



CHRONIC NON-MALIGNANT PAIN (CNMP) General Pharmacological Considerations – Supplement Tables

The attached tables supplement the RxFiles newsletter – Opioids in Chronic Non-Malignant Pain ^{Oct-2005}.

Table 1: Pain Conditions – Specific Drug Therapy Options

- This table lists various specific pain related conditions that are often included in CNMP. It lists specific drug therapy options that may be considered. Where possible it notes evidence from randomized controlled trials (RCTs) including numbers needed to treat (NNT) for one patient to benefit, and numbers needed to harm (NNH) for one person to withdraw from therapy due to an adverse event. Where possible, Cochrane / systematic reviews or meta-analysis of RCTs have been included. In some cases, evidence is very limited.
- Dosages noted are those that were commonly studied or required to see a benefit. This often varies for the conditions listed. For example, the usual effective doses of amitriptyline in fibromyalgia are in the 10-50mg/day range; in post-herpetic neuralgia, the average effective amitriptyline dose was 75mg/day.
- In some cases, therapies that have conflicting evidence or have been ineffective are also noted as such.
- Although the chart focuses on drug therapies, the reader is reminded that non-drug therapies are essential for the effective long-term management of chronic pain.

Table 2: Overview of Drugs Used in Treatment of Chronic Non-Malignant Pain (CNMP)

- Most of the drugs listed on this table are covered in more detail in the RxFiles Drug Comparison Chart book. However, this chart notes some of the CNMP drug options, initial and usual doses, comparative cost, and comments related to their use in pain.

Pearls that might change your Practice

- Amitriptyline is one of the best studied TCAs used in various pain conditions, but nortriptyline in a dose of 25-≥50mg HS may often be effective and better tolerated (less sedation, less dry mouth, less weight gain, etc.).
- Gabapentin doses with evidence for effectiveness in neuropathic pain are often in the 900-1800mg/day range (~1800mg commonly required in trials); some patients lack benefit due to subtherapeutic dose.
- If you want a patient to have an adequate trial on a drug that often has side effects, start at a low dose, titrate up gradually, and counsel that side effects often diminish with 1-2 weeks. Initial and usual target doses are noted where applicable in Table 2. A gradual tapering can also reduce withdrawal syndromes.
- Choose a drug that may cover multiple complaints. (e.g. a person with frequent headache/migraine and weight gain concerns may benefit from topiramate; however remember tolerability, cost and evidence lacking in CNMP)
- Topical agents (capsaicin, NSAIDs, lidocaine 5%, morphine ^{if painful open ulcer}) may have a role in select conditions.
- Sleep is a frequent concern. If pain is a cause of poor sleep, consider a longer-acting analgesic to cover the nighttime period and/or agents that are helpful in sleep/pain disorders (amitriptyline ^{10-50mg HS}, methotrimeprazine ^{5-25mg HS}).
- Other anecdotal pearls: 1) corticosteroid spray topically to decrease fentanyl patch irritation. 2) Haldol 0.5mg HS-BID PRN to reduce severe nausea but avoid sedation. 3) Weight gabapentin dosing towards bedtime (e.g. 300mg BID, 600mg HS) to reduce daytime side effects. 4) If fentanyl patch required but too potent, uncover only half of patch (or tape half) to decrease dose. 5) In some locales, generic hydromorphone has lower street value than Dilaudid. 6) 10% of Caucasians can not metabolize ^{CYP2D6} codeine or tramadol to active metabolites; thus considered opioid naïve

New Drugs Included in the Tables

1. **Pregabalin LYRICA**
 - an anticonvulsant indicated for post-herpetic neuralgia and diabetic neuropathy in Canada.
 - has not been directly compared to current alternative – gabapentin. It is new – thus lacking long-term safety data, and costs a fair bit more than gabapentin or TCAs (see chart). Side effects such as dizziness, somnolence, weight gain, edema and abnormal thinking are likely to be a concern at higher dosages.
 - the risk of peripheral edema increases with glitazones (e.g. **ACTOS**, **AVANDIA**)
2. **Tramadol/Acetaminophen TRAMACET**
 - Tramadol is a weak mu opioid agonist with actions on serotonin and noradrenaline. It has been previously available in other countries but is new to North America. It is indicated in Canada for acute pain for a maximum of 5 days. It carries an increased seizure risk, and the potential for addiction although this is often thought to be lower than comparative opioids. Its use in CNMP will be limited by the need for frequent dosing, the acetaminophen component, and the relatively high cost compared to Tylenol #3 and other opioids. (The long-acting form of tramadol is not yet available in Canada.)
3. **SATIVEX** – some brief information will be included in our Q&A - Cannabinoids an Overview ^{Oct 2005}

Medication / Analgesic History:	Non-pharmacologic Therapy:	Approach to analgesics:
<ul style="list-style-type: none"> Ask about use of over-the-counter (OTC) products including acetaminophen, Tylenol #1 with codeine, ibuprofen, relaxants, herbals, laxatives, etc. <u>Trends</u> in when various medications are used is helpful. Evaluate <u>total acetaminophen</u> dose & risk of toxicity from overuse. Common Statements: <ul style="list-style-type: none"> ♦“I’ve tried that and it didn’t work!” Assess whether dose & duration of trial was adequate: what exactly was taken, at what dose, and for how long? ♦“It had too many side effects!” Evaluation of side effect history should consider whether initial dose was too high, and whether patient knew that many side effects go away over time. Dry mouth is common, and can often be relieved with an artificial saliva agent (e.g. Oral Balance Gel). Ask about drugs of abuse: street drugs, alcohol, etc. These can affect how drugs may work or are tolerated. 	<ul style="list-style-type: none"> Behavioral, psychosocial & physical therapies are essential in the successful long-term management. Interdisciplinary intervention may ↓drug requirements Pain reduction and improved function, not pain elimination, is the goal of drug therapy. Those with CNMP must be helped to refocus on positive, incremental gains. Dedicated therapists and/or CNMP programs are helpful. {Consider role of: exercise, pacing, heat, ice, TENS, cognitive-behavioral, relaxation, spiritual, acupuncture, etc.} 	<ul style="list-style-type: none"> ♦“<u>One at a time</u>” <u>drug therapy changes</u> allow for more accurate assessment of any beneficial or adverse effect. ♦<u>Specific pain syndromes</u> or <u>types of pain</u> may have preferred drug options based on varying levels of evidence and practicality (see Table 1: Pain Conditions). {Evidence is limited in chronic pain; most trials are small, of short duration, and moderate in design quality.} ♦<u>Adequate trial of suitable non-opioid analgesics</u> and/or adjunct agents is recommended before considering opioids. ♦<u>Try alternate drugs</u> within a therapeutic class before determining that the class is ineffective. ♦<u>Continuous pain</u>: use regularly administered agent(s); this will serve to prevent pain, and allows tolerance to develop to most of the bothersome side effects. ♦<u>Intermittent pain</u>: consider whether an agent can be used just prior to activity or in conditions that trigger pain.
	Medication Induced Headache (MIH):	
	<ul style="list-style-type: none"> ♦Also called <i>analgesic rebound headache</i> ♦Generally resolves on discontinuation of drug ^{up to 6-8wks} {acetaminophen, NSAIDs, opioids, caffeine, ergots, etc.} ♦Outpatient: gradual tapering; if on short acting agents, may switch to long-acting first; Migraine prevention ♦Inpatient: dihydroergotamine (DHE) IV in NS Protocol given with metoclopramide 10mg may be effective.^{2,3} 	

Table 1: Pain Conditions – Specific Drug Therapy Options

Pain Related Conditions	Specific Drug Therapy Options – {Daily target doses based on trials to date} ¹
Trigeminal Neuralgia (TN)	Anticonvulsants: carbamazepine ^{DOC,FDA} 200mg qid; NNT=1.8 ⁴ , may ↓effect at 3yrs, (+/-baclofen 60mg/d synergistic?); gabapentin 900-2400mg/d; lamotrigine 150-400mg/d; phenytoin; Topical anaesthetics: 4% tetracaine & 0.5% bupivacaine option if do not tolerate carbamazepine; BOTOX ⁵ {Drug Causes (rare): digoxin, nitrofurantoin}
Diabetic Neuropathy (DN) ^{6,7}	TCAs NNT≤2; NNH=16: (amitriptyline, desipramine or imipramine) ~100mg/d; nortriptyline 20-50mg/d; TCA +/- fluphenazine 2-3mg/d; venlafaxine 150-225mg/d NNT=4.5 @6wks ⁸ ; Anticonvulsants: gabapentin ~1800mg/d; Cochrane:NNT=3, pregabalin 300-600mg/d; NNT>3, sodium valproate 1000mg/d ⁹ , lamotrigine 200-400mg/d ¹⁰ ; SSRI’s: less effective than TCAs Topical Anaesthetics: lidocaine patch 5%, capsaicin crm 0.025% or 0.075% qid; glucose control ^{intensive} - prevent progression; Vitamin: thiamine 25mg/d & pyridoxine 50mg/d; Opioids (oxycodone CR 10-40mg q12h NNT=2.6) ¹¹ ; mexiletine 300-900mg/d ^{ineffective in RCT’s} ; {Not in Canada: Duloxetine CYMBALTA ^x 60-120mg/d an SNRI approved for DN ^{FDA} ; no comparative trials}
Post-Herpetic Neuralgia (PHN) ^{12,13,14,15}	TCAs: (nortriptyline, amitriptyline ^{75mg/d} , desipramine) NNT=1.6; Anticonvulsants: gabapentin 1800mg/d, NNT=2.2; NNH=11.2, pregabalin 600mg/d, NNT=3.3; NNH=3.7 (16 for 300mg/d dose), divalproex sodium 1000mg/d; Opioids morphine, (oxycodone NNT=2.5; NNH=38); Topical: lidocaine 5% gel or patch; [negligible or marginal benefit: capsaicin 0.075% cream & ASA cream/oint]
Post-Stroke Pain	TCAs: amitriptyline ^{75mg/d} more effective than carbamazepine ¹⁶ (consider nortriptyline if elderly); Anticonvulsants: lamotrigine 200mg/d ¹⁷ ; BOTOX for spasticity
Spinal Cord Injury (SCI) Pain	Gabapentin ≤3600mg/d-conflicting results (dose related?) ^{18,19} ; most effective if duration <6months. Lamotrigine 400mg/d benefit only if incomplete SCI; allodynia a predictor of benefit ²⁰ . Ketamine infusion ²¹ ; Baclofen intrathecal infusion for refractory spasm/spasticity ²² Amitriptyline– not useful-1 RCT ²³ . Valproate– not useful-1 RCT ²⁴ .
Post Mastectomy Pain	Topical capsaicin 0.025% (open label trials only) ^{25,26} ; TCA (amitriptyline 100mg/d NNT=2.5; NNH=5); NSAIDS
Complex Regional Pain Syn. Type I: Reflex Sympathetic Dystrophy (RSD) (Type II: previously “Causalgia”) ^{27,28,29,30}	DMSO 50% Crm 5x/day x2 months; Bisphosphonates IV short course in early phase; Prednisone short-term tapering regimen; Calcitonin: conflicting data; Nifedipine ≤60mg/d; Baclofen intrathecal for leg/foot pain in MS; TCAs & Anticonvulsants - options but lack data. [Gabapentin 1800mg/d NO long-term benefit ³¹ .] Opioids?; Lidocaine 5% topical, 10% SC infusion ≤5 days; Clonidine 0.05mg BID, ↑d to 0.1mg BID may be useful if sweating or changes in skin temp/color. Max- 0.4mg/BID.
Musculoskeletal - Non-OA	NSAIDs -useful in acute; less useful in chronic? Opioids (long-acting). Injection therapies sometimes option but evidence of benefit poor or inconsistent.
Osteoarthritis (OA)	Acetaminophen ³² - effective for some; some consider DOC if effective; NSAIDs -more effective than acetaminophen for pain but not function (consider SE, cost) some consider DOC; Glucosamine ³³ -safe, possibly effective ^{conflicting data} ; Intra-articular Corticosteroid ^{Knee} ³⁴ - short-term benefit; Viscosupplementation ^{Knee} ³⁵ -effective; lack benefit on fx ³⁶ ; Opioids (including Tramacet) – option in more severe patients, or if CI to other agents. Herbal: Avocado/soybean unsaponifiables + NSAID ^{37,38,39} -possible benefit NNT=4
Psychological Factors - (Concomitant): Consider using...	Depression/Anxiety ⁴⁰ : nortriptyline, venlafaxine, mirtazapine, SSRIs. Insomnia: amitriptyline, nortriptyline, fluvoxamine, trazodone, ^{50-100mg HS} methotrimeprazine NOZINAN . Bipolar/Mood: carbamazepine, divalproex, lamotrigine. Weight Gain: topiramate; gabapentin over pregabalin; nortriptyline over amitriptyline
Headache, Chronic Daily ⁴¹	Amitriptyline ≥25mg HS; SSRIs; Divalproex 500mg-1.5g/d (retrospective study); Other: Topiramate, Gabapentin, Propranolol, BOTOX. See also: RxFiles Migraine Prophylaxis chart.
Phantom Limb Pain (PLP)	Carbamazepine 200mg QID effective in case report; Gabapentin: somewhat effective in RCT ⁴² ≤2400mg/d; n=19 & case series n=7 (some patients able to taper off); Ketamine effective in case reports; Propranolol 80mg/d effective in 3 case reports; Opioids; Amitriptyline – not effective ≤125mg/d, RCT 6wk, n=39 ⁴³ ; Memantine – not effective.
Fibromyalgia ^{44,45,46} (may try trigger point injections if myofascial)	Amitriptyline 10-50mg hs, NNT=4 ⁴⁷ , cyclobenzaprine 10-30mg hs, NNT=5 ⁴⁸ ; SSRIs – fluoxetine ^{conflicting results} ; combination- {fluoxetine 20mg AM + amitriptyline 25mg HS} ⁴⁹ ; venlafaxine ≥150mg; {antiepileptics-marginal benefit pregabalin≤450mg/d ⁵⁰ }; zopiclone for sleep short-term; [tramadol ≤400mg/day?; only TRAMACET in Canada]; Non-drug therapies useful!

DOC=drug of choice fx=function NNT=number needed to treat to benefit one NNH=number needed to treat for one extra harm resulting in discontinuation of treatment RCT=randomized controlled trial SE=side effect ↓=dose for renal dysfunction

Table 2: Overview of Drugs Used in Treatment of Chronic Non-Malignant Pain (CNMP) ^{1,51}

Therapeutic Class	Drug	TRADE NAME	Initial Dose	Usual Dose (Usual Max)	\$/mo	General Comments for Use in CNMP
Analgesic	Acetaminophen	TYLENOL	650-1,000mg q6-8h (Max 4g/d)		15	<ul style="list-style-type: none"> ◆ Consider LFTs q6-12mo if hepatic risk (hx, long-term, EtOH, DI's-e.g. muscle relaxants) ◆ Limit to 3200_{mg/d} & 2600_{mg/d} in chronic & high risk use respectively (EtOH, cirrhosis)
	Acetaminophen ER	ER = Extended Release → TYLENOL ARTHRITIS	1,300mg q8h		25	
NSAID / Analgesic (various: see also RxFiles NSAIDs/COXIBs chart)	Celecoxib	CELEBREX	200mg OD <small>Max 400mg/d</small>		54	<ul style="list-style-type: none"> ◆ Effective in osteoarthritis ◆ Dose listed is usual lowest anti-inflammatory dose; allow 1-2weeks for full effect ◆ Avoid in renal dysfunction, GI ulcer; Caution if cardiovascular disease ◆ Coxibs celecoxib: equal efficacy, similar renal toxicity to other NSAIDs; less GI ulcer <small>Non-ASA pts</small>; minimal platelet effects; concern re: ↑cardiac/serious^{52,53,54} events esp VIOXX, BEXTRA
	Diclofenac	VOLTAREN	75mg SR BID <small>Max 200mg/d</small>		39	
	Diclofenac+Misoprostol	ARTHRONEX 75	75mg+200mcg BID (or 50mg+200mcg BID-TID)		63	
	Ibuprofen	MOTRIN, ADVIL	600mg po TID <small>Max 2400mg/d</small>		13	
	Meloxicam	MOBICOX	7.5mg OD <small>Max 15mg/d</small>		25	
	Naproxen	NAPROSYN	375mg BID <small>Max 1000mg/d</small>		16	
Opioid See also Opioids-CNCP newsletter: www.RxFiles.ca Note: ◆ Recent concerns of abuse with oxycodone ; some consultants note report of psychological symptoms (anxiety, apprehension) prior to end of dosing interval ◆ Dextromethorphan (DM) in doses of 360-960mg/day effective in DN; but 1) high-dose=high cost & 2) potential abuse. Also used pre-op)	Codeine+Acetamin	TYLENOL #3	<u>Lowest available:</u> 2 tablets q6h <small>Max 12tabs/d</small>		35	<ul style="list-style-type: none"> ◆ Role in carefully selected CNMP patients, although long-term trials lacking! ◆ Advantages: potent analgesics, lack of major organ toxicity with opioids ◆ Disadvantages: concerns regarding abuse, diversion, tolerance, dependence ◆ Keys to Success: 1) careful patient selection 2) documentation 3) use as part of comprehensive treatment plan <small>non-drug components</small> 4) use a treatment agreement 5) use long-acting formulations & minimize reliance/use of short-acting/PRN formulations 6) prevent/manage SE's <small>constipation</small> 7) Early follow-up for dose titration, etc. ◆ Codeine: requires metabolism <small>CYP2D6</small>, ≤10% ↓ analgesia but ↑ SEs ◆ DURAGESIC: potent; delayed but prolonged effect requires caution; not for opioid naive or <18yrs; adjust dose q3-6days ◆ TRAMACET: short acting; expensive; requires metab by <small>CYP2D6</small>; some effect in neuropathic ⁵⁶; SE: dose related ↑ seizure risk; ↑ serotonin (5HT); caution with other 5HT or acetaminophen drugs.
	Tramadol+Acetam.	TRAMACET [⊗] <small>New</small>	2 tablets q6h <small>Max 8 tabs/d</small>		170	
	Codeine	CODEINE CONTIN	150mg q12h		70	
	Morphine q12h	MS-CONTIN, M-ESLON	60mg q12h		75	
	Morphine q24h	KADIAN	100mg q24h		94	
	Hydromorphone	HYDROMORPH CONTIN	12mg q12h		122	
	Oxycodone	OXYCONTIN	10-20mg q12h		95	
	Fentanyl	DURAGESIC PATCH	25ug/hr q48-72h		116	
	Methadone ⁵⁵ powder ↓ ⁵⁶	METADOL <small>scored tablets</small>	1-2.5mg			
		Methadone requires special license to prescribe in SK; useful in rotation strategies or patients with chronic pain + addiction; used OD to prevent craving, but Q8H for pain. Caution: long half-life (~22hrs); dose ↑'s after 5+ days.				
Antidepressant-TCA ◆ inhibit reuptake of 5HT & NE; block α-adrenergic, H1, ACH & NMDA receptors; block Na+ & Ca++ channels ◆ higher doses if neuropathic pain: dose limited by side effects, CV disease	Amitriptyline <small>5HT & NE</small>	ELAVIL	10-25mg HS	10-30mg HS pain/sleep	10	<ul style="list-style-type: none"> ◆ Adequate trial requires 2 weeks at suitable target dose; titrate dosage up gradually every 1-2wks to minimize side effects & assess response; requires regular admin. ◆ Avoid/Caution if arrhythmias or prolonged QT interval ◆ Effective-neuropathic pain NNT=2-3 ^{57,58} Adverse effects causing withdrawal NNT≥13 ◆ Consider nortriptyline-less side effects, esp anticholinergic; preferred in elderly
	Desipramine <small>NE > 5HT</small>	NORPRAMIN	(suggest taking @ 8 or 9 PM)	75 - ≥ 100mg HS if neuropathic <small>Max 300mg/d</small>	21	
	Imipramine <small>5HT & NE</small>	TOFRANIL				
	Nortriptyline <small>NE > 5HT</small>	AVENTYL	10mg HS	25-50mg HS <small>Max 150mg/d</small>	21	
Antidepressant-Other ⁵⁹	Venlafaxine <small>5HT & NE</small>	EFFEXOR XR	37.5mg	75-150mg OD <small>Max 225mg/d</small>	65	<ul style="list-style-type: none"> ◆ Somewhat effective in neuropathic pain <small>NNT≥4</small>; Less effective than TCAs <small>NNT=2</small>; more effective than SSRIs <small>NNT=7</small>; doses of 150mg-225mg/d often required ⁶⁰
	Duloxetine CYMBALTA - (Not yet in Canada) - 60mg OD - BID [⊗] <small>Recently approved for DN & depression by FDA</small>					
Anticonvulsant ⁶¹ ◆ often require relatively high doses; often more expensive than TCAs without additional benefit ◆ if SE's, ↑dose more slowly ◆ may be useful for <i>sharp, stabbing, zinging</i> ◆ all: pharmacodynamic DI's (e.g. ↑somnia)	Gabapentin ⁶² <small>-few metabolic DI's</small>	NEURONTIN	300mg HS ↑by 100-300mg per day or weekly	300mg am+600mg HS 600mg TID-QID 2.4-3.6g/d common in trials	58 107 130	<ul style="list-style-type: none"> ◆ Cochrane⁶³: evidence for pain in diabetic neuropathy <small>NNT=3</small> & PHN <small>NNT=4</small>; doses <900mg not effective; no major harm <small>NNH=ns</small>; minor harm <small>NNH=3.7</small> ◆ SE: dizziness^{24%}, somnolence^{20%}, headache^{10%}, diarrhoea^{10%}, confusion^{10%}, nausea^{8%}; weight ↑ or ↓ ◆ Cochrane⁶⁴: effective for trigeminal neuralgia <small>NNT=2</small>; no major harm <small>NNH=ns</small>; minor harm <small>NNH=3.7</small> ◆ SE: drowsiness, dizziness, constipation, nausea, ataxia, ↑LFT ◆ Option in chronic daily headache, migraine prophylaxis. CI: liver disease ◆ limited role in CNMP; useful in migraine prevention & preventing weight gain ◆ Effective in PHN & DN <small>NNT ≥3; NNH=13</small>; unknown if advantages over other agents. ^{65,66,67} ◆ SERD: dizziness^{20%}, somnolence^{14%}, periph edema^{5.3%}, ≥7% ↑weight^{5%}, dry mouth^{4.8%}, blurred vision^{4.5%}; abnormal thinking/euphoria^{3.4%} ◆ SE's causing withdrawal: overall <small>NNH=13</small>; 600mg/d <small>NNH=4</small> ◆ glitazones: ↑edema
	Carbamazepine <small>-many metabolic DI's</small>	TEGRETOL	100mg BID	200mg BID 400mg BID	10 15	
	Divalproex (DVA)	EPIVAL	250mg OD ^{↑1wk}	500mg BID cc	33	
	Topiramate	TOPAMAX	25mg HS ^{↑weekly}	100mg BID or 50mg am; 100mg HS	164	
	Pregabalin <small>-few metabolic DI's</small>	LYRICA (New 2005)	75mg BID ^{↑1wk} (or 25-50mg TID)	150mg BID [⊗] 300mg BID <small>Max 600mg/d</small>	164 164	
	No comparative trials yet; side effects common; high cost; new thus lack long-term data; vying for market now that gabapentin generic.					
Herbal / Natural	Glucosamine	Various	500mg OD	500mg TID or 1500mg OD [⊗]		<ul style="list-style-type: none"> ◆ OA <small>knee</small>-benefit NNT=5 <small>some conflicting data 70,71,72</small>; allow 4-8wks; well tolerated <small>trials ≤3yrs</small> ◆ Viscosupplementation - Cartilaginous Defect Repair Agent – OA (benefit up to 52wks <small>knee</small>) ◆ Dosing varies with product/indication (Knee -initial: weekly x3^{Symvisc} or x3-5 <small>others</small>)
	Hylan G-F-20	SYNVISC <small>Rooster Combs</small>	16mg/2ml intra-articular-knee / hip	200-330 per 3	200-330	
	Hyaluronic acid Na+ Na+ Hyaluronate	ALYGAN <small>Combs</small> NEOVISC	20mg/2ml intra-articular-shoulder / knee / hip <small>\$330/3</small> 2ml intra-articular to joint - avian protein free <small>\$200/3</small>			
Other	Calcitonin Salmon Nasal	MIACALCIN	200 I.U.	OD alternating nostrils [⊗]	65	◆ for pain from vertebral fractures ◆ Adequate trial 1 wk ◆ well tolerated
Topical Anesthetic	Lidocaine top 5%	USA: LIDODERM 5% Patch	Also Compounded Gel 5%	[⊗] ?		◆ Effective in PHN ⁷³ , apply patch to painful area (systemic absorption is negligible)
Topical Capsaicin {from hot peppers}	Capsaicin 0.025%	ZOSTRIX <small>also A535 with Capsaicin 45g/\$15</small>		Apply TID (OA, RA) [⊗]		<ul style="list-style-type: none"> ◆ Adequate trial 4-8wks ◆ neuropathic pain NNT=6 <small>0.075% 8wks</small>; musculoskeletal NNT=8 <small>4wks</small> ◆ Adverse events causing withdrawal <small>NNH=10</small> ⁷⁴; local burning, stinging, erythema
	Capsaicin 0.075%	ZOSTRIX HP <small>60g</small>	TID	Apply TID (for PHN, DN)	26	
Topical NSAID ^{75,76} (various base options for varying levels of penetration)	Diclofenac 1.5%	PENNSAID Soln	Apply 40drops to affected knee QID	[⊗] 100		<ul style="list-style-type: none"> ◆ OA; allow 1wk; CI: GI ulcer; 40drops=16mg/dose; may be ineffective if using less ◆ Limited evidence in CNMP <small>musculoskeletal</small> NNT=4.4 (at 2 weeks). ◆ high concentrations in meniscus/cartilage & tendon sheath; [serum] 5% of oral. ◆ ketoprofen may be preferred
	Ketoprofen 5-15%	Compounded	Apply to affected area/joint TID	[⊗] ?		
Topical-Compounded	Topical Salicylates - limited evidence suggests little <small>NNT=5.3</small> or no effect. Small clinical trials suggest possible effect: amitriptyline 1%+ketamine 0.5% in chronic neuropathic pain <small>n=20; 7d</small> ⁷⁷ ; clonidine 0.2% crm in oral neuralgia-like, but not neuropathic pain <small>n=17</small> ⁷⁸ ; morphine -painful open ulcers. ⁷⁹ Single or multiple ingredient preps from pharmacies specializing in compounding: amitriptyline ^{1-4%} , baclofen ^{2-5%} , capsaicin ^{0.025-0.1%} , carbamazepine ^{2%} , clonidine ^{0.1-0.3%} , doxepin ^{3%} , gabapentin ^{6-10%} , ketamine ^{0.5-1.5%} , lidocaine ^{1-10%} .					

CI=contraindications CV=cardiovascular DI=drug interaction EtOH=alcohol GI=gastrointestinal HA=headache LFTs=liver function tests ns=not statistically significant RD=risk difference vs placebo SE=side effect \$=retail cost/month SK =non formulary SK
Muscle Relaxants-CNMP- not generally recommended for use >2 wks; effect more from sedation than relaxation; PRN use - habit forming; ↑hepatic toxicity with chronic use & DI's e.g. with chronic acetaminophen; RA=rheumatoid arthritis
 baclofen LIORESAL 5-10mg TID-QID, tizanidine ZANAFLEX 2-4mg TID, dantrolene DANTRIN 25-50mg TID: effective for MS spasticity, spinal cord injury, cerebral palsy or stroke (not musculoskeletal injury). Gradual taper to discontinuence. Also-BOTOX inj.
Benzodiazepines-CNMP: not generally recommended except for short term use; even then, the chronic nature of pain, and resultant pain behavior can easily result in long-term abuse (multiple adverse effects long-term e.g. falls)
 See also - RxFiles Drug Comparison Charts at www.RxFiles.ca (NSAID/COXIB, Opioid, Antidepressant & Antiepileptic). ⊗=EDS Exception Drug Status in SK ⊕=prior approval for NIHB coverage ▼=covered by NIHB ⊘=not covered by NIHB

- ¹ Micromedex 2005 – Drug Evaluations.
- ² Pringsheim T, Howse D. In-patient treatment of chronic daily headache using dihydroergotamine: a long-term follow-up study. *Can J Neurol Sci.* 1998 May 25(2):146-50.
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- ⁵ Turk U, Ihan S, Alp R, Sur H. Botulinum Toxin and Intractable Trigeminal Neuralgia. *Clin Neuropharmacol.* 2005 July/August;28(4):161-162.
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