mean score: 1.61 at 4 weeks
			Average pain intensity (0-10), 0-10 (NPS hot pain) Mean score: 4.54 at 4 weeks
			Average pain intensity (0-10), 0-10 (NPS itchy pain) Mean score: 0.03 at 4 weeks
			Average pain intensity (0-10), 0-10 (NPS sensitive pain) Mean score: 1.76 at 4 weeks
			Average pain intensity (0-10), 0-10 (NPS sharp pain) Mean score: 2.01 at 4 weeks
			Average pain intensity (0-10), 0-10 (NPS surface pain) Mean score: 2.00 at 4 weeks
			Average pain intensity (0-10), 0-10 (NPS unpleasant pain) Mean score: 5.33 at 4 weeks
			Average pain intensity (0-10), Neuropathic Pain Scale (NPS) 0-10 (intense) Mean score: 5.29 at 4 weeks
Yildirim 2003 Turkey Efficacy quality: FAIR	RCT Parallel	Gabapentin 900 mg-3600 mg N=25	Pain at rest, 0-4 (none, mild, moderate, severe) Mean score: 0.56 at 2 months (p<0.001) 95% CI: 0.33, 0.79
			Pain at rest, 0-4 (none, mild, moderate, severe) Mean score: 0.73 at 1 month (p<0.05) 95% CI: 0.44, 1.02
		Placebo N=25	Pain at rest, 0-4 (none, mild, moderate, severe) Mean score: 1.36 at 2 months 95% CI: 1.13, 1.59
			Pain at rest, 0-4 (none, mild, moderate, severe) Mean score: 1.47 at 1 month 95% CI: 1.20, 1.74
Simpson (A) Part 1 2001 US Efficacy quality: FAIR	RCT Parallel Single Center	Gabapentin 900-2700 mg N=30	Average pain intensity, SF-MPQ Present Pain Intensity Mean score: data NR at 8 weeks (pNR(significant))
			Average pain, 11-point Likert scale (0-10) Mean score: 4.0 at 8 weeks (p<0.01)
			Average pain, SF-MPQ Total Mean score: data NR at 8 weeks (pNR(significant))
			Average pain, SF-MPQ VAS (0-100) Mean score: data NR at 8 weeks (pNR(significant))
			Global Impression of Change, Much/moderately improved % of patients: data NR at 8 weeks (p=NR)
		Placebo N=30	Average pain intensity, SF-MPQ Present Pain Intensity Mean score: data NR at 8 weeks
			Average pain, 11-point Likert scale (0-10) Mean score: 6.0 at 8 weeks
			Average pain, SF-MPQ Total Mean score: data NR at 8 weeks
			Average pain, SF-MPQ VAS (0-100) Mean score: data NR at 8 weeks

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Global Impression of Change, Much/moderately improved % of patients: data NR at 8 weeks
Dworkin 2003 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 300-600 mg N=89	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.58 at 8 weeks (p=0.127) 95% CI: 1.34, 1.82
			Average pain, 11-point scale (0-10) Least squares mean: 3.60 at 8 weeks (p=0.0001) 95% CI: 3.13, 4.07
			Average pain, SF-MPQ Total (0-45) Least squares mean: 9.85 at 8 weeks (p=0.0002) 95% CI: 7.99, 11.71
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 38.68 at 8 weeks (p=0.0001) 95% CI: 33.00, 44.36
			Response, >=30% decrease in pain % of patients: 63% at 8 weeks (p=0.001)
			Response, >=50% decrease in pain % of patients: 50% at 8 weeks (pNR(significant))
		Placebo N=84	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.98 at 8 weeks 95% CI: 1.74, 2.22
			Average pain, 11-point scale (0-10) Least squares mean: 5.29 at 8 weeks 95% CI: 4.82, 5.76
			Average pain, SF-MPQ Total (0-45) Least squares mean: 14.72 at 8 weeks 95% CI: 12.84, 16.60
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 56.30 at 8 weeks 95% CI: 50.56, 62.04
			Response, >=30% decrease in pain % of patients: 25% at 8 weeks
			Response, >=50% decrease in pain % of patients: 20% at 8 weeks
Freynhagen 2005 Multiple European Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150-600 mg N=141	Average pain, 11-point scale (0-10) Mean score: Reported graphically only at 12 weeks (p=NR)
			Global Impression of Improvement, "much improved" or "very much improved" % of patients: 52.0% at 12 weeks (p<0.01)
			Response, >=30% reduction in pain % of patients: 59.0% at 12 weeks (p=0.003)
			Response, >=50% reduction in pain % of patients: 48.2% at 12 weeks (p<0.001)
		Pregabalin 600 mg N=132	Average pain, 11-point scale (0-10) Mean score: Reported graphically only at 12 weeks (p=NR)
			Global Impression of Improvement, "much improved" or "very much improved" % of patients: 53.6% at 12 weeks (p<0.01)
			Response, >=30% reduction in pain % of patients: 66.4% at 12 weeks (p<0.001)
			Response, >=50% reduction in pain % of patients: 52.3% at 12 weeks (p<0.001)

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
		Placebo N=65	Average pain, 11-point scale (0-10) Mean score: Reported graphically only at 12 weeks
			Global Impression of Improvement, "much improved" or "very much improved" % of patients: 30.5% at 12 weeks
			Response, >=30% reduction in pain % of patients: 37.1% at 12 weeks
			Response, >=50% reduction in pain % of patients: 24.2% at 12 weeks
Lesser 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 75 mg N=77	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.67 at 5 weeks (p=0.4286) 95% CI: 1.45, 1.89
			Average pain, SF-MPQ Total (0-45) Least squares mean: 15.06 at 5 weeks (p=0.9966) 95% CI: 13.22, 16.90
			Average pain, SF-MPQ VAS (0-40) Least squares mean: 49.70 at 5 weeks (p=0.2947) 95% CI: 44.33, 55.07
			Average pain, VAS (0-10) Least squares mean: 4.91 at 5 weeks (p=0.6267) 95% CI: 4.44, 5.38
			Global impression of improvement, "much improved" or "very much improved" % of patients: data NR at 5 weeks (p=NR)
			Response, >=50% reduction in pain % of patients: data NR at 5 weeks
		Pregabalin 300 mg N=81	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.20 at 5 weeks (p=0.0001) 95% CI: 0.98, 1.42
			Average pain, SF-MPQ Total (0-45) Least squares mean: 10.17 at 5 weeks (p=0.0001) 95% CI: 8.37, 11.97
			Average pain, SF-MPQ VAS (0-40) Least squares mean: 37.40 at 5 weeks (p=0.0001) 95% CI: 32.13, 42.67
			Average pain, VAS (0-10) Least squares mean: 3.80 at 5 weeks (p=0.0001) 95% CI: 3.35, 4.25
			Global impression of improvement, "much improved" or "very much improved" % of patients: 55.7% at 5 weeks (p=0.001)
			Response, >=50% reduction in pain % of patients: 46% at 5 weeks (pNR(significant))
		Pregabalin 600 mg N=82	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.18 at 5 weeks (p=0.0001) 95% CI: 0.96, 1.40
			Average pain, SF-MPQ Total (0-45) Least squares mean: 9.88 at 5 weeks (p=0.0001) 95% CI: 8.10, 11.66

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Average pain, SF-MPQ VAS (0-40) Least squares mean: 34.48 at 5 weeks (p=0.0001) 95% CI: 29.29, 39.67
			Average pain, VAS (0-10) Least squares mean: 3.60 at 5 weeks (p=0.0001) 95% CI: 3.15, 4.05
			Global impression of improvement, "much improved" or "very much improved" % of patients: 69.2% at 5 weeks (p=0.001)
			Response, >=50% reduction in pain % of patients: 48% at 5 weeks (pNR(significant))
		Placebo N=97	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.79 at 5 weeks 95% CI: 1.59, 1.99
			Average pain, SF-MPQ Total (0-45) Least squares mean: 15.06 at 5 weeks 95% CI: 13.41, 16.71
			Average pain, SF-MPQ VAS (0-40) Least squares mean: 53.49 at 5 weeks 95% CI: 48.67, 58.31
			Average pain, VAS (0-10) Least squares mean: 5.06 at 5 weeks 95% CI: 4.65, 5.47
			Global impression of improvement, "much improved" or "very much improved" % of patients: 24.2% at 5 weeks
			Response, >=50% reduction in pain % of patients: 18% at 5 weeks
Richter 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=79	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.78 at 6 weeks (p=0.2836) 95% CI: 1.54, 2.02
			Average pain, 11-point numeric rating scale (0-10) Least squares mean: 5.11 at 6 weeks (p=0.1763) 95% CI: 4.64, 5.58
			Average pain, SF-MPQ Total Least squares mean: 15.48 at 6 weeks (p=0.0651) 95% CI: 13.54, 17.42
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 53.27 at 6 weeks (p=0.2058) 95% CI: 47.88, 58.66
			Global impression of change, "much improved" or "very much improved" % of patients: reported graphically only at 6 weeks (p=NS)
		Pregabalin 600 mg N=82	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.30 at 6 weeks (p=0.0002) 95% CI: 1.06, 1.54
			Average pain, 11-point numeric rating scale (0-10) Least squares mean: 4.29 at 6 weeks (p=0.0002) 95% CI: 3.78, 4.80

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Average pain, SF-MPQ Total Least squares mean: 12.14 at 6 weeks (p=0.0002) 95% CI: 10.24, 14.04
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 43.38 at 6 weeks (p=0.0002) 95% CI: 38.09, 48.67
			Global impression of change, "much improved" or "very much improved" % of patients: reported graphically only at 6 weeks (p=0.002)
		Placebo N=85	Average pain intensity (0-10), SF-MPQ Present Pain Intensity (0-5) Least squares mean: 1.96 at 6 weeks 95% CI: 1.74, 2.18
			Average pain, 11-point numeric rating scale (0-10) Least squares mean: 5.55 at 6 weeks 95% CI: 5.10, 6.00
			Average pain, SF-MPQ Total Least squares mean: 17.97 at 6 weeks 95% CI: 16.09, 19.85
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 58.05 at 6 weeks 95% CI: 52.80, 63.30
			Global impression of change, "much improved" or "very much improved" % of patients: reported graphically only at 6 weeks
Rosenstock 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 300 mg N=76	Average pain intensity (0-10), SF-MPQ Present Pain Intensify (0-5) Least squares mean: 1.42 at 8 weeks (p=0.0364) 95% CI: 1.17, 1.67
			Average pain, 11-point numeric rating scale (0-10) Least squares mean: 3.99 at 8 weeks (p=0.0001) 95% CI: 3.48, 4.50
			Average pain, SF-MPQ Total score Least squares mean: 10.51 at 8 weeks (p=0.0033) 95% CI: 8.43, 12.59
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 40.83 at 8 weeks (p=0.0002) 95% CI: 34.87, 46.79
			Global Impression of Change, Improved (items not specified) % of patients: 64.5% at 8 weeks (p=0.001)
		Placebo N=70	Average pain intensity (0-10), SF-MPQ Present Pain Intensify (0-5) Least squares mean: 1.79 at 8 weeks 95% CI: 1.54, 2.04
			Average pain, 11-point numeric rating scale (0-10) Least squares mean: 5.46 at 8 weeks 95% CI: 4.91, 6.01
			Average pain, SF-MPQ Total score Least squares mean: 14.92 at 8 weeks 95% CI: 12.71, 17.13

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 57.02 at 8 weeks 95% CI: 50.73, 63.31
			Global Impression of Change, Improved (items not specified) % of patients: 38.6% at 8 weeks
Sabatowski 2004 Multiple European and Australia Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=81	Average pain, 11-point numeric scale (0-10) Least squares mean: 5.14 at 8 weeks (p=0.0002) 95% CI: 4.71, 5.57
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 52.03 at 8 weeks (p=0.0060) 95% CI: 47.01, 57.05
			Global Impression of Change, "much improved" or "very much improved" % of patients: 31% at 8 weeks (p=0.064)
			Response, >=50% reduction in pain % of patients: 26% at 8 weeks (p=0.006)
		Pregabalin 300 mg N=76	Average pain, 11-point numeric scale (0-10) Least squares mean: 4.76 at 8 weeks (p=0.0001) 95% CI: 4.31, 5.21
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 48.41 at 8 weeks (p=0.0003) 95% CI: 43.26, 53.56
			Global Impression of Change, "much improved" or "very much improved" % of patients: 40% at 8 weeks (p=0.002)
			Response, >=50% reduction in pain % of patients: 28% at 8 weeks (p=0.003)
		Placebo N=81	Average pain, 11-point numeric scale (0-10) Least squares mean: 6.33 at 8 weeks 95% CI: 5.90, 6.76
			Average pain, SF-MPQ VAS (100 mm) Least squares mean: 62.05 at 8 weeks 95% CI: 57.03, 67.07
			Global Impression of Change, "much improved" or "very much improved" % of patients: 14% at 8 weeks
			Response, >=50% reduction in pain % of patients: 10% at 8 weeks
van Seventer 2006 US and Multiple European Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=87	Average pain, 11-point numerical rating scale (0-10) Least squares mean: 5.26 at 13 weeks (p=0.0077) 95% CI: 4.79, 5.73
			Global Impression of Change, "much improved" or "very much improved" % of patients: 22.6% at 13 weeks (p=NR)
			Response, >=30% reduction in pain % of patients: 39.1% at 13 weeks (p<=0.001)
			Response, >=50% reduction in pain % of patients: 26.4% at 13 weeks (p=0.001)
		Pregabalin 300 mg N=98	Average pain, 11-point numerical rating scale (0-10) Least squares mean: 5.07 at 13 weeks (p=0.0016) 95% CI: 4.62, 5.52
			Global Impression of Change, "much improved" or "very much improved" % of patients: 27.2% at 13 weeks (p=NR)

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Response, >=30% reduction in pain % of patients: 40.8% at 13 weeks (p<=0.001)
			Response, >=50% reduction in pain % of patients: 26.5% at 13 weeks (p=0.001)
		Pregabalin 300-600 mg N=90	Average pain, 11-point numerical rating scale (0-10) Least squares mean: 4.35 at 13 weeks (p=0.0003) 95% CI: 3.88, 4.82
			Global Impression of Change, "much improved" or "very much improved" % of patients: 36.5% at 13 weeks (p=NR)
			Response, >=30% reduction in pain % of patients: 52.3% at 13 weeks (p<=0.001)
			Response, >=50% reduction in pain % of patients: 37.5% at 13 weeks (p=0.001)
		Placebo N=93	Average pain, 11-point numerical rating scale (0-10) Least squares mean: 6.14 at 13 weeks 95% CI: 5.69, 6.59
			Global Impression of Change, "much improved" or "very much improved" % of patients: 16.2% at 13 weeks
			Response, >=30% reduction in pain % of patients: 17.2% at 13 weeks
			Response, >=50% reduction in pain % of patients: 7.5% at 13 weeks
Goldstein 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 20 mg daily N=115	24h worst pain score, 11-point Likert scale (0-10) Mean change from baseline: -2.78 at 12 weeks (p=NS) 95% CI: -3.23, -2.33
			24-hour average pain score, 11-point Likert scale (0-10) Mean change from baseline: -2.36 at 12 weeks (p=NS) 95% CI: -2.77, -1.95
			Average pain severity, BPI Mean change from baseline: -2.25 at 12 weeks (p=NS) 95% CI: -2.66, -1.84
			Improvement, PGI-Improvement Mean change from baseline: 2.68 at 12 weeks (p=NS) 95% CI: 2.44, 2.92
			Night pain score, 11-point Likert scale (0-10) Mean change from baseline: -2.48 at 12 weeks (p=NS) 95% CI: -2.91, -2.05
			Severity of pain, SF McGill Pain Questionnaire Mean change from baseline: -7.23 at 12 weeks (p≤0.05) 95% CI: -8.54, -5.92
		Duloxetine 60 mg daily N=114	24h worst pain score, 11-point Likert scale (0-10) Mean change from baseline: -3.31 at 12 weeks (p≤0.05) 95% CI: -3.78, -2.84

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			24-hour average pain score, 11-point Likert scale (0-10) Mean change from baseline: -2.89 at 12 weeks (p=NS) 95% CI: -3.32, -2.46
			Average pain severity, BPI Mean change from baseline: -2.81 at 12 weeks (p≤0.01) 95% CI: -3.22, -2.40
			Improvement, PGI-Improvement Mean change from baseline: 2.21 at 12 weeks (p≤0.001) 95% CI: 1.97, 2.45
			Night pain score, 11-point Likert scale (0-10) Mean change from baseline: -2.91 at 12 weeks (p≤0.05) 95% CI: -3.36, -2.46
			Severity of pain, SF McGill Pain Questionnaire Total score Mean change from baseline: -8.25 at 12 weeks (p≤0.001) 95% CI: -9.52, -6.98
		Duloxetine 60 mg BID Total daily dose: 120 mg/d N=113	24h worst pain score, 11-point Likert scale (0-10) Mean change from baseline: -3.72 at 12 weeks (p≤0.001) 95% CI: -4.19, -3.25
			24-hour average pain score, 11-point Likert scale (0-10) Mean change from baseline: -3.24 at 12 weeks (p=NS) 95% CI: -3.69, -2.79
			Average pain severity, BPI Mean change from baseline: -3.07 at 12 weeks (p≤0.001) 95% CI: -3.50, -2.64
			Improvement, PGI-Improvement Mean change from baseline: 2.24 at 12 weeks (p≤0.01) 95% CI: 2.00, 2.48
			Night pain score, 11-point Likert scale (0-10) Mean change from baseline: -3.45 at 12 weeks (p≤0.001) 95% CI: -3.92, -2.98
			Severity of pain, SF McGill Pain Questionnaire Total score Mean change from baseline: -9.18 at 12 weeks (p≤0.001) 95% CI: -10.43, -7.93
		Placebo N=115	24h worst pain score, 11-point Likert scale (0-10) Mean change from baseline: -2.09 at 12 weeks 95% CI: -2.56, -1.62
			24-hour average pain score, 11-point Likert scale (0-10) Mean change from baseline: -1.91 at 12 weeks 95% CI: -2.34, -1.48

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Average pain severity, BPI□ Mean change from baseline: -2.04 at 12 weeks□ 95% CI: -2.45, -1.63
			Improvement, PGI-Improvement□ Mean change from baseline: 2.91 at 12 weeks□ 95% CI: 2.67, 3.15
			Night pain score, 11-point Likert scale (0-10)□ Mean change from baseline: -2.20 at 12 weeks□ 95% CI: -2.65, -1.75
			Severity of pain, SF McGill Pain Questionnaire Total score□ Mean change from baseline: -5.39 at 12 weeks□ 95% CI: -6.68, -4.10
Raskin (B) 2005 and 2006 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine□ 60 mg once daily□ Total daily dose: 60 mg□ N=116	24-hour average pain score, 11-point Likert scale□ Mean change from baseline: -2.50 at 12 weeks (p≤0.001)□ 95% CI: -2.85, -2.15
			24-hour worst pain score, Likert scale□ Mean change from baseline: -2.97 at 12 weeks (p≤0.001)□ 95% CI: -3.36, -2.58
			Average pain, BPI□ Mean change from baseline: -2.65 at 12 weeks (p≤0.01)□ 95% CI: -3.02, -2.28
			Average pain, SF-McGill Pain Questionnaire□ Mean change from baseline: -7.47 at 12 weeks (p≤0.01)□ 95% CI: -8.67, -6.27
			Improvement, PGI-Improvement□ Mean change from baseline: 2.50 at 12 weeks (p≤0.001)□ 95% CI: 2.30, 2.70
			Night pain score, Likert scale□ Mean change from baseline: -2.81 at 12 weeks (p≤0.001)□ 95% CI: -3.18, -2.44
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=116	24-hour average pain score, 11-point Likert scale□ Mean change from baseline: -2.47 at 12 weeks (p≤0.001)□ 95% CI: -2.82, -2.12
			24-hour worst pain score, Likert scale□ Mean change from baseline: -2.84 at 12 weeks (p≤0.01)□ 95% CI: -3.23, -2.45
			Average pain, BPI□ Mean change from baseline: -2.62 at 12 weeks (p≤0.01)□ 95% CI: -2.99, -2.25
			Average pain, SF-McGill Pain Questionnaire□ Mean change from baseline: -7.82 at 12 weeks (p≤0.001)□ 95% CI: -9.02, -6.62
			Improvement, PGI-Improvement□ Mean change from baseline: 2.54 at 12 weeks (p≤0.001)□ 95% CI: 2.34, 2.74

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Night pain score, Likert scale Mean change from baseline: -2.78 at 12 weeks (p≤0.001) 95% CI: -3.15, -2.41
		Placebo N=116	24-hour average pain score, 11-point Likert scale Mean change from baseline: -1.60 at 12 weeks 95% CI: -1.95, -1.25
			24-hour worst pain score, Likert scale Mean change from baseline: -2.03 at 12 weeks 95% CI: -2.42, -1.64
			Average pain, BPI Mean change from baseline: -1.82 at 12 weeks 95% CI: -2.19, -1.45
			Average pain, SF-McGill Pain Questionnaire Mean change from baseline: -4.96 at 12 weeks 95% CI: -6.14, -3.78
			Improvement, PGI-Improvement Mean change from baseline: 3.04 at 12 weeks 95% CI: 2.84, 3.24
			Night pain score, Likert scale Mean change from baseline: -1.87 at 12 weeks 95% CI: -2.24, -1.50
Wernicke 2006 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 60 mg once daily Total daily dose: 60 mg N=114	24-hour average pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -2.72 at 12 weeks (p<0.001) 95% CI: -3.15, -2.29
			24-hour worst pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -3.21 at 12 weeks (p<0.001) 95% CI: -3.70, -2.72
			Average pain severity, BPI Mean change from baseline: -2.66 at 12 weeks (p<0.001) 95% CI: -3.11, -2.21
			Improvement, PGI-Improvement Mean change from baseline: 2.61 at 12 weeks (p<0.01) 95% CI: -0.21, 5.43
			Night pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -2.95 at 12 weeks (p<0.01) 95% CI: -3.44, -2.46
			Worst pain, BPI Mean change from baseline: -3.33 at 12 weeks (p<0.001) 95% CI: -3.86, -2.80
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=112	24-hour average pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -2.84 at 12 weeks (p<0.001) 95% CI: -3.29, -2.39

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			24-hour worst pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -3.39 at 12 weeks (p<0.001) 95% CI: -3.90, -2.88
			Average pain severity, BPI Mean change from baseline: -3.05 at 12 weeks (p<0.001) 95% CI: -3.52, -2.58
			Improvement, PGI-Improvement Mean change from baseline: 2.40 at 12 weeks (p<0.001) 95% CI: -0.13, 4.93
			Night pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -3.08 at 12 weeks (p<0.001) 95% CI: -3.57, -2.59
			Worst pain, BPI Mean change from baseline: -3.50 at 12 weeks (p<0.001) 95% CI: -4.05, -2.95
		Placebo N=108	24-hour average pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -1.39 at 12 weeks 95% CI: -1.84, -0.94
			24-hour worst pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -1.94 at 12 weeks 95% CI: -2.43, -1.45
			Average pain severity, BPI Mean change from baseline: -1.48 at 12 weeks 95% CI: -1.93, -1.03
			Improvement, PGI-Improvement Mean change from baseline: 3.17 at 12 weeks 95% CI: 0.35, 5.99
			Night pain score, 11-point Likert scale (0=no pain, 10=worst pain) Mean change from baseline: -1.83 at 12 weeks 95% CI: -2.30, -1.36
			Worst pain, BPI Mean change from baseline: -1.98 at 12 weeks 95% CI: -2.53, -1.43
Rowbotham (C) 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Venlafaxine 75 mg daily N=81	Pain intensity, VAS (0-100) Mean change from baseline (adjusted): 22.4 at 6 weeks (p=NS)
			Pain relief, Global pain relief (0-5) Mean score: 2.8 at 6 weeks (p=NS)
			Pain relief, VAS (0-100) Mean change from baseline (adjusted): 51.0 at 6 weeks (p=NS)
		Venlafaxine 150-225 mg daily N=82	Pain intensity, VAS (0-100) Mean change from baseline (adjusted): 33.8 at 6 weeks (p<0.001)
			Pain relief, Global pain relief (0-5) Mean score: 3.3 at 6 weeks (p<0.01)

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain relief, VAS (0-100) Mean change from baseline (adjusted): 59.9 at 6 weeks (p<0.001)
		Placebo N=81	Pain intensity, VAS (0-100) Mean change from baseline (adjusted): 18.7 at 6 weeks
			Pain relief, Global pain relief (0-5) Mean score: 2.7 at 6 weeks
			Pain relief, VAS (0-100) Mean change from baseline (adjusted): 43.6 at 6 weeks
Tasmuth 2002 Finland Efficacy quality: FAIR	RCT Crossover Single Center	Venlafaxine 37.5 mg N=13	Pain intensity, Current VAS (0-100) Median score (range): 13 (0-62) at 4 weeks (p=NS)
			Pain intensity, Current VRS (0-7) Median score (range): 0 (0-4) at 4 weeks (p=NS)
			Pain relief, Current VAS (0-100) Median score (range): 20 (0-100) at 4 weeks (p=NS)
			Pain relief, Current VRS (0-5) Median score (range): 1 (0-4) at 4 weeks (p=NS)
		Venlafaxine 75 mg N=11	Pain intensity, Current VAS (0-100) Median score (range): 0 (0-35) at 4 weeks (p=NS)
			Pain intensity, Current VRS (0-7) Median score (range): 0 (0-4) at 4 weeks (p=NS)
			Pain relief, Current VAS (0-100) Median score (range): 42 (0-100) at 4 weeks (p=NS)
			Pain relief, Current VRS (0-5) Median score (range): 1.5 (0-4) at 4 weeks (p=NS)
		Placebo N=13	Pain intensity, Current VAS (0-100) Median score (range): 8 (0-67) at 4 weeks
			Pain intensity, Current VRS (0-7) Median score (range): 1 (0-4) at 4 weeks
			Pain relief, Current VAS (0-100) Median score (range): 0 (0-69) at 4 weeks
			Pain relief, Current VRS (0-5) Median score (range): 0 (0-3) at 4 weeks
		Placebo N=11	Pain intensity, Current VAS (0-100) Median score (range): 0.6 (0-70) at 4 weeks
			Pain intensity, Current VRS (0-7) Median score (range): 1 (0-2) at 4 weeks
			Pain relief, Current VAS (0-100) Median score (range): 25 (0-100) at 4 weeks
			Pain relief, Current VRS (0-5) Median score (range): 1 (0-3) at 4 weeks
Yucel 2005 Turkey Efficacy quality: Fair	RCT Parallel Single Center	Venlafaxine 75 mg N=19	Improvement, Global efficacy rated excellent or good % of patients: 68% at 6 weeks (p=NS)
			Pain intensity, VAS (0-10) Median score (range): 4 (0-6) at 6 weeks (p=NS)
		Venlafaxine 150 mg N=17	Improvement, Global efficacy rated excellent or good % of patients: 41% at 6 weeks (p=NS)

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain intensity, VAS (0-10) Median score (range): 4 (0-8) at 6 weeks (p=NS)
		Placebo N=19	Improvement, Global efficacy rated excellent or good % of patients: 42% at 6 weeks
			Pain intensity, VAS (0-10) Median score (range): 7 (0-10) at 6 weeks
Estanislao 2004 US Efficacy quality: Fair	RCT Crossover Multicenter	Lidocaine gel 5% N=32	Average pain, Gracely Pain Scale Mean score (Phase A, before crossover): 1.09 at 2 weeks (p=NS) 95% CI: 1.01, 1.17
			Average pain, Gracely Pain Scale Mean score (Phase B, after crossover): 1.16 at 2 weeks (p=NS) 95% CI: 1.05, 1.27
			Pain relief, Global pain relief Mean score: 2.25 at 2 weeks (p=0.715) 95% CI: 1.99, 2.51
		Placebo N=32	Average pain, Gracely Pain Scale Mean score (Phase B, after crossover): 1.10 at 2 weeks 95% CI: 0.99, 1.21
			Average pain, Gracely Pain Scale Mean score: 1.15 at 2 weeks 95% CI: 1.04, 1.26
			Pain relief, Global pain relief Mean score: 2.23 at 2 weeks 95% CI: 1.98, 2.48
Rowbotham (A) 1995 US Efficacy quality: Fair	RCT Crossover Single Center	Lidocaine gel 5% N=39	Allodynia, 4-item scale (0-3) Mean change from baseline: -0.47 at After gel removal (p=0.021)
			Pain intensity, VAS (0-100) Mean change from baseline: Reported graphically only at 30 min, 1, 2, 3, 4, and 8 hours
			Pain relief, Category scale (6 items, worse to complete relief) Mean change from baseline: Reported graphically only at 30 min, 1, 2, 3, 4, and 8 hours
		Placebo N=39	Allodynia, 4-item scale (0-3) Mean change from baseline: -0.14 at After gel removal
			Pain intensity, VAS (0-100) Mean change from baseline: Reported graphically only at 30 min, 1, 2, 3, 4, and 8 hours
			Pain relief, Category scale (6 items, worse to complete relief) Mean change from baseline: Reported graphically only at 30 min, 1, 2, 3, 4, and 8 hours
Galer (A) 2002 US Efficacy quality: Poor	RCT Parallel Multicenter	Lidocaine topical patch N=67	Pain, NPS 4 Score (0-100) Mean change from baseline: 18.0 at 3 weeks (p=0.013)
			Pain, NPS Composite Score (0-100) Mean change from baseline: 15.3 at 3 weeks (p=0.043)

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain, NPS Nonallodynic Score (0-100) Mean change from baseline: 15.1 at 3 weeks (p=0.022)
			Pain, NPS Total Descriptor Score (0-100) Mean change from baseline: 14.1 at 3 weeks (p=0.042)
		Placebo N=29	Pain, NPS 4 Score (0-100) Mean change from baseline: 6.6 at 3 weeks
			Pain, NPS Composite Score (0-100) Mean change from baseline: 7.7 at 3 weeks
			Pain, NPS Nonallodynic Score (0-100) Mean change from baseline: 6.8 at 3 weeks
			Pain, NPS Total Descriptor Score (0-100) Mean change from baseline: 6.6 at 3 weeks
Galer (B) 1999 US Efficacy quality: FAIR	RCT Crossover Multicenter	Lidocaine topical patch N=32	Pain relief, Verbal pain relief scale (0- 5) % of patients: 90.6% at 2-14 days (p=NR)
			Pain relief, Verbal pain relief scale (0- 5) Median "time to exit": >14 days at 2-14 days (p<0.001)
		Placebo N=32	Pain relief, Verbal pain relief scale (0- 5) % of patients: 40.6% at 2-14 days
			Pain relief, Verbal pain relief scale (0- 5) Median "time to exit": 3.8 days at 2-14 days
Meier 2003 Germany and Switzerland Efficacy quality: POOR	RCT Crossover Multicenter	Lidocaine topical patch 5% N=28	Allodynia, VAS (0-100) Mean change from baseline: Reported graphically only at 2 hours to 7 days
			Pain intensity, VAS (0-100) Mean change from baseline: Reported graphically only at 2 hours to 7 days
		Placebo N=30	Allodynia, VAS (0-100) Mean change from baseline: Reported graphically only at 2 hours to 7 days
			Pain intensity, VAS (0-100) Mean change from baseline: Reported graphically only at 2 hours to 7 days
Rowbotham (B) 1996 US Efficacy quality: Fair	RCT Crossover Single Center	Lidocaine topical patch 5%; up to 3 patches to cover area N=40	Pain intensity, VAS (0-100) Mean change from baseline: 10.2 mm at 30 min, 1, 2, 4, 6, 9, 12 hours (p=<0.001-p=0.038)
			Pain relief, Category scale (0-4; 0=worse, 4= "a lot" Mean score: 2.17 at 30 min, 1, 2, 4, 6, 9, 12 hours (p=0.033)
		Placebo N=35	Pain intensity, VAS (0-100) Mean change from baseline: Reported graphically only at 30 min, 1, 2, 4, 6, 9, 12 hours

Evidence Table 4. Patient-reported pain outcomes in placebo controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain relief, Category scale (0-4; 0=worse, 4= "a lot" Mean change from baseline: Reported graphically only at 30 min, 1, 2, 4, 6, 9, 12 hours

Evidence Table 5. Observer-reported pain outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Observer-reported pain
Rice 2001 UK Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 1800 mg N=115	Global impression of improvement, Very much or much improved % of patients: 44% at 7 weeks (p=0.002)
		Gabapentin 2400 mg N=108	Global impression of improvement, Very much or much improved % of patients: 44% at 7 weeks (p=0.001)
		Placebo N=111	Global impression of improvement, Very much or much improved % of patients: 19% at 7 weeks
Rowbotham (D) 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 3600 mg N=113	Global impression of improvement, Moderately or much improved % of patients: 39.5% at 8 weeks (p=NR)
		Placebo N=116	Global impression of improvement, Moderately or much improved % of patients: 12.9% at 8 weeks
Serpell 2002 UK and Republic of Ireland Efficacy quality: Fair	RCT Paralle Multicenter	Gabapentin N=153	Global impression of improvement, Very much or much improved % of patients: 38% at 8 weeks (p=0.01)
		Placebo N=152	Global impression of improvement, Very much or much improved % of patients: 18% at 8 weeks
Simpson (A) Part 1 2001 US Efficacy quality: Fair	RCT Parallel Single Center	Gabapentin 900-2700 mg N=30	Global impression of Change, Much/moderately improved % of patients: 55.5% at 8 weeks (p<0.01)
		Placebo N=30	Global impression of Change, Much/moderately improved % of patients: 25.9% at 8 weeks
		Gabapentin 900-2700 mg N=30	Global impression of Change, Much/moderately improved % of patients: 55.5% at 8 weeks (p<0.01)
		Placebo N=30	Global impression of Change, Much/moderately improved % of patients: 25.9% at 8 weeks
Lesser 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 75 mg N=77	Global impression of improvement, "much improved" or "very much improved" % of patients: data NR at 5 weeks (p=NR)
		Pregabalin 300 mg N=81	Global impression of improvement, "much improved" or "very much improved" % of patients: 58.2% at 5 weeks (p=0.001)

Evidence Table 5. Observer-reported pain outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Observer-reported pain
		Pregabalin 600 mg N=82	Global impression of improvement, "much improved" or "very much improved" % of patients: 64.1% at 5 weeks (p=0.001)
		Placebo N=97	Global impression of improvement, "much improved" or "very much improved" % of patients: 26.3% at 5 weeks
Richter 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=79	Global impression of change, "much improved" or "very much improved" % of patients: reported graphically only at 6 weeks (p=NS)
		Pregabalin 600 mg N=82	Global impression of change, "much improved" or "very much improved" % of patients: reported graphically only at 6 weeks (p=0.002)
		Placebo□ □ N=85	Global impression of change, "much improved" or "very much improved" % of patients: reported graphically only at 6 weeks
Rosenstock 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 300 mg N=76	Global impression of change, Improved (items not specified) % of patients: 59.2% at 8 weeks (p=0.004)
		Placebo N=70	Global impression of change, Improved (items not specified) % of patients: 38.6% at 8 weeks
Sabatowski 2004 Multiple European and Australia Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=81	Global impression of Change, "much improved" or "very much improved" % of patients: data NR at 8 weeks
		Pregabalin 300 mg N=76	Global impression of Change, "much improved" or "very much improved" % of patients: data NR at 8 weeks
		Placebo N=81	Global impression of Change, "much improved" or "very much improved" % of patients: data NR at 8 weeks
Goldstein 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 20 mg daily N=115	Severity, CGI-Severity Mean change from baseline: -1.28 at 12 weeks (p≤0.05) 95% CI: -1.50, -1.06
		Duloxetine 60 mg daily N=114	Severity, CGI-Severity Mean change from baseline: -1.42 at 12 weeks (p≤0.001) 95% CI: -1.66, -1.18

Evidence Table 5. Observer-reported pain outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Observer-reported pain
		Duloxetine 60 mg BID Total daily dose: 120 mg/d N=113	Severity, CGI-Severity Mean change from baseline: -1.70 at 12 weeks (p≤0.001) 95% CI: -1.94, -1.46
		Placebo N=115	Severity, CGI-Severity Mean change from baseline: -0.83 at 12 weeks 95% CI: -1.07, -0.59
Raskin (B) 2005 and 2006 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 60 mg once daily Total daily dose: 60 mg N=116	Severity, CGI-Severity Mean change from baseline: -1.42 at 12 weeks (p≤0.001) 95% CI: -1.60, -1.24
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=116	Severity, CGI-Severity Mean change from baseline: -1.40 at 12 weeks (p≤0.001) 95% CI: -1.60, -1.20
		Placebo N=116	Severity, CGI-Severity Mean change from baseline: -0.93 at 12 weeks 95% CI: -1.11, -0.75
Wernicke 2006 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 60 mg once daily Total daily dose: 60 mg N=114	Severity of pain, CGI-Severity Mean change from baseline: -1.37 at 12 weeks (p<0.05) 95% CI: -1.59, -1.15
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=112	Severity of pain, CGI-Severity Mean change from baseline: -1.47 at 12 weeks (p<0.01) 95% CI: -1.71, -1.23
		Placebo N=108	Severity of pain, CGI-Severity Mean change from baseline: -0.98 at 12 weeks 95% CI: -1.22, -0.74
Rowbotham (C) 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Venlafaxine 75 mg daily N=81	Global impression of improvement, CGI-Improvement (1-7) Mean score: 2.5 at 6 weeks (p=NS)
			Severity, CGI-Severity (1-7) Mean score: 3.2 at 6 weeks (p=NS)

Evidence Table 5. Observer-reported pain outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Observer-reported pain
		Venlafaxine 150-225 mg daily N=82	Global impression of improvement, CGI-Improvement (1-7) Mean score: 2.1 at 6 weeks (p<0.001)
			Severity, CGI-Severity (1-7) Mean score: 2.8 at 6 weeks (p<0.001)
		Placebo N=81	Global impression of improvement, CGI-Improvement (1-7) Mean score: 2.8 at 6 weeks
			Severity, CGI-Severity (1-7) Mean score: 3.5 at 6 weeks

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
Backonja 1999 US Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 3600 mg N=84	Quality of life, SF-36 Bodily Pain Mean score: 55.2 at 8 weeks (p=0.01)
			Quality of life, SF-36 Mental Health Mean score: 75.7 at 8 weeks (p=0.03)
			Quality of life, SF-36 Vitality Mean score: 53.5 at 8 weeks (p=0.001)
		Placebo N=81	Quality of life, SF-36 Bodily Pain Mean score: 47.4 at 8 weeks
			Quality of life, SF-36 Mental Health Mean score: 70.4 at 8 weeks
			Quality of life, SF-36 Vitality Mean score: 43.7 at 8 weeks
Bone 2002 UK and Ireland Efficacy quality: Fair	RCT Crossover Single Center	Gabapentin 2400 mg N=10	Activities of Daily Living, Barthel Index Median score: 85 at 6 weeks (p=NS) IQR: (70-105)
		Placebo N=9	Activities of Daily Living, Barthel Index Median score: 87 at 6 weeks IQR: (65-105)
Gilron (A) 2005 Canada Efficacy quality: Fair	RCT Crossove Single Center	Gabapentin 3200 mg N=48	Quality of life, SF-36 Bodily Pain (0-100) Mean score: 65.6 at 5 weeks (p<0.05) 95% CI: 59.92, 71.28
			Quality of life, SF-36 Mental Health (0-100) Mean score: 80.9 at 5 weeks (p<0.05) 95% CI: 75.80, 86.00
			Quality of life, SF-36 Physical Functioning (0-100) Mean score: 61.1 at 5 weeks (p<0.05) 95% CI: 53.26, 68.94
		Lorazepam 1.6 mg N=44	Quality of life, SF-36 Bodily Pain (0-100) Mean score: 56.0 at 5 weeks 95% CI: 50.12, 61.88
			Quality of life, SF-36 Mental Health (0-100) Mean score: 73.4 at 5 weeks 95% CI: 68.30, 78.50
			Quality of life, SF-36 Physical Functioning (0-100) Mean score: 56.0 at 5 weeks 95% CI: 48.16, 63.84

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
Rice 2001 UK Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 1800 mg N=115	Quality of life, : Reported graphically only at 7 weeks
		Gabapentin 2400 mg N=108	Quality of life, : Reported graphically only at 7 weeks
		Placebo N=111	Quality of life, : Reported graphically only at 7 weeks
Rowbotham (D) 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 3600 mg N=113	Quality of life, SF-36 Bodily pain Mean score: 57.4 at 8 weeks (p<0.001) 95% CI: 53.77, 61.03
			Quality of life, SF-36 General health Mean score: 63.1 at 8 weeks (p=0.65) 95% CI: 59.04, 67.16
			Quality of life, SF-36 Mental health Mean score: 74.6 at 8 weeks (p<0.001) 95% CI: 71.54, 77.66
			Quality of life, SF-36 Physical functioning Mean score: 66.2 at 8 weeks (p=0.01) 95% CI: 61.70, 70.70
			Quality of life, SF-36 Vitality Mean score: 55.1 at 8 weeks (p<0.001) 95% CI: 51.36, 58.84
		Placebo N=116	Quality of life, SF-36 Bodily pain Mean score: 47.3 at 8 weeks 95% CI: 43.61, 50.99
			Quality of life, SF-36 General health Mean score: 64.3 at 8 weeks 95% CI: 60.15, 68.45
			Quality of life, SF-36 Mental health Mean score: 69.9 at 8 weeks 95% CI: 66.15, 73.65
			Quality of life, SF-36 Physical functioning Mean score: 57.5 at 8 weeks 95% CI: 52.04, 62.96
			Quality of life, SF-36 Vitality Mean score: 43.7 at 8 weeks 95% CI: 39.73, 47.67
Serpell 2002 UK and Republic of	RCT Parallel Multicenter	Gabapentin N=153	Quality of life, SF-36 : Reported graphically only

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
Ireland Efficacy quality: Fair		Placebo N=152	Quality of life, SF-36 : Reported graphically only
Simpson (A) Part 1 2001 US Efficacy quality: Fair	RCT Parallel Single Center	Gabapentin 900-2700 mg N=30	Quality of life, SF-36 Bodily Pain Mean score: 60 at 8 weeks (p<0.01)
			Quality of life, SF-36 Mental Health Mean score: 80 at 8 weeks (p<0.01)
			Quality of life, SF-36 Vitality Mean score: 60 at 8 weeks (p<0.01)
		Placebo N=30	Quality of life, SF-36 Bodily Pain Mean score: 45 at 8 weeks
			Quality of life, SF-36 Mental Health Mean score: 65 at 8 weeks
			Quality of life, SF-36 Vitality Mean score: 40 at 8 weeks
		Gabapentin 900-2700 mg N=30	Quality of life, SF-36 Bodily Pain Mean score: 60 at 8 weeks (p<0.01)
			Quality of life, SF-36 Mental Health Mean score: 80 at 8 weeks (p<0.01)
			Quality of life, SF-36 Vitality Mean score: 60 at 8 weeks (p<0.01)
		Placebo N=30	Quality of life, SF-36 Bodily Pain Mean score: 45 at 8 weeks
			Quality of life, SF-36 Mental Health Mean score: 65 at 8 weeks
			Quality of life, SF-36 Vitality Mean score: 40 at 8 weeks
Dworkin 2003 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 300-600 mg N=89	Quality of life, SF-36 Bodily Pain Least squares mean: 55.14 at 8 weeks (p=0.0021) 95% CI: 50.97, 59.31
			Quality of life, SF-36 General Health Perception Least squares mean: 67.61 at 8 weeks (p=0.0488) 95% CI: 64.51, 70.71
			Quality of life, SF-36 Mental Health Least squares mean: 77.53 at 8 weeks (p=0.0676) 95% CI: 74.51, 80.55
			Quality of life, SF-36 Physical Functioning Least squares mean: 62.25 at 8 weeks (p=0.7449) 95% CI: 58.41, 66.09
			Quality of life, SF-36 Vitality Least squares mean: 49.99 at 8 weeks (p=0.6798) 95% CI: 46.29, 53.69

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
		Placebo N=84	Quality of life, SF-36 Bodily Pain Least squares mean: 46.14 at 8 weeks 95% CI: 41.97, 50.31
			Quality of life, SF-36 General Health Perception Least squares mean: 63.40 at 8 weeks 95% CI: 60.30, 66.50
			Quality of life, SF-36 Mental Health Least squares mean: 73.73 at 8 weeks 95% CI: 70.71, 76.75
			Quality of life, SF-36 Physical Functioning Least squares mean: 61.41 at 8 weeks 95% CI: 57.69, 65.13
			Quality of life, SF-36 Vitality Least squares mean: 48.94 at 8 weeks 95% CI: 45.26, 52.62
Lesser 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 75 mg N=77	Quality of life, SF-36 bodily pain data not reported: data NR at 5 weeks
			Quality of life, SF-36 vitality data not reported: data NR at 5 weeks (p<0.05)
		Pregabalin 300 mg N=81	Quality of life, SF-36 bodily pain data not reported: data NR at 5 weeks (p<0.005)
			Quality of life, SF-36 vitality data not reported: data NR at 5 weeks (p<0.01)
		Pregabalin 600 mg N=82	Quality of life, SF-36 bodily pain data not reported: data NR at 5 weeks (p<0.0005)
			Quality of life, SF-36 vitality data not reported: data NR at 5 weeks (p=NR)
		Placebo N=97	Quality of life, SF-36 bodily pain data not reported: data not reported at 5 weeks
			Quality of life, SF-36 vitality data not reported: data not reported at 5 weeks
Richter 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=79	Quality of life, SF-36 Bodily Pain Least squares mean: data NR at 6 weeks (p<0.016)
			Quality of life, SF-36 Other domains Least squares mean: data NR at 6 weeks (p=NS)

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
		Pregabalin 600 mg N=82	Quality of life, SF-36 Bodily Pain Least squares mean: data NR at 6 weeks (p<0.016)
			Quality of life, SF-36 Other domains Least squares mean: data NR at 6 weeks (p=NS)
		Placebo N=85	Quality of life, SF-36 Bodily Pain Least squares mean: data NR at 6 weeks
			Quality of life, SF-36 Other domains Least squares mean: data NR at 6 weeks
Rosenstock 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 300 mg N=76	Quality of life, SF-36 Bodily Pain Least squares mean: 53.83 at 8 weeks (p=0.0294) 95% CI: 49.44, 58.22
			Quality of life, SF-36 Mental Health Least squares mean: 75.82 at 8 weeks (p=0.1893) 95% CI: 72.10, 79.54
			Quality of life, SF-36 Vitality Least squares mean: 46.82 at 8 weeks (p=0.2343) 95% CI: 42.98, 50.66
		Placebo N=70	Quality of life, SF-36 Bodily Pain Least squares mean: 46.96 at 8 weeks 95% CI: 42.31, 51.61
			Quality of life, SF-36 Mental Health Least squares mean: 72.36 at 8 weeks 95% CI: 68.50, 76.22
			Quality of life, SF-36 Vitality Least squares mean: 43.57 at 8 weeks 95% CI: 39.55, 47.59
Sabatowski 2004 Multiple European and Australia Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=81	Quality of life, SF-36 Bodily Pain Least squares mean difference from placebo: NR at 8 weeks
			Quality of life, SF-36 Mental Health Least squares mean difference from placebo: 5.72 at 8 weeks (p=0.043)
			Quality of life, SF-36 Physical Functioning Least squares mean difference from placebo: NR at 8 weeks
			Quality of life, SF-36 Vitality Least squares mean difference from placebo: NR at 8 weeks

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
		Pregabalin 300 mg N=76	Quality of life, SF-36 Bodily Pain Least squares mean difference from placebo: 9.58 at 8 weeks (p=0.005)
			Quality of life, SF-36 Mental Health Least squares mean difference from placebo: 6.05 at 8 weeks (p=0.043)
			Quality of life, SF-36 Physical Functioning Least squares mean difference from placebo: data NR at 8 weeks
			Quality of life, SF-36 Vitality Least squares mean difference from placebo: 7.11 at 8 weeks (p=0.044)
		Placebo N=81	Quality of life, SF-36 Bodily Pain Least squares mean difference from placebo: NA at 8 weeks
			Quality of life, SF-36 Mental Health Least squares mean difference from placebo: NA at 8 weeks
			Quality of life, SF-36 Physical Functioning Least squares mean difference from placebo: NA at 8 weeks
			Quality of life, SF-36 Vitality Least squares mean difference from placebo: NA at 8 weeks
Goldstein 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 20 mg daily N=115	Interference, BPI Interference- average of 7 questions) Mean change from baseline: -1.73 at 12 weeks (p=NS) 95% CI: -2.06, -1.40
			Quality of life, Euro quality of life Mean change from baseline: 0.10 at 12 weeks (p=NS) 95% CI: 0.06, 0.14
			Quality of life, SF-36 bodily pain Mean change from baseline: 13.22 at 12 weeks (p=NS) 95% CI: 9.48, 16.96
			Quality of life, SF-36 Mental Health Mean change from baseline: 0.74 at 12 weeks (p=NS) 95% CI: -2.55, 4.03
			Quality of life, SF-36 physical Mean change from baseline: 3.67 at 12 weeks (p=NS) 95% CI: 2.14, 5.20

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
		Duloxetine 60 mg daily N=114	Interference, BPI Interference- average of 7 questions) Mean change from baseline: -2.33 at 12 weeks (p≤0.01) 95% CI: -2.66, -2.00
			Quality of life, Euro quality of life Mean change from baseline: 0.13 at 12 weeks (p≤0.05) 95% CI: 0.09, 0.17
			Quality of life, SF-36 bodily pain Mean change from baseline: 18.00 at 12 weeks (p≤0.01) 95% CI: 14.30, 21.70
			Quality of life, SF-36 Mental Health Mean change from baseline: 2.99 at 12 weeks (p<0.05) 95% CI: -0.24, 6.22
			Quality of life, SF-36 physical Mean change from baseline: 5.86 at 12 weeks (p=NS) 95% CI: 4.35, 7.37
		Duloxetine 60 mg BID Total daily dose: 120 mg/d N=113	Interference, BPI Interference-general activity Mean change from baseline: -2.30 at 12 weeks (p≤0.05) 95% CI: -2.65, -1.95
			Quality of life, Euro quality of life Mean change from baseline: 0.13 at 12 weeks (p≤0.05) 95% CI: 0.09, 0.17
			Quality of life, SF-36 bodily pain Mean change from baseline: 18.32 at 12 weeks (p≤0.01) 95% CI: 14.64, 22.00
			Quality of life, SF-36 Mental Health Mean change from baseline: 5.14 at 12 weeks (p<0.001) 95% CI: 1.96, 8.32
			Quality of life, SF-36 physical Mean change from baseline: 5.85 at 12 weeks (p=NS) 95% CI: 4.36, 7.34
		Placebo N=115	Interference, BPI Interference-general activity Mean change from baseline: -1.73 at 12 weeks 95% CI: -2.06, -1.40
			Quality of life, Euro quality of life Mean change from baseline: 0.08 at 12 weeks 95% CI: 0.04, 0.12

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
			Quality of life, SF-36 bodily pain Mean change from baseline: 10.32 at 12 weeks 95% CI: 6.62, 14.02
			Quality of life, SF-36 Mental Health Mean change from baseline: -2.63 at 12 weeks 95% CI: -5.94, 0.68
			Quality of life, SF-36 physical Mean change from baseline: 3.94 at 12 weeks 95% CI: 2.43, 5.45
Raskin (B) 2005 and 2006 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 60 mg once daily Total daily dose: 60 mg N=116	Interference, BPI Interference (average of 7 questions) Mean change from baseline: -2.43 at 12 weeks (p≤0.001) 95% CI: -2.78, -2.08
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=116	Interference, BPI Interference (average of 7 questions) Mean change from baseline: -2.54 at 12 weeks (p≤0.001) 95% CI: -2.89, -2.19
		Placebo N=116	Interference, BPI Interference (average of 7 questions) Mean change from baseline: -1.56 at 12 weeks 95% CI: -1.91, -1.21
Wernicke 2006 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 60 mg once daily Total daily dose: 60 mg N=114	Interference, BPI Interference average of 7 questions Mean change from baseline: -2.36 at 12 weeks (p<0.05) 95% CI: -2.73, -1.99
			Quality of life, Euro Quality of Life (EQ-5D) Mean change from baseline: 0.15 at 12 weeks (p<0.05) 95% CI: 0.11, 0.19
			Quality of life, SF-36 Bodily Pain Mean change from baseline: 15.3 at 12 weeks (p<0.05) 95% CI: 11.42, 19.18
			Quality of life, SF-36 General Health Mean change from baseline: 5.64 at 12 weeks (p=NS) 95% CI: 2.94, 8.34
			Quality of life, SF-36 Mental Health Mean change from baseline: 1.63 at 12 weeks (p=NS) 95% CI: -1.27, 4.53

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
			Quality of life, SF-36 Physical functioning Mean change from baseline: 11.96 at 12 weeks (p<0.01) 95% CI: 8.41, 15.51
			Quality of life, SF-36 Vitality Mean change from baseline: 8.47 at 12 weeks (p=NS) 95% CI: 5.08, 11.86
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=112	Interference, BPI Interference average of 7 questions Mean change from baseline: -2.79 at 12 weeks (p<0.001) 95% CI: -3.16, -2.42
			Quality of life, Euro Quality of Life (EQ-5D) Mean change from baseline: 0.15 at 12 weeks (p<0.05) 95% CI: 0.11, 0.19
			Quality of life, SF-36 Bodily Pain Mean change from baseline: 20.59 at 12 weeks (p<0.01) 95% CI: 16.59, 24.59
			Quality of life, SF-36 General Health Mean change from baseline: 7.73 at 12 weeks (p<0.01) 95% CI: 5.01, 10.45
			Quality of life, SF-36 Mental Health Mean change from baseline: 3.82 at 12 weeks (p<0.05) 95% CI: 0.90, 6.74
			Quality of life, SF-36 Physical functioning Mean change from baseline: 11.20 at 12 weeks (p<0.01) 95% CI: 7.55, 14.85
			Quality of life, SF-36 Vitality Mean change from baseline: 6.36 at 12 weeks (p=NS) 95% CI: 2.95, 9.77
		Placebo N=108	Interference, BPI Interference average of 7 questions Mean change from baseline: -1.72 at 12 weeks 95% CI: -2.09, -1.35
			Quality of life, Euro Quality of Life (EQ-5D) Mean change from baseline: 0.08 at 12 weeks 95% CI: 0.04, 0.12

Evidence Table 6. Functional outcomes in placebo-controlled trials of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention	Functional capacity
			Quality of life, SF-36 Bodily Pain Mean change from baseline: 12.17 at 12 weeks 95% CI: 8.05, 16.29
			Quality of life, SF-36 General Health Mean change from baseline: 2.39 at 12 weeks 95% CI: -0.39, 5.17
			Quality of life, SF-36 Mental Health Mean change from baseline: -0.31 at 12 weeks 95% CI: -3.29, 2.67
			Quality of life, SF-36 Physical functioning Mean change from baseline: 3.64 at 12 weeks 95% CI: -0.08, 7.36
			Quality of life, SF-36 Vitality Mean change from baseline: 2.79 at 12 weeks 95% CI: -0.70, 6.28
Yucel 2005 Turkey Efficacy quality: Fair	RCT Parallel Single Center	Venlafaxine 75 mg N=19	Daily activity, excellent, good, mild, none % of patients improved: 73.68% at 6 weeks (p=NS)
		Venlafaxine 150 mg N=17	Daily activity, excellent, good, mild, none % of patients improved: 47.05% at 6 weeks (p=NS)
		Placebo N=19	Daily activity, excellent, good, mild, none % of patients improved: 42.1% at 6 weeks

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
Backonja 1999 US Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 3600 mg N=84	Interference with sleep, 11-point Likert scale (0-10) Mean score: 2.3 at 8 weeks (p<0.001)
		Placebo N=81	Interference with sleep, 11-point Likert scale (0-10) Mean score: 3.8 at 8 weeks
Bone 2002 UK and Ireland Efficacy quality: Fair	RCT Crossover Single Center	Gabapentin 2400 mg N=10	Depression, Hospital Anxiety & Depression Scale (higher worse) Median score: 12 at 6 weeks (p=NS) IQR: (4-22)
			Interference with sleep, 11-point scale (0-10) Median score: 3 at 6 weeks (p=NS) IQR: (1-5)
		Placebo N=9	Depression, Hospital Anxiety & Depression Scale (higher worse) Median score: 14 at 6 weeks IQR: (5-25)
			Interference with sleep, 11-point scale (0-10) Median score: 4 at 6 weeks IQR: (1-5)
Gilron (A) 2005 Canada Efficacy quality: Fair	RCT Crossover Single Center	Gabapentin 3200 mg N=48	Depression, Beck Depression Inventory (0-63) Mean score: 6.4 at 5 weeks (p<0.05) 95% CI: 4.44, 8.36
			Interference with sleep, Brief Pain Inventory (Sleep, 0-10) Mean score: 1.5 at 5 weeks (p<0.05) 95% CI: 0.72, 2.28
		Lorazepam 1.6 mg N=44	Depression, Beck Depression Inventory (0-63) Mean score: 8.5 at 5 weeks 95% CI: 6.54, 10.46
			Interference with sleep, Brief Pain Inventory (Sleep, 0-10) Mean score: 3.4 at 5 weeks 95% CI: 2.62, 4.18

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
Hahn 2004 Germany Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 1200-2400 mg N=15	Interference with sleep, VAS (0-10) % change from baseline: -48.9% at 4 weeks (p=NS)
			Interference with sleep, VAS (0-10) Median score: 2.3 at 4 weeks (pNRvsplacebo)
		Placebo N=11	Interference with sleep, VAS (0-10) % change from baseline: -11.6% at 4 weeks
			Interference with sleep, VAS (0-10) Median score: 4.95 at 4 weeks
Rice 2001 UK Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 1800 mg N=115	Interference with sleep, Likert scale (0-10) Difference from placebo: 0.9 at 7 weeks (p<0.01) 95% CI: 0.4-1.4
		Gabapentin 2400 mg N=108	Interference with sleep, Likert scale (0-10) Difference from placebo: 1.1 at 7 weeks (p<0.01) 95% CI: 0.7-1.6
		Placebo N=111	Interference with sleep, Likert scale (0-10) Difference from placebo: NA at 7 weeks
Rowbotham (D) 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Gabapentin 3600 mg N=113	Average daily sleep rating score, Likert scale (0-10) Mean score: 2.4 at 8 weeks (p<0.001) 95% CI: 1.94, 2.86
		Placebo N=116	Average daily sleep rating score, Likert scale (0-10) Mean score: 3.6 at 8 weeks 95% CI: 3.05, 4.15
Simpson (A) Part 1 2001 US Efficacy quality: Fair	RCT Parallel Single Center	Gabapentin 900-2700 mg N=30	Interference with sleep, 11-point Likert scale (0-10) Mean score: data NR at 8 weeks (pNR(significant))
		Placebo N=30	Interference with sleep, 11-point Likert scale (0-10) Mean score: data NR at 8 weeks

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
		Gabapentin 900-2700 mg N=30	Interference with sleep, 11-point Likert scale (0-10) Mean score: data NR at 8 weeks (pNR(significant))
		Placebo N=30	Interference with sleep, 11-point Likert scale (0-10) Mean score: data NR at 8 weeks
Dworkin 2003 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 300-600 mg N=89	Interference with sleep, 11-point numeric scale (0-10) Least squares mean: 1.93 at 8 weeks (p=0.0001) 95% CI: 1.48, 2.38
			Interference with sleep, Medical Outcomes Study Sleep Scale (higher=worse) Least squares mean: 26.63 at 8 weeks (p=0.0001) 95% CI: 23.16, 30.10
		Placebo N=84	Interference with sleep, 11-point numeric scale (0-10) Least squares mean: 3.51 at 8 weeks 95% CI: 3.06, 3.96
			Interference with sleep, Medical Outcomes Study Sleep Scale (higher=worse) Least squares mean: 36.43 at 8 weeks 95% CI: 33.00, 39.86
Freynhagen 2005 Multiple European Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150-600 mg N=141	Interference with sleep, Medical Outcomes Study Sleep Scale Mean score: Reported graphically only at 12 weeks (p<0.001)
		Pregabalin 600 mg N=132	Interference with sleep, Medical Outcomes Study Sleep Scale Mean score: Reported graphically only at 12 weeks (p<0.001)
		Placebo N=65	Interference with sleep, Medical Outcomes Study Sleep Scale Mean score: Reported graphically only at 12 weeks

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
Lesser 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 75 mg N=77	Interference with sleep, Sleep interference score Mean difference from placebo: Reported graphically only at 5 weeks (p=NR)
		Pregabalin 300 mg N=81	Interference with sleep, Sleep interference score Mean difference from placebo: 1.3 at 5 weeks (p=0.0001)
		Pregabalin 600 mg N=82	Interference with sleep, Sleep interference score Mean difference from placebo: 1.6 at 5 weeks (p=0.0001)
		Placebo N=97	Interference with sleep, Sleep interference score Mean difference from placebo: NA at 5 weeks
Richter 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=79	Interference with sleep, 11-point numeric rating scale (0-10) Least squares mean difference: reported graphically only at 6 weeks (p=NS)
		Pregabalin 600 mg N=82	Interference with sleep, 11-point numeric rating scale (0-10) Least squares mean difference: -1.152 at 6 weeks (p=0.0004) 95% CI: -1.752 to -0.551
		Placebo N=85	Interference with sleep, 11-point numeric rating scale (0-10) Least squares mean: reported graphically only at 6 weeks
Rosenstock 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 300 mg N=76	Interference with sleep, 11-pont scale (0-10) Least squares mean: 2.78 at 8 weeks (p=0.0001) 95% CI: 2.25, 3.31
		Placebo N=70	Interference with sleep, 11-pont scale (0-10) Least squares mean: 4.32 at 8 weeks 95% CI: 3.75, 4.89

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
Sabatowski 2004 Multiple European and Australia Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=81	Depression, Zung Self-Rating Depression Scale Least squares mean: 47.66 at 8 weeks (p0.0560(adjusted)) 95% CI: 45.50, 49.82
			Interference with sleep, Sleep interference score Least squares mean: 3.13 at 8 weeks (p=0.0003) 95% CI: 2.72, 3.54
		Pregabalin 300 mg N=76	Depression, Zung Self-Rating Depression Scale Least squares mean: 46.62 at 8 weeks (p0.024(adjusted)) 95% CI: 44.41, 48.83
			Interference with sleep, Sleep interference score Least squares mean: 2.81 at 8 weeks (p=0.0001) 95% CI: 2.38, 3.24
		Placebo N=81	Depression, Zung Self-Rating Depression Scale Least squares mean: 50.64 at 8 weeks 95% CI: 48.48, 52.80
			Interference with sleep, Sleep interference score Least squares mean: 4.24 at 8 weeks 95% CI: 3.83, 4.65
van Seventer 2006 US and Multiple European Efficacy quality: Fair	RCT Parallel Multicenter	Pregabalin 150 mg N=87	Interference with sleep, 11-point numerical rating scale (0-10) Least squares mean: 3.07 at 13 weeks (p=0.0007) 95% CI: 2.64, 3.50
		Pregabalin 300 mg N=98	Interference with sleep, 11-point numerical rating scale (0-10) Least squares mean: 2.84 at 13 weeks (p=0.0002) 95% CI: 2.43, 3.25

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
		Pregabalin 300-600 mg N=90	Interference with sleep, 11-point numerical rating scale (0-10) Least squares mean: 2.17 at 13 weeks (p=0.0002) 95% CI: 1.74, 2.60
		Placebo N=93	Interference with sleep, 11-point numerical rating scale (0-10) Least squares mean: 4.10 at 13 weeks 95% CI: 3.69, 4.51
Goldstein 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 20 mg daily N=115	Depression, Beck Depression Inventory Mean change from baseline: -2.44 at 12 weeks (p=NS) 95% CI: -3.38, -1.50
		Duloxetine 60 mg daily N=114	Depression, Beck Depression Inventory Mean change from baseline: -2.71 at 12 weeks (p=NS) 95% CI: -3.67, -1.75
		Duloxetine 60 mg BID Total daily dose: 120 mg/d N=113	Depression, Beck Depression Inventory Mean change from baseline: -3.11 at 12 weeks (p≤0.05) 95% CI: -4.09, -2.13
		Placebo N=115	Depression, Beck Depression Inventory Mean change from baseline: -1.74 at 12 weeks 95% CI: -2.68, -0.80
Raskin (B) 2005 and 2006 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 60 mg once daily Total daily dose: 60 mg N=116	Depression, HAM-D Mean change from baseline: -1.17 at 12 weeks (p=NS) 95% CI: -1.66, -0.68
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=116	Depression, HAM-D Mean change from baseline: -0.65 at 12 weeks (p=NS) 95% CI: -1.14, -0.16

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
		Placebo N=116	Depression, HAM-D Mean change from baseline: -0.55 at 12 weeks 95% CI: -1.04, -0.06
Wernicke 2006 US Efficacy quality: Fair	RCT Parallel Multicenter	Duloxetine 60 mg once daily Total daily dose: 60 mg N=114	Depression, HAM-D Mean change from baseline: -0.65 at 12 weeks (p=NS) 95% CI: -1.16, -0.14
			Use of rescue analgesics, Median average daily dose: 108.7 mg at 12 weeks (p=NS)
		Duloxetine 60 mg twice daily Total daily dose: 120 mg N=112	Depression, HAM-D Mean change from baseline: 0.19 at 12 weeks (p<0.05) 95% CI: -0.32, 0.70
			Use of rescue analgesics, Median average daily dose: 23.81 mg at 12 weeks (p<0.001)
		Placebo N=108	Depression, HAM-D Mean change from baseline: -0.64 at 12 weeks 95% CI: -1.15, -0.13
			Use of rescue analgesics, Median average daily dose: 207.14 mg at 12 weeks
Forssell 2004 Finland Efficacy quality: Poor	RCT Crossove Multicenter	Venlafaxine 37.5 mg once daily for 2 weeks then twice daily Total daily dose: 37.5 mg to 75 mg N=15	Depression, Beck Depression Inventory (0-63) Mean score: 9 at 4 weeks (p=0.16)
		Placebo N=15	Depression, Beck Depression Inventory (0-63) Mean score: 11 at 4 weeks
Tasmuth 2002 Finland	RCT Crossover Single Center	Venlafaxine 37.5 mg N=13	Depression, Beck Depression Inventory (0-63) Median score (range): 7 (1-27) at 4 weeks (p=NS)

Evidence Table 7. Other outcomes in RCTs of pregabalin, gabapentin, SNRIs and topical lidocaine for neuropathic pain

Study	Design	Intervention and study arm characteristics	Other outcomes
Efficacy quality: Fair		Venlafaxine 75 mg N=11	Depression, Beck Depression Inventory (0-63) Median score (range): 7 (1-39) at 4 weeks (p=NS)
		Placebo N=13	Depression, Beck Depression Inventory (0-63) Median score (range): 8 (1-22) at 4 weeks
		Placebo N=11	Depression, Beck Depression Inventory (0-63) Median score (range): 7 (1-11) at 4 weeks
Galer (B) 1999 US Efficacy quality: Fair	RCT Crossover Multicenter	Lidocaine transdermal patch N=32	Use of rescue analgesics, % of patients: 9.4% at 2-14 days (p=NS)
		Placebo N=32	Use of rescue analgesics, % of patients: 12.5% at 2-14 days

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
Leijon 1989 Sweden Efficacy quality: Fair	CT Crossover Single Center	Central/post-stroke neuropathic pain N=15 Age	Amitriptyline 25 + 50 mg BID Carbamazepine 400 mg BID Placebo
Rull 1969 Mexico Efficacy quality: Fair	RCT Crossover	Painful diabetic neuropathy N=30 Age Mean 54.2 (range 21-81) 30% male, 70% female	Carbamazepine 600 mg Placebo
Killian 1968 US Efficacy quality: Poor	RCT Crossover	Mixed N=42	carbamazepine 600 to 800 mg placebo
Campbell 1966	RCT Crossover	Trigeminal neuralgia	Carbazepine Placebo
Dalessio 1966 US Efficacy quality: Poor	RCT Crossover Single Center	Trigeminal neuralgia N=10	Carbazepine 600 mg Placebo N=10
Rockliff 1966 US	RCT Crossover Single Center	Trigeminal neuralgia N=9	Carbazepine 600 mg Placebo
Eisenberg 2001 Israel Efficacy quality: Fair	RCT Parallel Single Center	Painful diabetic neuropathy N=53 Age Mean (SD): 55.2	Lamotrigine 200-400 mg Placebo N=26
Finnerup	RCT	Spinal cord injury-related pain	Lamotrigine

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
2002 Denmark Efficacy quality: Fair	Crossover Single Center	N=22 Age Mean (SD): 49 Range: 27-63	200-400 mg Placebo
McCleane 1999 UK	RCT Parallel Single Center	Mixed N=74	Lamotrigine 200 mg Placebo
Simpson (B) 2003 US Efficacy quality: Fair	RCT Parallel Multicenter	HIV-related neuropathic pain N=227 Age Mean (SD): 44.5 Range: 26-67 Male: 89.43% Female: 10.57% White: 59.9% Black: 33.5% Other: 6.6%	Lamotrigine 400 mg Lamotrigine 600 mg Placebo Placebo
Simpson (C) 2000 US	RCT Parallel Multicenter	HIV-related neuropathic pain N=29	Lamotrigine 300 mg Placebo
Vestergaard 2001 Denmark	RCT Crossover Multicenter	Central/post-stroke neuropathic pain N=30	Lamotrigine 200 mg Placebo
Zakrzewska 1997	RCT Crossover	Trigeminal neuralgia	Lamotrigine 400 mg

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
UK		N=14	Placebo
Beydoun 2006 US Efficacy quality: Fair	RCT Parallel	Painful diabetic neuropathy N=347 Age Mean (SD): 60.7	Oxcarbazepine 600 mg daily
			Oxcarbazepine 1200 mg daily
			Oxcarbazepine 1800 mg daily
			Placebo
Dogra 2005 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=146	Oxcarbazepine mean 1445 mg
			Placebo
Gilron (B) 2001 US	RCT Crossover	Trigeminal neuralgia N=3	Topiramate mean 308 mg (range 75-600 mg)
			Placebo
Khoromi 2005 US	RCT Crossover	Neuropathy associated with low back pain N=29	Topiramate mean 208 mg
			Diphenhydramine mean 40 mg
Raskin (A) 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Painful diabetic neuropathy N=317 Age Mean (SD): 59.2 (9.8) Male: 49.53% Female: 50.47% White: 87.4% Black: 11.4%	Topiramate mean 320 mg
			Placebo
Thienel 2004 Multiple	RCT Parallel Multicenter	Painful diabetic neuropathy N=1269	Topiramate 100 mg
			Topiramate 200 mg

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
Efficacy quality: Fair		Age	
		Mean (SD): 58.3	Topiramate
		Range: 21-81	400 mg
			Placebo
Kochar (A)□	RCT	Painful diabetic neuropathy	Valproic acid/divalproex/sodium
2002	Parallel		valproate
India	Single Center	N=52	600 mg
			Placebo
Kochar (B)	RCT	Painful diabetic neuropathy	Valproic acid/divalproex/sodium
2004	Parallel		valproate
India		N=39	500 mg
			Placebo
Efficacy quality: Fair		Age	
		Mean (SD): 55.2	
Kochar (C)	CT	Painful diabetic neuropathy	Valproic acid/divalproex/sodium
2005	Parallel		valproate
India	Single Center	N=40	1000 mg daily
Efficacy quality: Fair		Age	
		Mean (SD): 57.24	Placebo
		Male: 55%	
		Female: 45%	
Otto	RCT	Polyneuropathy	Valproic acid/divalproex/sodium
2004	Crossover		valproate
Denmark		N=31	Placebo
Carlsson	RCT	Post-traumatic neuropathic pain	Dextromethorphan
2004	Crossover		270 mg one dose
Norway		N=15	
			Placebo
Efficacy quality: Fair		Age	
		Mean (SD): 41 (13)	
McQuay	RCT	Mixed	Dextromethorphan
1994	Crossover		40.5 mg

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
UK Efficacy quality: Fair	Single Center	N=19 Age Mean (SD): 60.6 Range: 28-80 Male: 63.16% Female: 36.84%	
			Dextromethorphan 81 mg
Nelson (A: diabetic neuropathy) 1997 US	RCT Crossover	Painful diabetic neuropathy N=13 Age	Dextromethorphan mean 381 mg
			Placebo
Nelson (B: postherpetic neuralgia) 1997 US	RCT Crossover	Post-herpetic neuralgia N=13 Age	Dextromethorphan mean 439 mg
			Placebo
Sindrup (B) 1992 Denmark	RCT Crossover Multicenter	Painful diabetic neuropathy N=15	Citalopram 40 mg
			Placebo
Max (D) 1992 US	RCT Crossover NR	Painful diabetic neuropathy N=54 	Fluoxetine 20-40 mg
			Benztropine mesylate 0.125 to 1.5 mg
Sindrup (A) 1990 Denmark Efficacy quality: Poor	RCT Crossover Multicenter	Painful diabetic neuropathy N=20 Age Mean (SD): 41 Range: 28-75	Paroxetine 40 mg daily Total daily dose: 40 mg
			Imipramine 50 or 75 mg daily Total daily dose: 50 or 75 mg
			Placebo

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
Cardenas 2002 US	RCT Parallel Multicenter	Spinal cord injury-related pain N=84	Amitriptyline 10-125 mg daily Benztropine mesylate 0.5 mg daily
Kalso 1995 Finland Efficacy quality: Fair	RCT Crossover Single Center	Cancer-related neuropathic pain N=15 Age Mean (SD): 56.0 Range: 39-72 Male: 0% Female: 100%	Amitriptyline 50 mg Amitriptyline 100 mg Placebo
Kieburtz 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	HIV-related neuropathic pain N=145 Age Mean (SD): 40	Amitriptyline 25-100 mg Mexiletine 150 mg Benztropine mesylate 0.125 mg
Leijon 1989 Sweden Efficacy quality: Fair	CT Crossover Single Center	Central/post-stroke neuropathic pain N=15 Age Mean (SD): 66	Amitriptyline 25 + 50 mg BID Carbamazepine 400 mg BID Placebo
Max (A) 1987 US	RCT Crossover Single Center	Painful diabetic neuropathy N=29	Amitriptyline mean 90 mg Benztropine mesylate 1 mg
Max (C) 1988 US	RCT Crossover Single Center	Post-herpetic neuralgia N=58	Amitriptyline 12.5-150 mg (mean 65 mg) Lorazepam 0.5-6 mg (mean 2.4 mg)

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
Efficacy quality: Fair		Age Mean (SD): 72	Placebo
Robinson 2004 US Efficacy quality: Fair	RCT Parallel Single Center	Phantom limb pain N=39 Age Mean (SD): 44.8 Male: 87.2%	Amitriptyline Benztropine mesylate
Shlay 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	HIV-related neuropathic pain N=136 Age Mean (SD): 40.0 Male: 91.2%	Amitriptyline 75 mg Placebo
Vrethem 1997 Sweden Efficacy quality: Fair	RCT Crossover	Polyneuropathy N=36 Age	Amitriptyline 75 mg Maprotiline 75 mg Placebo
Watson 1982 Canada	RCT Crossover	Post-herpetic neuralgia N=24	Amitriptyline 75 mg (median) Placebo
Panerai 1990 Italy	RCT Crossover	Mixed N=39	Nortriptyline Chlorimipramine Placebo

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
Raja 2002 US Efficacy quality: Fair	RCT Crossover	Post-herpetic neuralgia N=76 Age Mean 71 (range 32-90) 45% male, 55% female 88% white, 11% black, 1% other	Nortriptyline mean 89 mg; switched to desipramine if not tolerated Placebo
Kishore-Kumar 1990 US	RCT Crossover Single Center	Post-herpetic neuralgia N=26	Desipramine mean 167 mg Benztropine mesylate 0.5-1 mg
Max (B) 1991 US	RCT Crossover	Painful diabetic neuropathy□ □ N=24□	Desipramine Benztropine mesylate
Sindrup (A) 1990 Denmark Efficacy quality: Poor	RCT Crossover Multicenter	Painful diabetic neuropathy N=20 Age Mean (SD): 41 Range: 28-75	Paroxetine 40 mg daily Total daily dose: 40 mg Imipramine 50 or 75 mg daily Total daily dose: 50 or 75 mg Placebo
Sindrup (C) 1989 Denmark	RCT Crossover	Painful diabetic neuropathy N=9	Imipramine 50 or 75 mg Placebo
Sindrup (E) 1992 Denmark Efficacy quality: Fair	RCT Crossover	Painful diabetic neuropathy N=18 Age Mean 55.8 (range 29-80)	Imipramine 50 or 75 mg Placebo
Hammack 2002	RCT Crossover	Cisplatinum-induced neuropathic pain	Nortriptyline

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/' Sample size and characteristics	Intervention
US	Multicenter	N=51	
			Placebo
Panerai	RCT	Mixed	Nortriptyline
1990	Crossover		Chlorimipramine
Italy		N=39	Placebo

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
Leijon 1989 Sweden Efficacy quality: Fair	Unequivocal stroke episode; should seek remedy for constant or intermittent pain after stroke; pain was not nociceptive, peripheral neuropathic or psychogenic in origin	Known contraindication to both amitriptyline and carbamazepine; could not be evaluated in a satisfactory way
Rull 1969 Mexico Efficacy quality: Fair	Diabetic patients with well established subjective sensory manifestations of somatic neuropathy.	Not reported
Killian 1968 US Efficacy quality: Poor		
Campbell 1966	Trigeminal neuralgia, in pain at the time of entry.	"A few" patients rejected because of difficulty in attending regularly due to age, infirmity, or geography. Pain
Dalessio 1966 US Efficacy quality: Poor	Not reported	Not reported
Rockliff 1966 US	Active, typical trigeminal neuralgia.	Atypical facial pain or postherpetic neuralgia.
Eisenberg 2001 Israel Efficacy quality: Fair	1) Established diagnosis of diabetes mellitus (type 1 or 2); 2) no change had been made in their antihyperglycemic medications within 3 weeks before screening; 3) evidence of peripheral neuropathy was indicated by at least tow of the three following measures: a) medical history, b) neurologic examination, or c)	1) age younger than 18 or older than 75 years; 2) impaired renal or liver function; 3) known epilepsy; 4) presence of other painful conditions; 5) receipt of anticonvulsants, antidepressants, or membrane-stabilizing agent s for reasons other than pain relief, or use of opioids; and 6) participation in any clinical trial within 30 days before screening.
Finnerup	Outpatients of a rehabilitation center for spinal cord	Known concomitant cerebral damage or dementia (total score

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
2002 Denmark Efficacy quality: Fair	injury, with neuropathic pain after traumatic spinal cord injury at or below level of spinal lesion. Other reasons for pain were either excluded or considered highly unlikely. Age 18-70 and pain intensity >=3 on a 0-10 point numeric rating scale.	on the MMSE below 26), pregnant or lactating women and fertile women with inappropriate contraception (a negative pregnancy test was required), previous serious allergic reaction or hypersensitivity to lamotrigine, serious hepatic or renal disease or other significant illness.
McCleane 1999 UK	Adult patients presenting to a Pain Clinic with intractable neuropathic pain (diagnosed on the presence of at least 3 of the cardinal symptoms of neuropathic pain-	Known sensitivity to lamotrigine or already taking an anticonvulsant.
Simpson (B) 2003 US Efficacy quality: Fair	Aged 18 to 65 years, weighed at least 40 kg, had HIV-associated sensory neuropathy (either distal sensory polyneuropathy or antiretroviral toxic neuropathy), and scored at least 60 on the Karnofsky Performance Scale. To be characterized as having HIV-associated sensory neuropathy, patients had to have experienced symptoms of neuropathic pain in both distal lower extremities for at least 6 weeks and exhibited either diminished reflexes at the ankles compared with the knees or distal diminution of sensations of vibration, pain, or temperature in the legs, as established by a neurologist. Must have been experiencing pain in spite of previous symptomatic treatment for neuropathy	Other neurologic disorders that could confound the diagnosis of peripheral neuropathy, such as myelopathy. Any use of valproate within 4 weeks before randomization and any previous or current use of lamotrigine.
Simpson (C) 2000 US	HIV-infected subjects with distal sensory polyneuropathy established by a study neurologist, based on the following criteria: primary symptoms of burning or	Alternative causes for neuropathy (e.g., diabetes mellitus, hereditary neuropathy, or vitamin B12 deficiency) or current treatment with drugs that could be considered as contributing
Vestergaard 2001 Denmark	Patients with a previous stroke episode and who had pain for more than 3 months; older than age 18 and had had pain following as stroke for which nociceptive,	Dementia or any other severe cognitive impairment, diabetic neuropathy, malignant disease, recent MI, severe heart insufficiency, liver/renal failure, or a known allergy to
Zakrzewska 1997	Refractory trigemina neuralgia; diagnosis made according to the following criteria: suffering from	Surgery for trigeminal neuralgia (including nerve injections but excluding local anesthetic injections) within the last year.

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
UK	paroxysmal pain, pain was in the distribution of the	Patients with facial pain other than idiopathic trigeminal
Beydoun 2006 US Efficacy quality: Fair	Men and non-pregnant women, 18 years of age or older, with a diagnosis of diabetes mellitus (type 1 or 2), and pain attributed to diabetic neuropathy for 6 months to 5 years. Pain rating score of at least 50 units on a 100-unit VAS at the screening visit, stable glycemic control (as evidenced by a hemoglobin A1c level of <=11% at baseline), and baseline serum sodium levels >=35	Patients with other types of pain, clinically significant medical or psychiatric illnesses, a prior history of hyponatremia or non-compliance, drug or alcohol abuse in the preceding year, amputations other than the toes, treatment with lithium or MAO inhibitors, previous treatment with oxcarbazepine, or a history of sensitivity to carbamazepine or its metabolites.
Dogra 2005 US	Male or female outpatients, age 18 or older, established clinical diagnosis of diabetes mellitus (type 1 or 2); stable diabetic control as evidence by a) hemoglobin A1c level <=11% at baseline; b) average HA1c over the 6 months	Presence of other pain that could confound assessment of neuropathic pain of diabetic origin; currently or had previously taken oxcarbazepine; presence of skin lesions that could affect the ability to assess neuropathic pain or if they had
Gilron (B) 2001 US	Idiopathic trigeminal neuralgia (which may include recurrent trigeminal neuralgia following invasive peripheral nerve or intracranial procedures).	Multiple sclerosis or continuous pain and dense sensory loss related to an invasive procedure (i.e., anesthesia dolorosa.
Khoromi 2005 US	Evidence of lumbar radiculopathy, on the basis of the presence of pain in one or both buttocks or legs for 3 months or greater for at least 5 days a week and at least one of the following features on the side corresponding	Hepatic and renal dysfunction; pregnancy or lactation; seizure disorder; pain of greater intensity in any other location than the low back or leg; narcotic abuse and/or drug or alcohol abuse during the past year; fibromyalgia as defined by American
Raskin (A) 2004 US Efficacy quality: Fair	Men and women aged 18 to 75 years with a history of symmetric painful diabetic neuropathy in the lower extremities for at least 3 months but <=10 years. Diabetic neuropathy was confirmed by clinical, electrophysiologic, or quantitative sensory testing, and subjects were required to have maintained stable glycemic control (HbA1c <=11%) with oral hypoglycemics, insulin, or diet for at least 3 months before randomization. Women were required to practice adequate contraception during the study or be incapable of becoming pregnant	Other potential causes of peripheral neuropathy (including drug-induced neuropathy), another painful condition that was more severe than the diabetic neuropathy, a degenerative neurologic diorder, open ulcer, amputation, active infection, or Charcot joint, a history of nephrolithiasis, attempted suicide, suicidal tendencies, or substance abuse, or a clinically significant medical condition, including abnormal renal or hepatic function, symptomatic coronary artery or peripheral vascular disease, malignancy within the past 5 years, or major psychiatric disorder. Subjects also ecluded if they required continued treatmen with anticonvulsant or antipsychotic therapy, if they used acetazolamide, triamterene, zonisamide,
Thienel 2004 Multiple	Adults ages 18-75 years with type 1 or type 2 diabetes controlled by oral hypoglycemics and/or insulin or by diet alone, with bilateral and simultaneous symptoms of painful peripheral polyneuropathy for at least 6 months.	Polyneuropathy due to causes other than diabetes, diabetic ulceration of extremities, non-traumatic amputation, hosptialization within past 3 months for hyper-/hypoglycemia while adherent to appropriate diabetic therapy, significant

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
Efficacy quality: Fair	Antidiabetic regimens had to be stable for at least 3 months before study entry; baseline dosages were to be maintained throughout the study. HbA1c levels less than 11% and creatinine clearance of at least 60 ml/min.	history (within previous 2 years) of unstable medical disease, progressive or degenerative neurologic disorders, history of hepatitis or HIV, any mental impairment that would confound participaton, history of alcohol or drug abuse within previous
Kochar (A) 2002 India	Patients with type 2 diabetes with painful neuropathy attending the diabetes clinic at one hospital.	Liver disease, pulmonary tuberculosis, thyroid disorders, uremia, vitamin deficiency, hereditary and paraneoplastic neuropathy, alcoholism, and patients on steroid therapy.
Kochar (B) 2004 India Efficacy quality: Fair	1) Diabetes for at least 6 months on stable dosage of insulin or oral hypoglycemic agent and having reasonable diabetic control (HvA1c <11%), 2) daily neuropathic pain of at least moderate severity for >3 months, which interfered with daily activity or sleep, 3) pain intensity of >4 on a visual analogue pain scale, and	Liver disease, pulmonary tuberculosis, thyroid disorders, uremia, vitamin deficiency, hereditary and paraneoplastic neuropathy, alcoholism, or on steroid therapy.
Kochar (C) 2005 India Efficacy quality: Fair	Post-herpetic neuralgia patients in a hospital-based outpatient department; first 48 consecutive attenders who gave consent; adult patients having persistent pain for >6 months after onset of herpes zoster rash and at least 40/100mm point on visual analog scale and 4/11 point on Likert scale	Insufficient pain score on subsequent examination (visual analog scale <40) or withdrawn consent; no topical or other oral drugs during study
Otto 2004 Denmark	Polyneuropathy >=6 months confirmed by electrophysiologic tests, and age >20 years. At study entry during 1-week off medication patients had a	Causes of pain other than polyneuropathy, previous allergic reactions to valproic acid, pregnancy and lactating, liver disease, thrombocytopenia, and severe terminal illness.
Carlsson 2004 Norway Efficacy quality: Fair	Neuropathic pain of traumatic origin.	Pregnancy, severe organ disease not associated with the pain, or used MAO inhibitors.
McQuay 1994	Patients of either sex attending the Oxford Regional Pain Relief Unit for treatment of neuropathic pain, using the	Not reported

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
UK Efficacy quality: Fair	definition of a proven pathological process related to the painful area with demonstrable somatosensory dysfunction. Signs on neurological examination of a lesion of the peripheral or central nervous system, and pain symptoms in an appropriate distribution characterized by burning, shooting, or stabbing, sometimes associated with allodynia or hyperalgesia. Patients had to be able to understand the assessments.	
Nelson (A: diabetic neuropathy) 1997 US	Age between 18 and 85 years, daily pain of at least moderate intensity for greater than 3 months that was present more than 50% of the day, a previous trial of a tricyclic antidepressant medication, score of 28-30 on the MMSE indicating normal cognitive function, and	Presence of another more painful condition, difficulty with ambulation, any unstable disease process, a history of significant substance abuse or alcoholism, liver or kidney disease, or concurrent use of a MAO inhibitor.
Nelson (B: postherpetic neuralgia) 1997 US	Age between 18 and 85 years, daily pain of at least moderate intensity for greater than 3 months that was present more than 50% of the day, a previous trial of a tricyclic antidepressant medication, score of 28-30 on the MMSE indicating normal cognitive function, and	Presence of another more painful condition, difficulty with ambulation, any unstable disease process, a history of significant substance abuse or alcoholism, liver or kidney disease, or concurrent use of a MAO inhibitor.
Sindrup (B) 1992 Denmark	One or more symptoms (pain, paresthesia, dysesthesia, and hypesthesia) and signs (reduction of sensibility, strength, or tendon reflexes) of peripheral neuropathy.	Ankle/arm systolic blood pressure index below 0.9, and alcoholism.
Max (D) 1992 US	Presence of diabetes mellitus with stable glycemic control as assessed by the patient's primary physician, signs of peripheral neuropathy not attributable to another cause, and there months or more of daily pain of at least	Other pain more severe than the neuropathic pain, severe depression, postural hypotension, symptomatic coronary artery or peripheral vascular disease, and nephropathy.
Sindrup (A) 1990 Denmark Efficacy quality: Poor	Neurological signs of peripheral neuropathy and several of the following symptoms for at least 1 year: pain, paresthesia, dysesthesia, numbness, nightly exacerbation, and sleep disturbances.	Renal or cardiac dysfunction, diagnosis of pernicious anemia, reduced levels of vitamin B12 or folic acid, untreated hypothyroidism, or a recent weight loss/major change in metabolic control.

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
Cardenas 2002 US	Spinal cord injury more than 6 months ago; pain for at least 3 months; and average pain rating in the last month of at least 3 on a scale of 0-10.	Less than age 18 or more than 65 years of age, history of cardiovascular disease, abnormalities in a screening ECG, seizures, hyperthyroidism, or glaucoma; if female, were pregnant or unwilling to use a contraceptive during the study;
Kalso 1995 Finland Efficacy quality: Fair	Neuropathic pain following treatment for breast cancer. Pain had to be either in the anterior chest wall, and/or axilla and/or medial upper arm in an area with sensory disturbances.	Relapses or metastases of the breast cancer and clinically overt cardiac, renal, or hepatic disease.
Kieburtz 1998 US Efficacy quality: Fair	HIV infection and clinical symptoms and signs sufficient for a diagnosis of painful neuropathy defined as 1) primary symptoms of symmetrical pain, burning or tingling discomfort in the feet for a least 2 weeks, and rated on the pain intensity scale as at least mild all the time or moderate for a total of at least 2 hours per day;	If painful neuropathy was clearly attributable to another neuropathic drug (e.g., cisplatin, nitrofurantoin), if they were taking cardiac antiarrhythmic agents or tricyclic or tetracyclic antidepressants, or if they had a greater than 50% change in the dosage per week of medications for ain control in the week before entry. Diabetes mellitus, documented history of cardiac
Leijon 1989 Sweden Efficacy quality: Fair	Unequivocal stroke episode; should seek remedy for constant or intermittent pain after stroke; pain was not nociceptive, peripheral neuropathic or psychogenic in origin	Known contraindication to both amitriptyline and carbamazepine; could not be evaluated in a satisfactory way
Max (A) 1987 US	1) symptoms and signs of diffuse, predominantly sensory neuropathy or single or multiple mononeuropathy; 2) pain during some part of every day; and 3) active diabetes or a history of diabetes, with a	1) evidence of another etiology for neuropathy; 2) another painful condition at least as severe as the neuropathic pain; 3) cognitive or language impairment revealed by difficulty in completing the pain diary, paper-and-pencil psychological
Max (C) 1988 US	1) daily pain, persisting at least 3 months after a segmental herpes zoster eruption, and 2) normal cognitive and communicative ability, as judged by performance in completing a pain diary, paper-and-	1) presence of another type of pain as severe as the postherpetic neuralgia, 2) depression severe enough (e.g., suicidal ideation) to mandate immediate treatment with tricyclic medication, and 3) medical contraindications to the use of

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
Efficacy quality: Fair	pencil psychological tests, and telephone conversations.	amitriptyline or lorazepam.
Robinson 2004 US Efficacy quality: Fair	Amputation more than 6 months before enrollment, pain for at least 3 months, and average pain rating in the last month of at least 2 on a scale of 0 to 10.	Less than 18 years or more than 65 years of age, history of cardiovascular disease or seizures, were pregnant, on any type of antidepressant medication, or reported consuming more than 2 alcoholic drinks per day. Those 50 years or older had a screening ECG and were excluded if they had conducting abnormalities.
Shlay 1998 US Efficacy quality: Fair	Aged 13 or older, documented HIV infection, symptoms of HIV-related lower extremity peripheral neuropathy, diagnosed by a physician based on history and clinical exam, and have completed a baseline pain diary prior to randomization.	Being treated for an acute opportunistic infection or malignancy except nonsystemic Kaposi sarcoma, pregnant, or had taken a tricyclic antidepressant or MAO inhibitor 2 weeks before randomization.
Vrethem 1997 Sweden Efficacy quality: Fair	Daily moderate or severe polyneuropathic pain for at least 6 months. No indication of central, nociceptive, or psychogenic pain. At least 2 of the following symptoms and signs were required for the diagnosis of polyneuropathy: distal sensory impairment (touch,	Other neurologic diseases.
Watson 1982 Canada	Not reported	Not reported
Panerai 1990 Italy	Men and women, in- or outpatients, aged 18-80 years, affected by central pain lasting at least 6 months following limb amputation, phantom or stump pain,	Clinically evident heart or renal failure, severe liver disease, A-V conduction disturbances or class III or IV left ventricular arrhythmias, epilepsy, glaucoma, prostatic hypertrophy,

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
Raja 2002 US Efficacy quality: Fair	Age >18 years, pain persisting for >=3 months after the resolution of the cutaneous lesions, and typical pin intensity of >=4 (0 to 10 numerical rating scale) during the previous week.	History of substance abuse or an allergic reaction to an opioid or a tricyclic antidepressant, a myocardial infarction in the previous 3 months, cardia conduction defects, severe pulmonary disease, or encephalopathy, HIV positive, life expectancy <6 months; patients on MAO inhibitors or with severe depression precluding withdrawal from antidepressants.
Kishore-Kumar 1990 US	Postherpetic neuralgia and 1) daily pain, persisting at least 3 months after a segmental herpes zoster eruption and 2) normal cognitive and communicative ability, as judged by performance in completing a pain diary, paper-	1) presence of another type of pain as severe as the postherpetic neuralgia, 2) depression severe enough (e.g., suicidal ideation) to mandate immediate treatment with tricyclic medications, and 3) medical contraindications to the use of
Max (B) 1991 US	1) Symptoms and signs of diffuse, predominantly sensory neuropathy or single or multiple mononeuropathy; 2) daily pain, persisting at least 3	1) evidence of another etiology for neuropathy; 2) presence of another type of pain as severe as the neuropathic pain; 3) depression severe enough (e.g., suicidal ideation) to mandate
Sindrup (A) 1990 Denmark Efficacy quality: Poor	Neurological signs of peripheral neuropathy and several of the following symptoms for at least 1 year: pain, paresthesia, dysesthesia, numbness, nightly exacerbation, and sleep disturbances.	Renal or cardiac dysfunction, diagnosis of pernicious anemia, reduced levels of vitamin B12 or folic acid, untreated hypothyroidism, or a recent weight loss/major change in metabolic control.
Sindrup (C) 1989 Denmark	Diabetics with one or more symptoms and signs of peripheral neuropathy.	Ankle/arm systolic blood pressure index below 0.8, or serum creatinine >130 mcM, suspicion of alcohol abuse or current depression.
Sindrup (E) 1992 Denmark Efficacy quality: Fair	Pain, paresthesia, dysesthesia, nightly worsening of these symptoms, and sleep disturbance. Localization of symptoms was typical of peripheral neuropathy.	Renal or cardiac dysfunction, ankle/arm systolic blood pressure index below 0.9, megaloblastic anemia or hypothyroidism.
Hammack 2002	Age 18 or older, have received cisplatin chemotherapy, and have had painful paresthesia for at least 1 months	History of diabetes, glaucoma, prostatism, dementia, HIV infection, major psychiatric disease, significant cardiac

Evidence Table 8. Characteristics of placebo-controlled trials of other antidepressants, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Eligibility	Exclusion
US	attributed to cisplatin neuropathy. Required to have evidence on examination of a sensory peripheral	disease, or postural hypotension; other identified causes of sensory neuropathy and paresthesia; pregnant or lactating
Panerai 1990 Italy	Men and women, in- or outpatients, aged 18-80 years, affected by central pain lasting at least 6 months following limb amputation, phantom or stump pain,	Clinically evident heart or renal failure, severe liver disease, A-V conduction disturbances or class III or IV left ventricular arrhythmias, epilepsy, glaucoma, prostatic hypertrophy,

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Leijon 1989 Sweden Efficacy quality: Fair	CT Crossover Single Center	Amitriptyline 25 + 50 mg BID Total daily dose: 75 mg N=15	Global Impression of Change, Improved % of patients: 66.7% at 4 weeks (p<0.05)
			Pain intensity, 10-step verbal rating scale Mean score: 4.2 at 4 weeks (p<0.05) 95% CI: 3.39, 5.01
		Carbamazepine 400 mg BID Total daily dose: 800 mg N=14	Global Impression of Change, Improved % of patients: 35.7% at 4 weeks (p=NS)
			Pain intensity, 10-step verbal rating scale Mean score: 4.2 at 4 weeks (p=NS) 95% CI: 3.31, 5.09
		Placebo N=15	Global Impression of Change, Improved % of patients: 6.7% at 4 weeks
			Pain intensity, 10-step verbal rating scale Mean score: 5.3 at 4 weeks 95% CI: 4.29, 6.31
Campbell 1966 England Efficacy quality: Poor	RCT Crossover	Carbazepine N=36	Improvement, % change on a numeric scale (0-3) Mean change from baseline: 58% at 2 weeks (p<0.01)
		Placebo N=34	Improvement, % change on a numeric scale (0-3) Mean change from baseline: 26% at 2 weeks
Dalessio 1966 US Efficacy quality: Poor	RCT Crossover Single Center	Carbazepine 600 mg N=10	Pain relief, Significant change in pain (not defined) % of patients: 100% at 3 days (p<0.002)
		Placebo N=10	Pain relief, Significant change in pain (not defined) % of patients: 0% at 3 days
Rockliff 1966 US Efficacy quality: Poor	RCT Crossover Single Center	Carbazepine 600 mg N=9	Response, Patients preferring carbamazepine % of patients: 88.9% at 24 hours (p=NR)
		Placebo N=9	Response, Patients preferring placebo % of patients: 0% at 24 hours
Eisenberg 2001 Israel Efficacy quality: Fair	RCT Parallel Single Center	Lamotrigine 200-400 mg N=27	Average pain intensity, numerical scale (0-10) Mean score: 4.2 at 6 weeks (pNR,significantat200,300,and400mg) 95% CI: 4.16, 4.24

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Average pain, McGill Pain Questionnaire, words Mean score: 12.5 at 6 weeks (p=NS) 95% CI: 12.16, 12.84
			Response, 50% or greater reduction in pain % of patients: 44.4% at 6 weeks (p=0.05)
		Placebo N=26	Average pain intensity, numerical scale (0-10) Mean score: 5.3 at 6 weeks 95% CI: 5.26, 5.34
			Average pain, McGill Pain Questionnaire, words Mean score: 10.7 at 6 weeks Null Type field
			Response, 50% or greater reduction in pain % of patients: 19.2% at 6 weeks
Finnerup 2002 Denmark Efficacy quality: Fair	RCT Crossover Single Center	Lamotrigine 200-400 mg N=30	Average daily pain score, Numeric rating scale (0-10) Median change from baseline: 1 at 9 weeks (p=0.11)
			Pain, McGill Pain Questionnaire Median score: 19 at 9 weeks (p=0.76)
			Pain, McGill Pain Questionnaire, words chosen Median score: 11 at 9 weeks (p=0.81)
			Response, Moderate or greater pain relief % of patients: 31.8% at 9 weeks (p=0.06)
		Placebo N=30	Average daily pain score, Numeric rating scale (0-10) Median change from baseline: 0 at 9 weeks
			Pain, McGill Pain Questionnaire Median score: 18.5 at 9 weeks
			Pain, McGill Pain Questionnaire, words chosen Median score: 9 at 9 weeks
			Response, Moderate or greater pain relief % of patients: 13.6% at 9 weeks
McCleane 1999 UK	RCT Paralle Single Center	Lamotrigine 200 mg N=36	Pain, VAS (0-10) Mean change from baseline: -0.01 at 8 weeks (p=NS)

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Efficacy quality: Poor		Placebo N=38	Pain, VAS (0-10) Mean change from baseline: 0.03 at 8 weeks
Simpson (B) 2003 US Efficacy quality: Fair	RCT Parallel Multicenter	Lamotrigine 400 mg N=62	Average daily pain score, Gracely pain score Mean change from baseline: -0.27 at 11 weeks (p=NS)
			Average pain, McGill Pain Assessment Mean change from baseline: -6.9 at 11 weeks (p<0.05)
			Global Impression of Change, Marked or moderate improvement % of patients: 53% at 11 weeks (p<0.05 for marked)
			Pain intensity, VAS (0-100) Mean change from baseline: -27.1 at 11 weeks (p<0.05)
			Response, at least 30% reduction in VAS % of patients: 57% at 11 weeks (p<0.05)
		Lamotrigine 600 mg N=88	Average daily pain score, Gracely pain score Mean change from baseline: -0.30 at 11 weeks (p=NS)
			Average pain, McGill Pain Assessment Mean change from baseline: -6.8 at 11 weeks (p=NS)
			Global Impression of Change, Marked or moderate improvement % of patients: 60% at 11 weeks (p=NS)
			Pain intensity, VAS (0-100) Mean change from baseline: -23.3 at 11 weeks (p=NS)
			Response, at least 30% reduction in VAS % of patients: 52% at 11 weeks (p=NS)
		Placebo N=30	Average daily pain score, Gracely pain score Mean change from baseline: -0.10 at 11 weeks
			Average pain, McGill Pain Assessment Mean change from baseline: -1.6 at 11 weeks

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Global Impression of Change, Marked or moderate improvement % of patients: 30% at 11 weeks
			Pain intensity, VAS (0-100) Mean change from baseline: -9.0 at 11 weeks
			Response, at least 30% reduction in VAS % of patients: 23% at 11 weeks
		Placebo N=47	Average daily pain score, Gracely pain score Mean change from baseline: -0.27 at 11 weeks
			Average pain, McGill Pain Assessment Mean change from baseline: -8.7 at 11 weeks
			Global Impression of Change, Marked or moderate improvement % of patients: 45% at 11 weeks
			Pain intensity, VAS (0-100) Mean change from baseline: -21.3 at 11 weeks
			Response, at least 30% reduction in VAS % of patients: 45% at 11 weeks
Simpson (C) 2000 US Efficacy quality: Fair	RCT Parallel Multicenter	Lamotrigine 300 mg N=20	Average pain, Gracely pain score (log 10) Mean score: 0.52 at 14 weeks (p=0.05) 95% CI: 0.36, 0.68
			Severity of pain, Worst pain (Gracely pain score, log 10) Mean change from baseline: -0.63 at 14 weeks (p=0.17) 95% CI: -0.70, -0.56
		Placebo N=22	Average pain, Gracely pain score (log 10) Mean score: 0.88 95% CI: 0.69, 1.07
			Severity of pain, Worst pain (Gracely pain score, log 10) Mean change from baseline: -0.35 95% CI: -0.40, -0.30
Vestergaard 2001 Denmark Efficacy quality: Fair	RCT Crossover Multicenter	Lamotrigine 200 mg N=30	Average pain, Likert scale (0-10) Median score: 5 at 8 weeks (p=0.01)
			Global Pain Rating, 0-5 Median score: 3 at 8 weeks (p=0.02) Range: 1-5

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
		Placebo N=30	Average pain, Likert scale (0-10) Median score: 7 at 8 weeks
			Global Pain Rating, 0-5 Median score: 4 at 8 weeks Range: 2-5
Zakrzewska 1997 UK Efficacy quality: Fair	RCT Crossover	Lamotrigine 400 mg N=14	Average daily pain score, Reported graphically only
			Global Impression of Improvement, Composite efficacy index % of patients preferring lamotrigine: 85% at 2 weeks 95% CI: 61%-97%
			Improvement, Pain better or much better % of patients: 76.9% at 2 weeks (p=NR)
		Placebo N=14	Average daily pain score, Reported graphically only
			Improvement, Pain better or much better % of patients: 57.1% at 2 weeks
Beydoun 2006 US Efficacy quality: Fair	RCT Parallel	Oxcarbazepine 600 mg daily N=83	Average daily pain score, VAS (0-100) Mean change from baseline: -25.9 at 16 weeks (p=NS)
			Global Impression of Change, Much or very much improved % of patients: 36.4% at 16 weeks (p=NS)
		Oxcarbazepine 1200 mg daily N=87	Average daily pain score, VAS (0-100) Mean change from baseline: -29.0 at 16 weeks (p=NS)
			Global Impression of Change, Much or very much improved % of patients: 50.0% at 16 weeks (p=NS)
		Oxcarbazepine 1800 mg daily N=88	Average daily pain score, VAS (0-100) Mean change from baseline: -26.5 at 16 weeks (p=NS)
			Global Impression of Change, Much or very much improved % of patients: 49.3% at 16 weeks (p=NS)
		Placebo N=89	Average daily pain score, VAS (0-100) Mean change from baseline: -19.1 at 16 weeks

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Global Impression of Change, Much or very much improved % of patients: 37.3% at 16 weeks
Dogra 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Oxcarbazepine mean 1445 mg N=69	Average daily pain score, VAS (0-100) Mean change from baseline: -24.3 at 16 weeks (p=0.0108) 95% CI: -30.72, -17.88
			Response, 30% or greater decrease in VAS % of patients: 45.6% at 16 weeks (p=0.0288)
			Response, 50% or greater decrease in VAS % of patients: 35.2% at 16 weeks (p=0.0156)
		Placebo N=77	Average daily pain score, VAS (0-100) Mean change from baseline: -14.7 at 16 weeks 95% CI: -20.60, -8.80
			Response, 30% or greater decrease in VAS % of patients: 28.9% at 16 weeks
			Response, 50% or greater decrease in VAS % of patients: 18.4% at 16 weeks
Gilron (B) 2001 US Efficacy quality: Poor	RCT Crossover	Topiramate mean 308 mg (range 75-600 mg) N=3	Average daily pain score, 0-10 Mean score: 2.4 at 12 weeks (p=0.04) Range: 1.0-4.5
		Placebo N=3	Average daily pain score, 0-10 Mean score: 4.1 at 12 weeks (p=0.04) Range: 2.8-6.6
Khoromi 2005 US Efficacy quality: Fair	RCT Crossover	Topiramate mean 208 mg N=29	Average pain (leg), numeric (0-10) Mean score: 3.06 at 2 weeks (p=0.06)
			Global Impression of Change, Moderate or greater pain relief % of patients: 54% at 2 weeks (p=0.005)
		Diphenhydramine mean 40 mg N=29	Average pain (leg), numeric (0-10) Mean score: 3.8 at 2 weeks
			Global Impression of Change, Moderate or greater pain relief % of patients: 23% at 2 weeks

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Raskin (A) 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Topiramate mean 320 mg N=208	Global Impression of Efficacy, Good, very good, or excellent efficacy % of patients: 53.8% at 12 weeks (p=NR)
			Pain intensity (current pain), 5-point numeric scale (1-5) Mean score: data reported graphically only at 12 weeks (p=0.093)
			Pain intensity (worst pain), 5-point numeric scale (1-5) Mean score: data reported graphically only at 12 weeks (p=0.003)
			Pain intensity, VAS (0-100) Mean score: 46.2 at 12 weeks (p=0.038)
			Response, >30% decrease in VAS % of patients: 49.5% at 12 weeks (p=0.004)
			Response, >50% decrease in VAS % of patients: 35.6% at 12 weeks (p=0.005)
		Placebo N=109	Global Impression of Efficacy, Good, very good, or excellent efficacy % of patients: 33.9% at 12 weeks
			Pain intensity (current pain), 5-point numeric scale (1-5) Mean score: data reported graphically only at 12 weeks
			Pain intensity (worst pain), 5-point numeric scale (1-5) Mean score: data reported graphically only at 12 weeks
			Pain intensity, VAS (0-100) Mean score: 54.0 at 12 weeks
			Response, >30% decrease in VAS % of patients: 33.9% at 12 weeks
			Response, >50% decrease in VAS % of patients: 21.1% at 12 weeks
Thienel 2004 Multiple Efficacy quality: Fair	RCT Parallel Multicenter	Topiramate 100 mg N=253	Average pain, VAS (0-100) Mean score (Study 001): 36.1 at 18 weeks (p=0.043) 95% CI: 32.63, 39.57
			Average pain, VAS (0-100) Mean score (Study 003): 44.7 at 22 weeks (p=0.156) 95% CI: 41.06, 48.34

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
		Topiramate 200 mg N=372	Average pain, VAS (0-100) Mean score (Study 001): 38.3 at 18 weeks (p=0.138) 95% CI: 35.41, 41.19
			Average pain, VAS (0-100) Mean score (Study 002): 37.8 at 22 weeks (p=0.247) 95% CI: 34.91, 40.69
			Average pain, VAS (0-100) Mean score (Study 003): 44.7 at 22 weeks (p=0.096) 95% CI: 41.78, 47.62
		Topiramate 400 mg N=260	Average pain, VAS (0-100) Mean score (Study 001): 39.7 at 18 weeks (p=0.612) 95% CI: 36.43, 42.97
			Average pain, VAS (0-100) Mean score (Study 002): 39.3 at 22 weeks (p=0.482) 95% CI: 36.10, 42.50
		Placebo N=384	Average pain, VAS (0-100) Mean score (Study 001): 43.1 at 18 weeks 95% CI: 40.35, 45.85
			Average pain, VAS (0-100) Mean score (Study 002): 41.6 at 22 weeks 95% CI: 38.74, 44.46
			Average pain, VAS (0-100) Mean score (Study 003): 55.3 at 22 weeks 95% CI: 53.19, 57.41
Kochar (A) 2002 India Efficacy quality: Fair	RCT□ Parallel□ Single Center	Valproic acid/divalproex/sodium valproate 600 mg N=29	Pain, McGill Pain Score Mean score: 3.41 at 4 weeks (p=0.028) 95% CI: 2.73, 4.09
		Placebo N=28	Pain, McGill Pain Score Mean score: 4.6 at 4 weeks 95% CI: 3.81, 5.39
Kochar (B) 2004 India Efficacy quality: Fair	RCT□ Parallel□	Valproic acid/divalproex/sodium valproate 500 mg N=22	Pain intensity, Present Pain Intesity Mean score: 1.33 at 3 months (p<0.001) 95% CI: 0.04, 2.62
			Pain, SF-McGill Pain Questionnaire Mean score: 9.66 at 3 months (p<0.001) 95% CI: -2.02, 21.34

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain, VAS (0-10) Mean score: 3.0 at 3 months (p<0.001) 95% CI: -1.16, 7.16
		Placebo N=21	Pain intensity, Present Pain Intesity Mean score: 2.61 at 3 months 95% CI: 0.81, 4.41
			Pain, SF-McGill Pain Questionnaire Mean score: 17.88 at 3 months 95% CI: 7.26, 28.50
			Pain, VAS (0-10) Mean score: 6.0 at 3 months 95% CI: 2.39, 9.61
Kochar (C) 2005 India Efficacy quality: Fair	CT Parallel Single Center	Valproic acid/divalproex/sodium valproate 1000 mg daily N=23	Pain intensity, Present Pain Intensity Mean score: 1.95 at 8 weeks (p<0.0001) 95% CI: -0.58, 4.48
			Pain, 11-point Likert scale (0-10) Mean score: 3.63 at 8 weeks (p<0.0001) 95% CI: -0.96, 8.22
			Pain, SF-McGill Pain Questionnaire Mean score: 11.9 at 8 weeks (p<0.0001) 95% CI: -0.88, 24.68
			Pain, VAS (0-100) Mean score: 31.27 at 8 weeks (p<0.0001) 95% CI: -27.12, 89.66
			Response, At least 50% pain relief % of patients: 59.1% at 8 weeks (p=NR)
		Placebo N=22	Pain intensity, Present Pain Intensity Mean score: 3.22 at 8 weeks 95% CI: 1.26, 5.18
			Pain, 11-point Likert scale (0-10) Mean score: 5.33 at 8 weeks 95% CI: 2.04, 8.62
			Pain, SF-McGill Pain Questionnaire Mean score: 16.11 at 8 weeks 95% CI: 9.45, 22.77
			Pain, VAS (0-100) Mean score: 54.94 at 8 weeks 95% CI: 20.58, 89.30
			Response, At least 50% pain relief % of patients: 11.1% at 8 weeks
Otto 2004 Denmark	RCT Crossover	Valproic acid/divalproex/sodium valproate 1500 mg	Pain relief, Complete, good, or moderate relief % of patients: 9.7% at 4 weeks (p=0.13)

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Efficacy quality: Fair		N=37	Pain, Numeric scale (0-10) Median score: 5 at 4 weeks (p=0.24) Range: 2-10
		Placebo N=37	Pain relief, Complete, good, or moderate relief % of patients: 25.8% at 4 weeks
			Pain, Numeric scale (0-10) Median score: 6 at 4 weeks Range: 1-10
Carlsson 2004 Norway Efficacy quality: Fair	RCT Crossover	Dextromethorphan 270 mg one dose N=15	Pain intensity, VAS (0-100 mm) Mean reduction from baseline: 30% at 4 hours (p=NR)
			Pain intensity, VAS (0-100 mm) Mean reduction from baseline: data not reported, superior to placebo at 1.5 hours (p<0.05)
			Pain intensity, VAS (0-100 mm) Mean reduction from baseline: data not reported, superior to placebo at 2.5-4 hours (p<0.0002)
		Placebo N=15	Pain intensity, VAS (0-100 mm) Mean reduction from baseline: data not reported at 1.5 hours
			Pain intensity, VAS (0-100 mm) Mean reduction from baseline: data not reported at 2.5-4 hours
			Pain intensity, VAS (0-100 mm) Mean reduction from baseline: data not reported at 4 hours
McQuay 1994 UK Efficacy quality: Fair	RCT Crossover Single Center	Dextromethorphan 40.5 mg N=19	Current pain intensity, VAS (0-100) Mean score: 57 at 10 days (pNS(vsplacebodays)) 95% CI: 45.24, 68.76
			Current pain intensity, Verbal rating scale (0, 1, 2, 3) Mean score: 2.3 at 10 days (pNS(vsplacebodays)) 95% CI: 1.91, 2.69
			Current Pain intensity, Verbal rating scale (0-7) Mean score: 5 at 10 days (p NS vs placebo days) 95% CI: 4.61, 5.39
			Current Pain relief, VAS (0-100) Mean score: 0.5 at 10 days (pNS(vsplacebodays)) 95% CI: 0.11, 0.89

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Global Rating of Treatment, Verbal rating scale (0-4) Mean score: 0.4 at 10 days (pNS(vsplacebodays)) 95% CI: 0.20, 0.60
			Pain intensity, McGill No of Words Mean score: 13 at 10 days (pNS(vsplacebodays)) 95% CI: 11.04, 14.96
			Pain intensity, McGill Total score Mean score: 27 at 10 days (pNS(vsplacebodays)) 95% CI: 21.12, 32.88
			Typical pain intensity, VAS (0-100) Mean score: 70 at 10 days (pNS(vsplacebodays)) 95% CI: 62.16, 77.84
			Typical pain intensity, Verbal rating scale (0, 1, 2, 3) Mean score: 2.5 at 10 days (pNS(vsplacebodays)) 95% CI: 2.11, 2.89
			Typical Pain intensity, Verbal rating scale (0-7) Mean score: 5 at 10 days (pNS(vsplacebodays)) 95% CI: 4.22, 5.78
			Typical Pain relief, VAS (0-100) Mean score: 0.6 at 10 days (pNS(vsplacebodays)) 95% CI: 0.21, 0.99
		Dextromethorphan 81 mg N=17	Current pain intensity, VAS (0-100) Mean score: 50 at 10 days (pNS(vsplacebodays)) 95% CI: 38.24, 61.76
			Current pain intensity, Verbal rating scale (0, 1, 2, 3) Mean score: 2 at 10 days (pNS(vsplacebodays)) 95% CI: 1.61, 2.39
			Current Pain intensity, Verbal rating scale (0-7) Mean score: 4 at 10 days (pNS(vsplacebodays)) 95% CI: 3.22, 4.78
			Current Pain relief, VAS (0-100) Mean score: 0.3 at 10 days (pNS(vsplacebodays)) 95% CI: 0.10, 0.50

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Global Rating of Treatment, Verbal rating scale (0-4) Mean score: 0.5 at 10 days (pNS(vsplacebodays)) 95% CI: 0.11, 0.89
			Pain intensity, McGill No of Words Mean score: 11 at 10 days (pNS(vsplacebodays)) 95% CI: 9.04, 12.96
			Pain intensity, McGill Total score Mean score: 25 at 10 days (pNS(vsplacebodays)) 95% CI: 19.12, 30.88
			Typical pain intensity, VAS (0-100) Mean score: 56 at 10 days (pNS(vsplacebodays)) 95% CI: 44.24, 67.76
			Typical pain intensity, Verbal rating scale (0, 1, 2, 3) Mean score: 2.4 at 10 days (pNS(vsplacebodays)) 95% CI: 2.20, 2.60
			Typical Pain intensity, Verbal rating scale (0-7) Mean score: 5 at 10 days (pNS(vsplacebodays)) 95% CI: 4.41, 5.59
			Typical Pain relief, VAS (0-100) Mean score: 0.7 at 10 days (pNS(vsplacebodays)) 95% CI: 0.11, 1.29
Nelson (A: diabetic neuropathy) 1997 US Efficacy quality: Fair	RCT Crossover	Dextromethorphan mean 381 mg N=14	Global Impression of Change, A lot or moderate relief % of patients: 53.8% at 6 weeks (p=NR)
			Global Impression of Change, Categorical scale (0-4) Mean score: 2.7 at 6 weeks (p=0.002)
			Improvement, 13-item descriptor scale Mean difference from placebo (%): 24% at 6 weeks (p=0.014) 95% CI: 6%-42%
		Placebo N=14	Global Impression of Change, A lot or moderate relief % of patients: 0% at 6 weeks
			Global Impression of Change, Categorical scale (0-4) Mean score: 1.3 at 6 weeks

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Nelson (B: postherpetic neuralgia) 1997 US Efficacy quality: Fair	RCT Crossover	Dextromethorphan mean 439 mg N=18	Global Impression of Change, A lot or moderate relief % of patients: 38.5% at 6 weeks (p=NR)
			Global Impression of Change, Categorical scale (0-4) Mean score: 2.2 at 6 weeks (p=NS)
			Improvement, 13-item descriptor scale Mean difference from placebo (%): 2% at 6 weeks (p=0.72) 95% CI: 10%-14%
		Placebo N=18	Global Impression of Change, A lot or moderate relief % of patients: 23.1% at 6 weeks
			Global Impression of Change, Categorical scale (0-4) Mean score: 1.7 at 6 weeks
Sindrup (B) 1992 Denmark Efficacy quality: Fair	RCT Crossover Multicenter	Citalopram 40 mg N=18	Total neuropathy score, See comments Median score: 4.5 at 3 weeks (p=0.02) Range: 1.5-7.75
		Placebo N=18	Total neuropathy score, See comments Median score: 7.0 at 3 weeks Range: 1.0-10.5
Max (D) 1992 US Efficacy quality: Fair	RCT Crossover NR	Fluoxetine 20-40 mg N=54	Pain intensity, Verbal descriptors Mean change from baseline: Reported graphcally only at 6 weeks (p=NS)
			Pain relief, Complete, a lot, or moderate relief % of patients: 48% at 6 weeks (p=NS)
		Benztropine mesylate 0.125 to 1.5 mg N=54	Pain intensity, Verbal descriptors Mean change from baseline: Reported graphcally only at 6 weeks
			Pain relief, Complete, a lot, or moderate relief % of patients: 41% at 6 weeks
Sindrup (A) 1990 Denmark Efficacy quality: Poor	RCT Crossover Multicenter	Paroxetine 40 mg daily N=29	Pain, VAS (100 mm) Median score: 81.5 at 2 weeks (p=0.0121)
		Imipramine 50 or 75 mg daily N=29	Pain, VAS (100 mm) Median score: 37.0 at 2 weeks (p=0.0002)

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
		Placebo N=29	Pain, VAS (100 mm) Median score: 141.5 at 2 weeks
Cardenas 2002 US Efficacy quality: Fair	RCT Parallel Multicenter	Amitriptyline 10-125 mg daily N=44	Interference with activities, BPI Mean score: 29.8 at 6 weeks (p=NS) 95% CI: 23.18, 36.42
			Pain intensity, API (0-10) Mean score: 4.5 at 6 weeks (p=NS) 95% CI: 3.94, 5.06
		Benztropine mesylate 0.5 mg daily N=40	Interference with activities, BPI Mean score: 22.2 at 6 weeks 95% CI: 19.94, 24.46
			Pain intensity, API (0-10) Mean score: 4.0 at 6 weeks 95% CI: 3.38, 4.62
Kalso 1995 Finland Efficacy quality: Fair	RCT Crossover Single Center	Amitriptyline 50 mg N=15	Pain intensity, VAS (10 cm) Median score (breast scar area): 1.8 at 1 week (pNSvsbaseline) Range: 0-5.1
			Pain intensity, VAS (10 cm) Median score (ipsilateral arm): 1.9 at 1 week (pNSvsbaseline) Range: 0-9.1
			Pain intensity, VRS (8-point) Median score (breast scar area): 2.2 at 1 week (pNSvsbaseline) Range: 1-5
			Pain intensity, VRS (8-point) Median score (ipsilateral arm): 2.6 at 1 week (pNSvsbaselne) Range: 1-5
			Pain relief, VRS (5-point) Median score (breast scar area): 3.0 at 1 week (pNSvsbaseline) Range: 1-5
			Pain relief, VRS (5-point) Median score (ipsilateral arm): 3.0 at 1 week (pNSvsbaseline) Range: 1-5
		Amitriptyline 100 mg N=15	Pain intensity, VAS (10 cm) Median score (breast scar area): 0.2 at 1 week (p=NS) Range: 0-4.3
			Pain intensity, VAS (10 cm) Median score (ipsilateral arm): 0.5 at 1 week (p<0.05) Range: 0-30

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain intensity, VRS (8-point) Median score (breast scar area): 1.9 at 1 week (p<0.05) Range: 1-5
			Pain intensity, VRS (8-point) Median score (ipsilateral arm): 1.8 at 1 week (p<0.05) Range: 1-4
			Pain relief, VRS (5-point) Median score (breast scar area): 3.0 at 1 week (p<0.05) Range: 2-5
			Pain relief, VRS (5-point) Median score (ipsilateral arm): 3 at 1 week (p<0.05) Range: 2-5
			Pain, MPQ Total score Median score (breast scar region): 1151 at 1 week (p<0.05)
			Pain, MPQ Total score Median score (ipsilateral arm): 1757 at 1 week (p<0.01)
		Placebo N=15	Pain intensity, VAS (10 cm) Median score (breast scar area): 2.6 at 1 week Range: 0-6.6
			Pain intensity, VAS (10 cm) Median score (ipsilateral arm): 2.5 at 1 week Range: 0-9.2
			Pain intensity, VRS (8-point) Median score (breast scar area): 2.3 at 1 week Range: 1-4
			Pain intensity, VRS (8-point) Median score (ipsilateral arm): 3.1 at 1 week Range: 1-8
			Pain relief, VRS (5-point) Median score (breast scar area): 1 at 1 week Range: 1-5
			Pain relief, VRS (5-point) Median score (ipsilateral arm): 1 at 1 week Range: 1-5
			Pain, MPQ Total score Median score (breast scar region): 3221 at 1 week

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain, MPQ Total score Median score (ipsilateral arm): 2766 at 1 week
Kieburtz 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Amitriptyline 25-100 mg N=47	Global Impression of Change, Moderate, a lot, or complete relief % of patients: 50% at Week 8 (p=0.164)
			Pain intensity, Gracely Pain Scale Mean change from baseline: 0.31 at Week 8 (p=0.38) 95% CI: 0.21, 0.41
		Mexiletine 150 mg N=48	Global Impression of Change, Moderate, a lot, or complete relief % of patients: 45.8% at Week 8
			Pain intensity, Gracely Pain Scale Mean change from baseline: 0.23 at Week 8 Null Type field
		Benztropine mesylate 0.125 mg N=50	Global Impression of Change, Moderate, a lot, or complete relief % of patients: 48% at Week 8
			Pain intensity, Gracely Pain Scale Mean change from baseline: 0.20 at Week 8 Null Type field
Leijon 1989 Sweden Efficacy quality: Fair	CT Crossover Single Center	Amitriptyline 25 + 50 mg BID Total daily dose: 75 mg N=15	Global Impression of Change, Improved % of patients: 66.7% at 4 weeks (p<0.05)
			Pain intensity, 10-step verbal rating scale Mean score: 4.2 at 4 weeks (p<0.05) 95% CI: 3.39, 5.01
		Carbamazepine 400 mg BID Total daily dose: 800 mg N=14	Global Impression of Change, Improved % of patients: 35.7% at 4 weeks (p=NS)
			Pain intensity, 10-step verbal rating scale Mean score: 4.2 at 4 weeks (p=NS) 95% CI: 3.31, 5.09
		Placebo N=15	Global Impression of Change, Improved % of patients: 6.7% at 4 weeks
			Pain intensity, 10-step verbal rating scale Mean score: 5.3 at 4 weeks 95% CI: 4.29, 6.31

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Max (A) 1987 US Efficacy quality: Fair	RCT Crossover Single Center	Amitriptyline mean 90 mg N=37	Pain relief, Reporting greater pain relief with amitriptyline % of patients: 79.3% at 12 weeks (p<0.0001)
		Benztropine mesylate 1 mg N=37	Pain relief, Reporting greater pain relief with placebo % of patients: 3.4% at 12 weeks
Max (C) 1988 US Efficacy quality: Fair	RCT Crossover Single Center	Amitriptyline 12.5-150 mg (mean 65 mg) N=58	Average pain intensity, Verbal descriptors converted to numerical scores Mean score: reported graphically only at 6 weeks
			Pain relief, Moderate or greater relief % of patients: reported graphically only at 6 weeks
		Lorazepam 0.5-6 mg (mean 2.4 mg) N=58	Average pain intensity, Verbal descriptors converted to numerical scores Mean score: reported graphically only at 6 weeks
			Pain relief, Moderate or greater relief % of patients: reported graphically only at 6 weeks
		Placebo N=58	Average pain intensity, Verbal descriptors converted to numerical scores Mean score: reported graphically only at 6 weeks
			Pain relief, Moderate or greater relief % of patients: reported graphically only at 6 weeks
Robinson 2004 US Efficacy quality: Fair	RCT Parallel Single Center	Amitriptyline N=20	Average pain intensity (Phantom Limb Pain), Numeric rating scale (0-10) Mean score: 3.1 at 6 weeks (p=NS) 95% CI: 1.92, 4.28
			Average pain intensity (Residual Limb Pain), Numeric rating scale (0-10) Mean score: 3.1 at 6 weeks (p=NS) 95% CI: 2.14, 4.06
			Average pain, SF McGill Pain Questionnaire Mean score: 11.6 at 6 weeks (p=NS) 95% CI: 7.22, 15.98

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Interference with activities, BPI Mean score: 30.3 at 6 weeks (p=NS) 95% CI: 16.89, 43.71
		Benztropine mesylate N=19	Average pain intensity (Phantom Limb Pain), Numeric rating scale (0-10) Mean score: 3.1 at 6 weeks 95% CI: 1.80, 4.40
			Average pain intensity (Residual Limb Pain), Numeric rating scale (0-10) Mean score: 2.3 at 6 weeks 95% CI: 1.40, 3.20
			Average pain, SF McGill Pain Questionnaire Mean score: 12.5 at 6 weeks 95% CI: 8.63, 16.37
			Interference with activities, BPI Mean score: 24.2 at 6 weeks 95% CI: 14.58, 33.82
Shlay 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Amitriptyline 75 mg N=71	Average pain intensity, Gracely Scale (0.0 to 7.75) Mean change from baseline: -0.23 at 6 weeks (p=0.38) 95% CI: -0.22 to 0.08
			Average pain intensity, Gracely Scale (0.0 to 7.75) Mean change from baseline: -0.26 at 14 weeks (p=0.99) 95% CI: -0.18 to 0.19
			Pain relief, Moderate or more pain relief % of patients: 46.4% at 14 weeks (p=0.81)
			Pain relief, Moderate or more pain relief % of patients: 50.8% at 6 weeks (p=0.68)
		Placebo N=65	Average pain intensity, Gracely Scale (0.0 to 7.75) Mean change from baseline: -0.18 at 6 weeks
			Average pain intensity, Gracely Scale (0.0 to 7.75) Mean change from baseline: -0.30 at 14 weeks
			Pain relief, Moderate or more pain relief % of patients: 46.7% at 6 weeks

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain relief, Moderate or more pain relief % of patients: 50.9% at 14 weeks
Vrethem 1997 Sweden Efficacy quality: Fair	RCT Crossover	Amitriptyline 75 mg N=37	Response, 20% reduction in verbal scale (0-10) % of patients: 63% at 4 weeks (p=NR)
			Response, Improved, much improved, or pain free % of patients: 67% at 4 weeks (p<0.001)
		Maprotiline 75 mg N=37	Response, 20% reduction in verbal scale (0-10) % of patients: 50% at 4 weeks (p=NR)
			Response, Improved, much improved, or pain free % of patients: 42% at 4 weeks (p<0.05)
		Placebo N=37	Response, 20% reduction in verbal scale (0-10) % of patients: 22% at 4 weeks
			Response, Improved, much improved, or pain free % of patients: NR at 4 weeks
Watson 1982 Canada Efficacy quality: Fair	RCT Crossover NR	Amitriptyline 75 mg (median) N=24	Response, Good or excellent response % of patients: 66.7% at 3 weeks (p<0.001)
		Placebo N=24	Response, Good or excellent response % of patients: 4.2% at 3 weeks
Panerai 1990 Italy Efficacy quality: Poor	RCT Crossover	Nortriptyline N=39	Pain intensity, VAS (0-100 mm) Mean score: reported graphically only, superior to placebo at 3 weeks (p<0.0001)
		Chlorimipramine N=39	Pain intensity, VAS (0-100 mm) Mean score: reported graphically only, superior to placebo at 3 weeks (p<0.0001)
		Placebo N=39	Pain intensity, VAS (0-100 mm) Mean score: reported graphically only at 3 weeks
Kishore-Kumar 1990 US Efficacy quality: Poor	RCT Crossover Single Center	Desipramine mean 167 mg N=26	Average pain intensity, Verbal descriptor scale (Gracely pain scale) Mean score: data not reported, superior to placebo at 6 weeks (p<0.001)

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
			Pain relief, Moderate or better relief % of patients: 63% at 6 weeks (p=NR)
		Benztropine mesylate 0.5-1 mg N=26	Average pain intensity, Verbal descriptor scale (Gracely pain scale) Mean score: data not reported at 6 weeks
			Pain relief, Moderate or better relief % of patients: 11% at 6 weeks
Max (B) 1991 US Efficacy quality: Fair	RCT Crossover	Desipramine N=24	Pain intensity, Verbal descriptor scale (Gracely) Mean score: data reported graphically, superior to placebo at 6 weeks (p<0.01)
			Pain relief, Moderate or better relief % of patients: 55% at 6 weeks (p=NR)
		Benztropine mesylate N=24	Pain intensity, Verbal descriptor scale (Gracely) Mean score: dta reported graphically only at 6 weeks
			Pain relief, Moderate or better relief % of patients: 11% at 6 weeks
Sindrup (A) 1990 Denmark Efficacy quality: Poor	RCT Crossover Multicenter	Paroxetine 40 mg daily N=29	Pain, VAS (100 mm) Median score: 81.5 at 2 weeks (p=0.0121)
		Imipramine 50 or 75 mg daily N=29	Pain, VAS (100 mm) Median score: 37.0 at 2 weeks (p=0.0002)
		Placebo N=29	Pain, VAS (100 mm) Median score: 141.5 at 2 weeks
Sindrup (C) 1989 Denmark Efficacy quality: Poor	RCT Crossover	Imipramine 50 or 75 mg N=13	Pain relief, Most relieved of symptoms % of patients: 88.9% at 3 weeks (p<0.01)
			Pain, Lower score on a 6-item scale (0-2) % of patients: 88.9% at 3 weeks (p<0.01)
		Placebo N=13	Pain relief, Most relieved of symptoms % of patients: 11% at 3 weeks
			Pain, Lower score on a 6-item scale (0-2) % of patients: 11% at 3 weeks (p=0.01)

Evidence Table 9. Patient-reported pain outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Patient-reported pain
Hammack 2002 US Efficacy quality: Fair	RCT Crossover Multicenter	Nortriptyline N=26	Improvement, 13-item descriptor scale Mean difference from placebo (%): 24% at 6 weeks (p=0.014) 95% CI: 6%-42%
			Severity of pain, Verbal descriptor scale (5 points) Mean change from baseline: -0.5 at 4 weeks (p=0.99)
			Severity of pain, Visual analogue scale (0-100) Mean change from baseline: -7.7 at 4 weeks (p=0.78)
		Placebo N=25	Severity of pain, Verbal descriptor scale (5 points) Mean change from baseline: -0.4 at 4 weeks
			Severity of pain, Visual analogue scale (0-100) Mean change from baseline: -2.7 at 4 weeks
Panerai 1990 Italy Efficacy quality: Poor	RCT Crossover	Nortriptyline N=39	Pain intensity, VAS (0-100 mm) Mean score: reported graphically only, superior to placebo at 3 weeks (p<0.0001)
		Chlorimipramine N=39	Pain intensity, VAS (0-100 mm) Mean score: reported graphically only, superior to placebo at 3 weeks (p<0.0001)
		Placebo N=39	Pain intensity, VAS (0-100 mm) Mean score: reported graphically only at 3 weeks

Evidence Table 10. Functional outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Functional capacity
Eisenberg 2001 Israel Efficacy quality: Fair	RCT Parallel Single Center	Lamotrigine 200-400 mg N=27	Disability, Pain Disability Index□ Mean score: 3.8 at 6 weeks (p=NS)□ 95% CI: 3.54, 4.06
		Placebo N=26	Disability, Pain Disability Index□ Mean score: 4.3 at 6 weeks□ Null Type field
Finnerup 2002 Denmark Efficacy quality: Fair	RCT Crossover Single Center	Lamotrigine 200-400 mg N=30	Quality of life, SF-36 Mental Component summary□ Median score: 60.7 at 9 weeks (p=0.80)□
			Quality of life, SF-36 Physical component summary□ Median score: 32.6 at 9 weeks (p=1.00)□
		Placebo N=30	Quality of life, SF-36 Mental Component summary□ Median score: 61.9 at 9 weeks□
			Quality of life, SF-36 Physical component summary□ Median score: 33.9 at 9 weeks□
McCleane 1999 UK Efficacy quality: Poor	RCT Parallel Single Center	Lamotrigine 200 mg N=36	Mobility, VAS (0-10)□ Mean change from baseline: -0.36 at 8 weeks (p=NS)
			Quality of life, VAS (0-10)□ Mean change from baseline: -0.38 at 8 weeks (p=NS)
		Placebo N=38	Mobility, VAS (0-10)□ Mean change from baseline: -0.17 at 8 weeks
			Quality of life, VAS (0-10)□ Mean change from baseline: -0.15 at 8 weeks
Vestergaard 2001 Denmark Efficacy quality: Fair	RCT Crossover Multicenter	Lamotrigine 200 mg N=30	Interference, 1-5□ Median score: 3 at 8 weeks (p=0.11)□ Range: 1-5
		Placebo N=30	Interference, 1-5□ Median score: 4 at 8 weeks□ Range: 1-5
Beydoun 2006 US Efficacy quality: Fair	RCT Parallel	Oxcarbazepine 600 mg daily N=83	Quality of life, SF-36□ : Data NR, no difference from placebo at 16 weeks (p=NS)
		Oxcarbazepine 1200 mg daily N=87	Quality of life, SF-36□ : Data NR, no difference from placebo at 16 weeks (p=NS)
		Oxcarbazepine 1800 mg daily N=88	Quality of life, SF-36□ : Data NR, no difference from placebo at 16 weeks (p=NS)
		Placebo N=89	Quality of life, SF-36□ : Data NR, at 16 weeks
Dogra 2005 US Efficacy quality: Fair	RCT Parallel Multicenter	Oxcarbazepine mean 1445 mg N=69	Quality of life, SF-36 Mental Health□ Mean score: 47.2 at 16 weeks (p=0.03)
			Quality of life, SF-36 other subscales□ Mean score: data not reported, no difference from placebo at 16 weeks (p=NS)
		Placebo	Quality of life, SF-36 Mental Health□ Mean score: 50.2 at 16 weeks

Evidence Table 10. Functional outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Functional capacity
		N=77	Quality of life, SF-36 other subscales□ Mean score: data not reported at 16 weeks
Khoromi 2005 US Efficacy quality: Fair	RCT Crossover	Topiramate mean 208 mg N=29	Disability, Oswestry Low Back Pain Disability Questionnaire (%□ Mean score: 25 at 2 weeks (p=NS)□ 95% CI: 19.18, 30.82
			Quality of life, SF-36 Physical Functioning□ Mean score: 67 at 2 weeks (p=NS)
			Quality of life, SF-36 Bodily Pain□ Mean score: 51 at 2 weeks (p=NS)
			Quality of life, SF-36 General Health Perception□ Mean score: 72 at 2 weeks (p=NS)
			Quality of life, SF-36 Mental Health□ Mean score: 74 at 2 weeks (p0.019(treatmentworse))
			Quality of life, SF-36 Vitality□ Mean score: 54 at 2 weeks (p=NS)
		Diphenhydramine mean 40 mg N=29	Disability, Oswestry Low Back Pain Disability Questionnaire (%□ Mean score: 27 at 2 weeks□ 95% CI: 21.54, 32.46
			Quality of life, SF-36 Physical Functioning□ Mean score: 63 at 2 weeks
			Quality of life, SF-36 Bodily Pain□ Mean score: 50 at 2 weeks
			Quality of life, SF-36 General Health Perception□ Mean score: 72 at 2 weeks
			Quality of life, SF-36 Mental Health□ Mean score: 80 at 2 weeks
			Quality of life, SF-36 Vitality□ Mean score: 56 at 2 weeks
Raskin (A) 2004 US Efficacy quality: Fair	RCT Parallel Multicenter	Topiramate mean 320 mg N=208	Quality of life, SF-36 Mental Component Summary□ Mean score: 46.9 at 12 weeks (p=0.023)□ 95% CI: 45.28, 48.52
			Quality of life, SF-36 Physical Component Summary□ Mean score: 37.2 at 12 weeks (p=0.066)□ 95% CI: 35.76, 38.64
		Placebo N=109	Quality of life, SF-36 Mental Component Summary□ Mean score: 49.9 at 12 weeks□ 95% CI: 48.00, 51.80
			Quality of life, SF-36 Physical Component Summary□ Mean score: 34.9 at 12 weeks□ 95% CI: 33.14, 36.66
Cardenas 2002 US Efficacy quality: Fair	RCT Parallel Multicenter	Amitriptyline 10-125 mg daily N=44	Disability, CHART□ Mean score: 384.1 at 6 weeks (p=NS)□ 95% CI: 357.24, 410.96
			Disability, FIM□ Mean score: 66.3 at 6 weeks (p=NS)□ 95% CI: 61.37, 71.23
		Benztropine mesylate 0.5 mg daily N=40	Disability, CHART□ Mean score: 63.7 at 6 weeks□ 95% CI: 58.03, 69.37
			Disability, FIM□ Mean score: 24.4 at 6 weeks□ 95% CI: 18.08, 30.72

Evidence Table 10. Functional outcomes in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs, and dextromethorphan for neuropathic pain

Study	Design	Intervention	Functional capacity
Kieburtz 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Amitriptyline 25-100 mg N=47	Quality of life, General Health Self-Assessment form□ Data not reported: Data not reported at Week 8
		Mexiletine 150 mg N=48	Quality of life, General Health Self-Assessment form□ Data not reported: Data not reported at Week 8
		Benztropine mesylate 0.125 mg N=50	Quality of life, General Health Self-Assessment form□ Data not reported: Data not reported at Week 8
Robinson 2004 US Efficacy quality: Fair	RCT Parallel Single Center	Amitriptyline N=20	Activities of Daily Living, FIM Instrument□ Mean score: 74.5 at 6 weeks (p=NS)□ 95% CI: 66.26, 82.74
			Disability, CHART□ Mean score: 360 at 6 weeks (p=NS)□ 95% CI: 297.77, 422.23
			Quality of life, Satisfaction with Life Scale□ Mean score: 21.2 at 6 weeks (p0.004(placebobetter))□ 95% CI: 18.40, 24.00
		Benztropine mesylate N=19	Activities of Daily Living, FIM Instrument□ Mean score: 79.1 at 6 weeks□ 95% CI: 77.62, 80.58
			Disability, CHART□ Mean score: 417 at 6 weeks□ 95% CI: 383.28, 450.72
			Quality of life, Satisfaction with Life Scale□ Mean score: 21.8 at 6 weeks□ 95% CI: 17.89, 25.71
Shlay 1998 US Efficacy quality: Fair	RCT Parallel Multicenter	Amitriptyline 75 mg N=71	Quality of life, Medical Outcome Study, Physical functioning□ Mean change from baseline: 5.9 at 6 weeks (p=0.94)□ 95% CI: -8.3 to 8.9
			Quality of life, Medical Outcome Study, Physical functioning□ Mean change from baseline: 7.1 at 14 weeks (p=0.17)□ 95% CI: -2.7 to 15.5
		Placebo N=65	Quality of life, Medical Outcome Study, Physical functioning□ Mean change from baseline: 0.6 at 14 weeks
			Quality of life, Medical Outcome Study, Physical functioning□ Mean change from baseline: 5.1 at 6 weeks
Hammack 2002 US Efficacy quality: Fair	RCT Crossover Multicenter	Nortriptyline N=26	Interference, Verbal descriptor scale (5 points)□ Mean change from baseline: -0.3 at 4 weeks (p=0.04)
			Quality of life, Visual analogue scale (0-100)□ Mean change from baseline: -4.6 at 4 weeks (p=0.74)
		Placebo N=25	Interference, Verbal descriptor scale (5 points)□ Mean change from baseline: 0.2 at 4 weeks
			Quality of life, Visual analogue scale (0-100)□ Mean change from baseline: -7.7 at 4 weeks

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Backonja 1999 US	Fair	Yes	Method not described	Yes	Yes
Beydoun 2006 US	Fair	Yes	Yes	Yes	Yes
Bone 2002 UK and Ireland	Fair	Yes	Yes	NR Only baseline pain levels reported as NSD between groups	Yes
Campbell 1966 England	Poor	Yes	Method not described	No 6% of carbazepine first group vs 29% of placebo first group had been injected for pain; otherwise similar	No
Cardenas 2002 US	Fair	Method not described	Yes	Yes	Yes
Carlsson 2004 Norway	Fair	No	Method not described	NR	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Chandra 2006 India	Fair	Yes	Yes	Yes	Yes
Dalessio 1966 US	Poor	Method not described	Method not described	NR	No
Dallocchio 2000 Italy	Fair	Method not described	Method not described	Yes	Yes
Dogra 2005 US	Fair	Yes	Method not described	Yes	Yes
Drewes 1994 Denmark	Fair	Method not described	Method not described	NR Crossover	Yes
Dworkin 2003 US	Fair	Yes	Yes	Yes	Yes
Eisenberg 2001 Israel	Fair	Yes	Method not described	No duration of sx's longer in lamotrigine arm	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Estanisla 2004 US	Fair	Method not described	Method not described	NR On baseline pain score; other characteristic NR	Yes
Finnerup 2002 Denmark	Fair	Yes	Yes	NR	Yes
Freynhagen 2005 Multiple European	Fair	Method not described	Method not described	Yes	Yes
Galer (A) 2002 US	Poor	Method not described	Method not described	Yes	Yes
Galer (B) 1999 US	Fair	Method not described	Method not described	NR	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Gilron (A) 2005 Canada	Fair	Method not described	Yes	Yes	Yes
Gilron (B) 2001 US	Poor	Method not described	Method not described		Yes
Goldstein 2005 US	Fair	Yes	Yes	Yes More women in placebo group (48.7% vs 35%, p=0.033); otherwise similar	Yes
Gorson 1999	Fair	Method not described	Method not described	NR	Yes
Hahn 2004 Germany	Fair	Method not described	Yes	Yes	Yes
Hammack 2002 US	Fair	Balanced allocation	Not applicable	Yes	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Kalso 1996 Finland	Fair	Method not described	Yes	NR	Yes
Khoromi 2005 US	Fair	Yes	Yes	NR	Yes
Kieburtz 1998 US	Fair	Yes		Yes	Yes
Killian 1968 US	Poor	Method not described	Method not described	NR	Yes
Kishore-Kumar 1990 US	Poor	Method not described	Method not described	NR	Yes
Kochar (A) 2002 India	Fair	Method not described	Method not described	Yes	Yes
Kochar (B) 2004 India	Fair	Method not described	Method not described	NR Baseline characteristics reported on 39/43 analyzed	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Kochar (C) 2005 India	Fair	Method not described	Method not described	Yes Baseline data reported for 40/45 completers only	Yes
Kvinesdal 1984 Denmark	Fair	Method not described	Method not described	NR Crossover	Yes
Leijon 1989 Sweden	Fair	Method not described	Method not described	NR	Yes
Lesser 2004 US	Fair	Method not described	Yes	Yes	Yes
Levendoglu 2004 Turkey	Fair	Method not described	Method not described	NR	Yes
Max (A) 1987 US	Fair	Method not described	Method not described	NR	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Max (B) 1991 US	Fair	Method not described	Method not described	NR	Yes
Max (C) 1988 US	Fair	Method not described	Method not described	NR	Yes
Max (D) 1992 US	Fair	Method not described	Method not described	NR	Yes
McCleane 1999 UK	Poor	Yes	Method not described	NR Data only reported for 74/100 patients completing trial	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Carry Over Effects Handling (if crossover design)	Withdrawal Rate high (>85%)
Backonja 1999 US	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes 16.7% gabapentin, 19.8% placebo
Beydoun 2006 US	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes
Bone 2002 UK and Ireland	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	washout	Yes 5/19 (26.3%) withdrew
Campbell 1966 England	NR	NR	Yes	Attrition: Yes Crossover: Yes Adherence: No Contamination: No		No
Cardenas 2002 US	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	No 11/84 (13.1%)
Carlsson 2004 Norway	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	washout	No

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Carry Over Effects Handling (if crossover design)	Withdrawal Rate high (>85%)
Chandra 2006 India	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	No 7.9% overall (2/38 nortriptyline, 4/38 gabapentin)
Dalessio 1966 US	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: No Contamination: No	none	Yes 20%
Dallocchio 2000 Italy	No	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	NA	No
Dogra 2005 US	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes 40/146
Drewes 1994 Denmark	Yes	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	washout	No
Dworkin 2003 US	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes 34.8% pregabalin, 11.9% placebo
Eisenberg 2001 Israel	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes 13/59 (22%)

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Carry Over Effects Handling (if crossover design)	Withdrawal Rate high (>85%)
Estanisla 2004 US	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	washout	No
Finnerup 2002 Denmark	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	washout	Yes
Freynhagen 2005 Multiple European	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes 129/338 (38.2%)
Galer (A) 2002 US	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: No Crossover: No Adherence: No Contamination: No	NA	Unable to determine
Galer (B) 1999 US	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	NR	No

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Carry Over Effects Handling (if crossover design)	Withdrawal Rate high (>85%)
Gilron (A) 2005 Canada	Unclear, reported as double blind	Yes	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	analysis	Yes Attrition 16/57
Gilron (B) 2001 US	Unclear, reported as double blind	Yes	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	washout	No
Goldstein 2005 US	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	NA	Yes
Gorson 1999	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: No Crossover: No Adherence: No Contamination: No	washout	No
Hahn 2004 Germany	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes 19%
Hammack 2002 US	Unclear, reported as double blind	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	washout	No

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Carry Over Effects Handling (if crossover design)	Withdrawal Rate high (>85%)
Kalso 1996 Finland	Unclear, reported as double blind	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No		Yes 5/20 (25%)
Khoromi 2005 US	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: No Contamination: No	washout	Yes
Kieburtz 1998 US	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	Yes 35/145 (24%)
Killian 1968 US	Unclear, reported as double blind	Yes	Yes	Attrition: No Crossover: No Adherence: No Contamination: No	NA	Unable to determine
Kishore-Kumar 1990 US	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	none	Yes 7/26
Kochar (A) 2002 India	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	No
Kochar (B) 2004 India	Yes	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	No

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Carry Over Effects Handling (if crossover design)	Withdrawal Rate high (>85%)
Kochar (C) 2005 India	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	NA	No
Kvinesdal 1984 Denmark	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	none	Yes
Leijon 1989 Sweden	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	washout	No
Lesser 2004 US	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	NA	No
Levendoglu 2004 Turkey	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	washout	No
Max (A) 1987 US	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	none	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Carry Over Effects Handling (if crossover design)	Withdrawal Rate high (>85%)
Max (B) 1991 US	Unclear, reported as double blind	Yes	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	none	Yes 16.7% withdrew
Max (C) 1988 US	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	washout	Yes 21/62 (34%)
Max (D) 1992 US	Unclear, reported as double blind	Yes	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	washout	Yes 8/28 entered into fluoxetine vs. placebo withdrew
McCleane 1999 UK	Unclear, reported as double blind	Unclear, reported as double blind	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	NA	Yes

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Loss to Followup Differential or High	Intention to Treat Analysis (at least 95% analyzed)	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Backonja 1999 US	No	Yes <5% not analyzed	Yes lack of compliance (n=6 total)	Screened: 232 Eligible: 221 Enrolled: 165	Yes	Parke-Davis
Beydoun 2006 US	No	Yes Used LOCF, but number analyzed not clear	No	Screened: NR Eligible: NR Enrolled: 347	Yes	Novartis
Bone 2002 UK and Ireland	No	Yes	No	Screened: 33 Eligible: 27 Enrolled: 19	Yes	Pfizer provided study medication
Campbell 1966 England	No	No 70/76 analyzed	Yes 7/77 post-randomization exclusions	Screened: NR Eligible: NR Enrolled: 77	No	Not reported (Geigy Pharmaceuticals supplied carbazepine)
Cardenas 2002 US	No	Yes	No	Screened: 282 Eligible: 157 Enrolled: 84	Yes	Government funded (NIH and Dept of Education)
Carlsson 2004 Norway	No	No 13/15 (86%) analyzed	No	Screened: 22 Eligible: 21 Enrolled: 15	Yes	Not reported

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Loss to Followup Differential or High	Intention to Treat Analysis (at least 95% analyzed)	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Chandra 2006 India	No	No 70/76 analyzed (92.1%)	No	Screened: 110 Eligible: 79 Enrolled: 76	Yes	Pfizer (partly)
Dalessio 1966 US	No	Yes	No	Screened: NR Eligible: NR Enrolled: 10	No	Geigy provided study drug, otherwise NR
Dallocchio 2000 Italy	No	Yes	No	Screened: NR Eligible: NR Enrolled: 25	Yes	Not reported
Dogra 2005 US	No	Yes	No	Screened: 289 Eligible: 156 Enrolled: 146	Yes	Novartis
Drewes 1994 Denmark	No	Yes	Yes 1/20	Screened: NR Eligible: NR Enrolled: 20	Yes	Rhone-Poulenc Rorer A/S
Dworkin 2003 US	No	Yes LOCF	 excluded for lack of efficay (n=6)	Screened: 245 Eligible: 188 Enrolled: 173	Yes	Pfizer
Eisenberg 2001 Israel	No	No	No	Screened: 160 Eligible: NR Enrolled: 59	Yes	Glaxo-Wellcome

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Loss to Followup Differential or High	Intention to Treat Analysis (at least 95% analyzed)	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Estanisla 2004 US	No	Unable to determine says analysis was ITT, but no details.	Yes compliance (1)	Screened: NR Eligible: 64 Enrolled: 64	Yes	Hind Health Care and NIH
Finnerup 2002 Denmark	No	No 22/30 analyzed	No	Screened: 436 Eligible: 100 Enrolled: 30	Yes	Foundation and government; Glaxo provided medication
Freynhagen 2005 Multiple European	No	Yes 2/338 not analyzed (<1%)	Yes 7.3% for lack of compliance of other reason	Screened: 503 Eligible: NR Enrolled: 338	Yes	Pfizer
Galer (A) 2002 US	Unable to determine	No Only analyzed those with final data; Number randomized NR (only number analyzed)	Unable to determine	Screened: 150 Eligible: NR Enrolled: NR	No	Endo Pharmaceuticals
Galer (B) 1999 US	No	Yes	No <5% (1 patient who had a stroke)	Screened: NR Eligible: NR Enrolled: 33	Yes	Hind Health Care, Inc.

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Loss to Followup Differential or High	Intention to Treat Analysis (at least 95% analyzed)	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Gilron (A) 2005 Canada	Unable to determine	Unable to determine Not clear- states no patients excluded for missing data, but number analyzed not explicit, and 16 withdrawals	Unable to determine Reasons for withdrawal NR (13/57)	Screened: 86 Eligible: 70 Enrolled: 57	Yes	Government (Canadian Institutes of Health Research). Study medication provided by Pfizer and Aventis-Pharma
Gilron (B) 2001 US	No	Yes	No	Screened: NR Eligible: NR Enrolled: 3	Yes	Government (NIH) and Ortho-McNeil
Goldstein 2005 US	No	No 347/457 analyzed for primary outcome	Yes 17 subjects in total due to sponsor decision or protocol violation	Screened: 763 Eligible: 457 Enrolled: 457	Yes	Eli Lilly and PRN Consulting
Gorson 1999	No	Yes	No	Screened: NR Eligible: NR Enrolled: 40	Yes	Warner-Lambert (Parke-Davis Pharmaceuticals)
Hahn 2004 Germany	No	No 24/26 analyzed (92.3%)	No	Screened: NR Eligible: NR Enrolled: 26	Yes	Pfizer
Hammack 2002 US	No	Yes Imputation for missing data	Yes 6/57	Screened: NR Eligible: NR Enrolled: 57	Yes	

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Loss to Followup Differential or High	Intention to Treat Analysis (at least 95% analyzed)	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Kalso 1996 Finland	No	No	Yes 1/20 excluded due to noncompliance	Screened: NR Eligible: NR Enrolled: 20	Yes	Academy of Finland, Paulo Foundation, Centre for International Mobility
Khoromi 2005 US	No	No	Yes 1/42	Screened: NR Eligible: 42 Enrolled: 42	Yes	Government (NIH) and Ortho McNeil
Kieburtz 1998 US	No	No	No	Screened: NR Eligible: NR Enrolled: 145	Yes	Government (NIH); medication provided by Boerhinger-Ingelheim.
Killian 1968 US	Unable to determine	No 36/42 analyzed	Unable to determine	Screened: NR Eligible: NR Enrolled: 42		
Kishore-Kumar 1990 US	No	No 19/26 (73%)	No	Screened: NR Eligible: NR Enrolled: 26	Yes	Not reported
Kochar (A) 2002 India	No	No	Yes	Screened: 60 Eligible: NR Enrolled: 57	Yes	Not reported
Kochar (B) 2004 India	No	No	No	Screened: 48 Eligible: 44 Enrolled: 43	Yes	Not reported

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Loss to Followup Differential or High	Intention to Treat Analysis (at least 95% analyzed)	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Kochar (C) 2005 India	No	No	No	Screened: 48 Eligible: 45 Enrolled: 45	Yes	Not reported
Kvinesdal 1984 Denmark	No	No	No	Screened: NR Eligible: NR Enrolled: 15	Yes	Not reported (tablets provided by Dumex Ltd)
Leijon 1989 Sweden	No	No	No	Screened: 27 Eligible: 15 Enrolled: 15	Yes	Government and foundation (County Council of Ostergotland and Swedish Association of the Neurologically Disabled)
Lesser 2004 US	No	Yes	No	Screened: 578 Eligible: NR Enrolled: 338	Yes	Pfizer
Levendoglu 2004 Turkey	No	Yes	No	Screened: NR Eligible: NR Enrolled: 20	Yes	No funds received
Max (A) 1987 US	No	No	Unable to determine	Screened: NR Eligible: NR Enrolled: 37	Yes	Not reported

Evidence Table 11. Quality assessment of included randomized controlled trials

Author Year Country	Loss to Followup Differential or High	Intention to Treat Analysis (at least 95% analyzed)	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Max (B) 1991 US	No	No 20/24 analyzed (83.3%)	No	Screened: NR Eligible: NR Enrolled: 24	Yes	Not reported
Max (C) 1988 US	No	No 41/62 who completed both arms (partial sensitivity analysis on 11/21)	Unable to determine	Screened: NR Eligible: NR Enrolled: NR	Yes	
Max (D) 1992 US	No	No	Unable to determine	Screened: NR Eligible: NR Enrolled: 54	Yes	Not reported
McCleane 1999 UK	No	No 74/100 analyzed	Unable to determine	Screened: NR Eligible: NR Enrolled: 100	Yes	Not reported

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
Backonja 1999 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=165	Gabapentin 3600 mg	Total: 14 (16.67%) AE: 7 (8.33%)	Confusion: 8.3% (7/84)
					Diarrhea: 10.7% (9/84)
					Dizziness: 23.8% (20/84)
					Headache: 10.7% (9/84)
					Nausea: 8.3% (7/84)
					Somnolence: 22.6% (19/84)
			Placebo	Total: 16 (19.75% AE: 5 (6.17%)	Confusion: 1.2% (1/81)
					Diarrhea: 8.6% (7/81)
					Dizziness: 4.9% (4/81)
					Headache: 3.7% (3/81)
					Nausea: 4.9% (4/81)
					Somnolence: 6.2% (5/81)
Bone 2002 UK and Ireland	RCT Crossover Single Center	Phantom limb pain N=19	Gabapentin 2400 mg	Total: 2 (20%)	Dizziness: 20.0% (2/10)
					Headache: 20.0% (2/10)
					Nausea: 10.0% (1/10)
					Somnolence: 70.0% (7/10)
			Placebo	Total: 3 (33.33%)	Dizziness: 11.1% (1/9)
					Headache: 11.1% (1/9)
					Nausea: 11.1% (1/9)
					Somnolence: 22.2% (2/9)
Hahn 2004 Germany	RCT Parallel Multicenter	HIV-related neuropathic pain N=26	Gabapentin 1200-2400 mg	Total: 2 (13.33% AE: 1 (6.67%)	Dizziness: 60.0% (9/15)
					Gait abnormal: 46.7% (7/15)
					Headache: 6.7% (1/15)
					Nausea: 33.3% (5/15)
					Somnolence: 80.0% (12/15)
			Placebo	Total: 3 (27.27%) AE: 0 (0%)	Dizziness: 45.5% (5/11)
					Gait abnormal: 27.3% (3/11)
					Headache: 9.1% (1/11)
					Nausea: 18.2% (2/11)
					Somnolence: 18.2% (2/11)
Levendoglu 2004 Turkey	RCT Crossover	Spinal cord injury-related pain N=20	Gabapentin 3600 mg	Total: 0 AE: 0	Blurred vision: 0.0% (0/20)
					Diarrhea: 0.0% (0/20)
					Edema: 15.0% (3/20)
					Headache: 5.0% (1/20)
					Itching: 10.0% (2/20)
					Muscle twitching: 0.0% (0/20)
					Nausea: 0.0% (0/20)
					Somnolence: 15.0% (3/20)
					Vertigo: 15.0% (3/20)
					Vomiting: 0.0% (0/20)
					Weakness: 25.0% (5/20)
			Placebo	Total: 0 AE: 0	Blurred vision: 0.0% (0/20)
					Diarrhea: 0.0% (0/20)
					Edema: 0.0% (0/20)
					Headache: 5.0% (1/20)
					Itching: 0.0% (0/20)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Muscle twitching: 0.0% (0/20)
					Nausea: 5.0% (1/20)
					Somnolence: 0.0% (0/20)
					Vertigo: 5.0% (1/20)
					Vomiting: 5.0% (1/20)
					Weakness: 10.0% (2/20)
Rice 2001 UK	RCT Parallel Multicenter	Post-herpetic neuralgia N=334	Gabapentin 1800 mg	Total: 22 (19.13%) AE: 15 (13.04%)	Any adverse event: 70.4% (81/115)
					Asthenia: 6.1% (7/115)
					Diarrhea: 6.1% (7/115)
					Dizziness: 31.3% (36/115)
					Dry mouth: 6.1% (7/115)
					Edema, peripheral: 5.2% (6/115)
					Serious AEs: 2.6% (3/115)
					Somnolence: 17.4% (20/115)
			Gabapentin□ 2400 mg	Total: 23 (21.3%)□ AE: 19 (17.59%)	Any adverse event: 75.0% (81/108)
					Asthenia: 5.6% (6/108)
					Diarrhea: 4.6% (5/108)
					Dizziness: 33.3% (36/108)
					Dry mouth: 4.6% (5/108)
					Edema, peripheral: 11.1% (12/108)
					Serious AEs: 0.9% (1/108)
					Somnolence: 20.4% (22/108)
			Placebo□ □ N=111□ □ Age, mean (SD): 75 (28.9-94.8 (range))□ Gender□ Male: 46 (41%)□	Placebo□ □ N=111□ □ Age, mean (SD): 75 (28.9-94.8 (range))□ Gender□ Male: 46 (41%)□	Any adverse event: 49.5% (55/111)
					Asthenia: 3.6% (4/111)
					Diarrhea: 0.9% (1/111)
					Dizziness: 9.9% (11/111)
					Dry mouth: 0.9% (1/111)
					Edema, peripheral: 0.0% (0/111)
					Serious AEs: 0.9% (1/111)
					Somnolence: 6.3% (7/111)
Rowbotham (D) 1998 US	RCT Parallel Multicenter	Post-herpetic neuralgia N=225	Gabapentin 3600 mg	Total: 24 (21.24%) AE: 21 (18.58%)	Any adverse event: 54.9% (62/113)
					Ataxia: 7.1% (8/113)
					Dizziness: 23.9% (27/113)
					Edema, peripheral: 9.7% (11/113)
					Infection: 8.0% (9/113)
					Somnolence: 27.4% (31/113)
			Placebo	Total: 21 (18.1%) AE: 14 (12.07%)	Any adverse event: 27.6% (32/116)
					Ataxia: 0.0% (0/116)
					Dizziness: 5.2% (6/116)
					Edema, peripheral: 3.4% (4/116)
					Infection: 2.6% (3/116)
					Somnolence: 5.2% (6/116)
Serpell 2002 UK and Republic of Ireland	RCT Parallel Multicenter	Mixed N=305	Gabapentin	Total: 32 (21.05%) AE: 24 (15.79%)	Abdominal pain: 6.5% (10/153)
					Accidental injury: 5.9% (9/153)
					Any adverse event: 76.5% (117/153)
					Diarrhea: 5.2% (8/153)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Dizziness: 24.2% (37/153)
					Flu syndrome: 7.2% (11/153)
					Headache: 9.2% (14/153)
					Infection: 9.2% (14/153)
					Nausea: 9.2% (14/153)
					Serious AEs: 2.6% (4/153)
					Somnolence: 14.4% (22/153)
			Placebo	Total: 41 (26.8%) AE: 25 (16.34%)	Abdominal pain: % (6/152)
					Accidental injury: % (8/152)
					Any adverse event: % (103/152)
					Diarrhea: % (6/152)
					Dizziness: % (12/152)
					Flu syndrome: % (7/152)
					Headache: % (21/152)
					Infection: % (19/152)
					Nausea: % (14/152)
					Serious AEs: % (4/152)
					Somnolence: % (8/152)
Simpson (A) Part 1 2001 US	RCT Parallel Single Center	Painful diabetic neuropathy N=60	Gabapentin 900-2700 mg	Total: 3 (10%) AE: 2 (6.67%)	Confusion: 7.4% (2/27)
					Diarrhea: 11.1% (3/27)
					Dizziness: 22.2% (6/27)
					Headache: 11.1% (3/27)
					Nausea: 7.4% (2/27)
					Somnolence: 22.2% (6/27)
			Placebo	Total: 3 (10%) AE: 2 (6.67%)	Confusion: 0.0% (0/27)
					Diarrhea: 3.7% (1/27)
					Dizziness: 3.7% (1/27)
					Headache: 3.7% (1/27)
					Nausea: 3.7% (1/27)
					Somnolence: 3.7% (1/27)
Yildirim 2003 Turkey	RCT Parallel	Radiculopathy N=50	Gabapentin 900 mg-3600 mg	Total: 2 (8%)	Dizziness: 4.0% (1/25)
					Somnolence: 4.0% (1/25)
			Placebo	Total: 5 (20%)	Dizziness: 0.0% (0/25)
					Somnolence: 0.0% (0/25)
Simpson (A) Part 1 2001 US	RCT Parallel Single Center	Painful diabetic neuropathy N=60	Gabapentin 900-2700 mg	Total: 3 (10%) AE: 2 (6.67%)	Confusion: 7.4% (2/27)
					Diarrhea: 11.1% (3/27)
					Dizziness: 22.2% (6/27)
					Headache: 11.1% (3/27)
					Nausea: 7.4% (2/27)
					Somnolence: 22.2% (6/27)
			Placebo	Total: 3 (10%) AE: 2 (6.67%)	Confusion: 0.0% (0/27)
					Diarrhea: 3.7% (1/27)
					Dizziness: 3.7% (1/27)
					Headache: 3.7% (1/27)
					Nausea: 3.7% (1/27)
					Somnolence: 3.7% (1/27)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
Dworkin 2003 US	RCT Parallel Multicenter	Post-herpetic neuralgia N=173	Pregabalin 300-600 mg	Total: 31 (34.83% AE: 28 (31.46%)	Amblyopia: 11.2% (10/89)
					Ataxia: 6.7% (6/89)
					Confusion: 6.7% (6/89)
					Diarrhea: 6.7% (6/89)
					Dizziness: 28.1% (25/89)
					Dry mouth: 11.2% (10/89)
					Edema, peripheral: 19.1% (17/89)
					Gait abnormal: 7.9% (7/89)
					Headache: 7.9% (7/89)
					Somnolence: 24.7% (22/89)
					Speech disorder: 5.6% (5/89)
			Placebo	Total: 10 (11.9%) AE: 4 (4.76%)	Amblyopia: 1.2% (1/84)
					Ataxia: 0.0% (0/84)
					Confusion: 0.0% (0/84)
					Diarrhea: 4.8% (4/84)
					Dizziness: 11.9% (10/84)
					Dry mouth: 2.4% (2/84)
					Edema, peripheral: 2.4% (2/84)
					Gait abnormal: 1.2% (1/84)
					Headache: 8.3% (7/84)
					Somnolence: 7.1% (6/84)
					Speech disorder: 0.0% (0/84)
Freynhagen 2005 Multiple European	RCT Parallel Multicenter	Mixed N=338	Pregabalin 150-600 mg	Total: 49 (34.75%) AE: 24 (17.02%)	Asthenia: 6.4% (9/141)
					Dizziness: 2.1% (3/141)
					Dry mouth: 2.8% (4/141)
					Edema, peripheral: 2.1% (3/141)
					Headache: 5.0% (7/141)
					Nausea: 5.0% (7/141)
					Somnolence: 10.6% (15/141)
					Vertigo: 7.8% (11/141)
					Weight gain: 0.7% (1/141)
			Pregabalin 600 mg	Total: 50 (37.88%) AE: 33 (25%)	Asthenia: 9.1% (12/132)
					Dizziness: 28.8% (38/132)
					Dry mouth: 6.1% (8/132)
					Edema, peripheral: 7.6% (10/132)
					Headache: 2.3% (3/132)
					Nausea: 10.6% (14/132)
					Somnolence: 12.9% (17/132)
					Vertigo: 9.8% (13/132)
					Weight gain: 13.6% (18/132)
			Placebo	Total: 30 (46.15%) AE: 5 (7.69%)	Asthenia: 0.0% (0/65)
					Dizziness: 4.6% (3/65)
					Dry mouth: 4.6% (3/65)
					Edema, peripheral: 3.1% (2/65)
					Headache: 3.1% (2/65)
					Nausea: 1.5% (1/65)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Somnolence: 0.0% (0/65)
					Vertigo: 1.5% (1/65)
					Weight gain: 3.1% (2/65)
Lesser 2004 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=337	Pregabalin 75 mg	Total: 10 (12.99%) AE: 2 (2.6%)	Accidental injury: 5.2% (4/77)
					Amblyopia: 2.6% (2/77)
					Amnesia: 2.6% (2/77)
					Asthenia: 3.9% (3/77)
					Ataxia: 6.5% (5/77)
					Confusion: 0.0% (0/77)
					Constipation: 0.0% (0/77)
					Diarrhea: 5.2% (4/77)
					Dizziness: 7.8% (6/77)
					Dry mouth: 2.6% (2/77)
					Edema, peripheral: 3.9% (3/77)
					Euphoria: 0.0% (0/77)
					Headache: 6.5% (5/77)
					Infection: 3.9% (3/77)
					Somnolence: 3.9% (3/77)
			Pregabalin 300 mg	Total: 5 (6.17%) AE: 3 (3.7%)	Accidental injury: 2.5% (2/81)
					Amblyopia: 4.9% (4/81)
					Amnesia: 0.0% (0/81)
					Asthenia: 4.9% (4/81)
					Ataxia: 3.7% (3/81)
					Confusion: 4.9% (4/81)
					Constipation: 3.7% (3/81)
					Diarrhea: 1.2% (1/81)
					Dizziness: 27.2% (22/81)
					Dry mouth: 7.4% (6/81)
					Edema, peripheral: 7.4% (6/81)
					Euphoria: 6.2% (5/81)
					Headache: 8.6% (7/81)
					Infection: 9.9% (8/81)
					Somnolence: 23.5% (19/81)
			Pregabalin 600 mg	Total: 12 (14.63%) AE: 10 (12.2%)	Accidental injury: 4.9% (4/82)
					Amblyopia: 8.5% (7/82)
					Amnesia: 6.1% (5/82)
					Asthenia: 7.3% (6/82)
					Ataxia: 8.5% (7/82)
					Confusion: 8.5% (7/82)
					Constipation: 8.5% (7/82)
					Diarrhea: 3.7% (3/82)
					Dizziness: 39.0% (32/82)
					Dry mouth: 4.9% (4/82)
					Edema, peripheral: 13.4% (11/82)
					Euphoria: 4.9% (4/82)
					Headache: 9.8% (8/82)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Infection: 1.2% (1/82)
					Somnolence: 26.8% (22/82)
			Placebo	Total: 8 (8.25%) AE: 3 (3.09%)	Accidental injury: 0.0% (0/97)
					Amblyopia: 1.0% (1/97)
					Amnesia: 1.0% (1/97)
					Asthenia: 3.1% (3/97)
					Ataxia: 2.1% (2/97)
					Confusion: 2.1% (2/97)
					Constipation: 1.0% (1/97)
					Diarrhea: 7.2% (7/97)
					Dizziness: 5.2% (5/97)
					Dry mouth: 0.0% (0/97)
					Edema, peripheral: 2.1% (2/97)
					Euphoria: 0.0% (0/97)
					Headache: 10.3% (10/97)
					Infection: 7.2% (7/97)
					Somnolence: 4.1% (4/97)
Richter 2005 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=246	Pregabalin 150 mg	Total: 4 (5.06%) AE: 2 (2.53%)	Accidental injury: 2.5% (2/79)
					Amblyopia: 2.5% (2/79)
					Asthenia: 3.8% (3/79)
					Constipation: 3.8% (3/79)
					Diarrhea: 5.1% (4/79)
					Dizziness: 10.1% (8/79)
					Dry mouth: 0.0% (0/79)
					Edema, peripheral: 3.8% (3/79)
					Headache: 7.6% (6/79)
					Infection: 12.7% (10/79)
					Somnolence: 5.1% (4/79)
					Weight gain: 1.3% (1/79)
			Pregabalin 600 mg	Total: 10 (12.2%) AE: 7 (8.54%)	Accidental injury: 9.8% (8/82)
					Amblyopia: 8.5% (7/82)
					Asthenia: 12.2% (10/82)
					Constipation: 6.1% (5/82)
					Diarrhea: 2.4% (2/82)
					Dizziness: 37.8% (31/82)
					Dry mouth: 8.5% (7/82)
					Edema, peripheral: 17.1% (14/82)
					Headache: 15.9% (13/82)
					Infection: 6.1% (5/82)
					Somnolence: 22.0% (18/82)
					Weight gain: 9.8% (8/82)
			Placebo	Total: 13 (15.29%) AE: 4 (4.71%)	Accidental injury: 5.9% (5/85)
					Amblyopia: 5.9% (5/85)
					Asthenia: 3.5% (3/85)
					Constipation: 4.7% (4/85)
					Diarrhea: 3.5% (3/85)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Dizziness: 2.4% (2/85)
					Dry mouth: 2.4% (2/85)
					Edema, peripheral: 4.7% (4/85)
					Headache: 10.6% (9/85)
					Infection: 9.4% (8/85)
					Somnolence: 3.5% (3/85)
					Weight gain: 0.0% (0/85)
Rosenstock 2004 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=146	Pregabalin 300 mg	Total: 11 (14.47%) AE: 8 (10.53%)	Accidental injury: 3.9% (3/76)
					Amblyopia: 5.3% (4/76)
					Asthenia: 3.9% (3/76)
					Constipation: 5.3% (4/76)
					Diarrhea: 3.9% (3/76)
					Dizziness: 35.5% (27/76)
					Edema, peripheral: 10.5% (8/76)
					Euphoria: 5.3% (4/76)
					Flatulence: 3.9% (3/76)
					Flu syndrome: 3.9% (3/76)
					Headache: 6.6% (5/76)
					Hyperglycemia: 3.9% (3/76)
					Infection: 14.5% (11/76)
					Nausea: 7.9% (6/76)
					Somnolence: 19.7% (15/76)
					Vomiting: 3.9% (3/76)
			Placebo	Total: 8 (11.43%) AE: 2 (2.86%)	Accidental injury: 5.7% (4/70)
					Amblyopia: 1.4% (1/70)
					Asthenia: 2.9% (2/70)
					Constipation: 0.0% (0/70)
					Diarrhea: 2.9% (2/70)
					Dizziness: 11.4% (8/70)
					Edema, peripheral: 1.4% (1/70)
					Euphoria: 0.0% (0/70)
					Flatulence: 1.4% (1/70)
					Flu syndrome: 4.3% (3/70)
					Headache: 10.0% (7/70)
					Hyperglycemia: 0.0% (0/70)
					Infection: 5.7% (4/70)
					Nausea: 8.6% (6/70)
					Somnolence: 2.9% (2/70)
					Vomiting: 1.4% (1/70)
Sabatowski 2004 Multiple European and Australia	RCT Parallel Multicenter	Post-herpetic neuralgia N=238	Pregabalin 150 mg	Total: 10 (12.35%) AE: 9 (11.11%)	Asthenia: 6.2% (5/81)
					Diarrhea: 4.9% (4/81)
					Dizziness: 12.3% (10/81)
					Dry mouth: 11.1% (9/81)
					Edema, peripheral: 2.5% (2/81)
					Headache: 11.1% (9/81)
					Infection: 2.5% (2/81)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Somnolence: 14.8% (12/81)
			Pregabalin 300 mg	Total: 16 (21.05%) AE: 12 (15.79%)	Asthenia: 2.6% (2/76) Diarrhea: 5.3% (4/76) Dizziness: 27.6% (21/76) Dry mouth: 6.6% (5/76) Edema, peripheral: 13.2% (10/76) Headache: 10.5% (8/76) Infection: 6.6% (5/76) Somnolence: 23.7% (18/76)
			Placebo	Total: 20 (24.69%) AE: 8 (9.88%)	Asthenia: 4.9% (4/81) Diarrhea: 4.9% (4/81) Dizziness: 14.8% (12/81) Dry mouth: 3.7% (3/81) Edema, peripheral: 0.0% (0/81) Headache: 3.7% (3/81) Infection: 0.0% (0/81) Somnolence: 7.4% (6/81)
Siddall 2006	RCT Parallel Multicenter	Spinal cord injury-related pain N=137	Carbazepine	Total: 21 (30%) AE: 15 (21.43%)	Amblyopia: 8.6% (6/70) Amnesia: 10.0% (7/70) Asthenia: 15.7% (11/70) Constipation: 12.9% (9/70) Dizziness: 24.3% (17/70) Dry mouth: 15.7% (11/70) Edema: 20.0% (14/70) Infection: 8.6% (6/70) Myasthenia: 8.6% (6/70) Paresthesia: 5.7% (4/70) Serious AEs: 18.6% (13/70) Somnolence: 41.4% (29/70) Thinking abnormal: 8.6% (6/70) Urinary incontinence: 5.7% (4/70)
			Placebo	Total: 30 (44.78%) AE: 9 (13.43%)	Amblyopia: 3.0% (2/67) Amnesia: 3.0% (2/67) Asthenia: 6.0% (4/67) Constipation: 6.0% (4/67) Dizziness: 9.0% (6/67) Dry mouth: 3.0% (2/67) Edema: 6.0% (4/67) Infection: 6.0% (4/67) Myasthenia: 4.5% (3/67) Paresthesia: 1.5% (1/67) Serious AEs: 11.9% (8/67) Somnolence: 9.0% (6/67) Thinking abnormal: 1.5% (1/67) Urinary incontinence: 3.0% (2/67)
van Seventer	RCT	Post-herpetic neuralgia	Pregabalin	Total: 26 (29.89%)	Amblyopia: 2.3% (2/87)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
2006 US and Multiple European	Parallel Multicenter	N=368	150 mg	AE: 7 (8.05%)	Asthenia: 4.6% (4/87)
					Ataxia: 3.4% (3/87)
					Confusion: 3.4% (3/87)
					Constipation: 1.1% (1/87)
					Diarrhea: 5.7% (5/87)
					Diplopia: 0.0% (0/87)
					Dizziness: 16.1% (14/87)
					Dry mouth: 5.7% (5/87)
					Edema, face: 3.4% (3/87)
					Edema, peripheral: 12.6% (11/87)
					Edema, peripheral: 3.4% (3/87)
					Flatulence: 1.1% (1/87)
					Gait abnormal: 1.1% (1/87)
					Headache: 4.6% (4/87)
					Incoordination: 2.3% (2/87)
					Nausea: 1.1% (1/87)
					Somnolence: 9.2% (8/87)
					Sweating increased: 1.1% (1/87)
					Thinking abnormal: 2.3% (2/87)
					Vision abnormal: 0.0% (0/87)
					Weight gain: 3.4% (3/87)
			Pregabalin 300 mg	Total: 36 (36.73%) AE: 15 (15.31%)	Amblyopia: 3.1% (3/98)
					Asthenia: 3.1% (3/98)
					Ataxia: 6.1% (6/98)
					Confusion: 3.1% (3/98)
					Constipation: 8.2% (8/98)
					Diarrhea: 0.0% (0/98)
					Diplopia: 0.0% (0/98)
					Dizziness: 32.7% (32/98)
					Dry mouth: 4.1% (4/98)
					Edema, face: 1.0% (1/98)
					Edema, peripheral: 14.3% (14/98)
					Edema, peripheral: 3.1% (3/98)
					Flatulence: 0.0% (0/98)
					Gait abnormal: 2.0% (2/98)
					Headache: 1.0% (1/98)
					Incoordination: 1.0% (1/98)
					Nausea: 0.0% (0/98)
					Somnolence: 11.2% (11/98)
					Sweating increased: 0.0% (0/98)
					Thinking abnormal: 2.0% (2/98)
					Vision abnormal: 2.0% (2/98)
					Weight gain: 8.2% (8/98)
			Pregabalin□ 300-600 mg	Total: 34 (37.78%)□ AE: 19 (21.11%)	Amblyopia: 5.6% (5/90)
					Asthenia: 5.6% (5/90)
					Ataxia: 12.2% (11/90)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Confusion: 3.3% (3/90)
					Constipation: 8.9% (8/90)
					Diarrhea: 0.0% (0/90)
					Diplopia: 3.3% (3/90)
					Dizziness: 36.7% (33/90)
					Dry mouth: 12.2% (11/90)
					Edema, face: 4.4% (4/90)
					Edema, peripheral: 13.3% (12/90)
					Edema, peripheral: 5.6% (5/90)
					Flatulence: 3.3% (3/90)
					Gait abnormal: 4.4% (4/90)
					Headache: 4.4% (4/90)
					Incoordination: 3.3% (3/90)
					Nausea: 2.2% (2/90)
					Somnolence: 25.6% (23/90)
					Sweating increased: 0.0% (0/90)
					Thinking abnormal: 4.4% (4/90)
					Vision abnormal: 4.4% (4/90)
					Weight gain: 8.9% (8/90)
			Placebo	Total: 34 (36.56%) AE: 5 (5.38%)	Amblyopia: 1.1% (1/93)
					Asthenia: 5.4% (5/93)
					Ataxia: 0.0% (0/93)
					Confusion: 1.1% (1/93)
					Constipation: 2.2% (2/93)
					Diarrhea: 1.1% (1/93)
					Diplopia: 0.0% (0/93)
					Dizziness: 9.7% (9/93)
					Dry mouth: 0.0% (0/93)
					Edema, face: 2.2% (2/93)
					Edema, peripheral: 10.8% (10/93)
					Edema, peripheral: 3.2% (3/93)
					Flatulence: 2.2% (2/93)
					Gait abnormal: 0.0% (0/93)
					Headache: 3.2% (3/93)
					Incoordination: 0.0% (0/93)
					Nausea: 5.4% (5/93)
					Somnolence: 4.3% (4/93)
					Sweating increased: 3.2% (3/93)
					Thinking abnormal: 1.1% (1/93)
					Vision abnormal: 0.0% (0/93)
					Weight gain: 0.0% (0/93)
Goldstein 2005 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=457	Duloxetine 20 mg daily	Total: 24 (20.87%) AE: 5 (4.35%)	Anorexia: 2.6% (3/115)
					Appetite decreased: 2.6% (3/115)
					Constipation: 5.2% (6/115)
					Dizziness: 6.1% (7/115)
					Dry mouth: 5.2% (6/115)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Nausea: 13.9% (16/115)
					Somnolence: 7.8% (9/115)
					Sweating increased: 6.1% (7/115)
					Weakness: 0.9% (1/115)
			Duloxetine 60 mg daily	Total: 28 (24.56%) AE: 15 (13.16%)	Anorexia: 2.6% (3/114)
					Appetite decreased: 2.6% (3/114)
					Constipation: 14.9% (17/114)
					Dizziness: 9.6% (11/114)
					Dry mouth: 7.0% (8/114)
					Nausea: 16.7% (19/114)
					Somnolence: 20.2% (23/114)
					Sweating increased: 3.5% (4/114)
					Weakness: 2.6% (3/114)
			Duloxetine 60 mg BID Total daily dose: 120 mg	Total: 33 (29.2%) AE: 22 (19.47%)	Anorexia: 8.0% (9/113)
					Appetite decreased: 12.4% (14/113)
					Constipation: 10.6% (12/113)
					Dizziness: 23.0% (26/113)
					Dry mouth: 15.0% (17/113)
					Nausea: 27.4% (31/113)
					Somnolence: 28.3% (32/113)
					Sweating increased: 8.8% (10/113)
					Weakness: 7.1% (8/113)
			Placebo	Total: 28 (24.35%) AE: 7 (6.09%)	Anorexia: 0.9% (1/115)
					Appetite decreased: 0.0% (0/115)
					Constipation: 3.5% (4/115)
					Dizziness: 7.0% (8/115)
					Dry mouth: 6.1% (7/115)
					Nausea: 9.6% (11/115)
					Somnolence: 7.8% (9/115)
					Sweating increased: 2.6% (3/115)
					Weakness: 0.0% (0/115)
Raskin (B) 2005 and 2006 2005 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=348	Duloxetine 60 mg once daily	Total: 15 (12.93%) AE: 5 (4.31%)	Any adverse event: 61.2% (71/116)
					Serious AEs: 3.4% (4/116)
			Duloxetine 60 mg twice daily	Total: 21 (18.1%) AE: 14 (12.07%)	Any adverse event: 62.9% (73/116)
					Serious AEs: 1.7% (2/116)
			Placebo	Total: 16 (13.79%) AE: 3 (2.59%)	Any adverse event: 49.1% (57/116)
					Serious AEs: 3.4% (4/116)
Wernicke 2006 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=334	Duloxetine 60 mg once daily Total daily dose: 60 mg N=114	Duloxetine 60 mg once daily Total daily dose: 60 mg N=114	Constipation: 7.0% (8/114)
					Diarrhea: 11.4% (13/114)
					Dizziness: 15.8% (18/114)
					Fatigue: 12.3% (14/114)
					Headache: 10.5% (12/114)
					Insomnia: 5.3% (6/114)
					Nasopharyngitis: 7.0% (8/114)
					Nausea: 28.1% (32/114)
					Somnolence: 7.9% (9/114)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Sweating increased: 8.8% (10/114)
			Duloxetine 60 mg twice daily Total daily dose: 120 mg	Total: 34 (30.36%) AE: 20 (17.86%)	Constipation: 18.8% (21/112)
					Diarrhea: 4.5% (5/112)
					Dizziness: 10.7% (12/112)
					Fatigue: 12.5% (14/112)
					Headache: 13.4% (15/112)
					Insomnia: 9.8% (11/112)
					Nasopharyngitis: 6.3% (7/112)
					Nausea: 32.1% (36/112)
					Somnolence: 15.2% (17/112)
					Sweating increased: 7.1% (8/112)
			Placebo	Total: 23 (21.3%) AE: 8 (7.41%)	Constipation: 1.9% (2/108)
					Diarrhea: 1.9% (2/108)
					Dizziness: 5.6% (6/108)
					Fatigue: 2.8% (3/108)
					Headache: 6.5% (7/108)
					Insomnia: 1.9% (2/108)
					Nasopharyngitis: 4.6% (5/108)
					Nausea: 6.5% (7/108)
					Somnolence: 0.9% (1/108)
					Sweating increased: 0.9% (1/108)
Rowbotham (C) 2004 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=244	Venlafaxine 75 mg daily	Total: 12 (14.81%) AE: 6 (7.41%)	Anorexia: 8.6% (7/81)
					Dyspepsia: 11.1% (9/81)
					Flatulence: 1.2% (1/81)
					Impotence (men only): 10.9% (6/55)
					Insomnia: 6.2% (5/81)
					Myalgia: 6.2% (5/81)
					Nausea: 27.2% (22/81)
					Sinusitis: 3.7% (3/81)
					Somnolence: 17.3% (14/81)
					Sweating increased: 6.2% (5/81)
					Vomiting: 7.4% (6/81)
			Venlafaxine 150-225 mg daily	Total: 18 (21.95%) AE: 8 (9.76%)	Anorexia: 6.1% (5/82)
					Dyspepsia: 12.2% (10/82)
					Flatulence: 7.3% (6/82)
					Impotence (men only): 11.9% (5/42)
					Insomnia: 12.2% (10/82)
					Myalgia: 7.3% (6/82)
					Nausea: 12.2% (10/82)
					Sinusitis: 8.5% (7/82)
					Somnolence: 18.3% (15/82)
					Sweating increased: 12.2% (10/82)
					Vomiting: 6.1% (5/82)
			Placebo	Total: 12 (14.81%) AE: 3 (3.7%)	Anorexia: 3.7% (3/81)
					Dyspepsia: 1.2% (1/81)
					Flatulence: 3.7% (3/81)

Evidence Table 12. Adverse events in placebo controlled trials of pregabalin, gabapentin, SNRIs, and topical lidocaine for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs	Specific adverse events
					Impotence (men only): 0.0% (0/48)
					Insomnia: 4.9% (4/81)
					Myalgia: 0.0% (0/81)
					Nausea: 6.2% (5/81)
					Sinusitis: 3.7% (3/81)
					Somnolence: 1.2% (1/81)
					Sweating increased: 4.9% (4/81)
					Vomiting: 0.0% (0/81)
Tasmuth 2002 Finland	RCT Crossover Single Center	Cancer-related neuropathic pain N=13	Venlafaxine 37.5 mg		Anorexia: 23.1% (3/13)
					Constipation: 30.8% (4/13)
					Difficult to urinate: 15.4% (2/13)
					Dry mouth: 61.5% (8/13)
					Fatigue: 69.2% (9/13)
					Headache: 46.2% (6/13)
					Nausea: 30.8% (4/13)
					Nightmares: 15.4% (2/13)
					Palpitations: 23.1% (3/13)
					Sweating increased: 61.5% (8/13)
			Placebo		Anorexia: 30.8% (4/13)
					Constipation: 23.1% (3/13)
					Difficult to urinate: 15.4% (2/13)
					Dry mouth: 46.2% (6/13)
					Fatigue: 76.9% (10/13)
					Headache: 30.8% (4/13)
					Nausea: 30.8% (4/13)
					Nightmares: 30.8% (4/13)
					Palpitations: 23.1% (3/13)
					Sweating increased: 53.8% (7/13)
Yucel 2005 Turkey	RCT Paralle Single Center	Mixed N=55	Venlafaxine 75 mg	Total: 1 (5% AE: 1 (5.26%)	Any adverse event: 45.0% (9/20)
			Venlafaxine 150 mg	Total: 3 (15%) AE: 3 (17.65%)	Any adverse event: 70.0% (14/20)
			Placebo	Total: 1 (5%) AE: 1 (5.26%)	Any adverse event: 55.0% (11/20)
Estanislao 2004 US	RCT Crossover Multicenter	HIV-related neuropathic pain N=64	Lidocaine gel 5%	Total: 5 (15.62%) AE: 2 (6.25%)	Dermatologic reaction: 6.3% (2/32)
			Placebo	Total: 3 (9.38%) AE: 0 (0%)	Dermatologic reaction: 0.0% (0/32)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
Leijon 1989 Sweden	CT Crossover Single Center	Central/post-stroke neuropathic pain N=15	Amitriptyline 25 + 50 mg BID	Total: 0 (0%) AE: 0 (0%)
			Carbamazepine 400 mg BID Total daily dose: 800 mg	Total: 0 (0%) AE: 0 (0%)
			Placebo	Total: 0 (0%) AE: 0 (0%)
Eisenberg 2001 Israel	RCT Paralle Single Center	Painful diabetic neuropathy N=53	Lamotrigine 200-400 mg	Not reported
			Placebo	Not reported
Finnerup 2002 Denmark	RCT Crossover Single Center	Spinal cord injury-related pain N=22	Lamotrigine 200-400 mg	Total: 3 (10%) AE: 1 (3.33%)
			Placebo	Total: 5 (16.67%) AE: 2 (6.67%)
Simpson (B) 2003 US	RCT Parallel Multicenter	HIV-related neuropathic pain N=227	Lamotrigine 400 mg	Total: 17 (27.42%) AE: 5 (8.06%)
			Lamotrigine 600 mg	Total: 17 (19.32%) AE: 5 (5.68%)
			Placebo	Total: 7 (23.33%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
				AE: 2 (6.67%)
			Placebo	Total: 14 (29.79%) AE: 5 (10.64%)
Vestergaard 2001 Denmark	RCT Crossover Multicenter	Central/post-stroke neuropathic pain N=30	Lamotrigine 200 mg	Total: 4 (13.33%) AE: 0 (0%)
			Placebo	Total: 6 (20%) AE: 0 (0%)
Zakrzewska 1997 UK	RCT Crossover	Trigeminal neuralgia N=14	Lamotrigine 400 mg	Total: 0 (0%) AE: 0 (0%)
			Placebo	Total: 1 (7.14%) AE: 0 (0%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
Beydoun 2006 US	RCT Parallel	Painful diabetic neuropathy N=347	Oxcarbazepine 600 mg daily	Total: 16 (19.28%) AE: 9 (10.84%)
			Oxcarbazepine 1200 mg daily	Total: 34 (39.08%) AE: 20 (22.99%)
			Oxcarbazepine 1800 mg daily	Total: 48 (54.55%) AE: 36 (40.91%)
			Placebo	Total: 17 (19.1%) AE: 6 (6.74%)
Dogra 2005 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=146	Oxcarbazepine mean 1445 mg	Total: 25 (36.23%) AE: 19 (27.54%)
			Placebo	Total: 15 (19.48%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
				AE: 6 (7.79%)
Khoromi 2005 US	RCT Crossover	Neuropathy associated with low back pain N=29	Topiramate mean 208 mg	Total: 10 (34.48%) AE: 10 (34.48%)
			Diphenhydramine mean 40 mg	Total: 1 (3.45%) AE: 1 (3.45%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
Raskin (A) 2004 US	RCT Parallel Multicenter	Painful diabetic neuropathy N=317	Topiramate mean 320 mg	Total: 102 (49.04%) AE: 52 (25%)
			Placebo	Total: 29 (26.61%) AE: 9 (8.26%)
Thienel 2004 Multiple	RCT Parallel Multicenter	Painful diabetic neuropathy N=1269	Topiramate 100 mg	Total: 116 (45.85%) AE: 41 (16.21%)
			Topiramate 200 mg	Total: 197 (52.96%) AE: 93 (25%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
			Topiramate 400 mg	Total: 151 (58.08%) AE: 79 (30.38%)
			Placebo	Total: 156 (40.62%) AE: 32 (8.33%)
Drewes 1994 Denmark	RCT Crossover Single Center	Spinal cord injury-related pain N=20	Sodium valproate median 1800 mg (600-2400 mg)	Total: 0 (0%) AE: 0 (0%)
			Placebo	Total: 0 (0%) AE: 0 (0%)
Max (D) 1992 US	RCT Crossover NR	Painful diabetic neuropathy N=54	Fluoxetine 20-40 mg	Not reported
			Benztropine mesylate	Not reported

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
			0.125 to 1.5 mg	
Cardenas 2002 US	RCT Parallel Multicenter	Spinal cord injury-related pain N=84	Amitriptyline 10-125 mg daily	Not reported
			Benztropine mesylate 0.5 mg daily	
Kalso 1996 Finland	RCT Crossover Single Center	Cancer-related neuropathic pain N=15	Amitriptyline 50 mg	Not reported
			Amitriptyline 100 mg	Not reported
			Placebo	Not reported

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
Kieburtz 1998 US	RCT Parallel Multicenter	HIV-related neuropathic pain N=145	Amitriptyline 25-100 mg	Total: 13 (27.66%) AE: 3 (6.38%)
			Mexiletine 150 mg	Total: 14 (29.17%) AE: 4 (8.33%)
			Benztropine mesylate 0.125 mg	Total: 12 (24%) AE: 4 (8%)
Leijon 1989 Sweden	CT Crossover Single Center	Central/post-stroke neuropathic pain N=15	Amitriptyline 25 + 50 mg BID Total daily dose: 75 mg	Total: 0 (0%) AE: 0 (0%)
			Carbamazepine 400 mg BID Total daily dose: 800 mg	Total: 0 (0%) AE: 0 (0%)
			Placebo	Total: 0 (0%) AE: 0 (0%)
Max (A) 1987 US	RCT Crossover Single Center	Painful diabetic neuropathy N=29	Amitriptyline mean 90 mg	Not reported

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
			Benztropine mesylate 1 mg	Not reported
Max (C) 1988 US	RCT Crossover Single Center	Post-herpetic neuralgia N=58	Amitriptyline 12.5-150 mg (mean 65 mg)	Not reported
			Lorazepam 0.5-6 mg (mean 2.4 mg)	Not reported
			Placebo	Not reported
Robinson 2004 US	RCT Parallel Single Center	Phantom limb pain N=39	Amitriptyline	Total: 2 (10%) AE: 2 (10%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
			Benztropine mesylate	Total: 0 (0%) AE: 0 (0%)
Vrethem 1997 Sweden	RCT Crossover	Polyneuropathy N=36	Amitriptyline 75 mg	AE: 3 (8.11%)
			Maprotiline 75 mg	AE: 2 (5.41%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
			Placebo	AE: 0 (0%)
Panerai 1990 Italy	RCT Crossover	Mixed N=39	Nortriptyline	Total: 7 (17.95%) AE: 2 (5.13%)
			Chlorimipramine	Total: 1 (2.56%) AE: 0 (0%)
			Placebo	Total: 7 (17.95%) AE: 1 (2.56%)
Kishore-Kumar 1990 US	RCT Crossover Single Center	Post-herpetic neuralgia N=26	Desipramine mean 167 mg	Total: 5 (19.23%) AE: 5 (19.23%)
			Benztropine mesylate 0.5-1 mg	Total: 3 (11.54%) AE: 3 (11.54%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
Max (B) 1991 US	RCT Crossover	Painful diabetic neuropathy N=24	Desipramine	Total: 2 (8.33%) AE: 2 (8.33%)
			Benztropine mesylate	Total: 2 (8.33%) AE: 1 (4.17%)
Kvinesdal 1984 Denmark	RCT Crossover Single Center	Painful diabetic neuropathy N=12	Imipramine 100 mg	Total: 3 (20%) AE: 1 (6.67%)
			Placebo	Total: 0 (0%) AE: 0 (0%)
Sindrup (C) 1989 Denmark	RCT Crossover	Painful diabetic neuropathy N=9	Imipramine 50 or 75 mg	Total: 1 (7.69%) AE: 1 (7.69%)
			Placebo	Total: 2 (15.38%) AE: 2 (15.38%)
Hammack 2002 US	RCT Crossover Multicenter	Cisplatinum-induced neuropathic pain N=51	Nortriptyline	Total: 2 (7.69%) AE: 2 (7.69%)
			Placebo	Total: 4 (16%) AE: 4 (16%)
Panerai 1990	RCT Crossover	Mixed 	Nortriptyline	Total: 7 (17.95%) AE: 2 (5.13%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Design	Type of pain/ Sample size	Intervention	Withdrawals/ Withdrawals due to AEs
Italy		N=39	Chlorimipramine	Total: 1 (2.56%) AE: 0 (0%)
			Placebo	Total: 7 (17.95%) AE: 1 (2.56%)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
Leijon 1989 Sweden	Any adverse event: 93.3% (14/15)
	Any adverse event: 92.9% (13/14)
	Any adverse event: 46.7% (7/15)
Eisenberg 2001 Israel	Dizziness: 12.5% (3/24)
	Headache: 8.3% (2/24)
	Nausea: 16.7% (4/24)
	Rash: 8.3% (2/24)
	Somnolence: 4.2% (1/24)
	Stomach problems: 12.5% (3/24)
	Dizziness: 18.2% (4/22)
	Headache: 9.1% (2/22)
	Nausea: 18.2% (4/22)
	Rash: 0.0% (0/22)
	Somnolence: 18.2% (4/22)
	Stomach problems: 4.5% (1/22)
Finnerup 2002 Denmark	Any adverse event: 48.1% (13/27)
	CNS AEs: 44.4% (12/27)
	Gastrointestinal AEs: 14.8% (4/27)
	Skin AEs: 14.8% (4/27)
	Any adverse event: 50.0% (14/28)
	CNS AEs: 32.1% (9/28)
	Gastrointestinal AEs: 10.7% (3/28)
	Skin AEs: 14.3% (4/28)
Simpson (B) 2003 US	Diarrhea: 10.7% (16/150)
	Headache: 10.7% (16/150)
	Infection: 11.3% (17/150)
	Nausea: 11.3% (17/150)
	Rash: 14.0% (21/150)
	Diarrhea: % (/)
	Headache: % (/)
	Infection: % (/)
	Nausea: % (/)
	Rash: % (/)
	Diarrhea: 9.1% (7/77)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Headache: 10.4% (8/77)
	Infection: 9.1% (7/77)
	Nausea: 10.4% (8/77)
	Rash: 11.7% (9/77)
	Diarrhea: % (/)
	Headache: % (/)
	Infection: % (/)
	Nausea: % (/)
	Rash: % (/)
Vestergaard 2001 Denmark	CNS AEs: 26.7% (8/30)
	Gastrointestinal AEs: 23.3% (7/30)
	Respiratory AEs: 13.3% (4/30)
	Skin AEs: 16.7% (5/30)
	CNS AEs: 43.3% (13/30)
	Gastrointestinal AEs: 6.7% (2/30)
	Respiratory AEs: 16.7% (5/30)
	Skin AEs: 10.0% (3/30)
Zakrzewska 1997 UK	Amblyopia: 7.7% (1/13)
	Any adverse event: 53.8% (7/13)
	Asthenia: 7.7% (1/13)
	Ataxia: 7.7% (1/13)
	Constipation: 23.1% (3/13)
	Difficult to urinate: 7.7% (1/13)
	Diplopia: 15.4% (2/13)
	Dizziness: 38.5% (5/13)
	Nausea: 23.1% (3/13)
	Somnolence: 23.1% (3/13)
	Sweating increased: 7.7% (1/13)
	Tremor: 7.7% (1/13)
	Vomiting: 15.4% (2/13)
	Amblyopia: 0.0% (0/14)
	Any adverse event: 50.0% (7/14)
	Asthenia: 7.1% (1/14)
	Ataxia: 0.0% (0/14)
	Constipation: 14.3% (2/14)
	Difficult to urinate: 7.1% (1/14)
	Diplopia: 0.0% (0/14)
	Dizziness: 7.1% (1/14)
	Nausea: 7.1% (1/14)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Somnolence: 7.1% (1/14)
	Sweating increased: 7.1% (1/14)
	Tremor: 7.1% (1/14)
	Vomiting: 0.0% (0/14)
Beydoun 2006 US	Dizziness: 6.0% (5/83)
	Fatigue: 4.8% (4/83)
	Headache: 10.8% (9/83)
	Nausea: 2.4% (2/83)
	Somnolence: 2.4% (2/83)
	Tremor: 1.2% (1/83)
	Dizziness: 18.8% (16/85)
	Fatigue: 12.9% (11/85)
	Headache: 10.6% (9/85)
	Nausea: 15.3% (13/85)
	Somnolence: 5.9% (5/85)
	Tremor: 1.2% (1/85)
	Dizziness: 34.5% (30/87)
	Fatigue: 14.9% (13/87)
	Headache: 11.5% (10/87)
	Nausea: 19.5% (17/87)
	Somnolence: 10.3% (9/87)
	Tremor: 12.6% (11/87)
	Dizziness: 2.2% (2/89)
	Fatigue: 6.7% (6/89)
	Headache: 7.9% (7/89)
	Nausea: 5.6% (5/89)
	Somnolence: 3.4% (3/89)
	Tremor: 2.2% (2/89)
Dogra 2005 US	Back pain: 9.1% (5/55)
	Blurred vision: 1.8% (1/55)
	Diarrhea: 1.8% (1/55)
	Dizziness: 12.7% (7/55)
	Fatigue: 5.5% (3/55)
	Headache: 9.1% (5/55)
	Nausea: 3.6% (2/55)
	Somnolence: 9.1% (5/55)
	Tremor: 3.6% (2/55)
	Vomiting: 3.6% (2/55)
	Back pain: 2.9% (2/70)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Blurred vision: 1.4% (1/70)
	Diarrhea: 5.7% (4/70)
	Dizziness: 1.4% (1/70)
	Fatigue: 1.4% (1/70)
	Headache: 1.4% (1/70)
	Nausea: 1.4% (1/70)
	Somnolence: 0.0% (0/70)
	Tremor: 1.4% (1/70)
	Vomiting: 1.4% (1/70)
Khoromi 2005 US	Anorexia: 0.0% (0/29)
	Any adverse event: 86.2% (25/29)
	Blurred vision: 3.4% (1/29)
	Constipation: 6.9% (2/29)
	Diarrhea: 31.0% (9/29)
	Edema: 3.4% (1/29)
	Fatigue: 34.5% (10/29)
	Headache: 10.3% (3/29)
	Joint pain: 6.9% (2/29)
	Memory difficulty: 3.4% (1/29)
	Paresthesia: 37.9% (11/29)
	Sedation: 34.5% (10/29)
	Speech disorder: 3.4% (1/29)
	Thirst (severe): 3.4% (1/29)
	Tremor: 0.0% (0/29)
	Anorexia: 3.4% (1/29)
	Any adverse event: 72.4% (21/29)
	Blurred vision: 0.0% (0/29)
	Constipation: 0.0% (0/29)
	Diarrhea: 10.3% (3/29)
	Edema: 0.0% (0/29)
	Fatigue: 31.0% (9/29)
	Headache: 10.3% (3/29)
	Joint pain: 3.4% (1/29)
	Memory difficulty: 0.0% (0/29)
	Paresthesia: 20.7% (6/29)
	Sedation: 3.4% (1/29)
	Speech disorder: 0.0% (0/29)
	Thirst (severe): 0.0% (0/29)
	Tremor: 3.4% (1/29)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
Raskin (A) 2004 US	Accidental injury: 3.8% (8/211)
	Anorexia: 10.9% (23/211)
	Bad taste: 6.6% (14/211)
	Concentration poor: 5.2% (11/211)
	Diarrhea: 11.4% (24/211)
	Dizziness: 7.1% (15/211)
	Fatigue: 7.1% (15/211)
	Headache: 5.7% (12/211)
	Joint pain: 3.8% (8/211)
	Nausea: 9.5% (20/211)
	Paresthesia: 8.5% (18/211)
	Sinusitis: 6.2% (13/211)
	Somnolence: 10.0% (21/211)
	Upper respiratory tract infection: 9.0% (19/211)
	Accidental injury: 7.3% (8/109)
	Anorexia: 0.9% (1/109)
	Bad taste: 0.0% (0/109)
	Concentration poor: 0.9% (1/109)
	Diarrhea: 3.7% (4/109)
	Dizziness: 5.5% (6/109)
	Fatigue: 1.8% (2/109)
	Headache: 9.2% (10/109)
	Joint pain: 5.5% (6/109)
	Nausea: 5.5% (6/109)
	Paresthesia: 1.8% (2/109)
	Sinusitis: 5.5% (6/109)
	Somnolence: 3.7% (4/109)
	Upper respiratory tract infection: 5.5% (6/109)
Thienel 2004 Multiple	Anorexia: 5.1% (13/253)
	Bad taste: 4.0% (10/253)
	Confusion: 3.2% (8/253)
	Fatigue: 11.1% (28/253)
	Memory difficulty: 3.2% (8/253)
	Nausea: 9.9% (25/253)
	Paresthesia: 9.1% (23/253)
	Somnolence: 7.9% (20/253)
	Weight loss: 4.0% (10/253)
	Anorexia: 12.1% (45/372)
	Bad taste: 8.1% (30/372)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Confusion: 3.0% (11/372)
	Fatigue: 16.9% (63/372)
	Memory difficulty: 5.1% (19/372)
	Nausea: 12.9% (48/372)
	Paresthesia: 14.0% (52/372)
	Somnolence: 12.1% (45/372)
	Weight loss: 8.9% (33/372)
	Anorexia: 11.9% (31/260)
	Bad taste: 8.1% (21/260)
	Confusion: 6.9% (18/260)
	Fatigue: 20.0% (52/260)
	Memory difficulty: 6.9% (18/260)
	Nausea: 13.1% (34/260)
	Paresthesia: 11.9% (31/260)
	Somnolence: 8.8% (23/260)
	Weight loss: 6.9% (18/260)
	Anorexia: 3.1% (12/384)
	Bad taste: 1.0% (4/384)
	Confusion: 1.0% (4/384)
	Fatigue: 10.9% (42/384)
	Memory difficulty: 2.1% (8/384)
	Nausea: 7.0% (27/384)
	Paresthesia: 4.9% (19/384)
	Somnolence: 3.9% (15/384)
	Weight loss: 1.0% (4/384)
Drewes 1994 Denmark	Dizziness: 20.0% (4/20)
	Dizziness: 0.0% (0/20)
Max (D) 1992 US	Constipation: 2.2% (1/46)
	Dry mouth: 10.9% (5/46)
	Fatigue: 13.0% (6/46)
	Headache: 23.9% (11/46)
	Insomnia: 15.2% (7/46)
	Orthostatic symptoms: 2.2% (1/46)
	Palpitations: 2.2% (1/46)
	Sweating increased: 10.9% (5/46)
	Constipation: % (3/46)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Dry mouth: % (16/46)
	Fatigue: % (8/46)
	Headache: % (4/46)
	Insomnia: % (0/46)
	Orthostatic symptoms: % (0/46)
	Palpitations: % (0/46)
	Sweating increased: % (1/46)
Cardenas 2002 US	Any adverse event: 97.7% (43/44)
	Any adverse event: 90.0% (36/40)
Kalso 1996 Finland	Anorexia: 20.0% (3/15)
	Constipation: 40.0% (6/15)
	Difficult to urinate: 20.0% (3/15)
	Dizziness: 6.7% (1/15)
	Dry mouth: 86.7% (13/15)
	Fatigue: 80.0% (12/15)
	Headache: 33.3% (5/15)
	Nausea: 20.0% (3/15)
	Nightmares: 40.0% (6/15)
	Palpitations: 46.7% (7/15)
	Paresthesia: 0.0% (0/15)
	Sweating increased: 80.0% (12/15)
	Anorexia: 20.0% (3/15)
	Constipation: 13.3% (2/15)
	Difficult to urinate: 0.0% (0/15)
	Dizziness: 0.0% (0/15)
	Dry mouth: 26.7% (4/15)
	Fatigue: 40.0% (6/15)
	Headache: 20.0% (3/15)
	Nausea: 20.0% (3/15)
	Nightmares: 26.7% (4/15)
	Palpitations: 33.3% (5/15)
	Paresthesia: 0.0% (0/15)
	Sweating increased: 40.0% (6/15)
	Anorexia: 21.4% (6/28)
	Constipation: 10.7% (3/28)
	Difficult to urinate: 3.6% (1/28)
	Dizziness: 0.0% (0/28)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Dry mouth: 32.1% (9/28)
	Fatigue: 50.0% (14/28)
	Headache: 28.6% (8/28)
	Nausea: 17.9% (5/28)
	Nightmares: 32.1% (9/28)
	Palpitations: 32.1% (9/28)
	Paresthesia: 3.6% (1/28)
	Sweating increased: 50.0% (14/28)
Kieburtz 1998 US	Confusion: 2.1% (1/47)
	Difficult to urinate: 0.0% (0/47)
	Dizziness: 0.0% (0/47)
	Nausea: 0.0% (0/47)
	Sedation: 21.3% (10/47)
	Confusion: 0.0% (0/48)
	Difficult to urinate: 6.3% (3/48)
	Dizziness: 2.1% (1/48)
	Nausea: 20.8% (10/48)
	Sedation: 0.0% (0/48)
	Confusion: 4.0% (2/50)
	Difficult to urinate: 2.0% (1/50)
	Dizziness: 0.0% (0/50)
	Nausea: 20.0% (10/50)
	Sedation: 0.0% (0/50)
Leijon 1989 Sweden	Any adverse event: 93.3% (14/15)
	Any adverse event: 92.9% (13/14)
	Any adverse event: 46.7% (7/15)
Max (A) 1987 US	Any adverse event: 96.6% (28/29)
	Constipation: 13.8% (4/29)
	Difficult to urinate: 3.4% (1/29)
	Dizziness: 27.6% (8/29)
	Dry mouth: 89.7% (26/29)
	Mood change: 6.9% (2/29)
	Sedation: 65.5% (19/29)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Tinnitus: 3.4% (1/29)
	Any adverse event: 86.2% (25/29)
	Constipation: 0.0% (0/29)
	Difficult to urinate: 3.4% (1/29)
	Dizziness: 10.3% (3/29)
	Dry mouth: 69.0% (20/29)
	Mood change: 0.0% (0/29)
	Sedation: 41.4% (12/29)
	Tinnitus: 0.0% (0/29)
Max (C) 1988 US	Concentration poor: 5.2% (3/58)
	Difficult to urinate: 12.1% (7/58)
	Dizziness: 19.0% (11/58)
	Dry mouth: 62.1% (36/58)
	Mood change: 5.2% (3/58)
	Sedation: 62.1% (36/58)
	Tinnitus: 5.2% (3/58)
	Concentration poor: 0.0% (0/58)
	Difficult to urinate: 0.0% (0/58)
	Dizziness: 32.8% (19/58)
	Dry mouth: 29.3% (17/58)
	Mood change: 17.2% (10/58)
	Sedation: 65.5% (38/58)
	Tinnitus: 0.0% (0/58)
	Concentration poor: 0.0% (0/58)
	Difficult to urinate: 0.0% (0/58)
	Dizziness: 24.1% (14/58)
	Dry mouth: 39.7% (23/58)
	Mood change: 0.0% (0/58)
	Sedation: 39.7% (23/58)
	Tinnitus: 3.4% (2/58)
Robinson 2004 US	Blurred vision: 5.6% (1/18)
	Constipation: 22.2% (4/18)
	Diarrhea: 5.6% (1/18)
	Difficult to urinate: 5.6% (1/18)
	Dizziness: 11.1% (2/18)
	Dry mouth: 72.2% (13/18)
	Gastrointestinal AEs: 0.0% (0/18)
	Headache: 0.0% (0/18)
	Insomnia: 11.1% (2/18)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Nausea: 11.1% (2/18)
	Palpitations: 0.0% (0/18)
	Somnolence: 50.0% (9/18)
	Sweating increased: 0.0% (0/18)
	Tinnitus: 5.6% (1/18)
	Tremor: 0.0% (0/18)
	Blurred vision: 26.3% (5/19)
	Constipation: 15.8% (3/19)
	Diarrhea: 5.3% (1/19)
	Difficult to urinate: 5.3% (1/19)
	Dizziness: 15.8% (3/19)
	Dry mouth: 68.4% (13/19)
	Gastrointestinal AEs: 15.8% (3/19)
	Headache: 5.3% (1/19)
	Insomnia: 10.5% (2/19)
	Nausea: 0.0% (0/19)
	Palpitations: 10.5% (2/19)
	Somnolence: 47.4% (9/19)
	Sweating increased: 5.3% (1/19)
	Tinnitus: 5.3% (1/19)
	Tremor: 5.3% (1/19)
Vrethem 1997 Sweden	Cold feet: 0.0% (0/35)
	Difficult to urinate: 2.9% (1/35)
	Dry mouth: 34.3% (12/35)
	Hyperglycemia: 2.9% (1/35)
	Nausea: 2.9% (1/35)
	Nose stuffy: 2.9% (1/35)
	Sedation: 34.3% (12/35)
	Tachycardia: 0.0% (0/35)
	Thirst (severe): 2.9% (1/35)
	Urticaria: 0.0% (0/35)
	Vertigo: 20.0% (7/35)
	Cold feet: 2.9% (1/34)
	Difficult to urinate: 0.0% (0/34)
	Dry mouth: 41.2% (14/34)
	Hyperglycemia: 0.0% (0/34)
	Nausea: 2.9% (1/34)
	Nose stuffy: 0.0% (0/34)
	Sedation: 8.8% (3/34)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Tachycardia: 2.9% (1/34)
	Thirst (severe): 2.9% (1/34)
	Urticaria: 2.9% (1/34)
	Vertigo: 29.4% (10/34)
	Cold feet: 0.0% (0/33)
	Difficult to urinate: 0.0% (0/33)
	Dry mouth: 6.1% (2/33)
	Hyperglycemia: 0.0% (0/33)
	Nausea: 0.0% (0/33)
	Nose stuffy: 0.0% (0/33)
	Sedation: 9.1% (3/33)
	Tachycardia: 0.0% (0/33)
	Thirst (severe): 0.0% (0/33)
	Urticaria: 0.0% (0/33)
	Vertigo: 3.0% (1/33)
Panerai 1990 Italy	Any adverse event: 56.4% (22/39)
	Any adverse event: 59.0% (23/39)
	Any adverse event: 25.6% (10/39)
Kishore-Kumar 1990 US	Bad taste: 10.5% (2/19)
	Constipation: 73.7% (14/19)
	Difficult to urinate: 26.3% (5/19)
	Dizziness: 36.8% (7/19)
	Dry mouth: 73.7% (14/19)
	Insomnia: 21.1% (4/19)
	Itching: 0.0% (0/19)
	Palpitations: 10.5% (2/19)
	Sedation: 31.6% (6/19)
	Shakiness: 10.5% (2/19)
	Sweating increased: 21.1% (4/19)
	Bad taste: 10.5% (2/19)
	Constipation: 15.8% (3/19)
	Difficult to urinate: 5.3% (1/19)
	Dizziness: 26.3% (5/19)
	Dry mouth: 47.4% (9/19)
	Insomnia: 0.0% (0/19)
	Itching: 10.5% (2/19)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
	Palpitations: 0.0% (0/19)
	Sedation: 0.0% (0/19)
	Shakiness: 5.3% (1/19)
	Sweating increased: 0.0% (0/19)
Max (B) 1991 US	Constipation: 30.0% (6/20)
	Dry mouth: 40.0% (8/20)
	Insomnia: 35.0% (7/20)
	Orthostatic symptoms: 30.0% (6/20)
	Palpitations: 15.0% (3/20)
	Sedation: 40.0% (8/20)
	Sweating increased: 15.0% (3/20)
	Constipation: 20.0% (4/20)
	Dry mouth: 45.0% (9/20)
	Insomnia: 15.0% (3/20)
	Orthostatic symptoms: 5.0% (1/20)
	Palpitations: 5.0% (1/20)
	Sedation: 40.0% (8/20)
	Sweating increased: 5.0% (1/20)
Kvinesdal 1984 Denmark	Difficult to urinate: 13.3% (2/15)
	Dry mouth: 60.0% (9/15)
	Difficult to urinate: 0.0% (0/15)
	Dry mouth: 6.7% (1/15)
Sindrup (C) 1989 Denmark	Dry mouth: 61.5% (8/13)
	Dry mouth: 30.8% (4/13)
Hammack 2002 US	Constipation: 41.3% (19/46)
	Difficult to urinate: 4.3% (2/46)
	Dry mouth: 63.0% (29/46)
	Nausea: 8.7% (4/46)
	Sedation: 30.4% (14/46)
	Constipation: 22.2% (10/45)
	Difficult to urinate: 6.7% (3/45)
	Dry mouth: 31.1% (14/45)
	Nausea: 6.7% (3/45)
	Sedation: 26.7% (12/45)
Panerai 1990	Any adverse event: 56.4% (22/39)

Evidence Table 13. Adverse events in placebo-controlled trials of other antiepileptics, tricyclic antidepressants, SSRIs and dextromethorphan for neuropathic pain

Study	Specific adverse events
Italy	Any adverse event: 59.0% (23/39)
	Any adverse event: 25.6% (10/39)