Management of Acute Pain in Adults

Assessment of Acute Pain (pain less than 3 months) should include the steps in the Initial Assessment of Pain Protocol including the HPI, PE, and any diagnostic testing determined to be indicated based on findings or 'red flags'

The Initial Plan of Care should prioritize function first and opioids last and is strongly recommended to consist of Non-Opioid Pharmacologic Therapies and Non-Pharmacologic Therapies. In general the following therapies are recommended as first choice options regardless of the cause or type of pain.

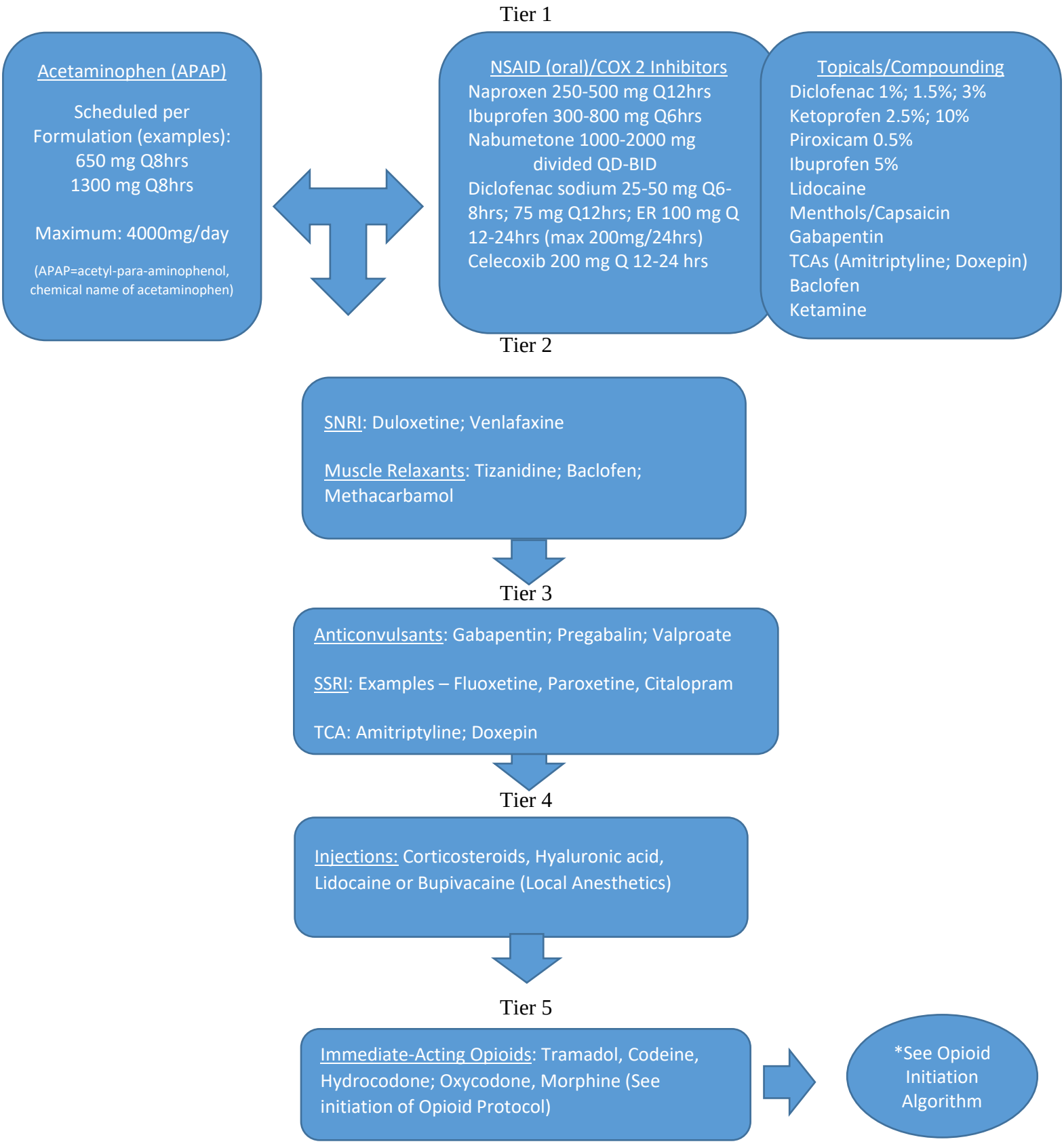
Either acetaminophen or Non-Steroidal Anti-inflammatory Drugs (NSAIDs) should be first line for mild to moderate pain with the choice dependent on individual benefits outweighing the risk of use as well as patient-specific factors, i.e., age, hepatic and renal impairment, co-existing cardiovascular, respiratory, or cerebrovascular disease. Topical medications are preferred when pain is localized to limited areas. Other factors to consider are the potential for drug-drug interactions and the co-administration with central nervous system (CNS) depressants. These medications are most effective when prescribed on a regular schedule than on an 'as needed' basis, for the shortest period of time, with the choice patient-centered, and individualized.

Recommendation: Maximize Non-Pharmacologic and Non-Opioid Pharmacologic Therapies

Neuropathic Pain Treatment Options	**Musculoskeletal Pain Treatment Options**	**Inflammatory Pain Treatment Options**	**Multiple Etiologies Treatment Options**
Pharmacologic Agents -Anticonvulsant meds (A) -Antidepressant meds (B) -Topical medications (C) Adjunct Therapies -Physical Therapy (PT) -Exercise Therapy -OMM -Injection (epidural/facet) -Acupuncture -Surgery	Pharmacologic Agents -Acetaminophen/NSAIDS (D) -Muscle relaxants (E) -Topical medications (C) Antidepressant meds (B) Adjunct Therapies -RICE* -Trigger point injections -OMM** -Massage therapy -Chiropractic -Acupuncture -Physical Therapy -Exercise Therapy *RICE-rest, ice, compression, elevation **OMM-Osteopathic manipulative medicine	Pharmacologic Agents -Acetaminophen/ -NSAIDS +/- H2RA* or PPI** (D) -Antidepressant meds (B) -Corticosteroids Adjunct Therapies -Ice/cold and Heat -Joint injections -PT and/or Occupational Therapy (OT) -Exercise Therapy *H2RA-Histamine-2 receptor Antagonist **PPI-Proton Pump Inhibitor	Pharmacologic Agents -Medication choice based on co-morbidities (F) Adjunct Therapies Based on etiology: -Sleep hygiene -Nutrition and Exercise Therapy -PT and/or OT -OMM -Acupuncture -CBT/counseling -Sleep (manage OSA*) -Surgery *OSA-Obstructive sleep apnea

Acute Adult Non-Opioid Pharmacological Pain Management Algorithm

Medications can be combined however topical and oral NSAIDs should not be used simultaneously. Medications can be combined with adjunct therapies. Non-Opioid Pharmacologic and Non-Pharmacologic Therapies should be maximized before starting Opioids.



Appendix A

Non-Opioid Neuropathic Pain Medications

Medication	Mechanism	Dose	Side Effects	Miscellaneous
Anticonvulsants – Sodium Channel Stabilizers				
Carbamazepine	Binds sodium channels causing ↓ nerve cell depolarization, blocking pain signal	100 mg BID; ↑by 200mg/day as needed to Max 1200 mg/day	Dizziness, SIADH, ↓ Na+, Pancytopenia, Hepatitis, Stevens-Johnson Syndrome	Drug of Choice-Trigeminal Neuralgia Baseline CBC, LFT, TSH
Oxcarbazepine	Binds sodium channels causing ↓ nerve cell depolarization, blocking pain signal	300 mg BID and up 600 mg/day weekly to Max 1200 mg/day	Dizziness, ↓ Na+	Baseline Na+
Topiramate	Binds sodium channels causing ↓ nerve cell depolarization, blocking pain signal; weakly inhibits carbonic anhydrase	25 mg every night; increase by 25 mg weekly to Max 100mg/day	Paraesthesias, Metabolic Acidosis, Renal Stones	Effective for HA Interferes w/glutamate Weight Loss Metabolic Acidosis
Valproic Acid	Increases gamma-Aminobutyric acid (GABA) blocking pain signals	500mg/day; increase 250-500 mg to Max 1250mg/day	Headache, drowsiness, N/V, ↑ LFT, Weight Gain	Effective for HA Caution in liver disease
Anticonvulsants – Calcium Channel Stabilizers				
Gabapentin	Blocks reuptake of serotonin > NE	37.5mg BID Max 225 mg	Increase Blood Pressure, at risk for serotonin syndrome	Increased suicide risk and active metabolite
Pregabalin	Blocks reuptake of serotonin = NE	30 mg per day for 7 days, then 60 mg per day	Headache, Gastrointestinal complaints, caution in liver disease	Increased suicide risk

Adapted from University of New Mexico Chronic Pain Management Toolkit, 2016

Appendix B

Non-Opioid Neuropathic Pain Medications

Tricyclic Antidepressants				
Medication	Mechanism	Dose	Side Effects	Miscellaneous
Amitriptyline	Blocks reuptake of serotonin & Norepinephrine (NE)	25-50 mg at bedtime Max 150 mg	Sedation, lethargy, weight gain, dry mouth, ↑ QTc, hypotension, urinary retention, constipation	Anticholinergic & Antihistamine side effects so avoid in cardiac disease and elderly; assess suicide risk
Nortriptyline	Blocks reuptake of serotonin & NE	10-25 mg at bedtime Max 75 mg	Sedation & lethargy (less than Amitriptyline) weight gain, dry mouth, ↑ QTc, urinary retention, constipation	Avoid in cardiac disease and assess for suicide risk
Desipramine	Blocks reuptake of serotonin & NE	25mg at bedtime Max 150 mg	Mild Sedation & lethargy, weight gain, dry mouth, ↑ QTc, urinary retention, constipation	Avoid in cardiac disease and assess for suicide risk
Selective Norepinephrine Reuptake Inhibitors				
Venlafaxine	Blocks reuptake of serotonin > NE	37.5mg BID Max 225 mg	Increase Blood Pressure, at risk for serotonin syndrome	Increased suicide risk and active metabolite
Duloxetine	Blocks reuptake of serotonin = NE	30 mg per day for 7 days, then 60 mg per day	Headache, Gastrointestinal complaints, caution in liver disease	Increased suicide risk

Adapted from University of New Mexico Chronic Pain Management Toolkit, 2016

Appendix C

Topical Pain Medications

Medication	Mechanism	Vehicle	Side Effects	Miscellaneous
Lidocaine	Na+ channel blocker	Cream, ointment, patch	Large amount can become systemic (Arrhythmias, seizures)	Every 12 hours on and 12 hours off
Menthols, Camphor	Counter-irritant	Cream, ointment, lotion	Redness or irritation at site; may cause serious burns	Keep away from eyes and sensitive areas
Capsaicin	Desensitization of sensory neurons; depletes Substance P	Cream, gel, ointment, patch	Erythema and pain	Quentza® (8% capsaicin patch) requires a prescription
Ketamine	NMDA receptor antagonist; blocks glutamate	Cream, ointment	Arrhythmia, airway obstruction, CNS effects; pain at site	If use systemically, give with benzodiazepines to reduce CNS side effects
Gabapentin	Ca++ antagonist	Cream, ointment	Increase Blood Pressure, at risk for serotonin syndrome	Increased suicide risk and active metabolite
Tri-cyclic Anti-depressants (TCAs)	Serotonin and NE reuptake inhibitors	Cream, ointment	Sedation, lethargy, weight gain, dry mouth, ↑ QTc, hypotension, urinary retention, constipation	Anticholinergic & Antihistamine side effects so avoid in cardiac disease and elderly; assess suicide risk
NSAIDs	COX inhibitor (varied selectivity of COX 1 and COX 2)	Cream, ointment	Increase in CV risk; potential for increase bleeding risk as well as gastrointestinal side effects	Most interact with anti-hypertensive meds; generally avoid in renal dz; may cause allergic reaction, i.e. with asthma
Baclofen	GABA-B agonist	Cream, ointment	Lethargy, drowsiness	Wean to stop with prolonged use; withdrawal phenomena

Adapted from University of New Mexico Chronic Pain Management Toolkit, 2016

APPENDIX D ***NSAIDs (last updated 09/2019) – Emily K. Flores, PharmD, BCPS/Beth A Fox, MD***

*** Generally, NSAIDS are not recommended for use in patients with advanced renal disease; manufacturer dosing recommendations have been included**

NSAID	Maximum daily dose (mg)	Time to peak (hours)	Half-life (hours)	Dose (mg)	Interval	Metabolism / Elimination	Renal / Hepatic dose adjustment
Acetic Acids							
Diclofenac potassium IR	200	1	1-2	50	BID-QID	Hepatic metabolism; 65% eliminated in urine, 35% in feces	Do not use in advanced renal disease; Elderly are more sensitive to adverse effects
Diclofenac sodium delayed release	225	2-3	1-2	100	QDay-BID		
Etodolac	1200	1-2	7.3	200-500	BID-QID	Hepatic metabolism; 73% eliminated in urine, 16% in feces	Not recommended in severe renal impairment
Indomethacin **Indomethacin SR**	200 150	1-2 2-4	4.5 4-5-6	25-50 75	BID-QID QDay-BID	Hepatic with significant enterohepatic recirculation; 60% eliminated in urine primarily as glucoronide conjugates, 33% eliminated in feces primarily as metabolites	Not recommended in patients with advanced renal disease; Start low in elderly
Ketorolac *MAXIMUM COMBINED PARENTERAL AND ORAL TREATMENT OF 5 DAYS*	IM: 120 (150 Day 1) PO: 40	0.5-1	3.8-8.6	***WATCH DAILY MAXs*** IM: 60mg single dose or 30 mg Q6H IV: 30mg single dose or 30 mg Q6H Oral: 20mg followed by 10mg Q4-6H – intended as continuation of IV/IM therapy only		Hepatic metabolism; 61% eliminated in urine as unchanged drug	Use with caution in hepatic impairment, may elevate liver enzymes; >65 years, <50 kg, or moderately elevated SCr: IV/IM use half doses, Oral omit loading dose, and half daily maximums; Not recommended in patients with advanced renal impairment
Sulindac	400	2-4	7.8 (16.4 for active metabolite)	150-200	BID	Hepatic metabolism to active and inactive metabolites; 50% eliminated in urine primarily as inactive metabolites, 25% in feces	Not recommended in advanced renal impairment, if required decrease dose and monitor closely; Reduce dose in hepatic impairment and discontinue if abnormal LFTs occur
Tolmetin	2000	0.5-1	1-1.5	400-600	TID	Urine elimination as inactive metabolites or conjugates within 24 hours	No adjustments noted

NSAID	Maximum daily dose (mg)	Time to peak (hours)	Half-life (hours)	Dose (mg)	Interval	Metabolism / Elimination	Renal / Hepatic dose adjustment
Fenamates (Anthranilic Acids)							
Meclofenamate	400	0.5-1	2 (3.3 with multiple doses)	50-100 (watch max)	Q4-6H	Primarily excreted in urine and feces as metabolites	No adjustments noted
Mefenamic acid Maximum therapy: 1 wk	1000	2-4	2-4	250 (500 mg initial dose)	Q4H	Conjugated hepatically; Eliminated in urine and feces	Not recommended for use in renal impairment
Propionic Acids							
Fenoprofen	3200	1-2	2-3	200-600	TID-Q4H	Extensively hepatic; Small elimination in urine and feces	Not recommended in patients with advanced renal disease
Flurbiprofen	300	1.5	5.7	50-100 (watch max)	BID-QID	Hepatic metabolism via CYP2C9 to inactive metabolites; Urinary elimination	Not recommended in patients with advanced renal disease
Ibuprofen Lower dosing limits (1200, 2400 mg) can be exceeded under physician supervision	3200	1-2	1.8-2.5	200-800	TID-QID Q4-8H	Hepatic metabolism via oxidation; Small elimination in urine and feces	Avoid use in severe hepatic impairment; Elderly start at lower end of dosing range
Ketoprofen	300	0.5-2	2-4	25-75	TID-QID ***Or*** extended release 200 mg QDay	Hepatic metabolism via glucoronidation; 80% urinary elimination via glucoronide conjugates	Mild renal impairment: maximum 150mg/day, severe renal impairment (CrCl<25 mL/min): maximum 100mg/day; In hepatic impairment and serum albumin <3.5 g/dL: maximum 100mg/day
Naproxen / Naproxen sodium	1250 naproxen base *(200mg naproxen base = 220mg naproxen sodium)*	1-4	12-15	250-500 naproxen base	Q6-12H (may use initial 500-750mg dose)	95% urinary elimination	Not recommended if CrCl<30 mL/min; >65 years : 200 mg Q12H

NSAID	Maximum daily dose (mg)	Time to peak (hours)	Half-life (hours)	Dose (mg)	Interval	Metabolism / Elimination	Renal / Hepatic dose adjustment
Oxaprozin	The lower of 1800mg or 26mg/kg; 1200mg if < 50 kg	3-5	42-50	600-1200	QDay	Hepatic metabolism via oxidation and glucoronidation, no active metabolites; 70% urinary and 35% fecal elimination	Use caution in patients with severe hepatic dysfunction; Severe renal impairment or dialysis: 600mg daily, may cautiously increase to 1200mg
Nonacidic Agent							
Nabumetone	2000	3-6	24	500-1000	QDay-BID Usually 1000mg QDay	Prodrug metabolized to active and inactive metabolites in liver, extensive first pass effect; 80% urinary and 9% fecal elimination	CrCl 30-49 mL/min: 750 mg/day, max 1500 mg/day, CrCl <30 mL/min: 500 mg/day, max 1000 mg/day
Salicylic Acid Derivative							
Diflunisal	1500	2-3	8-12	250-500	Q8-12H (Initial dose of 500-1000)	Extensive hepatic metabolism via saturable pathways; Urinary elimination within 72-96 hours	Use with caution in renal impairment, CrCl<50 mL/min: 50% of normal dose, not dialyzed off
Salsalate	3000	2-3	7-8	1000mg TID or 1500mg BID		Hepatically hydrolyzed to salicylic acid; Urinary elimination	ESRD on HD: 750mg BID with additional 500mg after dialysis
COX-2 Inhibitor							
Celecoxib Indication specific dosing *Acute pain: 400mg, 200 mg then 200mg BID*	400	3	11	100-400	Qday-BID	Hepatic metabolism via CYP2C9 to inactive metabolites; 30% urinary and 57% fecal elimination	Use low dose in elderly and if <50 kg; Decrease dose 50% in moderate hepatic impairment (Child-Pugh class B), not recommended in severe impairment; Not recommended in patients with severe renal dysfunction
Oxicam							
Meloxicam	15	4-5	15-20	7.5-15 (may benefit some)	Qday	Hepatic metabolism via CYP2C9 and 3A4(minor); Urinary and fecal elimination	Elderly may have increased concentrations; Child-Pugh class A-B: no adjustment, severe hepatic impairment not adequately studied; CrCL<15 mL/min: avoid use, not dialyzed off
Piroxicam	20	3-5	30-86	10-20	Qday	Hepatic metabolism; Urinary and fecal elimination	Reduce dose in hepatic impairment; Not recommended in patients with advanced renal disease

NSAIDs vary in their potency, duration of action, the way in which they are eliminated from the body, and their ability to cause ulcers and promote bleeding. The more an NSAID blocks Cox-1, the greater its tendency to cause ulcers and promote bleeding.

ASPIRIN: Unique because it is the only NSAID that is able to inhibit the clotting of blood for a prolonged period (4 to 7 days). This prolonged effect of aspirin makes it an ideal drug for preventing the blood clots that cause heart attacks and strokes. Most other NSAIDs inhibit the clotting of blood for only a few hours.

DICLOFENAC & KETOROLAC: The major NSAIDs of potency comparable to opioids. Moderate postoperative pain may be managed using these agents.

KETOROLAC: A very potent NSAID and is used for moderately severe pain that usually requires narcotics. The overall analgesic effect of 30 mg of ketorolac is equivalent to that of 6-12 mg of morphine. Efficacy has been demonstrated for postsurgical pain including oral, orthopedic, gynecologic, and abdominal procedures. Efficacy for acute musculoskeletal pain has also been shown. Its antipyretic activity is significant. Anti-inflammatory activity is achieved only at doses higher than those needed for analgesia. Ketorolac causes ulcers more frequently than any other NSAID and is, therefore, not used for more than five days.

DICLOFENAC: Selection of a specific formulation of diclofenac is important because only one of the available formulations (sodium or potassium salts) of diclofenac provides prompt relief (potassium formulation), which is essential in the management of acute pain. Efficacy has been demonstrated with postoperative pain including gynecologic, oral, and orthopedic surgery models, as well as dysmenorrhea.

NAPROXEN: Provides effective relief in acute traumatic injury and for acute pain associated with migraine, tension headache, postoperative pain, postpartum pain, pain consequent to various gynecologic procedures, and the pain of dysmenorrhea.

Choice of NSAID for chronic and disabling inflammatory joint diseases like rheumatoid arthritis and osteoarthritis is governed by age, diagnosis, degree of severity, relative gastrointestinal safety, tolerability, and relative efficacy in the given clinical situation.

Use of multiple NSAIDs should be discouraged.

An agent with comparatively less gastrointestinal (GI) side effects like ibuprofen and diclofenac should be preferred in place of indomethacin, piroxicam, or naproxen, which are more gastrotoxic. In conditions where inflammation of joints is minimal (e.g. osteoarthritis) analgesics, like acetaminophen should be preferred over anti-inflammatory drugs like ibuprofen. In conditions where diagnosis is uncertain, the medicine should be empirically chosen and given for a week or so and if the response is adequate it should be continued until side effects mandate its withdrawal.

Appendix E

Non-Opioid Muscle Pain Medications

Medication	Mechanism	Dose	Side Effects	Miscellaneous
Muscle Relaxants – Sedating				
Cyclobenzaprine	Blocks reuptake of serotonin & Norepinephrine (NE)	5 mg TID; ↑ to 10 mg TID in 3-5 days Max 30 mg/day	Sedation, lethargy, weight gain, dry mouth, ↑ QTc, hypotension, urinary retention, constipation	Think TCA; Reports of seizures with Tramadol
Chlorzoxazone	Inhibits polysynaptic reflex arcs involved in muscle spasms	500 mg TID-QID initially; may ↑ to 750mg TID-QID if needed	Dizziness, drowsiness Liver dysfunction	No dosage adjustment in renal or hepatic dysfunction
Methacarbamol **Metaxolone**	CNS depression	500mg -1.5gm QID x 2-3 days; Max 6gm/day 400mg TID-QID; may ↑to 800mg TID-QID	Dizziness, drowsiness	Discolors urine
Orphenadrine	Central atropine-like effects	100mg BID	Dizziness, drowsiness	Avoid in elderly
Muscle Relaxants – Non-Sedating				
Baclofen	Inhibits reflexes at spinal cord level, GABA-B agonist	5mg TID; in 3 days ↑ 10mg TID; in 3 days ↑ 20mg TID Max 80 mg/day	Lethargy, drowsiness	Wean to stop; withdrawal phenomena
Tizanidine	α 2 adrenergic presynaptic agonist	2 mg TID-QID; ↑ in 2-4 mg increments every 1-4 days Max 36mg/day	Reduces sympathetic outflow from the CNS (same as clonidine); ↓ BP at higher doses	May help with other central pain syndromes such as CVA or fibromyalgia; Do no use with cytochrome P450 inhibitors' such as ciprofloxacin

Adapted from University of New Mexico Chronic Pain Management Toolkit, 2016

Appendix F

Medication Choice by Comorbidities

Drug	Anxiety	Cardiac Disease: Arrhythmia	Cardiac Failure: Edema	Depression	Hepatic Disease	HTN	Insomnia: OSA	Obesity, Weight gain	Renal Disease
Gabapentin	+	NI	-	J	+	NI	+	-	J
Pregabalin	++	NI	J	J	+	NI	++	_	J
Venlafaxine	+	NI	+	++	J	-	J	J	J
Duloxetine	+	NI	+	++	-	J	J	J	+
TCA	+	CI	J	+	+	J	++	J	+
NSAIDs	NI	NI	-	NI	J	J	NI	NI	-
Muscle Relaxants	+	NI	NI	NI	-	J	++	NI	J

Adapted from University of New Mexico Chronic Pain Management Toolkit, 2016

Legend: “+” preferred; “- “non-preferred; “J” Medical Judgment; “CI” Contraindicated; “NI” No impact