Pediatric Palliative Care Approach to Pain & Symptom Management

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Revised by the BCH/DFCI Pediatric Palliative Care Approach to Pain & Symptom Management Committee in May 2020.

Dana-Farber Cancer Institute/Boston Children's Hospital Pediatric Palliative Care Approach to Pain & Symptom Management (Blue Book) is a pocket-guide to symptom management in children, a tool for identifying areas for self-study, and provides educational information for healthcare professionals at Dana-Farber and Boston Children's Hospital. <u>This information is not medical advice</u>. The Blue Book is not continually updated, and new safety information may emerge after the most recent publication date. Health care providers should always exercise their own independent clinical judgment and consult other relevant and up-to-date experts and resources. Use of medications requires adequate knowledge of side effects and drug-drug interactions. Many of these medications involve off-label use. Official prescribing information should be consulted before any product is used or recommendation made. Non-pharmacologic interventions are always an essential part of symptom management.

Table of Contents

Important Definitions

Addiction/Substance Use Disorder: A primary, chronic, neurobiological disease, with genetic, psychosocial and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Agitation: Unpleasant state of arousal manifesting as irritability, restlessness, and increased motor activity.

Chronic Pain: Pain that recurs for more than 3 months; requires a distinctly different approach from acute pain that can benefit from specialty involvement.

Diversion: The redirection of a prescription drug from its lawful purpose to illicit use.

GMFCS (Gross Motor Function Classification System): 5 level clinical classification system that describes the gross motor function of individuals with cerebral palsy (CP). Children with level 4 or 5 have are at increased risk for neuro-pain.

Harmful Drug Use: Self-administration of medications to alter one's state of consciousness. This is a maladaptive pattern of use of a medication leading to significant impairment or distress, and potentially leading to opioid or substance use disorders. Previously referred to as abuse, which has fallen out of favor since it uses stigmatizing, non-person-first language.

Irritability: An abnormal responsiveness to stimuli or physiological arousal; may be in response to pain, fright, a drug, an acute illness, or a medical condition.

Misuse: Use of a medication with therapeutic intent, but other than as directed, regardless of whether a harmful outcome occurs. Examples of misuse include taking an extra dose or opioid for uncontrolled pain, outside of how it was prescribed or altering of the route of delivery.

Neuro-Pain: Chronic pain sources due to alterations in the nervous system without diagnostic tests or features to differentiate one from another (i.e. central neuropathic pain, autonomic dysfunction, visceral hyperalgesia, chronic post-surgical pain), often with other co-morbid problems with overlapping features (spasticity, dystonia, seizures). Neuro-pain is recommended over neuro-irritability; word choice can impact how the problem is viewed.

Neuropathic Pain: Pain that arises from an alteration, insult and/or disease in the somatosensory nervous system.

Nociceptive Pain: Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors; further broken down into visceral and somatic types.

Opioid Use Disorder: Diagnosis defined in the DSM-5, characterized by the compulsive use of opioids despite adverse events from continued use and signs of withdrawal when stopped.

Pain Behaviors: Observable features expressed without words by an individual in pain.

***Physical Dependence:** A state of adaptation 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.

Pseudo-Addiction: Condition resembling drug addition, caused by undertreatment of symptoms causing the patient to seek more medication.

***Tolerance:** A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.

Withdrawal: The symptoms that occur when medications are stopped abruptly in a patient who has been chronically (most often opioids/ benzodiazepines) and has their dose stopped or reduced by greater than 50% abruptly. These symptoms include but are not limited to anxiety, agitation, muscle aches, sweating, diarrhea, nausea and vomiting.

***Opioid Tolerance** and **Physical Dependence:** Expected with long-term opioid treatment and should not be confused with addiction, which manifests as drug abuse behavior. The presence of opioid tolerance and physical dependence does not equate with addiction.

PACT Language	
Instead of	**Say/Write**
Complain	Endorse
Narcotic	Opioid
Compliance	Adherence
Refuse	Decline
Need	Consider

Evaluation & Approach to Pain Management[1, 2]	
1. Comprehensive assessment and workup as needed to make accurate diagnosis. Pain has a differential diagnosis. 2. Consider non-pharmacologic interventions and specific treatments that may resolve patient's pain 3. Utilize non-opioid agents (acetaminophen, ibuprofen) a. Scheduled non-opioid agents are preferred to PRN in continuous / uncontrolled pain 4. Add opioids and titrate dose as needed a. Schedule opioids or convert to long acting opioid if ≥ 3 as-needed doses used per day 5. Assess response closely and adjust opioid dose as needed a. Right dose is patient specific; there is no "max" dose	↕ - *Integrative therapies* and *adjuvants* should be continually considered to achieve broad spectrum analgesia - Consider adjuvants before opioids for neuropathic pain and children with impairment of the CNS *(See page 18-20)* ↕

Non-Opioids for Mild Pain		
Medication	**Initial Dose**	**Comments**
Acetaminophen 160 mg/5mL Supp: 120mg, 325mg, 650mg tabs	PO/PR: 10-15 mg/kg (325-650mg) max 3gm/day q4-6hr IV: 12.5 mg/kg q4hr or 15 mg/kg q6hr (650mg) Max 75 mg/kg/day q6hr	< 2 g/day appears to be well tolerated in adult patients with cirrhosis, monitor closely; essentially no anti-inflammatory activity; low risk of GI side effects; no effect on platelets
Ibuprofen 40mg/mL, 100mg/5 mL; 100mg, 200mg, 400mg, 600mg tabs	PO: 6-10 mg/kg (400-600mg) q6-8hr	Should be avoided in severe hepatic impairment and thrombocytopenia; may cause nephrotoxicity; avoid in infants <6 months
Naproxen 125mg/5 mL; 250mg tab	PO: 5-7 mg/kg (250-400mg) q12hr	↑ hepatotoxicity incidence versus other NSAIDs (↓ dose 50% in hepatic disease); avoid in thrombocytopenia; may cause to nephrotoxicity
Ketorolac 10mg tab	IV: 0.3-0.5 mg/kg (15-30mg) q6-8hr Max 24-hour dose: 120mg IV PO: 10mg q6-8hr *adult dosing Max 24-hour dose: 40mg PO	Do not use longer than 5 days; avoid in thrombocytopenia; may contribute to nephrotoxicity
Celecoxib 50mg, 100mg capsules	PO: 1-2 mg/kg (100-200mg) q12-24hr	↓ incidence of GI ulcerations; minimal to no inhibition of platelet function

Opioids for Severe Pain						
Medication **Formulations**	**Initial Dose PO***	**Initial PO Dose >50kg**	**Initial Dose IV***	**Long Acting Formulations**	**Hepatic Metabolism[3]**	**Renal Excretion[4]**
TraMADol *(not an opioid, binds to opioid receptors)* 50mg tab	1-2mg/kg PO q4-6hr	50-100mg q4-6hr PO	N/A	ER 100mg, 200mg, 300mg tabs Max 400mg/day	Prolong dose interval to q12h and avoid ER formulations	Prolong dose interval to q12h; may ↑ seizure threshold + uremia
OxyCODONE 5mg/5mL Concentrate: 100mg/5mL 5mg, 10mg, 15mg, 20mg, 30mg tabs	0.1-0.2 mg/kg (5-10 mg) q4-6hr PO	5-10mg q4-6hr PO	N/A	OxyCONTIN 10mg, 20mg, 30mg, 40mg, 60mg tabs	Dose reduce by 30-50% and prolong intervals; Half-life ↑, clearance ↓, Peak plasma conc. ↑	Reduce dose by at least 50%; avoid in mod-severe impairment; avoid in dialysis; Half-life ↑
Morphine 10mg/5mL 20mg/1mL 15mg, 30mg tabs	0.2-0.3 mg/kg q3-4hr PO	15-20mg q3-4hr PO	0.05-0.1 mg/kg (2.5-5 mg) q2-4hr IV	MS Contin 15mg, 30mg, 60mg, 100mg, 200mg tabs	↑ bioavailability ↑ half-life, ↓ clearance w/ cirrhosis	Reduce dose by 25-50%, up to 75% with moderate impairment. Use 10:20 IV:PO ratio rather than 10:30 with renal impairment; avoid in ESRD due to accumulation of active metabolites
HYDRO-morphone 1mg/mL 2mg, 4mg, 8mg tabs	0.04-0.08 mg/kg (1-2 mg) q3-4hr PO	2-4mg q3-4hr PO	0.015 mg/kg (0.2-0.6 mg) q2-4hr IV	Not available in USA	Preferred drug in liver impairment; may need dose reduction 25-50% with severe disease	Dose reduce 50-75% with renal impairment; drug accumulates though considered safe in mild ESRD; dialyzable
FentaNYL	*(See page 8) for TD FentaNYL*		0.5-2 mCg/kg (25-75 mCg) q30minIV	*(See page 8)*	Dose reduce TD patch by 50% with liver impairment; ↑half-life	Reduce dose by 25-50%, Preferred drug in renal impairment; not dialyzable
Methadone	*(See page 9-10)*			5mg/5mL, 10mg/5mL 5mg, 10mg tab	Generally considered safe, may accumulate with repeated doses	Not dialyzable, preferred drug in renal disease
*Infants < 6 months require lower initial opioid dosing, approximately 25-50% of the opioid doses provided						

Escalation of opioids:

a. Increase by 30% for mild pain, 50% for moderate pain, 75-100% for severe pain
b. Provide breakthrough (rescue) doses – typically 10-15% of the 24-hour opioid requirement, available as often as every 1-2hr PRN for oral opioids (except methadone)

Patient Controlled Analgesia (PCAs)[5] starting dose recommendations for opioid naïve pediatric patient*			
Medication	**Morphine**	**HYDROmorphone**	**FentaNYL**
Loading Dose	Loading: 0.03mg/kg	Loading: 0.006mg/kg	0.3mCg/kg
Continuous Infusion	0.015mg/kg/hr	0.003mg/kg/hr	0.15mCg/kg/hr
"Demand" Dose	0.025mg/kg	0.005mg/kg	0.25mCg/kg
Lockout Interval	7-12 minutes	7-12 minutes	7-12 minutes
Hourly Max Limit	0.1mg/kg/hr	0.02mg/kg/hr	1mCg/kg/hr
Available Concentration	Standard Concentration 1mg/1mL Standard Non-standard** Concentration 3mg/mL 25mg/mL *0.25mg/mL (diluted library)*	Standard Concentration 0.5mg/mL Standard Non-standard** Concentration 2mg/mL 10mg/mL *0.1mg/mL (diluted library)*	Standard Concentration 25mCg/mL Standard Non-standard** Concentration 50mCg/mL *10mCg/mL (diluted library)*
*__Opioid-Tolerant Patients__. Patients who are *opioid tolerant* (typically receiving oral morphine equivalent of 60 mg/day for ≥ 1 week) may require higher doses. Recommend starting PCA with total 24-hour dosing divided by 24 hours for hourly rate and titrate as needed.			
**__Standard non-standard concentration PCA.__ Initial order must be written by Pain Service. PACT and primary team can modify following initial order. *Consider in patients who may need more concentrated or more dilute solutions, and/or when escalating PCA at end-of-life.*			
Escalation of PCA b. Increase *continuous and demand* by 30% for mild, 50% for moderate, 75-100% for severe pain			

Transdermal FentaNYL (TDF)[6] *Use lowest dose possible and titrate based on patient response* See: www.TIRFREMSaccess.com	
Patch Formulations	12.5mCg/hr; 25mCg/hr; 50mCg/hr; 75mCg/hr; 100 mCg/hr
Conversion Factor	2:1 ratio of TDD (total daily dose) morphine: mCg/hr TDF Every 2 mg PO morphine/day ⇒ 1 mCg/hr TDF *calculate TDD morphine to determine patch dosing
Patient Characteristics	Good choice for chronic pain that is unlikely to fluctuate significantly **Patients must be taking at least 60mg of oral morphine, or equivalent, daily** Bad choice for patients who are opioid naive, with minimal subQ fat Increased absorption with fevers. Avoid use of heating pad near patch.
Initiating TD Patch **Takes at least 12 hours to achieve adequate analgesia, <u>max</u> concentration takes up to 36 hours, and 3-6 days to reach steady state*	Oral Opioid → TDF Apply patch at same time as last dose of ER opioid Continue to provide IR formulations for breakthrough pain as patch takes effect IV Infusion→ TDF Decrease IV infusion to 50% of the original rate 6hr after patch applied Discontinue IV infusion 12hr after patch applied
Discontinuing TD Patch **It takes 17-24 hours for 50% of FentaNYL to be eliminated from body after patch removal and > 50hours for 90% elimination*	For first 12hr after patch removal, use only IR rescue pain doses 12 hours after patch removal, begin with 50% calculated scheduled opioid regimen 24 hours after patch removal, increase to 100% calculated scheduled opioid regimen
Other Transmucosal Options	Transmucosal lozenge, Effervescent buccal tab, buccal soluble film, Sublingual tab, Sublingual spray, nasal spray

Methadone[7]	
Racemic mixture of two enantiomers with unique properties: **R- methadone**: opioid receptor activity (μ, Δ and K) **S- methadone**: NMDA antagonist; reuptake inhibitor of 5- HT, norepinephrine NMDA antagonism results in decreased opioid tolerance/increased sensitization/increased analgesic effect (relatively lower methadone dose has same effect)	
Pharmacokinetics (oral dosing) **significant variability between individuals**	
Bioavailability	Little first pass hepatic metabolism, >80% bioavailability High lipophilicity; high mucosal absorption
Metabolism	Largely by CYP2B6 and CYP3A4 → *Smoking*: induces CYP2B6 lowers methadone levels → *Genetics*: Wide range of genotypes → *Changes in concomitant medications*: ***check at every visit!***
Elimination	$t_{1/2}$ is variable, though long (about 22hr) Biphasic pattern α-elimination phase (8–12hr): correlates with analgesia duration β-elimination phase (30–60hr): levels sub-analgesic but prevent withdrawal No active metabolites
Excretion	Predominantly in feces Does not accumulate in renal failure Not appreciably filtered during hemodialysis
Analgesic Activity *both short and long-acting analgesic*	*Long analgesic activity* (approximately 3-6hr with initiation and 8-12hr with repeated dosing) *Onset of analgesia is short* (30-60min) → peak effect 2.5-4hr
Prescribing Recommendations	
Caution	**Use with Extreme Caution**
Structural heart disease Congenital heart disease Electrolyte abnormalities Disordered breathing syndromes	Congenital QTc syndrome (patient or family) Active illicit drug use Sole opioid for patients with prognosis <5 days (insufficient time to achieve steady state) QTc >500ms
Starting Dose	
0.1mg/kg/dose q8-12 hours PO 0.05-0.1mg/kg/dose q8-12 IV/SubQ	
Titration	
Given length of time needed to achieve steady state (~5 days) dose should be titrated every 3-5 days by 30% Initial doses should not start higher than 30-40mg/daily Initial dose increases of methadone should not be more than 10mg per day every 5-7 days	
Monitoring	
Opioid receptor mediated adverse effects (e.g. sedation, respiratory failure) QTc Monitoring: An Approach Based on Guidelines Issued by The American Pain Society Obtain EKG obtained prior to initiation of methadone (if consistent with goals of care) Obtain follow up ECGs with dose increases, (depending on risk and goals of care) Risk higher with IV methadone (due to chlorobutanol preservative). Be aware of concomitant drugs that may potentiate the repolarization caused by methadone. *For a list of QTC-prolonging medications: crediblemeds.org*	
*QTc prolongation: ≥460 milliseconds (ms) for prepubertal children, ≥470ms for pubertal males, and ≥480ms for pubertal females**[8]	

Methadone	
Selected Drug Interactions (*not comprehensive***)**	
Increase methadone levels	CYP 3A4 inhibitors, ciprofloxacin, isoniazid, diazePAM, clonazePAM, cimetidine, verapamil, dilTIAZem, nefazodone
Decrease methadone levels	CYP3A4 inducers, carBAMazepine, nevirapine, nelfinavir, phenytoin, PHENobarbital, rifAMpin
Prolong QT interval	5-HT3 antagonists, haloperidol, QUEtiapine, OLANZapine, chlorproMAZINE, amitriptyline, desipramine, imipramine, nortriptyline
Increase circulating methadone levels **AND** prolong QT	-azole antifungals, erythromycin, clarithromycin, azithromycin, fluvoxaMINE, PARoxetine, FLUoxetine, sertraline

Opioid Conversion → Methadone[9] (*requires expertise*)			
Equianalgesic Conversion to Methadone			
Oral morphine equivalent	mg of oral methadone	= ratio	mg of oral morphine
<100 mg/day	1		3-4
100-300 mg/day	1		5-8
301-600 mg/day	1		10
601-800 mg/day	1		12
801-1000 mg/day	1		15
>1000 mg/day	1		20
Due to incomplete cross-tolerance the initial calculated methadone dose should be reduced by 25-50% and then divided into 3 doses given q8hr *Convert to no more than 30mg/day methadone, then titrate upwards*			

Methadone → Morphine
PO methadone to PO morphine: 1:4.7 IV methadone to IV morphine: 1:13.5

Converting between Methadone IV and Methadone PO
Oral to IV ratio 2:1 IV to Oral ratio: 1:1.3
Due to variations in bioavailability, there is no consensus on IV to PO conversion *Recommended ratio is between 1:1 and 1:1.5*

Opioid Rotation: Making an equianalgesic opioid conversion[6] (5 Step Process)
1. Assess the pain and side effects to determine if rotation is the best intervention
2. Determine patient's total daily consumption of opioid
3. Set up ratio using data from equianalgesic table and calculate total daily dose of new opioid
4. Modify the calculated dose, generally reducing by 25-50% guided by the patient-specific situation. Determine new opioid regimen (specific dose, interval, and breakthrough analgesia)
5. Implement new dose and monitor patients' response carefully. Liberal access to breakthrough agent is necessary to ensure patient does not experience excess pain during the transition.

Opioid Equianalgesic Doses[6]

Recommend two-clinician verification with opioid conversions prior to placing order with additional confirmation using GlobalRPH.com.

Drug	PO/PR (mg)	SubQ/IV (mg)
Morphine	30	10
OxyCODONE	20	n/a
HYDROcodone	20	n/a
HYDROmorphone*	7.5	1.5
Methadone	*(see page 10)*	
FentaNYL *(see page 8)*	n/a	0.1 (100mCg)
OxyMORphone	10	1

Equianalgesic ratios are ***approximate***. The ratios chosen above reflect a consensus drawn from several sources. Other conversions tables exist and may show different ratios. Individual patients may have very different absorption or cross tolerance and ALL opioid conversion procedures should be conducted or overseen by clinicians with experience.

*Hydromorphone ratios have been shown to have large interpatient variability. Recent evidence suggests a different ratio when converting from IV to PO versus from PO to IV. New conversion methods based on this evidence risks overestimating the IV dose when converted from an oral opioid formulation. The table above represents bidirectional estimates; however, it is always recommended to dose reduce when using these tables.[10]

Opioid Regulatory Considerations	
Opioid Agreement	To be completed by primary opioid prescriber. Separate opioid agreements for DFCI / BCH. Copy opioid agreement and scan into electronic medical record.
MassPAT	**Massachusetts Prescription Awareness Tool** is the online prescription monitoring program in Massachusetts (https://massachusetts.pmpaware.net/login). All clinicians who write controlled substances must register with MassPAT. Checking MassPAT before issuing any prescription for a drug in schedule II or III and before each new benzodiazepine prescription is mandatory.
Naloxone RX	Consider co-prescription order for any patient being discharged on long-acting opioids. Typically Intranasal RX. (4mg:0.1mL).
Discussion of safe opioid practices	Safe storage of opioids Lock box
Documentation	**Document the above in PowerChart with every opioid prescription.**

Management of Opioid Side Effects	
Adverse Effect	**Management Considerations**
Constipation	Start with a stimulant ± stool softener, see constipation section (*see page 24)* For refractory opioid-induced (OI) constipation[11,12] Methylnaltrexone 0.15 mg/kg (max 8-12mg) q48hr subQ Relistor (PO) 450mg daily (adult dosing) PO PRN, Naloxegol (Movantik) PO 12.5-25mg daily (adult dosing), Lubiprostone (Amitiza) PO, Linzess PO
Delirium	Assess for coexisting factors (drugs: anticholinergics; metabolic alterations: infection, dehydration, renal, liver, electrolyte, brain metastases) Consider reducing opioid (if possible) or opioid rotation Consider neuroleptic (haloperidol, risperiDONE, OLANZapine, *(see pages 27-28))*
Myoclonus	Reduce dose (if possible) or add adjuvant / rotate opioid Increase hydration to enhance clearance of toxic metabolites Consider ClonazePAM 0.25-0.5mg PO TID; LORazepam 0.5-1 mg PO/IV QID; Baclofen 5-10mg PO TID
Hyperalgesia	Consider adjuvants (*see page 13-15, 20*) for pain to allow potential opioid reduction; consider ketamine (NMDA blockade, *see page 14*); consider opioid rotation
Nausea & vomiting	See N/V section *(pages 21-23)*
Neurotoxicity	Characterized by acute delirium, myoclonus, seizure, hyperesthesia, and hallucinations Rotate opioid, hydration, consider above for myoclonus, consider stimulant for sedation
Pruritus	Nalbuphine[13] 0.01-0.02 mg/kg (1.5mg) IV q6h PRN itching Naloxone (0.25-2 mCg/kg/hour) continuous IV infusion Antihistamines not effective (opioid induced itching not solely histamine mediated)
Respiratory Depression	Opioid antagonists can reverse opioid-induced respiratory depression; however, *they also may reverse analgesic effects* Naloxone should **NOT** be administered for a depressed RR but normal O2 saturation, or for a patient who is arousable In either of those cases, **reduce** the opioid dose, provide verbal and tactile stimulation, and continue to monitor the patient closely. If naloxone is needed: dilute 0.4 mg (1mL) in 9 mL of NS, and give IV in 1-2mL increments at 2-3 min intervals until response
Sedation & Hypersomnolence that persists	Tolerance typically develops. What initially appears to be sedation may be catch-up sleep made possible by controlled pain. Hold other less necessary drugs that are CNS depressants Methylphenidate for persistent fatigue in the morning and mid-day *(see page 28)*
Urinary Retention	Consider crede maneuver, bladder cathing Nalbuphine[14] q6hr IV PRN low dose (0.05-0.1mg/kg/dose) shown to be effective for opioid induced urinary retention Consider bethanechol (0.2 mg/kg, max 10mg, PO q8hr)

Adjuvant or First Line Analgesic Agents[15,16]

See table on page 20 for medications specific for neurologic symptoms, indicated by ✔

Medication	Indications	Usual Starting Dose & Interval	Comments
Anticonvulsants, Gabapentinoids			
Gabapentin✔ 50mg/1mL; 100mg, 300mg, 400mg capsules	Neuropathic Pain	Initial Dose: 2 mg/kg (100 mg) PO TID **OR** 5 mg/kg (250 mg <u>max</u>) PO QHS Increase by 2mg/kg/dose (5-6 mg/kg/day) q2-4 days until effective analgesia reached (often noted at 30-45 mg/kg/day) <u>Max</u> total dose of 50-72 mg/kg/day reached (2400-3600 mg/day) Give **half** of TDD QHS if symptoms occur mostly in evening/overnight	Pre-amputation to reduce post-op phantom pain Side effects experienced (nystagmus, sedation, tremor, ataxia, swelling) Adjust dose for renal dysfunction (CrCl <60mL/min) Younger children (<5 years) may require a 30% higher mg/kg/day dosing, (TDD of 40-60 mg/kg) Titrate more rapidly for severe pain or as tolerated
Pregabalin 20 mg/mL; 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 300mg capsules		Day 1-3: 1 mg/kg/dose (50mg <u>max</u>) PO QHS Day 4-6: 1 mg/kg/dose PO q12hr Increase q2-4 days to 3mg/kg/dose PO q12hr (<u>max</u> 6 mg/kg/dose)	Adjust dose for renal dysfunction (CrCl <60mL/min) CrCl 30-60: 150mg BID CrCl 15-30: 75 mg BID CrCl <15: 75mg daily

Converting Gabapentin to Pregabalin[17]

cross-titrating between gabapentin and pregabalin is not necessary. Recommend discontinuing gabapentin and initiating pregabalin with equivalent dosing at next interval

Total daily dose of Gabapentin in mg (pre-switch)	*Total daily dose of Pregabalin in mg (post-switch)*
0-300	*50*
301-450	*75*
451-600	*100*
601-900	*150*
901-1200	*200*
1201-1500	*250*
1501-1800	*300*

For total daily dose of Gabapentin > 1800mg;
every additional 300mg of Gabapentin = + 50mg Pregabalin
(up to <u>max</u> 3600mg Gabapentin & <u>max</u> 600mg Pregabalin)

Other Antiepileptics to Consider (3rd or 4th line in adult algorithms for neuropathic pain)[18, 19]

Valproic Acid, OXcarbazepine, LamoTRIgine, Topiramate

<table>
<tr><th colspan="4">Tricyclic Antidepressants (TCA)</th></tr>
<tr><td>Amitriptyline

10mg, 25mg, 50mg, 75mg, 100mg tabs

Nortriptyline

10mg/5mL;
10mg, 25mg, 50mg, 75mg capsules</td><td>Neuropathic Pain</td><td>Day 1-4: 0.2 mg/kg (<u>max</u> 10 mg) PO QHS
Increase q4-5 days by 0.2 mg/kg/day until effective analgesia OR dosing reaches 1 mg/kg/day (<u>max</u> 50 mg/day)
Consider twice daily dosing of 25-30% qAM and 70-75% qPM</td><td>Obtain plasma level and ECG before further dose escalation

Both have higher rate of side effects with higher doses (including anti-cholinergic)

Side effects: constipation, dry mouth, urinary retention, sedation. (Anticholinergic side effects Amitriptyline > nortriptyline)</td></tr>
<tr><th colspan="4">Selective Norepinephrine Reuptake Inhibitors (SNRI)</th></tr>
<tr><td>DULoxetine

20mg, 30mg, 40mg, 60mg capsules</td><td>Peripheral Diabetic Neuropathic Fibromyalgia</td><td>Initial dosing: 30 mg daily for two weeks
Titrating dose: After 2 weeks, increase dose to 60mg daily
If needed, increase by 30mg increments to <u>max</u> 120mg/day (may be divided into BID dosing)</td><td>Helpful for patients with comorbid anxiety/depression

Capsule may be opened and sprinkled onto food, though not recommended</td></tr>
<tr><th colspan="4">Topical Agents</th></tr>
<tr><td>Lidocaine patch²⁰
(4%)</td><td></td><td>Apply to intact skin over most painful area, may leave in place for up to 18-hr in a 24-hr period, OK to cut</td><td></td></tr>
<tr><td>Topical NSAIDs
[Diclofenac]

1% gel, 3% gel
Patch (for > 6yrs)</td><td>Joint pain</td><td>Gel→ apply using dosing card to measure, 3-4x daily up to 7 days
Patch → apply 1 patch 1-2x daily up to 14 days</td><td>Use lowest effective dose for shortest duration of time
Avoid over open skin or mucous membranes, allow at least one hour before bathing, wash hands immediately after applying</td></tr>
<tr><th colspan="4">N-Methyl-d asparate (NMDA) Antagonists</th></tr>
<tr><td>Ketamine²¹⁻²⁴

100mg/mL (5mL) use injection for oral doses</td><td>Analgesia; Opioid-sparing effects</td><td>Initial dosing: IV infusion: 0.05-0.1 mg/kg/hr = 2mCg/kg/min, increase IV infusion rate by 1mCg/kg/min increments
PO: 0.25-0.5 mg/kg PO q6-8hr
<table>
<tr><th>Dose (mg/kg)</th><th>Effect</th></tr>
<tr><td>01.-0.3</td><td>Analgesia</td></tr>
<tr><td>0.4-0.8</td><td>Partial dissociated</td></tr>
<tr><td>>0.7</td><td>Dissociative</td></tr>
</table></td><td><u>Converting from IV to PO ketamine</u>:
1:1 conversion ratio
Administer 1st oral dose 4-8hr after infusion discontinued
May utilize q4h → q12h dosing intervals</td></tr>
</table>

Alpha-2-adrenergic Agonists			
Dexmedetomidine[25]		0.2-1 mCg/kg/hr IV infusion * Doses as high as 2.5 mCg/kg/hr Infant may need higher infusion rates than older children	**must be done in ICU*
CloNIDine ◆ 100mCg/mL 0.1mg, 0.2mg tabs TD Patch Dosing: 0.1 mg/24hr 0.2 mg/24hr 0.3 mg/24hr *Patches can be cut to achieve 50mCg*	Neuropathic Pain; Opioid withdrawal	Day 1-3: 0.002 mg/kg (2mCg/kg) PO QHS (0.1 mg) Day 4-6: 0.002 mg/kg (2mCg/kg) q12hr Day 7-9: 0.002 mg/kg (2mCg/kg) q8hr Doses may be increased by 0.002 mg/kg (2mCg/kg) as tolerated (monitor for hypotension) May titrate more rapidly as tolerated	**Converting from PO → patch** (patch reapplied q7 days) Day 1: Apply patch, give 100% oral dose Day 2: Give 50% oral dose Day 3: Give 25% oral dose Day 4: Discontinue oral dose **Converting from CloNIDine patch→ PO CloNIDine** Remove patch Administer initial oral dose 8 hours later Due to lower metabolism and inability to stand eliminating orthostatic hypotension ◆
Corticosteroids			
Dexamethasone[26] 0.5mg/0.5mL; 0.5mg, 1.5mg, 4mg tabs	Dosing for Spinal Cord Compression Increased ICP Bowel obstruction Hepatic capsular distention	1-2 mg/kg (max 10mg) IV load **THEN** 1-1.5mg/kg/day IV divided into q6-12h dosing (max daily dose = 16mg) *Higher maintenance doses for spinal cord compression associated with higher incidence of side effects without greater benefit	
	Dosing for Bony Pain/Edema	0.02-0.03 mg/kg/day in 2-3 divided doses (max daily dose ~10-12mg/day)	
PredniSONE 1mg, 5mg, 10mg, 20mg, 50mg tabs	Bone pain	0.5-1 mg/kg (max 40 mg) PO q12hr	
Miscellaneous			
Pamidronate	Metastatic bone pain, delay of bone metastasis progression, hypercalcemia	0.5mg-1mg/kg IV q4 weeks, may decrease interval to q3 weeks (>60kg) 90mg IV q4 weeks, may decrease interval to q3 weeks	Reduce dose for renal dysfunction May cause myalgias and fevers
Zolendric Acid		1st time dose: (pts >2 years of age) 0.0125mg/kg/dose Subsequent doses (pts >2 years of age) 0.025-0.05mg/kg/dose 4mg IV q4 weeks, may decrease interval to q3 weeks	

Chronic Pain

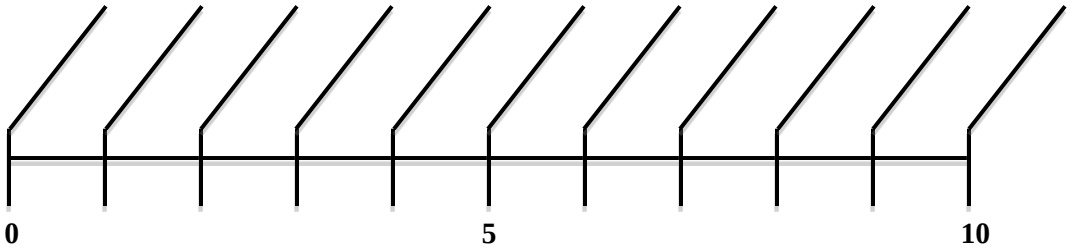
- Pain that occurs for more than 3 months
- Causes include musculoskeletal, visceral, post-surgical, neuropathic, and central pain syndromes
- The goal is pain control and improved function, as opposed to complete pain relief:
  o Elimination of symptoms is often not possible
  o Improved comfort is always possible and may require re-evaluation of treatment goals
- Approach must be multidisciplinary, including non-pharmacologic, psychological, emotional and pharmacological therapies
- *See page 19* for recommendations on **Interventional Language Strategies**
- *See page 19* for recommendations for screening children with SNI for risk of chronic neuro-pain

Weaning Guidelines[27-29]
- If drug has been in continuous **use > 5 days**, consider a wean (especially for opioids and benzodiazepines) - Rule of thumb when weaning any medication is to reduce by 20-30% and observe for breakthrough symptoms or withdrawal symptoms. There is no evidence to support any one weaning strategy, it should be individualized to patient. - Frequency of weaning steps depends on half-life of drug and how long patient has been on it - Longer half-life and longer duration of use = slower wean - Generally, the last step of wean is the starting dose. In some patients, doses below typical starting dose are needed to avoid withdrawal symptoms. - Patients on benzodiazepines > 3 months or with chronic pain on opioids > 6 months will likely need a VERY SLOW wean (5-10% of original dose per week)
Withdrawal - Symptoms include, (not limited to) anxiety, agitation, dysphoric mood, nausea/vomiting, muscle aches, lacrimation, rhinorrhea, pupillary dilation, piloerection, sweating, diarrhea, yawning, fever, insomnia - **CloNIDine** can be used to mitigate withdrawal symptoms   ▪ PO 5 mCg/kg/day, divided every 8-12 hours or rounded to nearest ¼ patch size for transdermal dosing (<u>max</u> initial dose 100 mCg/day)
WAT score > 3 indicates likely withdrawal, consider slowing wean.

Children with Impairment of the Central Nervous System

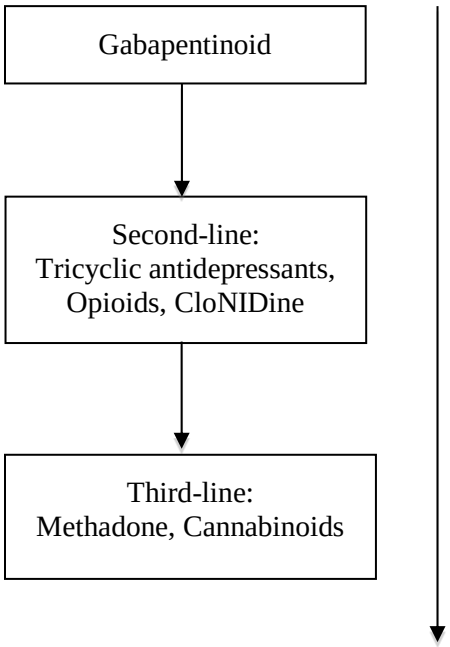
Pain behaviors in children with severe neurological impairment (SNI)
- *Vocalizations*: crying, moaning - *Facial expression*: grimacing, frowning, eyes wide open - *Unable to console*: difficult to calm, not soothed by parent comfort actions - *Interaction*: withdrawn, seeking comfort - *Physiological*: tachycardia, sweating, pale or flushed skin, tears - *Muscle tone*: intermittent stiffening of extremities, clenching of fists, muscle tensing, tremors, back arching - *Movement*: increased from baseline, restless, startles easily, pulls away when touched, twisting
Acute and Post-Surgical Pain Assessment
INRS **R-FLACC**
Evaluation of Pain
- Causes, history, and exam pg e6-e7 of AAP clinical report[30] - Initial tests: Blood (CMP, CBC, lipase), urine (UA/UCx), X-ray or bone scan if fracture suspected, and guided by history or exam (e.g. head imaging for shunt, place longer low profile G-tube if tight against abdomen due to growth) - *Consider* abdominal ultrasound, dental exam if no recent exam

Individualized Numeric Rating Scale (INRS): In the diagram below, write in your child's typical pain behaviors on the line that corresponds to its pain intensity, where 0 = no pain and 10 = worst possible pain (see article for further information)



Screening children with SNI for risk of chronic neuro-pain[31]
1. Does your child have any of the following? - Frequently not calm - Intermittently agitated, irritable, cranky, uncomfortable, without a consistent explanation - Chronic poor sleep - Symptoms that continue after 1 or more interventions for: o Autonomic dysfunction and storms o Spasticity or dystonia o Gastrointestinal reflux disease (GERD) and vomiting o Constipation with discomfort o Pain with feeds, not tolerating tube feeds 2. Review prior testing for sources of pain 3. Review for testable chronic pain sources, such as: - Dental, hip subluxation, chronic dry eyes, renal stones - Note: Some findings can be incidental and not the reason for symptoms 4. Screen for risk of chronic pain due to CNS sources without diagnostic tests - See History from N-PRAT (Neuro-Pain Risk Assessment Tool) below - Use score to guide decision to initiate medication trial

Suggested guidelines for pharmacologic management of chronic neuro-pain[32,33]



History from N-PRAT as guide to start / add drug

- Pain is Chronic: (*see definition above)*
- Level of disability: GMFCS level 4 to 5 or moderate to profound intellectual disability
- AND 1 or more of the following
  - Episodes with rapid onset, out of the blue
  - Intermittent increase in muscle tone, spasms, movement, posture
  - Autonomic dysfunction features: flushing of skin, sweating, tachycardia, hypertension
  - GI symptoms: pain with feeds, gas and constipation; improvement following flatus and a bowel movement
  - Chronic poor sleep
  - Post-surgical: pain >2 months post-surgery without a source
  - Intractable seizures
  - Planned surgery: gabapentinoids may decrease need for post-surgical opioids and development of postsurgical pain

Chronic Symptom Management Strategies[31]
- Scheduled medication(s): recurrent episodes that do not respond to typical comfort strategies, and are of significant severity, duration, and frequency (e.g. 3 or more episodes per week or a cycle of daily episodes for 4-7 days q2-4 weeks) - Breakthrough care plan: chronic neuro-symptoms can be decreased with scheduled medications but not cured; breakthrough symptoms can still occur - Lessen distention of the GI tract: causes of chronic neuro pain can decrease the amount of distention that triggers pain signals; assess for excessive calories[30] - Co-morbid problems: review management of other problems
Steps for each medication trial for chronic neuro-pain
- Initiate a gabapentinoid: N-PRAT can guide decision to start - Define goals of treatment: e.g. pain reduction, improved sleep, improved feeding tolerance - Initial trial: 3-4 weeks - Initial sedation: can mean the drug is working - Sedation that persists with good symptom control: decrease other sedating drugs (e.g. benzodiazepine, baclofen) before attributing sedation to gabapentinoid - When to consider a 2nd or 3rd drug: symptoms persist after 1st dose maximized, new sources and co-morbid problems assessed, continue other drugs if adding 2nd or 3rd - Potential for less benefit with 3 or more trials given the inability to eliminate sources due to the impaired CNS; a time to revisit goals of care

Chronic Symptom Management Strategies *continued*

New breakthrough symptoms at time of good symptom control

- Assess for new pain source: see Acute Pain for evaluation
- Lessen GI tract distention: manage constipation, consider calorie decrease as metabolism may have decreased[32]
- Adjust medication plan when symptoms persist after first steps:
  - Maximize dose of chronic pain medications
  - Initiate 2nd or 3rd drug trial if episodes frequent and prolonged
  - Continue other medications when adding 2nd or 3rd
- Review management of co-morbid problems: GERD, spasticity, dystonia, sleep
- Symptoms can worsen in the hospital and during puberty then improve

Non-Pharmacologic strategies to promote comfort in children with SNI

Comfort strategies	Cuddling, rocking, massage, warm baths, music, adjusting enteral feed rate, venting gastrostomy tube
Positional	Repositioning, supportive seating systems, supportive bedding/mattresses
Sensory	Weighted blankets, vibratory mats and pillows
Integrative	Essential oils, aromatherapy, Reiki, craniosacral therapy, acupressure

Interventional Language Strategies: A Framework for Families

- Neuro-pain is a chronic form of pain due to alterations in the nervous system, often with recurrent episodes of different intensity. It can be improved but not fixed; breakthrough symptoms can still occur, just like breakthrough seizures can occur on treatment.
- There are no tests to confirm neuro-pain. Your son is at risk for this type of pain and has many of the features that occur with this type of pain. As an example, the nerves that send pain signals between the gut and brain are often part of this type of pain, causing gut symptoms in some. I recommend that we try a medication for neuro-pain.
- Muscle spasms and increased movement are common. Everyone tenses when in pain. Your son's brain makes his muscles tense much more when pain occurs. This can result in back arching, stiffening of legs, muscle tremors, and startling in children like your son.
- We will give you a plan to manage breakthrough symptoms. We will update this plan as we learn what helps your son most.
- Treatment will not mask pain from a new cause, such as pain from a bladder infection.
- I wish this was an easy form of pain to treat. This will get better, but I can't promise it will improve as much as we hope with the first drug. We will focus on the hoped-for benefit. If this doesn't occur, we will discuss next steps to make this better.
- I wish I could guarantee that this would be better within a week. For many children, this is a slow process over weeks to several months to figure out the plan that works best. Our team is available when needed. This can be hard with support needed throughout.
- This is complex and confusing; here is a summary of some of the information we discussed:
  - Courageous Parents Network
  - Complex Care Journal (Table 3 of Chronic Pain article)

Management of Neurological Problems		
Medications	**Initial dose (max starting dose)**	**Comments**
Autonomic Dysfunction / Dysautonomia		
CloNIDine 100mCg/mL, 500mCg/mL; 0.1mg, 0.2mg tabs; 0.1mg, 0.2mg, 0.3mg transdermal patch sizes	Days 1–4: 0.002 mg/kg (2mCg/kg) PO TID Days 5-8: 0.004 mg/kg (4mCg/kg) PO TID Option to start with once a day dose to minimize risk of sedation Option to increase: 0.02 mg/kg (20mCg/kg) per day average dose identified for spasticity[33] Autonomic storm: 0.003-0.006 mg/kg (3-6mCg/kg) q4hr PRN Sleep: 0.003-0.006 mg/kg (3-6mCg/kg) nightly	Better tolerated in children unable to stand; eliminates risk of fall from orthostatic hypotension Central-acting alpha-2-adrenergic receptor agonist, reducing sympathetic outflow
Gabapentin *(see page 13)*	Higher doses may be beneficial for children with SNI, up to 60-72 mg/kg/day[34-36]	*(see page 13)*
Propranolol 20mg/5mL, 40mg/5mL; 10mg, 40mg tabs	0.2-0.4 mg/kg PO q8hr (20 mg), increase q3-4 days up to 1.6 mg/kg q8hr (80 mg)	Beta-1 adrenergic receptor antagonist
Central Neuropathic Pain / Visceral Hyperalgesia		
Gabapentinoids, Tricyclic Antidepressants: See pages 13-14 for dosing guidelines		
Gabapentin	See Autonomic Dysfunction (*page 20*) for higher dosing	(*see page 13)*
Insomnia in children with SNI		
Melatonin	Higher doses may be beneficial for children with SNI due to altered pathways of arousal/sleep, up to 10-12 mg nightly[37,38]	Natrol™ reportedly has highest purity *(see page 28)*
Spasticity		
Baclofen 10mg tab	2.5–5 mg PO TID; increase q 3 days by 5–15 mg/day up to a max of 60-80 mg/day	Modulates GABA-B receptors
TiZANidine	0.04–0.08 mg/kg (4 mg) PO QHS, increase up to 0.16 mg/kg q8hr (max 8-12mg q8hr)	Less experience in younger children *Recommend collaboration w/ neurology & psychiatry*
CloNIDine	*See Autonomic Dysfunction, page 20*	
DiazePAM 2mg, 5mg tabs	0.03–0.05 mg/kg (2 mg) PO or IV q6-8hr, titrate to effect (max 10 mg)	Not recommended for long term use
Dystonia		
Trihexyphenidyl 2mg/5mL; 2mg, 5mg tabs	0.1-0.2 mg/kg/day in 2 to 3 divided doses; doses as high as 2.6 mg/kg/day in 3 divided doses described in children	Anticholinergic *Recommend collaboration w/ neurology & psychiatry*
CloNIDine	Status dystonicus: 0.003-0.006 mg/kg (3-6mCg/kg) q4hr PRN[39]	Higher doses for inpatient
Myoclonus		
ClonazePAM 0.1mg/mL; 0.125mg, 0.25mg, & 0.5mg tabs	0.005–0.01 mg/kg PO q8-12hr (0.5 mg), up to 0.2 mg/kg/day	May result in hypersalivation

Management of Neurological Problems *continued*		
Seizures: acute therapy for prolonged seizure		
LORazepam 2mg/mL; 0.5mg, 1mg, 2mg tabs	0.1 mg/kg (4–6 mg) PO/SL/PR/IV q15 min x 2	Home care plans can be adjusted as goals of care change, such as repeating breakthrough benzo several times followed by scheduled taper dose for 2 days
Midazolam 2mg/mL, 5mg/mL	0.2 mg/kg SL, intranasal, or IV (10 mg) x 2; 5mg/mL with mucosal atomization device (MAD) for intranasal	
DiazePAM 2.5mg, 5mg, 10mg rectal gel	2–5 years: 0.5 mg/kg q15 minutes x 3 6–11 years: 0.3 mg/kg q15 minutes x 3 > 12 years: 0.2 mg/kg q15 minutes x 3	

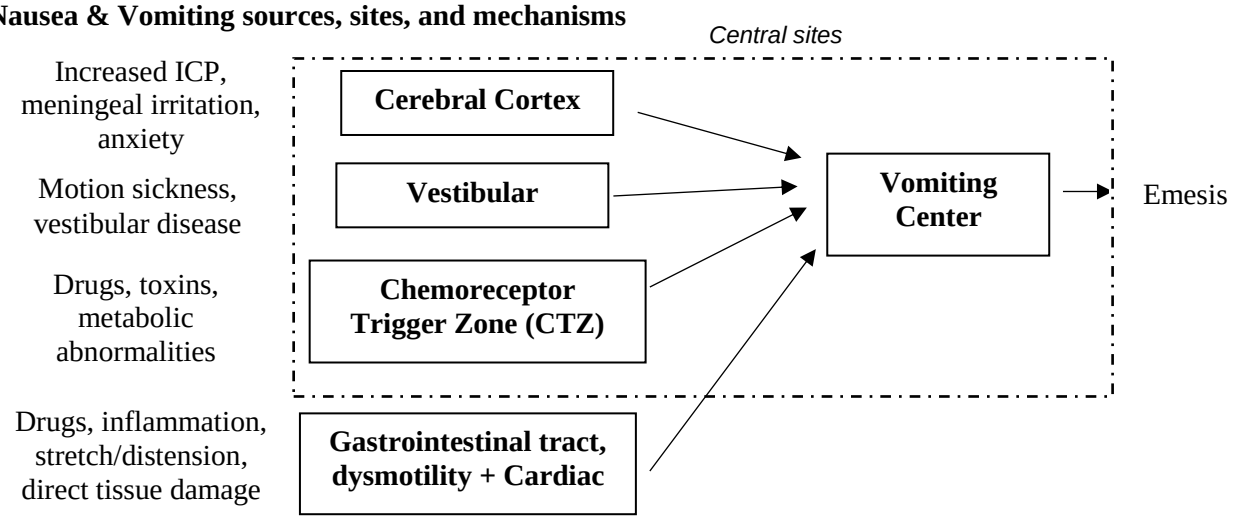
Clinical Framework to Approaching Headaches in PPC

1. Consider differential
2. Collaborate with primary and consulting teams (neurology, neuro-oncology, pain team, psychiatry)
3. Consider role of medication overuse
4. If this is a patient with a brain tumor, recommend providing recommendations as you would for severe cancer pain
   - Consider steroids, celecoxib, +/- opioids

Evaluation and Approach to Nausea & Vomiting

1. Thorough evaluation (H&P), in-depth assessment including other symptoms
2. Reverse or treat underlying cause (if possible)
3. Non-pharmacological approaches
   - Avoid noxious smells, small meals
   - Pericardium 6 (P6) pressure point; SeaBands
   - Ginger, peppermint
   - Aromatherapy (Lemon/citrus, peppermint)
4. Pharmacological approach based on underlying mechanism
   - May include multiple mechanisms
   - Use medications targeting different receptors
   - Reassess regularly

Nausea & Vomiting sources, sites, and mechanisms



Nausea & Vomiting			
Potential Causes	**Receptors / Mechanisms to Target**	**Therapeutic Agents**	**Sites**
Medications chemo, opioids, antibiotics, AEDs Metabolic hyponatremia, hypercalcemia, acidosis, uremia Toxins bacteremia, ischemic bowel	Serotonin (5-HT_3) Dopamine (D_2) Neurokinin (NK_1)	*Serotonin antagonists* (Olanzapine, Granisetron) *Butyrophenones* (Haloperidol, Droperidol) *Atypical antipsychotic* (OLANZapine) *NK_1 antagonists* (Aprepitant)	Chemoreceptor Trigger Zone (CTZ) *Floor of fourth ventricle, at blood brain barrier*
Disorders of the vestibular nucleus and CN VIII	Histamine (H_1) Acetylcholine (Ach)	*Antihistamines* (DiphenhydrAMINE) *Anticholinergics* (Scopolamine, meclizine)	Vestibular
Mechanism is unclear	Histamine (H_1) Acetylcholine (Ach)	*Anticholinergics* (Scopolamine)	Vomiting Center (VC) *Final common pathway*
	Serotonin	*$5HT_2$ antagonists* (Cyproheptadine)	
Increased intracranial pressure, tumor, infection	Stimulation of the VC	Corticosteroids	Meningeal Mechanoreceptors
Anxiety	Stimulation of CTZ and VC	Relaxation techniques, Benzodiazepines, Cannabinoid agents	Cortex
Acid reflux		*H2-Blockers*, *Proton pump inhibitors* (Ranitidine, Omeprazole)	
GI motility		*Prokinetic Agents*, (Metoclopramide, Cyproheptadine) *Constipation*	

Medications for Nausea/Vomiting/Retching (receptor blocking properties indicated)		
Medication Formulation	**Dosing and route**	**Comments**
$5HT_2$ and $5HT_3$ Serotonin Antagonists		
Ondansetron 4 mg/5 mL; 4mg, 8mg tabs	0.15 mg/kg PO/IV q8hr (4-8 mg; 24mg/day max)	Causes constipation
Granisetron 1 mg tab; 3.1mg/24hr patch	40 mCg/kg PO/IV q12-24hr (daily doing for <6 months, otherwise q12hr dosing)	
Atypical Antipsychotic		
OLANZapine 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20 mg tabs	1.25-2.5mg PO daily, increase weekly if needed, up to 20mg daily ODT not available in 2.5mg/7.5mg	Targets D_2, $5HT_2$, $5HT_3$, H_1; treatment of delayed CINV; also helpful with insomnia

Medications for Nausea/Vomiting/Retching (receptor blocking properties indicated) *continued*		
Medication / Formulation	**Dosing and route**	**Comments**
Dopamine Antagonists (D_2)		
Metoclopramide 5mg/5 mL; 5mg, 10mg tabs	1 mg/kg/dose IV prior to chemotherapy, then 0.0375 mg/kg/dose PO/IV q6hr	Higher doses for CINV; risk of EPS/NMS → *administer with diphenhydrAMINE; c*an also be helpful in dysmotility
Haloperidol 2mg/mL; 0.5mg, 1mg, 2mg tabs	0.01-0.02 mg/kg PO q8hr PRN (0.5-1 mg)	Risk of EPS
Anticholinergic		
Scopolamine 1.5mg TD patch	>age 12: 1.5mg by transdermal patch q72hr	
Neurokinin-receptor Antagonists		
Aprepitant 40mg, 80mg, 125mg tabs *Suspension form available*	>6 months: 3 mg/kg PO (max 125 mg) on day1, then 2 mg/kg q day (max 80mg) Adolescents: 125 mg PO 1hr prior to chemo, then 80mg q day	Increases neurotoxicity of some chemotherapy (ifosfamide)[40]
Corticosteroids		
Dexamethasone 0.5mg/5 mL, 1mg/1mL	0.1 mg/kg PO/IV q6hr (max 16 mg/day)	Best for edema; Can disrupt BBB, avoid in brain tumors
Dysmotility, Prokinetic Agents		
Cyproheptadine 2mg/5 mL; 4mg tab	0.08 mg/kg PO TID or QID (up to 8 mg) If no benefit in 5 days, increase each dose by 0.04-0.08 mg/kg	Targets $5HT_2$, H_1 & Ach; may benefit children with retching and feeding intolerance
Miscellaneous		
LORazepam 2mg/mL; 0.5mg, 1mg, 2mg tabs	0.02-0.05 mg/kg PO/SL/IV/subQ q6hr, PRN (1-2 mg)	Use for anticipatory nausea
Dronabinol 2.5mg, 5mg, 10mg capsules	0.05-0.1 mg/kg PO q12hr (2.5-5 mg) May increase if tolerated to max of 10mg bid Typically recommend use in ages > 6 years old	Cannabinoid – THC; avoid late PM dose (vivid dreams)

Abbreviations: CINV=chemotherapy-induced nausea and vomiting, EPS= extrapyramidal symptoms, NMS = neuromalignant syndrome, BBB= blood brain barrier

Anorexia/Weight Loss		
Medication Name	**Dosing and route**	**Comments**
Dronabinol *See above, page 23*	0.05-0.1 mg/kg PO q12hr (2.5-5 mg) May increase if tolerated to max of 10mg BID	Late afternoon/evening doses associated with colorful dreams (may be distressing)
Cyproheptadine *See above, page 23*	0.08 mg/kg PO TID or QID (up to 8 mg) If no benefit in 5 days, increase each dose by 0.04-0.08 mg/kg	May cause sedation, start dose low and escalate slowly

Constipation *(see management of opioid side effects page 12)*		
**** Mush (osmotic) + push (stimulant) + and whoosh (enema)****		
Polyethylene Glycol (osmotic) 17gm/packet	0.7-1.5 gm/kg q day (8.5 – 17 g q day)	Most effective given as 'bolus' dose (not sipped over long period)
Lactulose (osmotic) 10gm/15 mL	15-30 mL PO bid or 5-10 mL q2hr until stool	Also used for hyperammonemia; may cause cramping
Milk of Magnesia (osmotic) 400mg/mL	2-6 yrs: 400-1200 mg/day (single or divided doses) 6-12 yrs: 1200 -2400 mg/day >12 years and adolescents: 2400-4800/day	Best if taken with 8oz water
Bisacodyl (stimulant) 5mg tab; 10mg supp	3-10 yrs: 5 mg q day 10-12 yrs: 5-10 mg q day >12 yrs and adolescents: 5-15 mg q day	Tab should not be crushed or chewed
Senna (stimulant) 8.8mg/5 mL; 8.6mg, 15mg tabs; Sprinkles; 10mg supp	2-6 yrs: 2.5-3.75 mL q day; (1/2 tab q day) >6-12 yrs: 5 – 7.5 mL q day; (1 tab/day) >12 years and adolescents: 10-15mL q day; (2 tab/day)	Also available in combination with docusate; sprinkles may be eaten plain, mixed with liquids such as milk to make a drink, or sprinkled on food
Sodium phosphate (enema) Fleet®	1 PR every other day as needed	Risk of electrolyte disturbances, caution in patients with cardiac/renal disease; avoid in immunocompromised patients
Glycerin suppository	1 PR daily Pediatric supp for children <6 Adult supp for children >6	Avoid rectal medication administration in immunocompromised patients
Mu receptor antagonists (opioid-induced constipation)		
Methylnaltrexone	0.15 mg/kg (max 8-12 mg) q48hr IV/subQ[11]	Subsequent doses (no more than every 24 hours) may be needed
Naloxone[41, 42]	0.25-2 mCg/kg/hr IV continuous infusion	Doses over 2 mCg/kg/hr may reverse systemic opioid effects
Naloxegol[43] (pegylated form of naloxone) 12.5mg, 25mg tabs	25 mg PO q day If not tolerated, reduce dose to 12.5 mg q day	Take 1 hour before or 2 hours after meals; interacts with -azoles
Intestinal Motility		
Erythromycin 200mg/5 mL	2-5 mg/kg PO QID (max 250 mg per dose)	Risk of QTc prolongation with other meds; may cause nausea
Cyproheptadine 2mg/5 mL; 4mg tab	0.08 mg/kg PO TID (4 mg) If no benefit in 5 days, increase each dose by 0.04-0.08 mg/kg	May cause sedation, start dose low and escalate slowly
Metoclopramide 5mg/5 mL; 5mg, 10mg tabs	Prokinetic: 0.1-0.2 mg/kg PO/IV q6hr (5-10 mg)	Do not need diphenhydrAMINE for EPS with this dose
Bowel Obstruction		
Octreotide	0.001-0.002 mg/kg (1-2 mCg/kg) subQ, IV q8hr **OR** 0.003-0.006 mg/kg/day (3-6 mCg/kg/day) continuous	Concern for gut ischemia; initiated in ICU unless DNR order in place.

Evaluation and Approach to Diarrhea

1. Thorough evaluation (H&P), in-depth assessment including other symptoms
2. Reverse or treat underlying cause (if possible)
   - *Potential causes*: malabsorption (e.g. short gut), infection, bacterial overgrowth, medications (e.g. antibiotics, magnesium, laxatives), radiation therapy, constipation with overflow/leakage
3. Non-pharmacological approaches
   - Diet: bland, no dairy, added fiber to increase stool bulk
   - Barrier creams to protect skin
4. Pharmacological approach based on underlying mechanism
   - Loperamide (non-absorbable opioid that directly reduces intestinal motility): discontinue when no diarrhea for 12 hours; for radiation-induced diarrhea – continue for the duration of radiation
   - Low dose opioid, consider deodorized tincture of opium
   - Octreotide – for severe diarrhea, especially if bleeding; reduces output in cramping *(see page 24)*
   - Special cases:
     - Irinotecan acute diarrhea (cholinergic mechanism): Atropine
     - Irinotecan delayed diarrhea (direct epithelia toxicity): Antibiotics (cefixime), activated charcoal

Evaluation and Approach to Itching

1. Thorough evaluation (H&P), in-depth assessment including other symptoms
2. Reverse or treat underlying cause (if possible)
   - *Potential causes*: dermatologic (e.g. irritation), immunologic (e.g. allergy), drug effect (e.g. opioids), other systemic disease (lymphoma, iron deficiency, liver or renal failure), psychogenic
3. Non-pharmacological approaches
   - Emollients to reduce xerosis
   - Avoid hot baths/showers
   - Oatmeal baths, cooling agents (e.g. Calamine, Sarna™)
   - Cold packs to soothe skin
   - Address pain, boredom, or anxiety, which can worsen itch
4. Pharmacological approach based on underlying mechanism
   - Antihistamines if associated histamine release (diphenhydrAMINE, hydroxyZINE, doxepin for refractory cases)
   - Topical steroids for inflammation (ointment best, if severe consider systemic)
   - Ondansetron (*see page 22)*
   - Aprepitant[44] (cancer biologics, lymphoma) (*see page 23)*
   - Special cases:
     - Cholestatic pruritis: bile duct stenting, cholestyramine, ondansetron, naloxone, naltrexone
     - Uremic pruritis: gabapentinoid, aprepitant, paroxetine

Evaluation and Approach to Respiratory Symptoms

1. Thorough evaluation (H&P), in-depth assessment including other symptoms
2. Reverse or treat underlying cause (if possible)
3. Non-pharmacological approaches

Dyspnea	*Secretions*
- Air circulation and fan	- Optimize positioning
- Breathing training	- Provide gentle suction
- Relaxation and self-hypnosis	- Reduction of fluid intake
- Occupational and music therapy	
- Acupuncture and acupressure	
- Physical therapy	
- Modification of activity	
- Noninvasive positive pressure ventilation	

4. Pharmacological approach based on underlying mechanism
   - Reassess regularly

Respiratory Symptoms		
Medication Formulation	**Usual Starting Dose & Interval**	**Comments**
Dyspnea		
Morphine (or opioid equivalent) 10mg/5 mL, 20mg/mL	0.05-0.1 mg/kg PO or 0.015-0.03 mg/kg IV/subQ q3-4hr PRN (5 mg PO, 2.5 mg IV) (or other opioids at equivalent dose)	Typical starting dose 50% of starting dose for pain medication
LORazepam *(see page 23)*	0.02-0.05 mg/kg PO/SL/IV/subQ q4-6hr PRN (max 2 mg)	DiazePAM and ClonazePAM may increase secretions
Oxygen	*Only helpful if patient is hypoxemic, otherwise recommend handheld fan directly to face to improve airflow*	
Secretions		
Ipratropium	250-500mCg nebulization/MDI q4-6hr PRN	
Glycopyrrolate 0.2mg/1mL; 1mg, 2mg tabs	40-100mCg/kg/dose (1-2mg) PO q4-8hr[45] 0.004-0.005 mg/kg (4-10 mCg/kg) IV q3-4hr	Does not cross BBB = less CNS toxicity and side effects
Atropine[46] 1% ophthalmic drops	Initial: 1 -2 drops q 2-4hrs Usual dose range: 2 to 4 drops q 2-4hrs	
Scopolamine Patch (HyoSCINE)	Adolescents: 1.5 mg transdermal patch q72hr	Takes 24 hours to reach steady state; for acute symptoms other drugs should be used
HyosCYAamine 0.125mg/1 mL; 125mCg tablet (SL)	0.125 mg/1 mL solution 3-4 kg 4 drops PO q4hrs PRN 10 kg 8 drops PO q4hrs PRN 50 kg 1 mL (0.125 mg) PO q4hrs PRN	0.125 mg/5 mL elixir also available

Evaluation and Approach to Mood & Sleep Disturbances
It can be difficult to distinguish anxiety, agitation (unpleasant state of arousal), and delirium (fluctuating disturbance of consciousness with acute onset over hours to days). **Consider sources with similar features**: pain, impaired sleep, depression, metabolic disturbances, medication reactions, and progression of a neurodegenerative condition. Children with neurological impairment (NI) of the CNS can have a number of problems that result in agitation and irritability (neuropathic pain, visceral hyperalgesia, dysautonomia, muscle spasms). *See pages 17-20* for symptom treatment guidelines and suggestions in children with NI.
1. Thorough evaluation (H&P), in-depth assessment including other symptoms 2. Reverse or treat underlying cause (if possible) 3. Non-pharmacological approaches - Close collaboration with psychosocial provider & psychiatry. Consider psychotherapy, hypnotherapy, and/or cognitive behavioral therapy - Create schedule/routine - Provide proper day/ night orientation o Remind the child of where he is and what time of day it is. o Keep lights on and window shades open during day/ off and closed at night. o Encourage the child to be out of bed during the day. o Turn screens off at night - Provide familiar and comforting items to the child (toys, blankets, music). - Provide glasses or hearing aids if needed 4. Pharmacological approach based on underlying mechanism - Reassess regularly

Mood & Sleep Disturbances		
Medication Formulation	**Usual Starting Dose & Interval**	**Comment**
Anxiety		
LORazepam *(see page 23)*	0.02-0.05 mg/kg PO/SL/IV/subQ q6hr PRN (1-2 mg)	May worsen delirium
ClonazePAM *(see page 20)*	0.005-0.01 mg/kg PO q8-12hr (up to 0.25-0.5mg/day)	*Consider collaboration with psychiatry*
Agitation, Delirium		
Haloperidol 2 mg/mL; 0.5mg, 1mg, 2mg tabs	0.01-0.02 mg/kg IV*/PO q8hr PRN (0.5-1 mg) For acute agitation: 0.025-0.05 mg/kg PO/IV, may repeat 0.025 mg/kg in one-hour PRN	IV side effects typically worse than PO; *IV administration limited to ICU unless DNR order in place Risk of QTc prolongation with other medications
RisperiDONE 1mg/1mL; 0.25mg, 0.5mg, 1mg tabs	0.25-0.5mg PO QHS or divided, titrate every 1-2 days, (max 3mg total/day)	Consider as short-term therapy with steroid induced behavior[47]

<table>
<tr><th colspan="3">Mood & Sleep Disturbances continued</th></tr>
<tr><td colspan="3">Anxiety, Agitation, Delirium, Insomnia (if insomnia related to anxiety, agitation, delirium)</td></tr>
<tr><td>OLANZapine
See page 22</td><td>1.25mg-2.5mg PO daily, increase weekly if needed, up to 20mg daily</td><td>Not available IV
ODT not available in 2.5mg or 7.5mg</td></tr>
<tr><td>QUEtiapine
25mg, 50mg, 100mg, 200mg tabs</td><td>25mg BID increase daily by 25 mg/dose, (titrate as necessary to 450mg/day)
ER 50mg, 150mg tabs</td><td></td></tr>
<tr><th colspan="3">Sleep Disturbances</th></tr>
<tr><th>Medication
Formulation</th><th>Usual Starting Dose & Interval</th><th>Comments</th></tr>
<tr><td colspan="3">Insomnia</td></tr>
<tr><td>Melatonin
2mg, 3mg, 5mg tabs</td><td>1mg in infants
2-3mg PO QHS may increase to 6mg
(see page 20)</td><td>Common side effects include nightmares and headaches; Natrol™ reportedly has highest purity</td></tr>
<tr><td>Hydrocortisone[48]</td><td>Physiologic dose (10 mg/m^2/d) while receiving steroid (dexamethasone) for steroid induced insomnia</td><td></td></tr>
<tr><td>TraZODone
50mg, 100mg, 150mg tabs</td><td>0.75-1 mg/kg PO QHS (25-50 mg), increase every 1-2 weeks up to 150mg</td><td></td></tr>
<tr><td>CloNIDine
(see page 20)</td><td>0.002 mg/kg (2mCg/kg) PO QHS (0.1 mg), increase by 0.002 mg/kg (2mCg/kg) PO QHS if needed, (max 0.008 mg/kg = 8mCg/kg QHS) (0.4 mg)</td><td></td></tr>
<tr><td>Zolpidem
5mg, 10mg tabs</td><td>Children <17 years limited data start at 0.25 mg/kg at bedtime; (max 10 mg/dose)

>18 years 5 mg QHS for females 5-10mg QHS for males; (max 10mg/daily)

Extended release 6.25mg Female and 6.25-12.5mg in Males[49]</td><td>Recommend avoiding driving the day after use
Available in immediate and extended release</td></tr>
<tr><td colspan="3">Fatigue</td></tr>
<tr><td>Methylphenidate[50]
5 mg/5 mL,
10 mg/5 mL
5mg, 10mg tabs

Chewable: 2.5mg, 5mg, 10mg tabs</td><td>0.05-0.1 mg/kg q am and q noon (2.5-5 mg) scheduled or use PRN for directed therapy
<table><tr><th>Patch Size Daytrana™ (mg/9 hour)</th><th>Immediate Release (mg/day)</th></tr><tr><td>15</td><td>22.5</td></tr><tr><td>20</td><td>30</td></tr><tr><td>30</td><td>45</td></tr></table></td><td>Duration of action 1-4 hours; give 30 minutes before desired effect (and 6 hours before bedtime to avoid insomnia)</td></tr>
</table>

Depression[51,52] *Close collaboration with psychosocial provider & psychiatry.*		
Medication Formulation	**Usual Starting Dose & Interval**	**Comments**
Psychostimulants		
Methylphenidate *(see page 28)*	2.5-5 mg before breakfast or twice daily before breakfast and lunch; may increase based on response 2.5-5 mg every 1-4 days up to 20 mg twice daily	Helps mood & fatigue associated with opioid usage, psychomotor slowing, & cognitive impairment within 24-48 hours Consider use for depression as monotherapy at the end of life, otherwise consider use as adjunct therapy until antidepressant effective Improved analgesia of opioids
Selective Serotonin Reuptake Inhibitor (SSRI)		
Escitalopram 5mg/5 mL; 5mg, 10mg, 20mg tabs	Children >12 yrs 5-10 mg daily *FDA indication for pediatric depression & few drug interactions*	Assess for suicidal ideation given black box warning Consider drug-drug interactions (such as serotonin syndrome risk)
Citalopram 10 mg/5 mL; 10mg, 20mg tabs	5-10 mg daily; may be increased 5mg/day q2 weeks up to 20-40 mg/day *Risk of QTc prolongation with other meds*	Because they lack anticholinergic effects, SSRIs are preferred for patients with slowed intestinal motility or urinary retention Dose-related side effects common (headache, jitteriness, agitation, sexual dysfunction, diarrhea, nausea, and insomnia) & may subside after 4-7 days
Selective Norepinephrine Reuptake Inhibitors (SNRI)		
DULoxetine *(see page 14)*	Children > 7 years old 20-40 mg daily; may be increased 20mg/day q2wks up to 60 mg/day	Also helpful with chronic pain *(see page 14)*
Tetracyclic Antidepressants (TeCA)		
Mirtazapine 15mg, 30mg tabs (available as dissolving tab)	7.5mg QHS; may be increased 15mg/day weekly up to 45 mg/day	Anti-emetic & few drug interactions; side effects sedation & weight gain; sedating at lower doses and activating at higher doses

Significant Toxicity Syndromes		
The most common medication categories to consider include: antidopaminergic (neuroleptics) and SSRIs, paradoxical reactions possible with anticholinergics, benzodiazepines, and antihistamines ***Consider using the Lexicomp Drug Interactions Tool***		
Category	**Associated features**	**Potential causes** (partial list: drugs commonly implicated)
Serotonin syndrome	tachycardia, hypertension, hyperthermia, diaphoresis, mydriasis, diarrhea, hyperreflexia, clonus, agitation, and rigidity	selective serotonin reuptake inhibitors (SSRIs); other drugs, often when used in combination: traMADol, FentaNYL, traZODone, risperiDONE, linezolid, ondansetron, metoclopramide
Neuroleptic malignant syndrome	extrapyramidal effects, muscle rigidity, autonomic dysfunction, hyperthermia, altered mental status	most commonly caused by dopamine antagonists (metoclopramide, neuroleptics), abrupt stop of anticholinergics
Tardive dyskinesia, Dystonia	abnormal movement and posturing, agitation	dopamine antagonists (metoclopramide, haloperidol, risperiDONE)
Akathisia (unpleasant state of motor restlessness)	restlessness, distress, tension and discomfort	dopamine antagonists, TCAs, SSRIs, withdrawal from opioids, paradoxical reactions

PC Approach to Managing Escalating Symptoms at End-of-Life [53,54]

Must have an understanding of patient & family goals prior to escalation of medications

Consider the following interventions in all patients	**Specific considerations for children with sensory neural impairment**
Tailor medications and interventions so they are consistent with family goals Vital signs and respiratory support may be modified / weaned Consider holding feeds and/or fluids for the following: - Acute ileus presenting w/ abdominal distention and pain - Peripheral edema - Severe pulmonary congestion Discussion around labs &/or diagnostic procedures	Metabolism declines in the months preceding EOL Consider a reduction of feeds and fluids IF any of the following are noted: - Irritability and pain without a clear source and not responding to adjustments in medications - Escalating respiratory symptoms and secretions - Persistent emesis and feeding tolerance *Reduce by 30% or greater as initial trial, adjust further as needed* Continue medications for seizures, spasticity, and pain Tailor medications and respiratory therapies so they are consistent with family goals

Other Considerations

- Focus on what WILL be done to care for the child
- Consider touchpoints with team, bedside nurse, interdisciplinary team
- Determine most appropriate administration route for patient (oral, IV, TD, subQ)
- Consider adjuvants (e.g., NSAIDs, benzodiazepine, corticosteroids, ketamine)
- Use the term "discontinue" versus "withdrawal"
- Remember other distress (e.g. psychosocial, spiritual) can aggravate symptoms

Rapid Opioid Escalation

<u>If patient is on PCA:</u> → give loading dose 10% of total opioids from preceding 2 hours AND increase PCA/NCA settings

<u>If patient NOT on PCA:</u> → start PCA/NCA and give loading dose

- If symptoms recur, increase PCA dose and continuous by 30%-50% for moderate symptoms, 50-100% for severe symptoms
- Continue opioid titration until symptoms relieved
- No <u>MAX</u> dose for EOL symptoms.

Opioid Rotations

Inadequate analgesia at EOL usually requires dose escalation, not opioid rotation. Consider adding additional analgesics such as methadone or adjunctive therapies
If the patient has significant opioid adverse effects **<u>with</u>** adequate pain control, reduce the equianalgesic dose of the new opioid by 25-50%
If the patient has significant opioid adverse effects **<u>without</u>** adequate pain control, rotate opioid without a reduction in the equianalgesic dose

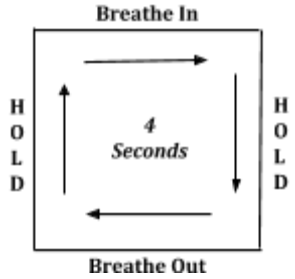
Frequently Used Medications at the End-of-Life (In-patient and/or Hospice Care)		
Symptom	**Medication** (Hospice formulation)	**Dosing**
Agitation, delirium, nausea	**Haloperidol** (2mg/mL) *PO/SubQ/SL/IV*	0.01-0.02 mg/kg PO q8hr PRN (0.5-1 mg) For acute agitation: 0.025-0.05 mg/kg PO, may repeat 0.025 mg/kg every hour PRN
Excessive bleeding / hemorrhage	**Aminocaproic Acid** Oral/IV/Topical	Apply topically to bleeding (i.e. gums, nose). Oral/IV 100-200mg/kg load, then 100mg/kg/dose q6hr, (max daily dose 30g)
	Tranexamic Acid Oral/IV	12-25mg/kg/dose PO or 10mg/kg/dose IV up to QID
Dyspnea, agitation, seizures	**LORazepam** (2mg/mL) *PO/SubQ/SL/IV*	0.05-0.1 mg/kg SL/IV q4h (max 2mg) Seizure dosing: 0.1 mg/kg/g SL/IV, may repeat dose in 5-10min (max 4mg)
	Intranasal Midazolam *(Nayzilam™)*	Adult dose: 0.2mg/kg <50kg: 5mg >50kg: 10mg 5mg one spray into one nostril. Can repeat after 10 minutes in the other nostril. Do not repeat if the patient has excessive sedation or hard time breathing. Max 10mg per dose per episode (2 sprays).
Pain, dyspnea	**Morphine** (20mg/mL) *PO/SubQ/SL/IV*	0.05-0.1 mg/kg PO q2-4hr PRN (max 5mg) *pain dosing depends on patients' prior opioid needs. (*See page 6 & 26 for initial starting doses)*
Secretions	**Atropine** 1% ophthalmic solution *Oral*	1-2 drops SL q4-6hr PRN
Seizures	**ClonazePAM** *PO*	0.005-0.01mg/kg PO q8-12hr (0.25-0.5mg) increase up to 0.05-0.1mg/kg PO q8-12hr
	DiazePAM Rectal	2.5, 5, 10mg rectal gel 2–5 years: 0.5 mg/kg q15 minutes x 3 6–11 years: 0.3 mg/kg q15 minutes x 3 > 12 years: 0.2 mg/kg q15 minutes x 3
	PHENobarbital PO/PR	1-5 years 3-4 mg/kg PO/IV/subQ BID 5-12 years 2-3 mg/kg PO/IV/subQ BID >12 years 1-2 mg/kg (50-100 mg) PO/IV/subQ BID For terminal seizures: 15-20mg/kg IV/subQ load, followed by maintenance dose 4-6mg/kg/day PO/PR

Palliative Sedation *Used for refractory and distressing symptoms, usually in patients with very limited prognosis.* *Requires close collaboration with family, primary teams, Pain Service (if inpatient) or hospice team* ***Refer to Boston Children's Hospital Palliative Sedation Reference***	
Medication	**Considerations**
Midazolam	Midazolam enhances inhibition at GABA-A receptor Anxiolysis, seizure management, sedation Rapid on/off activity, helpful for respite sedation
PHENobarbital	Phenobarbital enhances inhibition at GABA-A receptor Seizure management, sedation
PENTobarbital	Requires a dedicated lumen Continuous infusion is to be started concurrently with the initial loading dose Slower on/off activity

Alternative Routes to Administration[55] *Recommend consultation with hospice or inpatient pharmacist for alternative routes and formulations.* *Refer to BCH Non-Intravenous (IV) Methods of Symptom Relief at End-of-Life (EOL)* *Refer to BCH End of Life Symptom Management Using Subcutaneous Route*		
Route	**Medication**	**Comments**
Sub-Q	Most medications can be given subQ, with a 1:1 (IV:SubQ)	
Rectal Medication (given at same dose)	CarBAMazepine	Dilute oral suspension with equal volume of water Can have a cathartic effect
	LamoTRIgine	Crush chewable/dispersible or compressed tab and mix with 6 mL of room-temperature tap water
	PHENobarbital	Use parenteral solution
	Valproic acid	Dilute oral suspension with equal volume of water Can have a cathartic effect

Integrative Medicine/Non-Pharmacologic Symptom Management Strategies[56]

Breathing: Breathing exercises can help us to focus on our breath while calming our nervous system. *Exercise: "Square Breathing"- Complete each step for 4 seconds. If helpful, you can trace the square edges with your finger with each step. Get creative, try with different shapes!*



Helpful scents/ Aromatherapy:[57] Essential Oils are plant-based compounds which can be inhaled (using a "scent stick") to help with various symptoms, here are five common scents:

	Pain	Nausea	Insomnia	Fatigue	Anxiety
Lavender	✦		✦		✦
Sweet Orange			✦		✦
Lemon		✦		✦	
Peppermint	✦	✦		✦	
Grapefruit		✦		✦	✦

Meditation / Guided Imagery: Meditation and guided imagery can be helpful with calming your nervous system and providing a distraction to unwanted symptoms such as nausea, pain, anxiety, and insomnia. You can do this exercise alone, silently, or with a partner to read the exercise aloud.

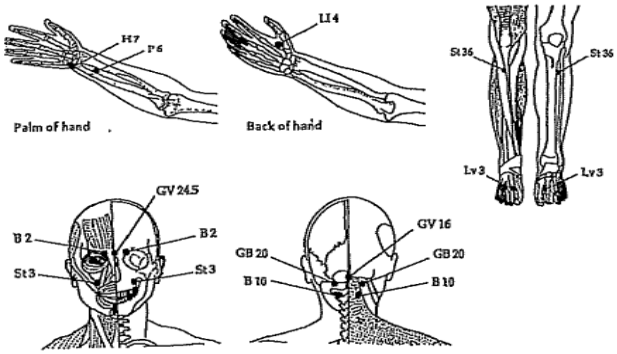
Exercise: Guided Imagery- Script
Begin by getting into a comfortable seat/lying position. Close your eyes or bring your focus to something in the room/environment. Begin focusing on your breathing, each inhale and exhale entering and leaving your body. Notice the pattern of your breath- without feeling the need to change the pattern at all.

Start to Imagine being in a place that makes you feel calm…What do you notice around you? What do you see, hear, smell, feel, or even taste? Now imagine you have come to this place to do your favorite activity… What activity is this? How does it make you feel? Bring your attention back to your breath. Each inhale and exhale. What do you notice about its pattern?

Begin to bring physical awareness back into your body by wiggling your fingers and toes. Open your eyes slowly if they were closed. Notice how you feel, physically, mentally, emotionally after this brief exercise

Art Therapy:[58] Art therapy can help reduce perceptions of pain experiences. It differs from a distraction tool and instead helps patients modify and move their mental focus away from difficult emotions (e.g. stress, anxiety, etc.) that accompany pain to promote self-soothing and relaxation. Art Therapy involves working with a registered or board-certified art therapist to create an art piece, then explore how it relates to their pain and reflect on its implications.

Acupressure: Acupressure stems from traditional Chinese medicine and involves stimulating acupuncture points, but pressure is used instead of needles to relieve pain. Acupressure can be helpful in the care of patients who experience nociceptive or neuropathic pain, both in the acute and chronic setting. (*Image below adapted from Acupressure's Potent Points by Michael Reed Gach*)



Commonly used acupressure points
Nausea/vomiting: P 6, St 36, K 9
Headache: LL4, Lv3, GB 20
General pain: LI4, Lv 3
Anxiety: H 7, P 6, GV 24.5
Other acupressure resources include weighted blankets, weighted vests, and SeaBands.

Music Therapy: Music therapy offers diversion, distraction, and enhanced relaxation and may benefit patients experiencing pain. Alongside a specialty trained music therapist, patients engage in active music making, lyric writing, and song selection that is meaningful to them

Self-Hypnosis:[59] Self-hypnosis strengthens a patient's existing or under-developed skills in self-regulation capacities in order to shift attention or maintain focused attention to transform the experience of symptoms or illness experience. Clinicians who receive specialty training in self-hypnosis can successfully "coach" patients to access therapeutic self-suggestions and exercises.

Yoga: Yoga is a physical, mental, and spiritual (not religious) practice that calms the mind and body using different poses, exercises, breathing and meditation.

**Exercise: Easy Relax/Wind Down yoga sequence:*

			
Head Tilt/Rotations	***Seated Spinal Twist***	***Seated Cat/Cow***	***Forward Fold***
can be done sitting / standing	*seated on floor or chair*	*seated on floor or chair*	*on ground or bed with pillow props*
Beginning w/ left ear touching left shoulder, circle head towards chest in clockwise rotation w/ eyes open or closed a few times and then reverse and repeat counterclockwise	In a comfortable seat, bring left hand to right knee, right hand behind you. Inhale extend spine upwards, exhale, twist deeper. Repeat, twisting to left.	Place both hands on knees. Inhale, pull chest through bent arms, providing a slight back bend. Exhale, round back, extending arms, gazing at your belly. Repeat.	Extend legs in front of you (w/ slight bend in knees if more comfortable). Place pillows on top of legs. Fold upper body & arms over pillows and breathe.

*****Helpful Applications & Additional Resources:*** There are many applications that offer additional resources and exercises related to mindfulness, meditation, yoga, self-hypnosis, breathing etc. These applications and more can be downloaded in the App Store.


Stop, Breathe, & Think


Headspace

Calm


Mind + Body

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