

Type 2 Diabetes – Neuropathy

Usual Presentation: Begins in feet and progresses proximally; often symmetrical but may present atypically.

Symptoms include chronic or undulating pain, numbness and tingling, burning or occasionally shooting or stabbing pain.

Prevention and Treatment of Neuropathic Pain Syndrome is as follows:

- Maintain glycemic control.
- Promote smoking cessation and or alcohol cessation or reduction.
- Consider alpha lipoic acid 600mg daily (OTC supplement).

Goal of therapy is to reduce symptoms by approximately 50%.

Non-Prescription Therapy

Consider alpha lipoic acid 600mg daily which is more effective than vitamin B therapy.

Prescription therapy

1st Line - Tricyclic Antidepressants (TCA) (Amitriptylline Nortriptylline Desipramine) are efficacious and low cost; consider contraindications.

2nd Line – If first line doesn't work use **Calcium Channel Modulators** (Gabapentin, Pregabalin) OR **Serotonin Norepinephrine Reuptake Inhibitors (SNRI)** (Venlafaxine, Duloxetine)

3rd Line – Last line of treatment is **long acting Opioids** (Morphine, Tramadol).

Common reasons for treatment failure:

- Dose is too low.
- Inadequate trial; requires 2 to 8 weeks of treatment to observe symptom reduction.
- Pt expecting elimination of symptoms; treatment reduces symptoms approximately a 50%.
- Incorrect diagnosis; if in doubt, refer to pain specialist or neurologist.
- If patient does not respond or has adverse effects, change the medication class.
- If patient has some but inadequate relief, raise the dose then consider adding or changing medications.

The following tables present information about the medications, dose, side effects, other benefits and cautions for using medications to treat neuropathy.

Table 1. 1st Line Medications - Tricyclic Antidepressant (TCA)

Medication	Dose	Comments
Nortriptylline	25-150mcg daily	May help with sleep disorders
Amitriptylline	25-150mcg daily	Less sedating, less anticholinergic
Desipramine*†	25-150mcg daily	Less sedating, less anticholinergic

* Drug not included in IHS National Core Formulary

Side effects of first line medications may include: sedation, dry mouth, blurred vision, weight gain, urinary retention.

Other benefits may include: improvement of depression and insomnia.

Caution: personal or family history of dysrhythmia or sudden cardiac death, glaucoma, suicide risk, seizure disorder; caution autonomic neuropathy (may cause orthostatic sx) - get standing Blood Pressures.

Table 2. 2nd Line Medications - Calcium Channel

Medication	Dose
Gabapentin*	100-1,200mg TID
Pregabalin*	50 – 200mg TID

* Drug not on IHS National Core Formulary

Side effects: sedation, dizziness, peripheral edema

Other benefits: improvement of insomnia, fewer drug interactions.

Caution: cardiac disease, glaucoma, suicide risk, seizure disorder.

Table 3. Other 2nd Line Medications - Serotonin Norepinephrine Reuptake Inhibitors (SNRI)

Medication	Dose
Venlafaxine* (Effexor®)	75-225 mg daily; starting dose: 37.5mg
Duloxetine*(Cymbalta®)	60 mg daily; starting dose: 30mg

*Drug not on IHS National Core Formulary

Side effects: sedation, dry mouth, blurred vision, weight gain, urinary retention

Other benefits: improvement of depression and insomnia

Caution: renal insufficiency; do not stop abruptly - taper dose

Table 4. 3^d Line Medications – Long Acting Opioids

Medication	Dose
Morphine* (MS Contin®) (or other long acting opioids)	Start at low dose and titrate gradually
Tramadol* (Ultram®)	Start at low dose and titrate gradually

* Drug included in the IHS National Core Formulary

Side effects: sedation, nausea, constipation (always prescribe stool softener)

Caution: abuse, suicide risk, short action-opioids not recommended for long term treatment.

Combination therapy is not well studied; some evidence exists for the combination of gabapentin and nortryptilline. Caution with drug interactions (e.g. serotonin syndrome risk with tramadol and many antidepressant meds).

If above medications are not efficacious, contraindicated, or if intolerable adverse events occur, may consider:

- **Bupropion* (Wellbutrin®)**
- **Topiramate* (Topamax®)**
- **Citalopram* (Celexa®)**
- **Paroxetine* (Paxil®)**
- **Topical capsaicin* (for localized pain)**
- **Topical lidocaine*(for localized pain)***

*Drug not included in the IHS National Core Formulary

References:

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

Rutkove SB. A 52-year old woman with disabling peripheral neuropathy: review of diabetic polyneuropathy. JAMA 2009;302(13):1451-1458.