

Neuromodulators & Opioids for Analgesia

12/4/02

Generic	Brand	Action	FDA Approved	Diagnoses Studied	Drug Interaction	Dose Titration and Dose Range <i>In elderly always start the lowest dose possible!</i>	Serum Levels	Labs	Side Effects – <i>all of these drugs are central Nervous system (CNS) active and toxic effects are frequently related to the CNS!</i> <i>*Serum levels and do not necessarily equate to clinical efficacy with pain management</i>	Discontinuation <i>*Generally, the rate you titrate up is also the rate you taper</i>
Carbamazepine +# (CBZ)	Tegretol, Carbatrol	Na+ channel (NMDA?)	Seizures	Trigeminal neuralgia, PHN, DN, tabetic neuralgia, central post-stroke pain, atypical facial pain, post sympathectomy neuralgia, migraine	VPA, LMT erythromycin, Ca++ blockers,	400-1800/day (in 2-3 divided doses); start low (100mg bid), increase weekly. Extended release available.	4-12	CBC, Plt Lytes (Na+)	Nausea is most common, sedation, ataxia, vomiting, diplopia. Rare but serious blood dyscrasias (aplastic anemia, agranulocytosis).	Titrate down by 25% per week. May stop with adverse effects.
Gabapentin (GBP)	Neurontin	Ca++ channel	Seizures	Diabetic neuropathy, PHN, neuropathic pain, low back myofascial pain, refractory mixed neuropathic pain syndromes, paroxysmal symptoms in MS, migraines.	Minimal	100-4800mg/day (in 3-4 divided doses and PRN– this is the only neuromodulator that can be given PRN).	5-20*	Baseline Sr. Cr	Sedation, ataxia, dizziness, nausea, vomiting, diplopia, edema. Most disturbing is “feeling totally out of it”. Most SE transient(2-4 wks)	May stop abruptly, no rebound, and no withdrawals.
Lamotrigine+ (LMT)	Lamictal	Na+ channel, glutamate	Seizures	Refractory trigeminal neuralgia, HIV-associated painful polyneuropathy, intractable neuropathic pain, DN, MS painful disorders.	VPA	25-600mg/day (in 2 divided doses). Start low (25mg bid), go very slowly following the package insert tables.	4-20*	NA	Rash: Stevens Johnson life threat esp. if on valproic acid and risk higher if dose accelerated faster than package insert recommendation. Sedation, ataxia, dizziness, nausea, vomiting, diplopia.	Titrate down by 25% per week. May stop with adverse effects.
Levetiracetam	Keppra	Unknown	Seizures	Seizures, bipolar d/o, migraine.	Minimal	1000-4000mg/day (in 2 divided doses). Start low (250mg bid), go slow, increase weekly.	NA	Baseline Sr. Cr	Somnolence, asthenia, cognitive dysfunction. behavioral abnormalities including irritability and mood changes.	Titrate down by 25% per week. May stop with adverse effects.
Oral Lidocaine	Mexiletine	Na+ channel	Cardiac arrhythmias	Ventricular arrhythmia, DN, CRPS.	Minimal	Start at 150mg and increase to 900-1200mg daily in divided doses, TID.	0.5-2	Lido levels, LFT	Analgesic doses are the same as those needed for antiarrhythmic effects. Dizziness, lightheadedness, <u>ataxia, nausea, vomiting.</u>	May stop abruptly with adverse effects.
Systemic Lidocaine	Lidocaine	Na+ channel	Cardiac antiarrhythmic, local anesthetic	Arrhythmia, neuropathy.	Minimal	Acute: 1mg/kg IV slow push - over 3-5 minutes -first dose, may repeat 1mg/kg IV push q20minutes; Chronic therapy SQ: 1-3mg/kg/hour.	2-4	Lido levels, LFT	Sedation, ataxia, dizziness, nausea, vomiting, diplopia. Most serious are seizures and cardiac arrhythmias.	May stop abruptly, no rebound and no withdrawals.
Topical Lidocaine	Lidoderm	Na+ channel. Peripheral membrane stabilizer	PHN	PHN, peripheral neuropathic pain conditions.	None	Apply up to 3 patches to affected area for 12 hours. Newer research indicates there is no limitation for length of application.	NA	None	Localized erythema or edema. Reactions are generally mild and transient. Resolves spontaneously within a few minutes to hours.	May stop abruptly.
Oxcarbazepine +#	Trileptal	Na+ channel	Seizures	Seizures, bipolar d/o, Neuralgia	Minimal	600-2400mg/day (in 2 divided doses) Start low (150mg bid), go slow increase weekly.	NA	Lytes (Na+)	Sedation, ataxia, nausea, vomiting, diplopia. Hyponatremia more often as compared to carbamazepine.	Titrate down by 25% per week. May stop with adverse effects.
Phenytoin	Dilantin	Na+ channel, glutamate	Seizures	Diabetic neuropathy, cancer pain, peripheral neuropathic pain, depression, migraine.	Allot	300mg at HS or as divided dose TID.	10-20	LFT	Rash (highest cause for Stevens-Johnson Syndrome), ataxia, mental confusion, decreased coordination, GI.	Titrate down by 25% per week. May stop with adverse effects.
Tiagabine	Gabapril	GABA	Seizures	Seizures, bipolar d/o, depression	Minimal, except with ethanol & triazolam	Initial dose 4mg QD. May inc dose by 4-8mg weekly to 56g/day max., BID-QID. 90% bioavailable, 96% protein bound, and rapidly absorbed on empty stomach.	NA	NA	Abdominal pain, dizziness, somnolence, difficulty w concentration, nervousness, speech disorder	Titrate down by 25% per week. May stop with adverse effects.
Topiramate+# (TOP)	Topamax	Mixed Na+ and Ca++ glutamate	Seizures	Migraine, diabetic neuropathy, migraines, neuropathic pain syndromes.	Minimal	15-800 mg/day (in 2 divided doses) Start low (15mg bid), go very slow increase weekly.	NA	Baseline Sr. Cr	Cognitive dysfunction, dizziness, fatigue, WEIGHT LOSS , nephrolithiasis, paresthesiae.	Titrate down by 25% per week. May stop with adverse effects.

*Therapeutic range not established; +Clearance increased by inducers of P450 enzymes; #Potential Birth Control Pill Failure

6/1/01 Prepared by the University of Wisconsin-Madison Hospital and Clinics Patient Pain Care Team, Madison, WI and the William S. Middleton Memorial Veterans Hospital, Madison WI. Updated 9/20/02 by Coatesville VAMC

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Generic	Brand	Action	FDA Approved	Diagnoses Studied	Drug Interaction	Dose Titration and Dose Range <i>In elderly always start the lowest dose possible!</i>	Serum Levels	Labs	Side Effects – <i>all of these drugs are central Nervous system (CNS) active and toxic effects are frequently related to the CNS!</i> <i>*Serum levels and do not necessarily equate to clinical efficacy with pain management</i>	Discontinuation <i>*Generally, the rate you titrate up is also the rate you taper</i>
TCAs amitriptyline Nortriptyline Desipramine	Elavil Aventyl	NE, 5HTP, Na+	Depression	Migraine, neuropathy, PHN, DN, polyneuropathy, nerve injury pain.	Minimal	10-200mg/day Start low (10-25mg qhs), go slow increase weekly.	50-150	Lytes (Na+)	Sedation, dry mouth, constipation, urinary retention, ataxia. WEIGHT GAIN. Hyponatremia is rare and frequently asymptomatic.	Titrate down by 50% per week. May stop with adverse effects.
Valproic Acid+ (VPA)	Depakote Depacon IV	GABA Na+ channel	Seizures Bipolar disorder Migraine	Migraine, bipolar d/o, central pain after spinal cord injury, various chronic pain disorders.	Everything	750-3000mg/day (in 2-3 divided doses) ER tab also. Start low (250mg bid), go very slow increase weekly.	50-125	AST, Plt	Sedation, dizziness, memory impairment. WEIGHT GAIN, hair loss. <i>There is no evidence that VA works for any pain diagnoses other than headaches.</i>	Titrate down by 25% per week. May stop with adverse effects.
Zonisamide+	Zonegran	Mixed Na+ and Ca++ DA, 5HTP	Seizures	Seizures, migraine, painful disorders	Minimal	200-600mg/day, Start slow (100mg qod), go very slow increase every other week by 100mg.	10-40*	Baseline Sr. Cr	Nephrolithiasis. Anemia. Leukopenia. Weight loss. Somnolence. Asthenia. Cognitive dysfunction. Rash. Paresthesiae.	Titrate down by 25% per week. May stop with adverse effects.
Clonazepam	Klonopin	GABA-A	Seizure, panic disorder	Facial neuralgia, trigeminal neuralgia, glossopharyngeal neuralgia, sluder's syndrome, various chronic pain disorders, deafferentiation disorders.	Minimal	0.25mg po BID-TID, increase by 0.125-0.25mg Q3D to max dose 4mg/day.	NA	Baseline Sr. Cr, LFT	Sedation, weakness, unsteadiness, confusion, upper respiratory tract infection.	Titrate down by 0.125 mg BID every 3 days until discontinued.
Lorazepam	Ativan	GABA-A	Anxiety	PHN, insomnia, panic d/o, status epilepticus.	Minimal	0.5-1.0 mg PO BID-TID, may inc q3-4 days to max dose 4mg/day.	NA	Baseline Sr. Cr., LFT	Sedation, weakness, unsteadiness, confusion.	Titrate down by 0.125 mg BID to TID every 3 days until discontinued.
SSRI	Paroxetine, Fluoxetine, Citalopram, Sertraline, Venlafaxine	Serotonin, NE	Depression	Depression, migraine.	Minimal	20-40mg QD 20-40mg QD 20-40mg QD 150-200mg QD	NA	NA	Agitation, GI, sexual dysfunction.	No taper. However, carefully DC if depression is also treated.
Opioids	Morphine	Mu opioid	Analgesia	PHN, DN, polyneuropathy, migraines, chronic pain syndromes.	Minimal	10 - as much as needed and tolerated, 10-30mg/75kg PO q4hrs, may increase by 20% per dose.	NA	NA	Sedation, constipation, urinary retention, ataxia, nausea, vomiting, asthenia, cognitive dysfunction, behavioral abnormalities, depression.	Titrate down by 25% per day, except methadone 5% per week Clonidine 0.1mg per day for withdrawals.
Cyclobenzaprine	Flexaril	Gamma & alpha motor dec tonic somatic motor activity	Muscle spasm of local origin, not centrally	Muscle spasticity.	Minimal	10 mg TID, with a range of 20 to 40 mg a day in divided doses. Dosage should not exceed 60 mg a day. Use of FLEXERIL for periods longer than two or three weeks is not recommended.	NA	NA	Syncope, malaise, GI.	No taper.
Metaxalone	Skelaxin	Unknown, possible CNS	Acute painful muscle conditions	Muscle pain.	Minimal	2 tabs, (total 800mg) PO TID-QID.	NA	Baseline Sr. Cr, BUN, LFT	Contraindicated in serious renal and hepatic insufficiency. GI, drowsiness, headache, nervousness.	No taper.

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Zanaflex	Tizanidine	Centrally acting (alpha) 2 - adrenergic agonist	Muscle spasticity	Multiple sclerosis and spinal cord injuries.	Minimal	4-8 mg p\PO Q6-8h PRN; max dose 36mg/day.	NA	Baseline Sr. Cr, BUN, LFT	Avoid with liver and renal insufficiency; dry mouth, somnolence, sedation, and dizziness.	No taper.
Tramadol	Ultram	Mu opioid receptor	Moderate to severe pain	Osteoarthritis.	Minimal	50-100mg po Q4-6H, max dose 400mg daily. If >75 yo, <300mg daily in divided doses. CC < 30ml/min increase dosing interval to 12h. If cirrhosis, 50mg Q12h.. If nauseated, start at 25mg daily & taper up by 25mg each dose every 2-3 days	NA	Baseline Sr. Cr, LFT	Seizures can occur with concurrent antidepressants or epileptics. May need dose adjustment with MAO inhibitors or w SSRI. Mostly GI adverse effects.	No taper.
Dextro-methorphan	Delysm, Benylin	NMDA antagonist	Cough	Cough, opioid tolerance, improving the efficacy of opioids.	Minimal	5-10 mg/day can be used to overcome sedation. 30mg po TID with an opioid to improve efficacy and decrease tolerance.	NA	NA	GI, nervousness.	No taper.
Methyl-phenidate	Ritalin	CNS stimulant	ADD, Narcolepsy	ADD, narcolepsy, various pain syndromes.	Minimal	5-10mg/day to overcome sedation. Av dose 20-30 and up to 60mg daily.	NA	CBC, Diff, PLT with long-term therapy	Nervousness, insomnia, weight loss. Patients with an element of agitation may react adversely.	Reduce dose or discontinue therapy if necessary.
Capsaicin Cream	Arthricare	Depletes substance P	Arthritis	DN, PHN, nerve injury pain.	None	Apply to affected area not more than 3-4 times daily.	NA	NA	Skin irritation.	No taper.

Equianalgesic opioid Conversion	Brand	Oral	Morphine : X opioid Ratio	Oral ratio There is incomplete cross tolerance between opioids	IV/IM	Morphine mg/24 h Conversion for Fentanyl	Fentanyl mcg/h Conversion for Morphine
Morphine Dosed TID to QID	Oramorph, MS Contin	30 mg	1:1		10	90	25
Oxycodone	Roxicodone, Percocet	30 mg	1:0.5 or MS is 2X the amount of oxycodone	30 mg MS = 15 mg Oxycodone	15	180	50
Codeine		200 mg	1:7 or codeine is 7X the amount of MS	30 mg MS = 210 mg Codeine	120	270	75
Meperidine USE NOT RECOMMENDED	Demerol	300 mg	1:10 MEPERIDINE NOT TO BE USED	30 mg MS = 300 mg Meperidine	100	360	100
Methadone Dosed TID-QID	Dolophine	5-6 mg	1: 0.2 or MS is 5X the amount of methadone	30 mg MS = 6 mg Methadone or 30 mg MS = 5(5-6 mg Methadone)	10	540	150
Methadone conversion				Methadone is approximately 20% of the Morphine dose <100mg/24h MS: Methadone= 30mg MS:1-3mg Methadone >100mg/24h MS: Methadone= 30mg MS:3-5mg Methadone		720	200
Hydrocodone	Vicodin, Loratab	30 mg	1:1	30mg MS= 30mg Hydrocodone	N/A	900	250
Hydromorphone	Dilaudid	7.5 mg	1:0.25 or MS is 4X the amount of	30 mg MS = 7.5 mg Hydromorphone or 30mg MS = 4(7.5mg)	1.5	1080	300

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			Hydromorphone			
Levorphanol	Levo-Dromoran	4 mg	1: 0.13 or MS is 7.5X the amount of Levorphanol	30 mg MS = 4 mg Levo-Dromoran or 30 mg MS = 7.5(4 mg)	2	
Propoxyphene USE NOT RECOMMENDED	Darvon	150 mg	No ratio	150mg Propoxyphene: 650 mg acetamenophen	NA	

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