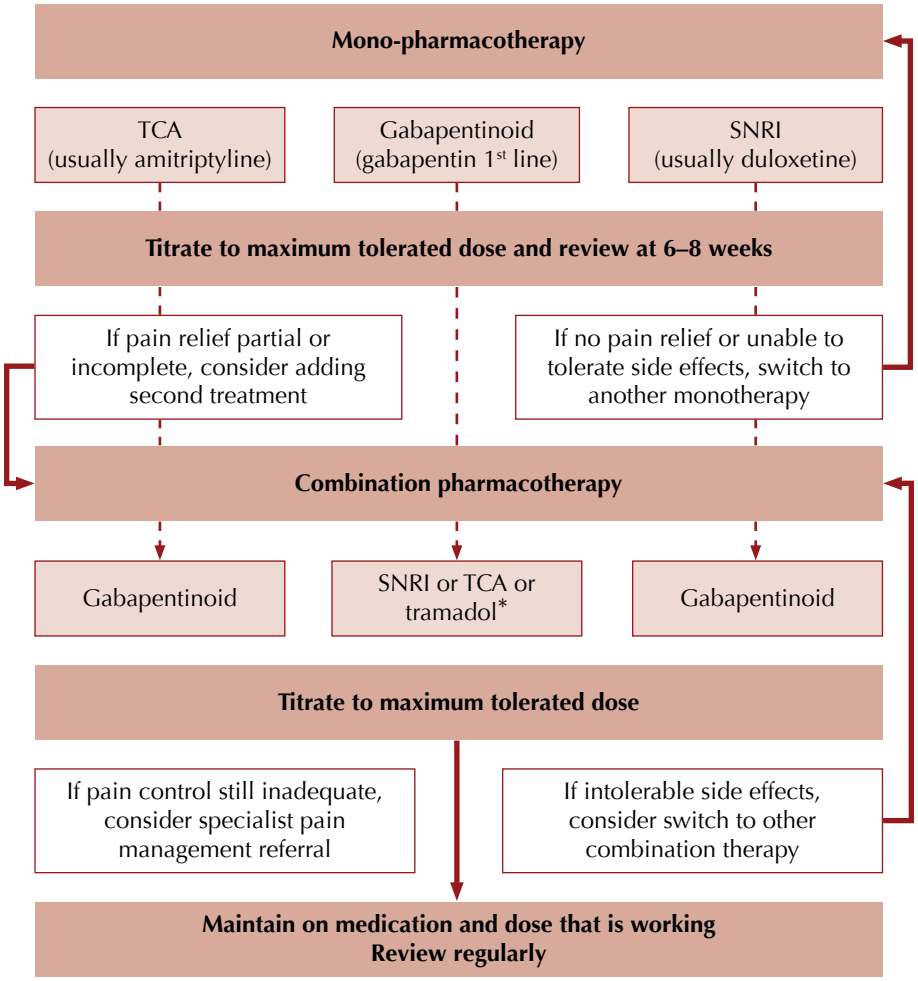
Prescribing guidance for neuropathic analgesia in painful diabetic neuropathy (click on drug names to access SmPCs).

Drug	Initial dosing	Titration	Max dose	Contraindications and cautions	Duration of trial
Amitriptyline	10–25 mg daily 2 hours before bed (to reduce hangover effect)	Increase in increments of 10–25 mg every 3–7 days	100 mg at night (in two divided doses if >75 mg) **Note:** Limited benefit over 50 mg but increased side effects	**Contraindications:** Arrhythmias; Recent MI; Manic phase of bipolar disorder; Heart block **Cautions:** Significant mental health history (e.g. psychosis, bipolar disorder, suicidal ideation); Age >75 years (due to cardiac and psychotropic adverse effects); Susceptibility to glaucoma; BPH; Chronic constipation; Cardiovascular disease; Epilepsy; Phaeochromocytoma Glycaemic control may be affected: adjust glucose-lowering therapy accordingly	If no response in 4–6 weeks (at least 2 weeks at maximum tolerated dose), withdraw slowly (over a minimum of 4 weeks; usually, reduce by 10 mg per week) to avoid withdrawal effects
Gabapentin	300 mg daily (100 mg daily in frail/elderly)	Increase by 300 mg every 2–3 days **Rapid titration:** Day 1: 300 mg o.n. Day 2: 300 mg b.d. Day 3: 300 mg t.d.s.	3600 mg/day in three divided doses Dose reductions required for renal impairment **CrCl (mL/min):** 50–79 = 600–1800 mg 30–49 = 300–900 mg 15–29 = 150–600 mg <15 = 150–300 mg If side-effects occur, remain at highest tolerated dose for 4 weeks before reassessment and further titration if required	**Cautions:** Substance misuse history (potential for dependence and abuse); Low body weight; Elderly; Suicidal ideation; Respiratory depression Seizure exacerbation in patients with absence, myoclonic, tonic or atonic seizures	3–8 weeks with at least 2 weeks at maximum tolerated dose If no benefit, gradually wean down over at least 1 week
Pregabalin	75 mg b.d. (25 mg b.d. in frail/elderly) **CrCl (mL/min):** 30–59: 75 mg o.d. 15–29: 25–50 mg o.d. <15: 25 mg o.d.	Increase by 75 mg b.d. after 3–7 days and can increase by a further 150 mg b.d. after another 7 days. 25 mg increments in frail elderly	300 mg b.d. **CrCl (mL/min):** 30–59: 150 mg b.d. or 100 mg t.d.s. 15–29: 150 mg o.d. or 75 mg b.d. <15: 75 mg o.d.	**Cautions:** Substance misuse history (potential for dependence and abuse); Suicidal ideation; Respiratory depression; Severe congestive heart failure; Elderly; Those at risk of encephalopathy Seizure exacerbation in patients with absence, myoclonic, tonic or atonic seizures	If no benefit after 8 weeks at maximum tolerated dose, reduce and gradually titrate down as titrated up
Duloxetine	60 mg daily	30 mg increments	120 mg (two divided doses)	**Contraindications:** Severe liver disease; Severe renal impairment (CrCl <30 mL/min). Do not use in combination with fluvoxamine, ciprofloxacin, enoxacin or MAOIs. **Cautions:** Bleeding disorders; Cardiac disease; Elderly; History of mania; History of seizures; Hypertension (uncontrolled); Raised interocular pressure; Susceptibility to closed-angle glaucoma	Stop after 8 weeks if providing no benefit
Capsaicin 0.075% cream	Apply 3–4 times daily	No titration	Apply 3–4 times daily sparingly, leave at least 4 hours between applications	**Contraindications:** Do not use on broken or irritated skin **Cautions:** Pain, burning sensation and erythema at application site	For period of 8 weeks then reassess

Dosing abbreviations: o.d.=once daily; o.n.=once nightly; b.d.=twice daily; t.d.s.=three times daily; PRN=when required.
CrCl=creatinine clearance; BPH=benign prostatic hyperplasia; MAOI=monoamine oxidase inhibitor; MI=myocardial infarction.
Note: Tramadol should be used as rescue therapy only when awaiting specialist pain services. Use 50–100 mg PRN up to four times a day. See SmPC for common side effects, cautions and contraindications.
Always consult the electronic BNF or Summaries of Product Characteristics (SmPCs) prior to prescribing any drug. Information correct on 9 March 2023.

Neuropathic pain treatment pharmacological treatment pathway



*Tramadol should only be used as acute rescue therapy.
SNRI=serotonin–norepinephrine reuptake inhibitor; TCA= tricyclic antidepressant.
Adapted from Ziegler et al (2022).

Common adverse events

Amitriptyline
Anticholinergic syndromes (dry mouth, blurry vision, constipation, drowsiness, sedation, urine retention, confusion), tremor, dizziness, headache, speech disorder, palpitations, tachycardia, orthostatic hypotension, weight gain, QT interval prolongation.

Gabapentin
Fatigue, fever, dizziness, ataxia, drowsiness, confusion, memory loss, emotional lability, gastrointestinal disturbance, infections.

Pregabalin
Gastrointestinal disturbance, dizziness, drowsiness, headache, dry mouth, memory loss, altered mood.

Duloxetine
Anxiety, headache, dizziness, dry mouth, nausea, flushing.

Capsaicin 0.075% cream
Nil.

Tramadol
Nausea, dizziness, confusion, constipation, hallucinations.

Switching from gabapentin to pregabalin

- Offer pregabalin if gabapentin is not tolerated or the person has not responded fully.
- One option is to gradually decrease and stop gabapentin over 1 week before starting pregabalin titration.
- If stopping gabapentin and switching immediately to pregabalin, see dosing advice below:

Daily dose of gabapentin pre-switch	Daily dose of pregabalin post-switch	Dosing schedule of pregabalin
0–900 mg	150 mg	75 mg twice daily
901–1500 mg	225 mg	75 mg in the morning and 150 mg in the evening
1501–2100 mg	300 mg	150 mg twice daily
2101–2700 mg	450 mg	150 mg in the morning and 300 mg in the evening
>2700 mg	600 mg	300 mg twice daily

Adapted from UK Medicines Information (2017).

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References

UK Medicines Information (2017) *Q&A 408.1: How do you switch between pregabalin and gabapentin for neuropathic pain, and vice versa?* https://bit.ly/3ZS4aMC

Ziegler D, Tesfaye S, Spallone V et al (2022) Screening, diagnosis and management of diabetic sensorimotor polyneuropathy in clinical practice: International expert consensus recommendations. *Diabetes Res Clin Pract* **186**: 109063

See also:

At a glance factsheet: Diabetes-related sensory peripheral neuropathy

The basics of diabetic neuropathy, including pathophysiology, screening and pain management.

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