

Table 21.3 Medications Used to Treat Pain Associated With Diabetic Neuropathy

Medication	Dosing	Side effects affecting rehab	Other side effects or considerations
NSAIDs: Used in acute treatment of neuropathy to relieve mild to moderate pain. Antipyretic, analgesic, anti-inflammatory. Reversible inhibition of platelet aggregation with NSAIDs lasts 1-3 days.			
Ibuprofen (Motrin)	400-800 mg by mouth every 6-8 h as needed. Take with meals.	Cog: + S: 0 A: 0 Motor: 0 D: ++ Com: + F: +	Gastrointestinal upset, dyspepsia, xerostomia, oral ulceration, glossitis, gastrointestinal mucosal hemorrhage, abrupt acute renal insufficiency, fluid retention, worsening of congestive heart failure, memory loss, confusion, dizziness, headache. Increased risk of bleeding with oral anticoagulant warfarin (Coumadin). Do not combine with aspirin. Antagonizes effects of antihypertensives; may cause confusion in elderly.
Naproxen (Naprosyn, Anaprox, Naprelan)	250-500 mg by mouth every 8-12 h as needed.	Cog: + S: 0 A: 0 Motor: 0 D: ++ Com: + F: +	
Skeletal muscle relaxants: Helpful in initial 2 wk of treatment of diabetic neuropathy.			
Carisoprodol (Soma)	Adults and adolescents: 250-350 mg 3 times/day and at bedtime. Children <12 yr: Not recommended.	Cog: ++ S: +++ A: 0 Motor: +++ D: ++ Com: ++ F: ++	Headache, dizziness, drowsiness, facial flushing, insomnia, coordination problems. Potential for addiction or abuse. Potentiates effects of opiates, allowing reduction of opiate dosage. Metabolized by CYP2C19 to meprobamate. Can result in dependence.
Cyclobenzaprine (Flexeril)	Adults: 10 mg 2-4 times/day; maximum dose of 60 mg/day. Available as 15 and 30 mg long-acting product which is dosed once/day. Children's dose: Not established.	Cog: ++++ S: ++++ A: 0 Motor: +++ D: ++ Com: ++ F: ++++	Somnolence, confusion, dizziness, paresthesias, seizures, arrhythmias. Avoid with monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, guanethidine, and concurrent central nervous system depressants. Structurally similar to tricyclic antidepressants with similar side effects. Use should be limited to no more than 3 wk.
Methocarbamol (Robaxin, Skelex)	Adults: 500-750 mg 4 times/day.	Cog: ++++ S: ++++ A: ++ Motor: +++ D: ++ Com: ++ F: +++	Somnolence, dizziness, vertigo, syncope, muscular incoordination, stomach upset, flushing, blurred vision, fever, skin rash, pruritus, bradycardia, jaundice, mood changes, slow heart rate, fainting, clumsiness, difficulty urinating; may cause discoloration of urine (black, blue, or green). Additive sedation when used with other central nervous system depressants. Metabolized by demethylation so no significant drug interactions.
Tricyclic antidepressants: Inhibit reuptake of serotonin and norepinephrine; should be used as first-line therapy in patients with underlying insomnia or depression; are effective for paresthetic pain (e.g., the feeling of pins and needles, electricity, numbness, or aches, knifelike shooting).			
Amitriptyline (Elavil)	10-25 mg at bedtime; titrate by 10-25 mg every 3-7 days to 75-150 mg/day	Cog: ++++ S: ++++ A: 0	Weight gain: +++ Seizure: +++ Cardiac: +++

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Dosing	Side effects affecting rehab	Other side effects or considerations
	as tolerated.	Motor: ++ D: ++++ Com: ++++ F: ++++	Sexual: ++ Not recommended in elderly due to high sedative and anticholinergic effects that increase risk of falls.
Desipramine (Norpramin)	Start at 25-50 mg 4 times/day and titrate slowly as needed. Maximum dose of 300 mg. Dose for elderly or adolescents is 25-100 mg/day. May take once/day at bedtime to minimize sedation.	Cog: ++ S: ++ A: + Motor: ++ D: ++ Com: ++ F: ++	Weight gain: + Seizure: ++ Cardiac: ++ Sexual: ++ Prolongs QT interval.
Nortriptyline (Pamelor)	Start at 25 mg/day and increase to 150 mg/day. Maximum dose of 150 mg. Dose for elderly or adolescents is 10-75 mg. May take once/day at bedtime.	Cog: ++ S: ++ A: 0 Motor: ++ D: ++ Com: ++ F: +	Weight gain: + Seizure: ++ Cardiac: ++ Sexual: ++ Preferred tricyclic antidepressant in elderly due to low anticholinergic and sedative effects.
Norepinephrine serotonin reuptake inhibitor (NSRI) antidepressant: Enhances norepinephrine and serotonin; used to treat depression, anxiety disorder, diabetic peripheral pain, neuropathic pain, chronic skeletal muscle pain, and fibromyalgia.			
Duloxetine (Cymbalta)	Start at 20 mg twice/day or 30 mg once/day and increase after 1 wk to 60 mg/day in 1-2 divided doses. Maximum dose of 60 mg/day. Do not use in patients with hepatic disease or with creatinine clearance <30 ml/min.	Cog: + S: 0 A: + Motor: 0 D: ++ Com: 0 F: +	Weight gain: 0/+ Seizure: 0 Cardiac: 0 Sexual: + Metabolized by CYP1A2 and CYP2D6, so there are potential drug interactions when combined with other medications metabolized by these pathways.
Anesthetic patch: Can be used for both dysesthetic and paresthetic pain as adjunct to oral therapy; may relieve intractable pain not relieved by other agents.			
Lidocaine 5% topical patch (Lidoderm)	One patch on for 12 h and then removed for 12 h; may titrate dose to up to 3 patches/12 h.	Cog: + S: + A: + Motor: + D: + Com: + F: +	Confusion, nervousness, lightheadedness, euphoria, tremors, blurred vision, vomiting, hypotension. Removing patch for 12 h reduces development of tolerance and maintains medication effectiveness.
Anticonvulsants: Used to treat pain by blocking sodium, potassium, calcium channels, and neurotransmitters such as gamma amino butyric acid (GABA) to relieve neuropathic pain.			
Gabapentin (Neurontin)	100-300 mg 3 times/day; can titrate by 100-300 mg every 1-7 days as tolerated to target dose of 1800-3600 mg/day in divided doses. Adjust dose for renal insufficiency.	Cog: ++ S: ++ A: + Motor: +++ D: 0 Com: ++ F: +++	Peripheral edema, tremor, dizziness, fatigue, ataxia, drowsiness, weight gain, behavior changes.
Pregabalin (Lyrica)	Start at 75 mg twice/day and increase to 150 mg twice/day in 1 wk; titrate to effective dose (usually 150-	Cog: ++ S: ++ A: + Motor: +++	Dizziness, somnolence, dry mouth, edema, blurred vision, weight gain, difficulty with concentration and attention.

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Medication	Dosing	Side effects affecting rehab	Other side effects or considerations
	225 mg twice/day). Adjust for renal insufficiency.	D: 0 Com: ++ F: +++	
Substance P enhancer: Topical agent used as an adjunct to oral therapy. Can relieve dysesthetic pain when applied to affected area.			
Capsaicin cream	Apply topically to affected area 3-4 times/day.	Cog: 0 S: 0 A: 0 Motor: 0 D: 0 Com: 0 F: 0	May cause stinging and burning pain during the initial few applications. Use gloves and applicator for administration and wash hands after application. Avoid contact with eyes.
Opiate analgesics: Used for severe pain that is not relieved with other agents.			
Oxycodone (Oxycontin SR) Roxycodone (Oxy-IR)	Immediate release: 10-30 mg every 3-4 h on as needed basis. Sustained release: 10-30 mg every 12 h on a scheduled basis.	Cog: ++ S: ++ A: + Motor: +++ D: ++ Com: ++ F: +++	Constipation, somnolence, dizziness, nausea, vomiting, itching, sedation, respiratory depression. Risk of addiction, physical dependence, and tolerance. Sustained-release product should be administered on a scheduled basis every 12 h to prevent or minimize pain development. Do not crush or chew SR products. SR products should be prescribed with an immediate-release product, which is administered on an as-needed basis for breakthrough pain. Drug interactions: Additive sedation when used with other CNS depressants.
Morphine SR (MS Contin, Morphine IR)	Immediate release: 10-30 mg every 4-6 h on as needed basis. Sustained release: 15-60 mg every 12 h on a scheduled basis.	Cog: ++ S: ++ A: + Motor: +++ D: ++ Com: ++ F: +++	
Tramadol (Ultram)	50-100 mg every 4-6 h. Maximum dose of 400 mg/day.	Cog: ++ S: ++ A: + Motor: +++ D: ++ Com: ++ F: +++	Constipation, somnolence, dizziness, nausea, vomiting, itching. Avoid use in those with seizure disorder or alcohol or drug abuse. Avoid serotonin syndrome by avoiding use with selective serotonin reuptake inhibitors. Risk of addiction, physical dependence, abuse and tolerance.

Cog = cognition; S = sedation; A = agitation or mania; Motor = discoordination; D = dysphagia; Com = communication; F = falls; NSAID = nonsteroidal anti-inflammatory drug; SR = sustained release; IR = immediate release; CNS = central nervous system.

The likelihood rating scale for encountering the side effects is as follows: 0 = Almost no probability of encountering side effects. 0/+ = Slight probability of encountering side effects with higher doses. + = Little likelihood of encountering side effects. +/++ = Low probability of encountering side effects; however, probability increases with increased dosage. ++ = Medium likelihood of encountering side effects. +++ = High likelihood of encountering side effects, particularly with high doses. ++++ = Highest likelihood of encountering side effects; best to avoid in at-risk patients.