FREQUENTLY ASKED QUESTIONS

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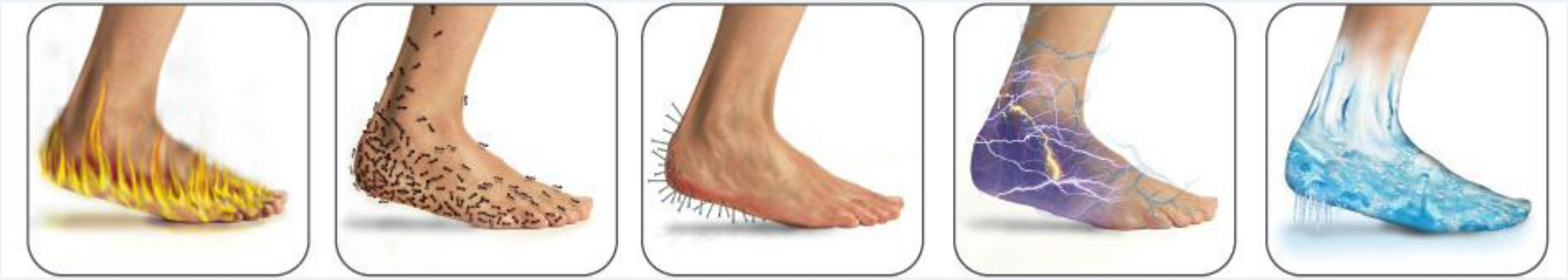
CCB = calcium channel blocker; NSAID = non-steroidal anti-inflammatory drug

How can neuropathic pain be identified?

Be alert for common verbal descriptors of neuropathic pain:



Burning ***Tingling*** ***Shooting*** ***Electric shock-like*** ***Numbness***

Baron R *et al. Lancet Neurol* 2010; 9(8):807-19; Gilron I *et al. CMAJ* 2006; 175(3):265-75.

Neuropathic Pain Screening Tools

	LANSS	DN4	NPQ	painDETECT	ID Pain
Symptoms					
Pricking, tingling, pins and needles	x	x	x	x	x
Electric shocks of shooting	X				
Hot or burning	X				
Numbness		x	x	x	x
Pain [illegible]	X				x
Painf [illegible]					
Clinical examination					
Brush allodynia	X	x			
Raised soft touch threshold					
Altered pin prick threshold	X				

Neuropathic pain screening tools rely largely on common verbal descriptors of pain

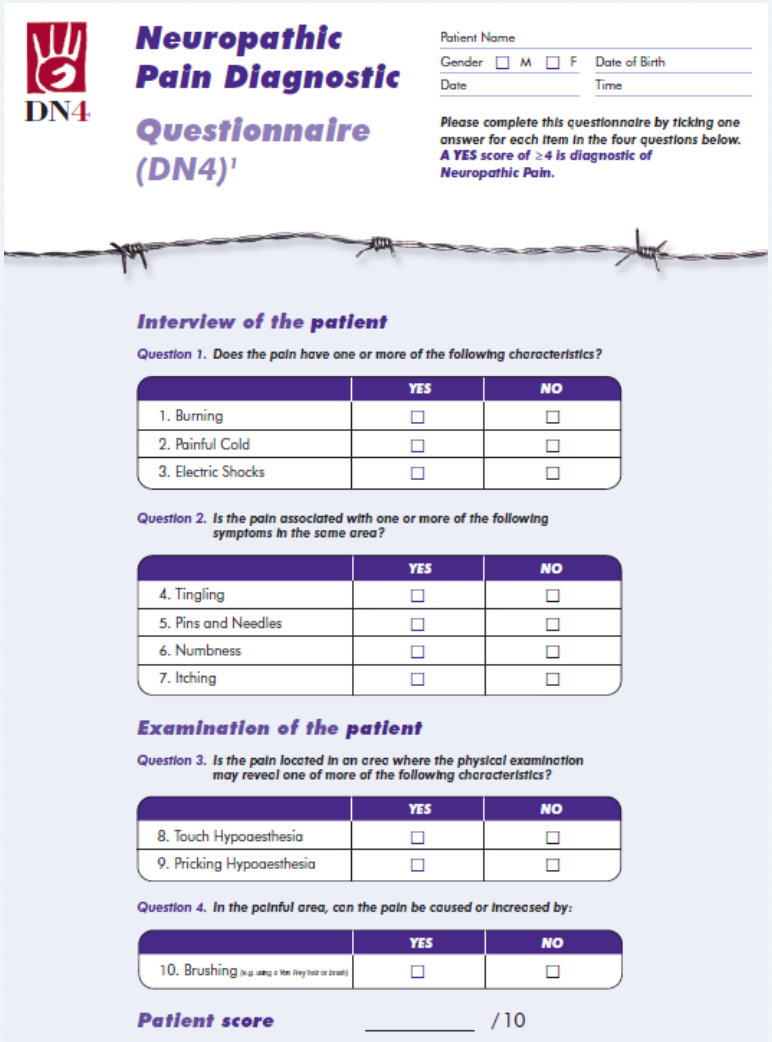
Select tool(s) based on ***ease of use*** and ***validation in the local language***

Some screening tools also include bedside neurological examination

DN4 = Douleur Neuropathique en 4 Questions (DN4) questionnaire;
LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; NPQ = Neuropathic Pain Questionnaire

Bennett MI *et al. Pain* 2007; 127(3):199-203; Haanpää M *et al. Pain* 2011; 152(1):14-27.

DN4



Neuropathic Pain Diagnostic Questionnaire (DN4)[1]

DN4

Patient Name

Gender ☐ M ☐ F Date of Birth

Date Time

Please complete this questionnaire by ticking one answer for each item in the four questions below. A YES score of ≥4 is diagnostic of Neuropathic Pain.

Interview of the patient

Question 1. Does the pain have one or more of the following characteristics?

	YES	NO
1. Burning	☐	☐
2. Painful Cold	☐	☐
3. Electric Shocks	☐	☐

Question 2. Is the pain associated with one or more of the following symptoms in the same area?

	YES	NO
4. Tingling	☐	☐
5. Pins and Needles	☐	☐
6. Numbness	☐	☐
7. Itching	☐	☐

Examination of the patient

Question 3. Is the pain located in an area where the physical examination may reveal one of more of the following characteristics?

	YES	NO
8. Touch Hypoaesthesia	☐	☐
9. Pricking Hypoaesthesia	☐	☐

Question 4. In the painful area, can the pain be caused or increased by:

	YES	NO
10. Brushing	☐	☐

Patient score _____ /10

- Completed by physician in office
- Differentiates neuropathic from nociceptive pain
- 2 pain questions (7 items)
- 2 skin sensitivity tests (3 items)
- Score ≥4 is an indicator for neuropathic pain
- Validated

DN4 = Douleur neuropathique en 4 questions

Bouhassira D *et al. Pain* 2005; 114(1-2):29-36.

What is the best non-pharmacological treatment for neuropathic pain?

Physiotherapy[1]

Psychotherapy/CBT[6,7]

Various non-pharmacological treatments are available for neuropathic pain and may be discussed with patients. Treatments should be selected based on presumed safety, patient interest and availability.

Various
ological
alities are
uidelines,
dality
ally
ded[1-5]

Alternative therapies and spiritual healing[1-4]

Patient education[1]

CBT = cognitive behavioral therapy

1. Chetty S *et al. S Afr Med J* 2012; 102(5):312-25; 2. Bril V *et al. Neurology* 2011; 76(20):1758-65; 3. Cruccu G *et al. Eur J Neurol* 2007; 14(9):952-70; 4. Pittler MH, Ernst E. *Clin J Pain* 2008; 24(8):731-35; 5. Dubinsky RM *et al. Neurology* 2004; 63(6):959-65; 6. Freynhagen R, Bennett MI. *BMJ* 2009; 339:b3002; 7. Morley S. *Pain* 2011;152(3 Suppl):S99-106.

Evidence for Non-pharmacological Therapies in Neuropathic Pain

- Studied therapies include:
  - Magnets
  - Dietary supplements
  - Imagery
  - Spiritual healing
- Limited evidence for most modalities
  - Cannabis extract
  - Carnitine
  - Electrostimulation
  - Magnets

The effectiveness of B vitamins in reducing chronic neuropathic pain has not been established

Ang CD *et al. Cochrane Database Syst Rev* 2008; 3:CD004573; Pittler MH, Ernst E. *Clin J Pain* 2008; 24(8):731-35.

What is the most effective way to relieve symptoms of allodynia?

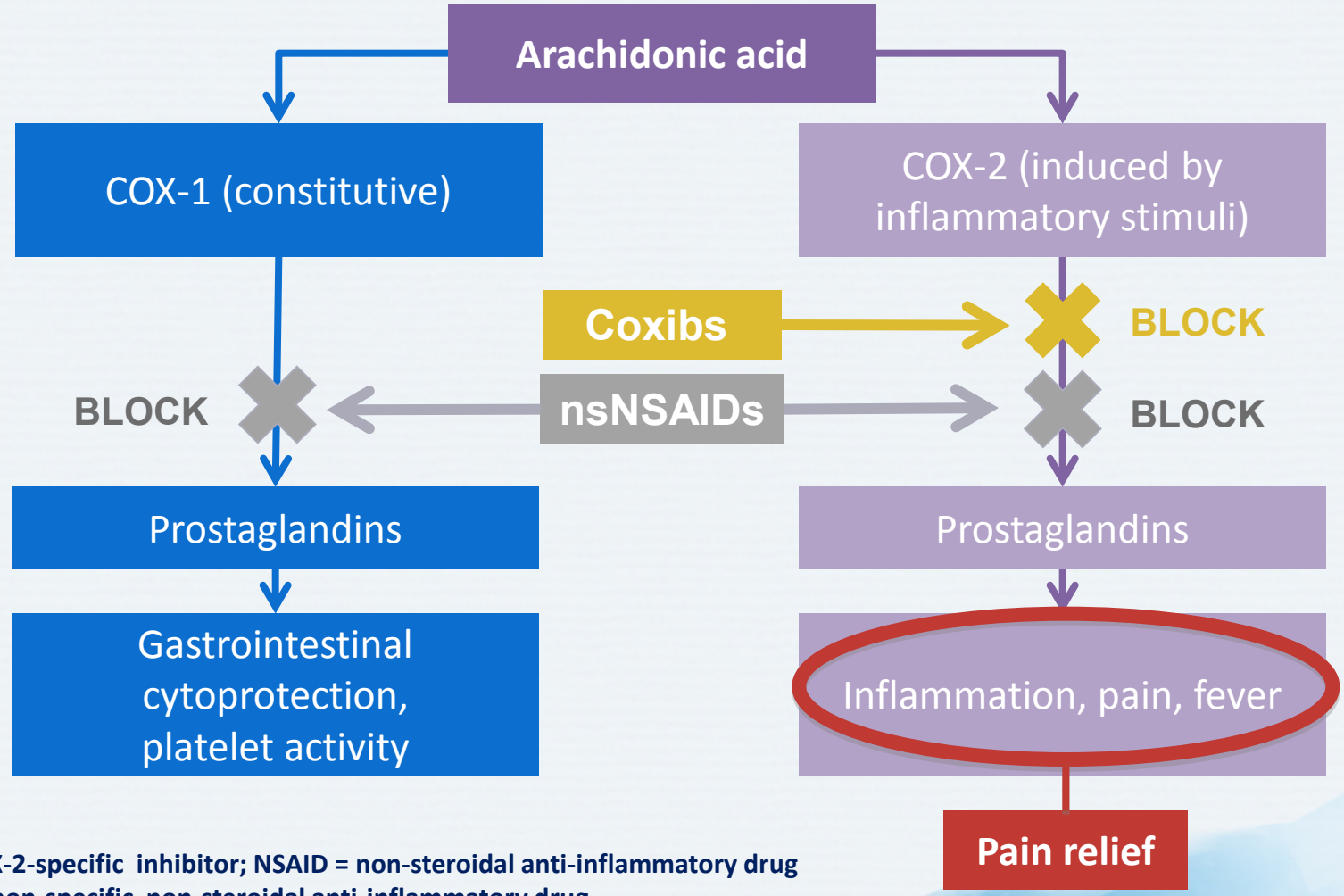
Drug Selection According to Clinical Presentation

Medications		Clinical presentation of neuropathic pain				
		Burning	Lancinating	Hyperalgesia	Allodynia	Parethesia, dysesthesia
TCA	Amitriptyline	++	+/-	++	++	+
SNRI	Venlafaxine	+	+/-	+	+	+/-
	Duloxetine	++	+/-	++	+	+/-
Na^+ channel blockers:	Carbamazepine	+/-	++	+	+	+
	Oxcarbazepine	+/-	++	+	+	+
Ca^{2+} channel $\alpha_2\delta$ ligands:	Gabapentin	++	+/-	++	++	+
	Pregabalin	++	+/-	++	++	+
Opioids:	Tramadol	+	+/-	+	+	+
	Morphine	+/-	+/-	+/-	+/-	+/-

SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Thai Association for the Study of Pain. *Clinical Practice Guidelines for Neuropathic Pain.* Available at: http://www.pain-tasp.com/download/cpg/CPG_Web5OK.pdf. Accessed: October 10, 2013.

Why are nsNSAIDs/coxibs not effetive in neuropathic pain?

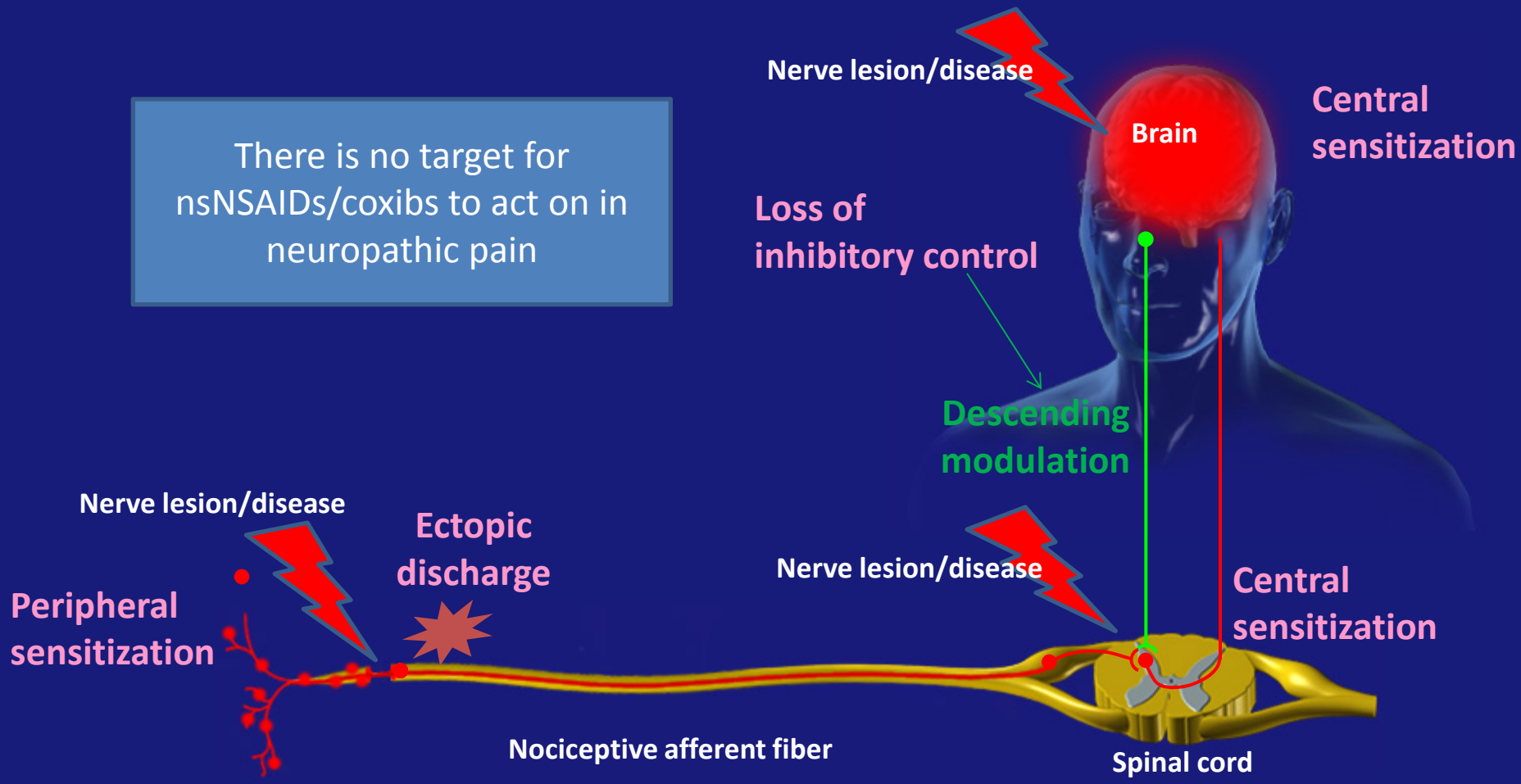


Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug
nsNSAID = non-specific non-steroidal anti-inflammatory drug

Gastrosource. *Non-steroidal Anti-inflammatory Drug (NSAID)-Associated Upper Gastrointestinal Side-Effects*. Available at: http://www.gastrosource.com/11674565?itemId=11674565. Accessed: December 4, 2010; Vane JR, Botting RM. *Inflamm Res* 1995;44(1):1-10.

Mechanisms of Neuropathic Pain

There is no target for nsNSAIDs/coxibs to act on in neuropathic pain



Gilron I *et al. CMAJ* 2006; 175(3):265-75; Jarvis MF, Boyce-Rustay JM. *Curr Pharm Des* 2009; 15(15):1711-6; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

What about surgery for neuropathic pain?

- Surgery may be useful in only very select cases:
  - Refractory cases of trigeminal neuralgia
  - Spinal cord stimulation for patients with failed back surgery syndrome and treatment-resistant complex regional pain syndrome
- Neurostimulation may be useful in cases of refractory neuropathic pain, though results appear to be variable
- Surgery is not generally recommended for radiculopathy

Pollock BE. *Curr Neurol Neurosci Rep* 2012; 12(2):125-31; Jacobs WC *et al. Eur* Spine J 2011; 20(4):513-22; Mailis A, Taenzer P. *Res Manag* 2012; 17(3):150-8; Nizard J *et al. Discov Med* 2012; 14(77):237-46.

When should combination therapy be used for neuropathic pain?

STEP 1

Initiate treatment with one or more **first-line** treatments:

- $\alpha_2\delta$ ligands (gabapentin, pregabalin)
- SNRIs (duloxetine, venlafaxine)
- TCAs* (nortriptyline, desipramine)
- Topical lidocaine (for localized peripheral pain)

STEP 2

- If there is partial pain relief, add another first-line medication
- If there is no or inadequate pain relief, switch to another first-line medication

STEP 3

If first-line medications alone and in combination fail, consider **second-line** medications (opioids, tramadol) or **third-line** medications (bupropion, citalopram, paroxetine, carbamazepine, lamotrigine, oxcarbazepine, topiramate, valproic acid, topical capsaicin, dextromethorphan, memantine, mexiletine) or referral to pain specialist

***Use tertiary amine TCAs such as amitiptyline only if secondary amine TCAs are unavailable**

Note: there is insufficient support for the use of nsNSAIDs in neuropathic pain

nsNSAID = non-specific non-steroidal anti-inflammatory drug; SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Dworkin RH *et al. Mayo Clin Proc* 2010 ; 85(3 Suppl):S3-14; Freynhagen R, Bennett MI. *BMJ* 2009; 339:b3002.

How should medications for neuropathic pain be titrated?

Medication	Starting dose	Titration	Max. dosage	Trial duration
$\alpha_2\delta$ ligands				
Gabapentin	100–300 mg at bedtime or tid	↑ by 100–300 mg tid every 1–7 days	3600 mg/day	3–8 weeks + 2 weeks at max. dose
Pregabalin	50 mg tid or 75 mg bid	↑ to 300 mg/day after 3–7 days, then by 150 mg/day every 3–7 days	600 mg/day	4 weeks
SNRIs				
Duloxetine	30 mg qd	↑ to 60 mg qd after 1 week	60 mg bid	4 weeks
Venlafaxine	37.5 mg qd	↑ by 75 mg each week	225 mg/day	4–6 weeks
TCAs (desipramine, nortriptyline	25 mg at bedtime	↑ by 25 mg/day every 3–7 days	150 mg/day	6–8 weeks, with ≥2 weeks at max. tolerated dosage
Topical lidocaine	Max. 3 5% patches/day for 12 h max.	None needed	Max. 3 patches/day for 12–18 h max.	3 weeks

SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Dworkin RH *et al. Mayo Clin Proc* 2010; 85(3 Suppl):S3-14.

Can you use $\alpha_2\delta$ ligands with CCBs?

- Yes!
  - Unlike CCBs, $\alpha_2\delta$ ligands do not completely block the calcium channel, resulting in virtually no change in systemic blood pressure or coronary blood flow changes

CCB = calcium channel blocker

Lowther C. *Pharmacotherapy Update* 2005; 8(5):1-6.

Can you stop $\alpha_2\delta$ ligands "cold turkey"?

No!

- Medications should be tapered gradually over **at least** one week
- Abrupt discontinuation may result in adverse effects, such as insomnia, nausea, headache, and diarrhea

Thomas JL, Walker RR. *Am Fam Physician* 2006; 74(12):2093-4.