

## Appendix H – Pharmaceutical Interventions for Neuropathic Pain

Drug	Dosage	Side effects, contraindications, and comments
<b>Daily Medications</b>		
<b>ANTICONVULSANTS</b>		
Gabapentin *	100 to 300 mg at bedtime; increase by 100-300 mg every three days up to 1,800 to 3,600 mg per day taken in divided doses three times daily. Higher doses might be used.	<b>Initial drug of choice.</b> Side effects: drowsiness, dizziness, fatigue, nausea, sedation, edema, weight gain. No significant drug-drug interactions. Reduce dose/increase interval in renal failure (give 10x creatinine clearance per day). <sup>1</sup>
Pregabalin *	50 mg - 75 mg twice daily-three times daily to start. Up to 150 mg three times daily.	<b>Initial drug of choice.</b> Side effects: drowsiness, dizziness, fatigue, nausea, sedation, edema, weight gain. No drug-drug interactions. Reduce dose/increase interval in renal failure (give 5x creatinine clearance per day). Schedule V medication. <sup>1</sup>
Lamotrigine	25 mg per day; increase by 25 mg - 50 mg every one to two weeks up to 400 mg per day.	Side effects: Stevens-Johnson syndrome, rare life-threatening rash unlikely with gradual dose titration. Dizziness, drowsiness, headache, nausea, blurred/double vision. <sup>1</sup>
Oxcarbazepine	Start 150 mg - 300 mg twice daily. Increase by 600 mg per day each week to maximum 1,200 mg twice daily.	Similar adverse effects to carbamazepine but less likely. Fewer drug-drug interactions. <sup>1</sup>
Carbamazepine *	100 mg - 200 mg twice daily. Increase to maximum 600 mg twice daily.	<b>Initial drug of choice for trigeminal neuralgia.</b> Watch for hyponatremia, leucopenia, allergic rash (Stevens-Johnson syndrome). Other side effects: dizziness, drowsiness, blurred/double vision, ataxia. Not favored for other neuropathic pain. Available in extended release. <sup>1,3</sup>
Topiramate	25 mg twice daily to start; increase by 25-50 mg per week up to 200-400 mg per day.	Most evidence is for migraine prevention, other neuropathic pains may respond. Side effects: drowsiness, abnormal thinking, weight loss, urinary tract stones, increased intraocular pressure. <sup>1</sup>
<b>ANTIDEPRESSANTS</b>		
<b>Serotonin &amp; Norepinephrine Reuptake Inhibitors (SNRIs)</b>		
Duloxetine *	20 to 60 mg per day taken once or twice daily in divided doses (for depression); 60 mg twice daily for fibromyalgia.	<b>Initial drug of choice.</b> Side effects: nausea, dry mouth, constipation, dizziness, insomnia. <sup>2</sup>
Venlafaxine	37.5 mg per day; increase by 37.5 mg per week up to 225 mg per day.	Side effects: headache, nausea, sweating, sedation, hypertension, seizures. Serotonergic properties in dosages below 150 mg per day; mixed serotonergic and noradrenergic properties in dosages above 150 mg per day. Available in extended-release formulation. <sup>2</sup>
<b>Tricyclic Antidepressants</b>		
Amitriptyline, Imipramine	10 to 25 mg at bedtime; increase by 10 to 25 mg per week up to 75 to 100 mg at bedtime or a therapeutic drug level.	<b>Initial drug of choice.</b> Tertiary amines have greater anticholinergic side effects and may cause arrhythmia, orthostatic hypotension; therefore, these agents should not be used in elderly patients. <sup>2</sup>
Desipramine, Nortriptyline	10 to 25 mg in the morning or at bedtime; increase by 25 mg per week up to 100 mg per day or a therapeutic drug level.	Secondary amines have fewer anticholinergic side effects, but should still be used cautiously in elderly patients. <sup>2</sup>

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Drug	Dosage	Side effects, contraindications, and comments
<b>Topical Medications</b>		
Lidocaine 5% patch *	Up to 3 patches to intact skin 12 hours per day (12 hours on/12 hrs off)	Indicated for postherpetic neuralgia. Commonly used for other neuropathic conditions. May be used daily or as needed.
Capsaicin	0.025% or 0.075% apply to intact skin 3-4 times per day	Burning irritation of skin, eyes, airway. Requires regular application for four to six weeks to achieve effect, then maintenance. Available without prescription.
<b>As-Needed Medications</b>		
Tramadol	50-100 mg 4 times daily as needed. Maximum 400 mg per day	Side effects: abdominal discomfort, dizziness, constipation, seizures. May interact with other serotonergic drugs to cause serotonin syndrome. Abuse potential despite unscheduled status. Available in extended-release form for daily use and in combination with acetaminophen.
Oxycodone	5 mg - 10 mg every 4 hours as needed	Schedule II medication. Side effects: constipation, drowsiness, confusion, nausea, itching, dependence, abstinence syndrome upon abrupt withdrawal at doses > 20 mg per day. Available in combination with acetaminophen. <sup>4</sup>

\* **Approved by the U.S. Food and Drug Administration for treatment of neuropathic pain.**

<sup>1</sup> FDA alert: Increased risk of suicidal behavior or ideation.

<sup>2</sup> Black box warning: Increased suicidal behavior in young adults

<sup>3</sup> Two black box warnings on carbamazepine:

- Aplastic anemia and agranulocytosis have been reported in association with the use of carbamazepine.
- The genetic testing is recommended prior to initiation of therapy in most patients of Asian ancestry for the presence of the HLA-B\*1502 allele genetic marker to decrease the risk of developing Stevens-Johnson syndrome (SJS) and/or toxic epidermal necrolysis (TEN).

<sup>4</sup> Black box warning on oxycodone: the concomitant use of oxycodone hydrochloride controlled-release tablets with all CYP3A4 inhibitors such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole) and protease inhibitors (e.g., ritonavir) may result in an increase in oxycodone plasma concentrations and may cause potentially fatal respiratory depression. Patients receiving oxycodone controlled-release tablets and a CYP3A4 inhibitors should be carefully monitored for an extended period of time and dose adjustment should be made if warranted.

Drugs labeled **initial drug of choice** based on a combination of evidence for efficacy from randomized controlled trials and safety profile. Does not imply superiority.

This table was completed using the following sources:

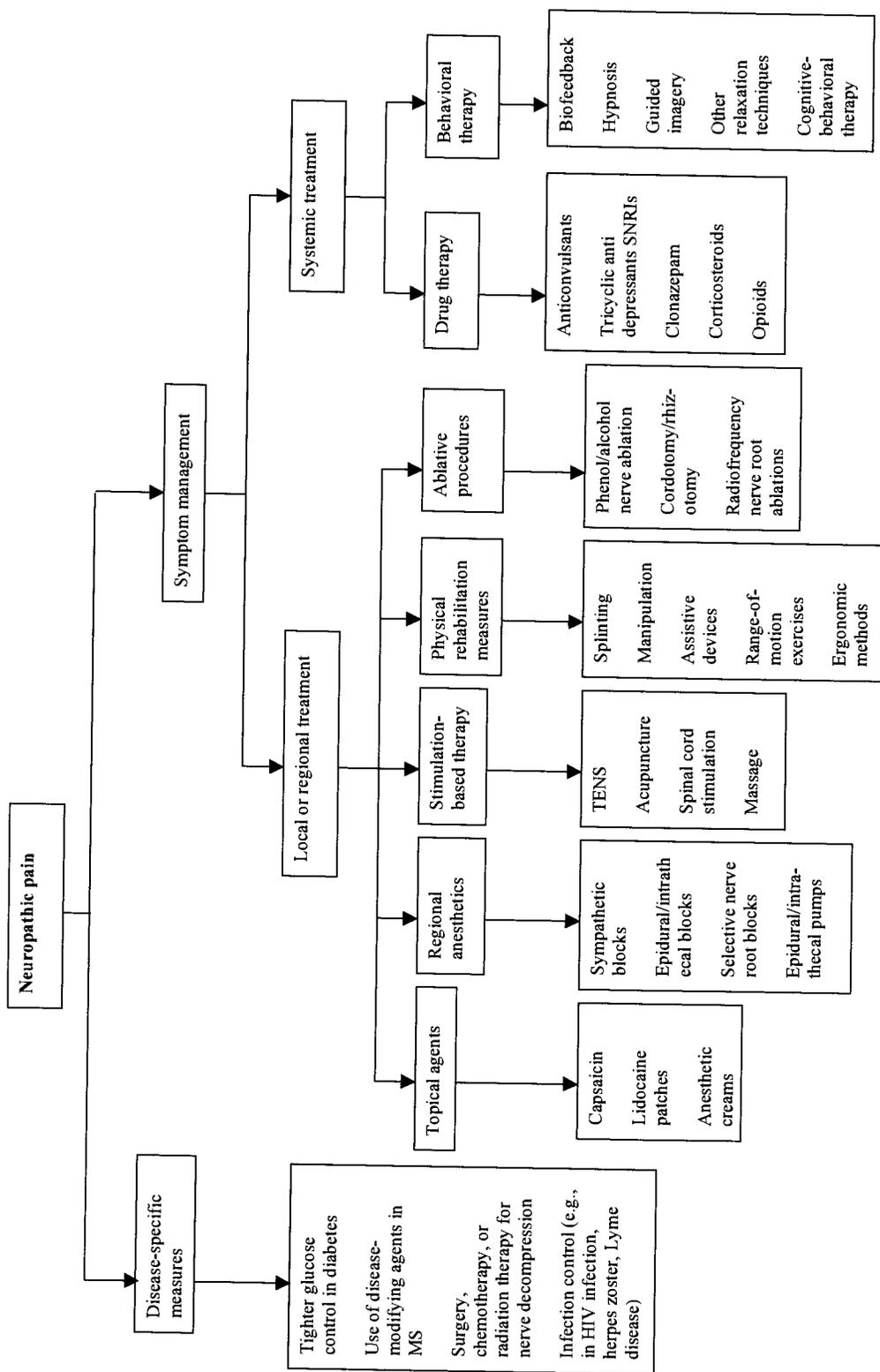
Argoff CE, Backonja MM, Belgrade MJ, et al. Consensus guidelines: treatment planning and options. *Mayo Clin Proc* 2006;81:S12-S25. (Guideline)

Chen H, Lamer TJ, Rho R, et.al. Contemporary Management of Neuropathic Pain for the Primary Care Physician. *Mayo Clinic Proceedings*. December 2004;79(12):1533-45. (Guideline)

This information is current as of September 2009. See prescribing information for complete details. For the most up-to-date medication information, consider the following sources: <http://www.epocrates.com>, <http://www.micromedex.com>, <http://www.updote.com>, <http://www.pdr.net>.

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# Appendix I – Neuropathic Pain Treatment Diagram



Source: Belgrade, MJ. Following the clues to neuropathic pain. PostGraduate Medicine, 106(6), November 1999.

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**BACK**

## Module 2

### Table 3: Pain Related Definitions

<u>Allodynia</u>	Pain caused by a stimulus that typically does not produce pain (e.g., light touch)
<u>Central Pain</u>	Pain resulting from a lesion or dysfunction in the central nervous system (e.g., post stroke pain)
<u>Dysesthesia</u>	Abnormal sensation that includes painful numbness, burning, tingling and allodynia
<u>Neuropathic Pain</u>	Pain initiated or caused by a primary lesion of dysfunction in the nervous system
<u>Nociceptors</u>	Neurons activated by noxious stimuli (also referred to as primary afferent neurons)
<u>Nociception</u>	The process of activation of primary afferent neurons by a noxious stimulus
<u>Noxious Stimulus</u>	A stimulus that is damaging or potentially damaging, that evokes activation of nociceptors (e.g., pinprick, extreme heat)
<u>Pain</u>	An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (IASP, 1979)
<u>Paresthesia</u>	Abnormal painful numbness, includes prickling, tingling and increased sensitivity
<u>Paroxysmal</u>	Sudden onset of escalation or recurrence of pain
<u>Physical Dependence</u>	A state of adaption that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist (AAPM, APS, ASAM 2001)
<u>Psychological Dependence (addiction)</u>	A primary, chronic, neurobiological disease with genetic, psychological, and environmental factors influencing its development and manifestations; characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm and craving (AAPM, APS, ASAM 2001)
<u>Radiculopathy</u>	Shooting pain usually coinciding with the distribution of spinal nerve root (e.g., sciatic pain)

### EQUIANALGESIC TABLE

(Dosing is always dependent on individual patient characteristics & response. Verify dosing for pediatric & geriatric patients.)

Drug	Dosage Form/Strengths	Approximate Equivalence	
		IV/SubQ	Oral
<b>Morphine</b>	<b>Immediate Release Tablets</b> Morphine Sulfate Immediate Release – 15, 30 mg <b>Sustained Release Tablets</b> MS Contin –15, 30, 60, 100, 200 mg q 8 or 12 hours Oramorph SR –15, 30, 60, 100 mg q 8 or 12 hours Avinza –30, 60, 90, 120 mg q 24 hours Kadian –10, 20, 30, 50, 60, 80, 100, 200 mg q 24 hours <b>Generics-Oral Liquid</b> Morphine Sulfate Immediate Release Solution -2mg/ml, 4 mg/ml Morphine Sulfate Immediate Release Concentrate – (Roxanol)-20 mg/ml <b>Suppository</b> Rectal Morphine Sulfate (RMS) - 5, 10, 20, 30 mg	10 mg	30 mg
<b>Hydromorphone</b>	<b>Tablets</b> Hydromorphone (Dilaudid) – 2, 4, 8 mg <b>Liquid</b> Hydromorphone (Dilaudid) – 5mg/5ml <b>Injection</b> -1, 2, 4mg/ml Dilaudid HP – 10mg/ml <b>Suppository</b> Hydromorphone (Dilaudid) – 3 mg Extended Release (Exalgo*) – 8, 12, 16 mg q 24 hrs *Consult drug insert for conversion	1.5 mg	7.5 mg
<b>Oxycodone</b>	<b>Immediate Release Tablets</b> Oxy IR – 5 mg Roxicodone – 5, 15, 30 mg Oxycodone/Acetaminophen ( <i>Do not exceed 2000 mg Acetaminophen q 24 hrs</i> ) Percocet - 5/325, 7.5/325, 7.5/500, 10/325mg Roxicet - 5/325, 5/500 mg <b>Sustained Release Tablets</b> Oxycontin – 10, 15, 20, 30, 40, 60, 80 mg <b>Liquid</b> Roxicodone – 1mg/ml, 20 mg/ml OxyFAST – 20mg/ml	----	20-30 mg
<b>Oxymorphone</b>	<b>Tablets</b> Opana-5, 10 mg Opana ER- 5, 10, 20, 30, 40 mg q 12 hrs (30 mg oral Morphine = 10 mg oral Oxymorphone)	---	10 mg
<b>Hydrocodone</b>	<b>Hydrocodone/Acetaminophen Tablets</b> ( <i>Do not exceed 2000 mg Acetaminophen/24 hr</i> ) Vicodin – 5/500 mg Vicodin ES - 7.5/750 mg Lorcet or Vicodin HP – 10mg/650 mg Lortab – 2.5/500, 5/500, 7.5/500, 10/500 mg Norco – 5/325 mg, 7.5/325 mg, 10/325 mg <b>Hydrocodone/Ibuprofen</b> Vicoprofen – 7.5/200 mg	----	1 mg Hydrocodone = 1 mg oral Morphine
<b>Tramadol Hydrochloride**</b>	<b>Tablets</b> Ultram- 50 mg Ultracet- 37.5/325 mg (Acetaminophen) ( <i>Do not exceed 2000 mg Acetaminophen q 24 hrs</i> ) <b>Extended Release</b> Ultram ER- 100, 200, 300 mg q 24 hrs Ryzolt- 100, 200, 300 mg q 24 hrs (Maximum dose: 400 mg q 24 hrs for ages 17-75; >75 ages is 300 mg q 24 hrs)	---	5 mg oral Morphine ≈ 50 mg oral Tramadol
<b>Fentanyl Transdermal</b>	<b>Skin Patch</b> ( <i>Not for post op/acute pain; Not for use in opiate naïve patients; 12-24 hours for full onset; 12-24 hours to leave system</i> ) 12.5, 25, 50, 75, 100 mcg/hr	100 mcg Transdermal Fentanyl ≈ 2 to 4 mg IV Morphine q hr	100 mcg patch q 2-3 days ≈ 200 mg oral Morphine q 24 hrs
<b>Fentanyl Transmucosal-- Buccal</b>	<b>Oral Lozenge</b> ( <i>Not for use in opiate naïve patients</i> ) Actiq – 200, 400, 600, 800, 1200, 1600 mcg Fentora – 100, 200, 400, 600, 800 mcg (Delivery system influences potency; Fentora is 2X strength of Actiq)	----	See package inserts for conversion
<b>Methadone</b>	Equivalency ratios for methadone are complex because of its long half-life, potency, and individual variations in pharmacokinetics; recommend consulting with Pain/ Palliative Care Specialist or consult with American Pain Society (APS) Guidelines. Warning: cross tolerance does not develop.		
<b>References</b>	American Pain Society. (2008). <i>Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain</i> . 6 <sup>th</sup> Edition. <a href="http://www.ampainsoc.org">www.ampainsoc.org</a> **Davis, M., Glare, P., & Hardy, J. (2005) <i>Opioids in cancer pain</i> . New York: Oxford University Press. Pasero, C & McCaffery, M. (2011). <i>Pain Assessment and Pharmacologic Management</i> . St. Louis, MO: Elsevier Mosby. For more resources, see the City of Hope Pain & Palliative Care Resource Center- City of Hope <a href="http://www.prc.coh.org">www.prc.coh.org</a>		

## SOURCES OF PAIN

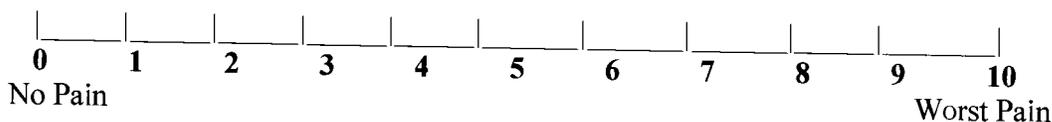
PAIN SOURCE	PAIN CHARACTER	DRUG CLASS/EXAMPLES
<b>Myofacial/Somatic Pain</b>	Constant and well localized.	<ul style="list-style-type: none"> <li>- Acetaminophen/ NSAIDs</li> <li>- Adjuvants</li> <li>- Opioids</li> </ul>
<b>Visceral Pain</b>	Injury to sympathetically innervated organs. Pain is vague in quality. Deep, dull, aching. Referred Pain.	<ul style="list-style-type: none"> <li>- NSAIDS</li> <li>- Corticosteroids</li> <li>- Opioids</li> </ul>
<b>Bone Pain</b>	Axial skeleton with thoracic and lumbar spine most common.	<ul style="list-style-type: none"> <li>- NSAIDS: Celecoxib (Celebrex), Ibuprofen (Motrin), Naproxen (Aleve), Ketorolac (Toradol) and others</li> <li>- Corticosteroids/ Bisphosphonates</li> <li>- Radiation Therapy, Radionuclides</li> <li>- Opioids</li> </ul>
<b>Neuropathic Pain Nerve Damage Dysesthesia</b>	Injury to some element of the nervous system (plexus or spinal root). Dysesthesia, burning, tingling, numbing, shooting electrical pain. May require higher doses of opioids.	<p>Adjuvants</p> <ul style="list-style-type: none"> <li>- Anticonvulsants: Gabapetin (Neurotin), Carbamazepine (Tegretol), Clonazepam (Klonopin), Pregabalin (Lyrica)</li> <li>- Tricyclic Antidepressants: Nortriptyline (Pamelor), Desipramine (Norpramin)</li> <li>- SNSRI'S Antidepressants: Duloxetine (Cymbalta), Venlafaxine (Effexor)</li> <li>- Corticosteroids</li> <li>- Topical Anesthetic: Lidocaine Patch 5% (Lidoderm)</li> </ul> <p>Opioids</p>
SIDE EFFECT	OPIOID SIDE EFFECT MANAGEMENT	
<b>Constipation</b>	Start with combined senna as stimulant and docusate (Colace) as softener. May increase to 4 tabs bid. If no bowel movement in 2 days, add a laxative (Dulcolax, Lactulose, Miralax, Milk of Magnesia). Increase fluids, activity; adjust to effect. Tolerance to opioid related constipation does not occur.	
<b>Nausea/vomiting</b>	Rule out reversible causes, e.g. constipation. Prochlorperazine (Compazine) 10 mg PO q 6 hr PRN or 25 mg suppository PR q 6 hr PRN. May add Lorazepam (Ativan) 0.5mg q 6 hr PO/SL PRN or Metoclopramide (Reglan) (also helpful for early satiety and constipation) 10 mg PO QID. Scopolamine TD (Transderm-Scop) patch 1.5 mg q 3 days is effective for movement related nausea q 72 hrs. Haloperidol (Haldol) 0.5 - 4 mg PO or IV/SQ q 6 hours.	
<b>Respiratory depression</b>	Rare – closely monitor opiate naïve patients. Increased risk with obstructive sleep apnea, obesity, on benzodiazepines, or in those with respiratory compromise.	

## CANCER PAIN MANAGEMENT REFERENCE CARD



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