

**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:

#### **1<sup>st</sup> line** – Tricyclic Antidepressants (Amitriptyline, Nortriptyline, Desipramine)

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

#### **2<sup>nd</sup> 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	
<b>1<sup>st</sup> Line Agents</b> <b>Tricyclic Antidepressants</b> TCA Improves neuropathy and depression	Amitriptyline / Elavil	25 – 100 mg* Avg dose 75mg	Usually 1 <sup>st</sup> choice	Take 1 hour before sleep. Side effects; dry mouth, tiredness, orthostatic hypotension. <b>Caution:</b> 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			
<b>Calcium Channel Modulators</b>	Gabapentin/ Neurontin	100 - 1,200mg TID	Improves insomnia, fewer drug interactions	Sedation, dizziness, peripheral edema, wt gain <b>Caution:</b> CHF, suicide risk, seizure disorder.	
	Pregabalin / Lyrica *FDA approved for neuropathy treatment	50 - 200mg TID			
<b>Serotonin Norepinephrine Reuptake Inhibitor</b> <b>SNRI</b>	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. <b>Caution:</b> adjust dose for renal insufficiency, do not stop abruptly, taper dose.	
	Venlafaxine/ Effexor	75 - 225 mg daily			
<b>2<sup>nd</sup> Line Agents</b> <b>Opioids</b> (avoid this class)	Weaker opioids Tramadol / Ultram	50 – 400 mg	Sedation, nausea, constipation <b>Caution:</b> ADA Standards no longer recommend this class due to addiction risk and lack of efficacy for painful neuropathy.		
	Stronger opioids Oxycodone	10 – 100 mg			
<b>Local Treatment</b>	Capsaicin Cream (0.025%) Apply 2-4 x daily for up to 8 wks				
<b>Other choices</b>	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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