



Clinician Summary Drugs for Neuropathic Pain June 2011

Based on the DERP report of October 2007

Produced by:
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Clinician Summary: Drugs for Neuropathic Pain

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Drugs included

Antiepileptics: gabapentin, pregabalin

SNRI antidepressants: duloxetine, venlafaxine

Topical analgesic: lidocaine patch and ointment

Tricyclic antidepressants: amitriptyline, desipramine, nortriptyline, imipramine, doxepin

SSRI antidepressants: citalopram, fluoxetine, paroxetine, sertraline, escitalopram

Limits of evidence

All of the trials included in this report are efficacy studies. None met criteria for effectiveness studies. The trials had narrow inclusion criteria, were conducted in specialty settings, and used rigid dosing regimens. Outcomes evaluated were short-term and poorly standardized. Most were sponsored by pharmaceutical companies.

Conclusions

Good evidence: Gabapentin, pregabalin, and duloxetine were more effective than placebo for pain relief or improvement in function

Fair evidence: Pregabalin is superior to duloxetine, venlafaxine, or SSRI's for pain relief with diabetic neuropathy

No conclusion can be made about the effectiveness of lidocaine for neuropathic pain due to poor quality studies.

Insufficient evidence to determine a difference in comparative effectiveness between gabapentin, pregabalin, duloxetine, or venlafaxine for neuropathic pain.

Insufficient evidence to determine comparative effectiveness between pregabalin, SNRI's (duloxetine and venlafaxine) and topical lidocaine vs. other drugs for neuropathic pain.

Adverse effects

Good evidence: Gabapentin and pregabalin are associated with more sedation than venlafaxine. **Fair evidence:** No difference in overall rates of withdrawal, somnolence/sedation or dizziness between gabapentin and pregabalin

Fair evidence: pregabalin and gabapentin have a higher incidence of somnolence and dizziness compared to other antiepileptic drugs and tricyclic antidepressants.

Insufficient evidence to differentiate between duloxetine, gabapentin, pregabalin or venlafaxine for other adverse events.

Insufficient evidence to determine comparative harms of pregabalin, gabapentin, SNRI's (duloxetine and venlafaxine) or topical lidocaine vs. other drugs for neuropathic pain.

Table 1. Included drugs

Drug	Trade Name(s)	Labeled indications for neuropathic pain	Recommended daily dosing for neuropathic pain	Range of daily doses used in RCTs of neuropathic pain (median)	FDA warnings/cautions*
<i>Gabapentin, pregabalin, SNRIs, and topical lidocaine</i>					
<i>Antiepileptics</i>					
Gabapentin	Neurontin®	Postherpetic neuralgia	Start at 300 mg, titrate to 900 mg, increase up to 1800 mg (divided TID)	900-3600 mg (1800 mg)	Central nervous system adverse events in pediatric patients with epilepsy.
Pregabalin	Lyrica®	Diabetic neuropathy Postherpetic neuralgia	Diabetic neuropathy: Start at 150 mg, increase up to 300 mg (divided TID) Postherpetic neuralgia: Start at 150 mg, increase up to 75 to 150 mg BID, or 50 to 100 mg TID in patients with creatinine clearance of at least 60 mL/min	75-600 mg (300 mg)	Angioedema, hypersensitivity reactions
<i>SNRI antidepressants</i>					
Duloxetine	Cymbalta®	Diabetic neuropathy	60 mg once daily; consider lower starting dose and gradual increase in patients with renal impairment	20-120 mg (90 mg)	Increased suicidality in children, adolescents, and young adults with major depressive disorder and other psychiatric conditions.
Venlafaxine	Effexor® Effexor XR®	None	NA	37.5-225 mg (75 mg)	Risk of serotonin syndrome when SNRIs and triptans are used together.
<i>Topical analgesic</i>					
Lidocaine patch 5%	Lidoderm®	Postherpetic neuralgia	Up to 3 patches for up to 12 hours within a 24-hour period	5%, up to 3 patches	Accidental exposure in children Excessive dosing by applying patch longer than or to a larger area than recommended
Lidocaine topical ointment	Anestacon® Xylocaine®	None	NA	5%	
<i>Other medications for neuropathic pain</i>					

Drug	Trade Name(s)	Labeled indications for neuropathic pain	Recommended daily dosing for neuropathic pain	Range of daily doses used in RCTs of neuropathic pain (median)	FDA warnings/cautions*
<i>Antiepileptics</i>					
Carbamazepine	Tegretol® Tegretol XR®	Trigeminal neuralgia	Start at 100 mg BID, increase up to a maximum of 1200 mg daily (divided BID). Most patients are maintained on 400-800 mg daily. Attempt to reduce dose to minimum effective level, or discontinue, at least every 3 months.	500-2400 mg (1000 mg)	
Lamotrigine	Lamictal®	None	NA	200-600 mg (350 mg)	Teratogenicity: Possible risk of cleft lip or palate
Topiramate	Topamax®	None	NA	75-600 mg (258 mg)	Use is associated with metabolic acidosis
Oxcarbazepine	Trileptal®	None	NA	600-1800 mg (900 mg)	Serious dermatological reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)
Valproic acid/divalproex	Depakote® Depakene®	None	NA	600-2400 mg (1000 mg)	BOXED WARNING: Teratogenicity
<i>Tricyclic antidepressants</i>					
Amitriptyline	Elavil®	None	NA	10-150 mg (70 mg)	Increased suicidality in patients with depression
Desipramine	Norpramin®	None	NA	50-200 mg (184 mg)	
Nortriptyline	Pamelor®	None	NA	25-100 mg	
Imipramine	Tofranil®	None	NA	50-150 mg (75 mg)	
Doxepin	Sinequan®	None	NA	No trials	
<i>SSRI antidepressants</i>					
Citalopram	Celexa®	None	NA	40 mg	Increased suicidality in patients with depression
Fluoxetine	Prozac®	None	NA	40 mg	
Paroxetine	Paxil®	None	NA	No trials	
Sertraline	Zoloft®	None	NA	No trials	
Escitalopram	Lexapro®	None	NA	No trials	
<i>NMDA receptor antagonist</i>					
Dextromethorphan	Several	None	NA	40.5-439 mg (270 mg)	BOXED WARNING: Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events.

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					FDA notification: There have been five recently reported deaths of teenagers that may be associated with the abuse/over-consumption of powdered dextromethorphan sold in capsules

*Please see package inserts and FDA labeling information for more detailed and specific cautions and black box warnings for medications included in this review.