

Behavioral Interventions: Improve glucose levels, quit smoking, alcohol reduction, exercise, massage, meditation, pain management clinic, adequate sleep, nutrition therapy, hobbies.

Pathogenetically Oriented Therapy

- Alpha lipoic acid 600 – 1,800 mg a day. Consider B12 replacement therapy.

Prescription Therapy:

1st line – Tricyclic Antidepressants (Amitriptyline, Nortriptyline, Desipramine)

- Calcium Channel Modulators (Gabapentin, Pregabalin)
- Serotonin Norepinephrine Reuptake Inhibitors (SNRI – Venlafaxine, Duloxetine)

2nd Line - Topical Capsaicin Cream for localized pain – Apply 2-4 x daily for up to 8 wks

- Opioids are no longer recommended due to addiction risk, lack of efficacy. (ADA Stds)

Common Reasons for Treatment Failure

- Dose too low or inadequate trial – requires 2-8 weeks of treatment to observe symptom reduction
- Expecting elimination of symptoms – only reduces symptoms by about 50%
- Incorrect diagnosis: If in doubt, refer to neurologist
- If there is no improvement or person has adverse effects, change medication class
- If some but inadequate relief, raise the dose and consider adding or changing meds.

References: Ziegler, D. Painful diabetic neuropathy. Diabetes Care 2009; 32 (Supp 2): S414-S419

Class	Generic / Trade Name	Usual Daily Dose Range	Comments	Side Effects/ Caution
1st Line Agents Tricyclic Antidepressants TCA Improves neuropathy and depression	Amitriptyline / Elavil	25 – 100 mg* Avg dose 75mg	Usually 1 st choice	Take 1 hour before sleep. Side effects; dry mouth, tiredness, orthostatic hypotension. Caution: not for pts w/ unstable angina (<6 mo), MI, heart failure, conduction system disorder.
	Nortriptyline / Pamelor	25 - 150 mg* (for burning mouth)	Less sedating and anticholinergic	
	Desipramine / Norpramine	25 – 150 mg* *Increase by 25mg weekly till pain relieved		
Calcium Channel Modulators	Gabapentin/ Neurontin	100 - 1,200mg TID	Improves insomnia, fewer drug interactions	Sedation, dizziness, peripheral edema, wt gain Caution; CHF, suicide risk, seizure disorder.
	Pregabalin / Lyrica *FDA approved for neuropathy treatment	50 - 200mg TID		
Serotonin Norepinephrine Reuptake Inhibitor SNRI	Duloxetine / Cymbalta *FDA approved for neuropathy treatment	60 mg daily Start at 30 mg	Improves depression, insomnia	Nausea, sedation, HTN, constipation, dizziness, dry mouth, blurred vision. Caution: adjust dose for renal insufficiency, do not stop abruptly, taper dose.
	Venlafaxine/ Effexor	75 - 225 mg daily		
2nd Line Agents Opioids (avoid this class)	Weaker opioids Tramadol / Ultram	50 – 400 mg	Sedation, nausea, constipation Caution: ADA Standards no longer recommend this class due to addiction risk and lack of efficacy for painful neuropathy.	
	Stronger opioids Oxycodone	10 – 100 mg		
Local Treatment	Capsaicin Cream (0.025%) Apply 2-4 x daily for up to 8 wks			
Other choices	If above medications not effective, contraindicated, or intolerable consider: Bupropion/Wellbutrin Paroxetine / Paxil Citalopram / Celexa Topiramate / Topamax Topical Lidocaine (for localized pain).			

*indicates medication is available in generic form.

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