

Palliative Care Symptom Guide | 2023

UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

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Table of Contents:

Pain Management	
Assessment	
Adjuvant and Non-Opioid Agents for Pain	
Principles of Opioid Therapy	
Select Opioid Products	
Opioid Equianalgesic Equivalencies	
Patient Controlled Analgesia (PCA)	
Buprenorphine	9
Opioid Induced Constipation	
Prescribing Outpatient Naloxone	
Interventional Pain Management	
Medical Cannabinoids	
Dyspnea Assessment	15
Treatment	
Nausea and Vomiting Treatment	
Delirium	
Diagnostic Criteria	
Treatment	
Depression and Anxiety Treatment	
Oral Secretions	
Spirituality Pearls	
Palliative Care and Pain Resources	
Spiritual Care Resources	
Acknowledgements	

Assessment of Pain

For Patients Who Can Communicate: Consider the acronym: "PQRSTUV":

P: Precipitating (and Alleviating) Factors	"What makes the pain better/worse?"
Q: Quality	"How would you describe the pain?"
R: Region or Radiating	"Where is the pain? Does it go anywhere?"
S: Severity	"What is the pain (on a scale of 0 -> 10) – now/at best/at worse/on average?" *Must ask: "What level of pain is acceptable or tolerable?"*
T: Time and Temporal	"When did the pain start? How does it change throughout the day?"
U: previous Utilization	"What have you used previously?"
V: Values	"How is this pain inhibiting your daily life?"

For Patients Who Are Cognitively Impaired, or Cannot Communicate:

e.g.: Pain Assessment in Advanced Dementia (PAIN-AD) Scale:

Parameter:	0 Points	1 Point	2 Points
Breathing Independent of Vocalization	Normal	Occasional labored breathing. Short period of hyperventilation	Noisy, labored breathing. Long period of hyperventilation. Cheyne-stokes respirations
Negative Vocalization None		Occasional moan or groan. Low level Repeated troubled calling out. Loud moaning groaning. Crying	
Facial Expression Smiling or inexpressive Sad, frightened or frowning		Sad, frightened or frowning	Facial grimacing
Body Language Relaxed Tense, distressed pacing, or fidgeting		Rigid. Fists clenched, knees pulled up. Pulling or pushing away. Striking out	
Consolability	No need to console Distracted or reassured by voice or touch		Unable to console, distract, or reassure
		Provides Approx. Severity Score: 0-3: Mild Pain; 4-7: Moderate Pain; 8-10: Severe Pain	

References: Chalkley AJ, Mulhall DJ. The PQRSTUV: The Personal Questionnaire Rapid Scaling Technique. Br J Clin Psychol. 1991 May;30 (Pt 2):181-3. Warden V, Hurley AC, Volicer L. Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) scale. J Am Med Dir Assoc. 2003 Jan-Feb;4(1):9-15.

Adjuvant and Non-Opioid Agents for Pain

Based on Perceived Etiology of Pain:

	Class or Drug	Starting Dose/Route	Maximum Daily Dose (MDD) and Duration	Comments
	АРАР	650mg PO/PR q4h	MDD: 3-4,000mg; 2,000mg/day for those with hepatic impairment	Lacks anti-inflammatory effects of NSAIDs
	Acetaminophen	1000mg IV q6h	 IV Duration: ≤2 doses per UPMC policy 	Avoid in severe hepatic disease
		Ibuprofen 400mg PO q8h	• MDD: 3,200mg	
		Naproxen 250mg PO q12h	• MDD: 1,250mg	Caution in patients with gastric disease, renal impairment, decompensated heart failure, liver
	Common NSAIDs	Ketorolac 15-30mg IM/IV q6h	 MDD: 120mg. Elderly, renally impaired, and/or weight <50kg/dose = 10-15mg IM/IV Max Therapeutic Duration: 3-5 days 	impairment or at risk for bleeding. Use not recommended in CrCl < 30
Pain		COX-2 Selective		
ptive		Celecoxib 100-200mg PO BID	MDD: 400mg/day	Caution in patients with renal impairment,
Nociceptive		Meloxicam 7.5-15mg PO daily	• MDD: 15mg/day	decompensated heart failure, or at risk for bleeding; Use not recommended in CrCl < 30
No	Common Steroids*	Dexamethasone 4-8mg/day	 MDD: 8mg/day. Short courses are advised (< 2 weeks) 	Use with caution in patients with heart failure, risk of bleeding, or on immunotherapy. Use in close coordination with primary teams.
	Common Topicals	Lidocaine 4 or 5% Patch 1-3 patches topically daily	MDD: 3 patches/day	Typically removed after 12 hours of administration to avoid toxicity. Do not use heating pad on patch to avoid skin reactions.
		Diclofenac 1% Gel 2-4g topically to painful area	• MDD: 32g/day	Dosage card for patients included in packaging. 2g for upper extremities, 4g for lower extremities. Minimal systemic absorption.

*limited to most used in the palliative care setting

References: UPMC Policy and Procedure Manual: Pain Management Policy (HS-NA0408). Available on UPMC infonet.

2

Based on Perceived Etiology of Pain:

	Class or Drug	Starting Dose/Route	Maximum Daily Dose (MDD) and Duration	Comments
	Anti-	Gabapentin 300mg PO HS	 MDD: 3,600mg No additional benefit seen >1800mg/day 	 Reduce dose in renal insufficiency (CrCl <60mL/min) Post-dialysis supplementation dose recommended
	epileptics	Pregabalin 75- 150mg/day in 2-3 divided doses	 MDD: 450mg-600mg/day depending on indication 	 Reduce in renal insufficiency (CrCl < 60mL/min). Use with caution in patients with congestive heart failure
Pain	SNDIa	Venlafaxine 37.5mg XR PO once daily	 MDD: 300mg/day No additional benefit seen >150mg/day 	 Reduce dose in mild and moderate renal insufficiency Avoid in severe renal and hepatic insufficiency
Neuropathic Pain	SNRIs	Duloxetine 30mg PO once daily	 MDD: 90mg/day No additional benefit seen > 60mg/day 	 Avoid in severe renal insufficiency Contraindicated in hepatic insufficiency
Neuro	Common	Amitriptyline 10mg- 25mg PO daily	 MDD: 75-150mg/day depending on indication 	 High anticholinergic burden; caution for use for older adults. QTc prolongation risk Reduce dose in severe hepatic impairment
	TCAs	Nortriptyline 10- 25mg PO daily	• MDD: 150mg/day	 Anticholinergic side effects; QTc prolongation risk Reduce dose in severe hepatic impairment
	Common Topicals	Capsaicin 0.075%- 0.1% cream	 MDD: 4 patches in one application, Cream can be used up to 4x/day 	 Do not apply on damaged or broken skin; do not use with external heat source (e.g. heating pad) Minimal systemic absorption

3

References: UPMC Policy and Procedure Manual: Pain Management Policy (HS-NA0408). Available on UPMC infonet.

Product Information: NEURONTIN®, gabapentin. Pfizer, Inc. (per FDA), NY, NY, 10/2017.; Product Information: LYRICA®, pregabalin. Pfizer, Inc. (per FDA), NY, NY, 6/2011. Product Information: EFFEXOR XR®, venlafaxine XR. Pfizer, Inc. (per FDA), NY, NY 1/2017. Product Information: CYMBALTA®, duloxetine. Eli Lilly and Company. (per FDA), Indianapolis, IN. 10/2010. Product Information: Amitriptyline. Sandoz, Inc. (per FDA) Princeton, NJ. Product Information: Notriptyline. Mallinckrodt, Inc. (per FDA), Hazelwood, MO.

Initiating Opioids:

	Are opioids appropriate for the patient's specific pain(s)? Some types of pains do not respond well to opioids
Appropriate?	Always screen patients for risk factors for opioid misuse upon initiation of opioid therapy. <i>Must check PA PDMP*</i> Can also consider utilizing the Opioid Risk Tool (ORT)
Adjuvants?	Adjuvants should always be considered for pain. See slide 2 for more information

Throughout Opioid Therapy: Monitor for the 4As

Analgesia	Has the current medication regimen improved the patient's pain scores?
Activity	What is the patient's specific goal? This may not be just a reduction in severity. Consider functional goals as well
ADRs	Is the patient experiencing any opioid-induced effects? Must ask the patient about each potential effect individually
Abuse	 Screen for abuse: Personal or family history of alcohol, tobacco or substance abuse Younger age (less than 35 years of age) Psychiatric disease such as anxiety, bipolar disorder, PTSD; particularly if uncontrolled Red flags suggesting opioid misuse: Asking for specific opioid medication/formulation/brand, or for early refills or early prescriptions; inability to control use; inappropriate urine drug screen results (negative for prescribed substances or positive for non- prescribed substances) Receiving prescriptions from different providers* Must check PA-PDMP prior to every opioid prescription * Pennsylvania PDMP website: <u>https://pdmp.health.pa.gov/cas/login</u>

Principles of Opioid Therapy (cont.)

Initiating Opioids:

- 1. Determine drug:
 - Morphine is considered first-line therapy. Consider for all patients (except for renal failure and true allergy)
- 2. Determine dose:
 - Start low and go slow
 - Be aware of commercially available oral formulations
- 3. Determine **route**:
 - PO route is preferred. IM route is not recommended
- 4. Determine **frequency**:
 - Never use long-acting opioids to control acute pain
 - For opioid naïve patients, only prescribe short-acting agents as needed (PRN)

Titrating Opioids:

- Titrate no faster than every 24 hours
 - First, calculate previous 24 hour OME total
 - If response is inadequate consider increasing 25-50% for moderate pain and 50-100% for severe pain
 - If adding a long-acting agent: Give 2/3 of total OME as long-acting. Give 10-15% of total daily long-acting agent OME as short acting breakthrough agent (PRN).

Recommended interval for breakthrough dose is 3-4hours.

Rotating Opioids:

Primary reasons to rotate opioids are: presence of intolerable adverse drug reaction or drug allergy and/or renal failure, and insurance coverage and/or cost issues

Converting Opioids:

- 1. Assess patient
- Determine total daily dose of opioid
- 3. Decide new opioid and route; consult equianalgesic table and calculate new opioid dose

mg of current opioid (& form) Equivalent mg current opioid (& form)

"X" mg of new opioid (& form) Equivalent mg new opioid (& form)

5

- Consider cross-tolerance when rotating to a different opioid (reduce new dose by 25-50%)
- Individualize based on assessment and monitor

Tapering Opioids:

- Reduce opioid dose 20-50% each week
- Once at the lowest commercially available formulation, either increase the interval between doses or reduce the dose every 2-5 days
 - As long as 25% of the previous steady-state dose is administered, the patient should not experience withdrawal

COMMONLY AVAILABLE OPIOID FORMULATIONS*

*Not all inclusive, does not include intravenous. Check with pharmacy for availability, and patient's insurance for coverage

Opioid	Short Acting (mg)	Long Acting (mg)
Morphine	Tabs (15, 30) MSIR ® Oral Solution (10mg/5mL, 20mg/5mL, 20mg/mL) §	MSContin ® Tabs (15, 30, 60, 100, 200) MorphaBond ER ® Tabs (15, 30, 60, 100)
Oxycodone	Roxicodone®, Tabs (5,10,15,20,30) Roxicodone® Oral Solution (5mg/mL) RoxyBond® Tabs (15, 30) OxyFAST®, Oxydose®, Roxicodone® Intensol Oral Concentrate (20mg/mL) § Endocet®, Percocet® Tabs (oxycodone/APAP) (2.5/325, 5/325, 7.5/325, 10/325)	OxyContin ® Tabs (10, 15, 20, 30, 40, 60, 80) Xtampza ER ® Caps (9, 13.5, 18, 27, 36)
Hydromorphone	Dilaudid® Tabs (2, 4, 8) Dilaudid® Oral Solution (1mg/mL) §	Exalgo ® Tabs (8, 12, 16, 32)
Oxymorphone	Opana ® Tabs (5, 10)	Oxymorphone ER Tabs (5, 7.5, 10, 15, 20, 30, 40)
Fentanyl	8	Duragesic® Transdermal Patch (12, 25, 37.5, 50, 75, 100mcg/hr)
Codeine	Tabs (15,30)	
Tramadol	Ultram® Tabs (50,100)	Ultram ER® Tabs (100, 200, 300)
Tapentadol	Nucynta ® Tabs (50, 75, 100)	Nucynta ER® Tabs (50, 100, 150, 200, 250)
Hydrocodone	Vicodin®, Lortab® Tabs (hydrocodone/APAP) (5/325, 7.5/325, 10/325)	Hysingla ER® Tabs (20, 30, 40, 60, 80, 100, 120) Zohydro ER® Tabs (10, 15, 20, 30, 40, 50)

Brand Name; Generic Name – most opioid preparations have generic formulations

§: orders for oral solutions must include drug name and strength (in mg/mL) to avoid confusion

All opioids are compared to morphine via oral morphine equivalents (OMEs).

*These are rough estimates; individual patients may vary **Equivalency for a one time dose of IV fentanyl only

Opioid Agonist	Oral (mg)	Parenteral (mg)	Comments
Morphine	30	10	Not recommended for patients with renal dysfunction (CrCl <30 mL/min), as metabolites can be neurotoxic Use with caution in patients with hepatic dysfunction
Hydrocodone	25-30		Reduce dose in patients with severe renal and hepatic dysfunction
Oxycodone*	20-30		Reduce dose in patients with hepatic dysfunction
Hydromorphone	7.5	1.5	Use with caution in patients with hepatic dysfunction
Oxymorphone	10		Reduce dose in patients with renal dysfunction (CrCl <50 mL/min) Contraindicated in patients with moderate or severe hepatic impairment. Reduce dose with mild hepatic impairment
Fentanyl		0.1** (100mcg)	Safe in renal dysfunction Consider major interactions with CYP 3A4 inhibitors or inducers For patch conversion, see box below; <u>Note</u> : IV fentanyl dose/hr = transdermal fentanyl dose
Tramadol	120		Maximum daily dose: 300mg; Reduce dose in patients with severe organ dysfunction Risk of serotonin syndrome and seizures

Note on Fentanyl Patches:

• THE 24 HOUR OME DIVIDED BY 2 IS EQUAL TO FENTANYL DOSE IN MCG/HR. Example: 50mg PO OME = 25mcg/hr fentanyl patch

• Patch takes 12-24 hours to achieve full effect. When removing a patch, remember the analgesic effect can still last up to 24 hours

*Xtampza ER 9mg = Oxycontin (Oxycodone ER) 10mg

References: McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010. Copyright ASHP.

Patient Controlled Analgesia (PCA)

The following are suggestions for PCA orders for adults. Like all opioid orders, doses must be individualized.

EDUCATE FAMILIES TO NOT PRESS THE PCA BUTTON!

Opioid Agonist	Opioid Status, Age	Loading Dose(s) (optional)	Starting Patient Administered Dose (mg)	Lockout Interval (min)	Starting RN Bolus Dose (mg)	Continuous Infusion Rate (mg/hr)
Morphine	Opioid Naïve	2-4mg q15 min	1	10-20	1	When indicated,
	Elderly (>70 years old)	2mg q20 min	0.5	10-20	0.5	calculate based on intermittent PCA use or previous opioid requirements
Hydromorphone	Opioid Naïve	0.2-0.3mg q15 mins	0.2	10-20	0.2	
	Elderly (>70 years old)	0.2mg q20 mins	0.1	10-20	0.1	

- Morphine is the opioid of choice (except for true drug allergy and renal failure)
- Capnography (EtCO2) monitoring is mandatory for all patients receiving PCA therapy, except those on mechanical ventilation, who are comfort measures only (CMO) or receiving for end of life care. See updated PCA policy for more information. In patients with RR <6 breaths/min for 1-2 minutes, PCA will alarm and pause from administering medication

References: UPMC Policy and Procedure Manual: UPMC PCA Monitoring and Managing Guidelines. Available on UPMC infonet.

Buprenorphine for Pain

Select FDA-Approved Buprenorphine Products for Pain*

Brand Name	Starting dose	Recommended Maximum Daily Dose (MDD)	Comments
	Not currently receiving opioids: 5mcg/h transdermal Q7days		 Dosing frequency every 7 days Use with caution in severe hepatic
Butrans ® (Transdermal patch)	Conversion from other opioids to Butrans: Previous OME < 30mg: 5mcg/h Q7days 30-80mg: 10mcg/h Q7days > 80mg**: consider alternate analgesic	 MDD: 20mcg/h given risk of QTc prolongation with higher doses 	 impairment given limited ability to alter the dose of transdermal formulation in this setting Consider major interactions with CYP 3A4 inhibitors or inducers
	Not currently receiving opioids: 75mcg once daily or Q12H		- Daga raduas in sovera bonstia
Belbuca ® (Buccal film)	Conversion from other opioids to Belbuca: Previous OME: < 30mg: 75mcg once daily-Q12H 30mg-89mg: 150mcg Q12H 90mg-160mg: 300mcg Q12H >160mg**: consider alternate analgesic	 MDD: 1800mcg/day (900mcg Q12H) given risk of QTc prolongation with higher doses 	 Dose reduce in severe hepatic impairment Consider major interactions with CYP 3A4 inhibitors or inducers

 If patient on full opioid agonists (e.g. oxycodone, morphine), package insert recommends tapering off current opioids prior to starting buprenorphine products to avoid withdrawal. This is not typically clinically possible prior to starting buprenorphine product for pain. In these instances, may utilize a smaller starting dose to avoid precipitated withdrawal upon initiation and increase to effect.

• It is possible to utilize simultaneous short-acting full opioid agonists for breakthrough pain while on buprenorphine.

*This is not meant to be a comprehensive review of buprenorphine or guide for initiation for opioid use disorder.

**This *starting* dosing is based on the package insert recommendations to avoid precipitated withdrawal, even though it is unlikely with the respective doses in these formulations. It is possible to start Butrans 20mcg/h patch on patients receiving > 80mg OME or Belbuca > 450mcg Q12H on patients receiving > 160mg OME.

References: Product Information: BUTRANS(R), buprenorphine. Purdue Pharma LP. (per FDA), Stamford, CT, 10/2019.; Product Information: :BELBUCA(R), buprenorphine. Collegium Pharmaceutical, Inc. (per FDA), Stoughton, MA, 6/2022.

Opioid-Induced Constipation (OIC)

All patients on opioid therapy should be prescribed a bowel regimen.

Medication	Site and Mechanism of Action	Usual Starting Dose	Onset of Action	Maximum Daily Dose
Stimulant Laxatives				
Bisacodyl	Colon; stimulates peristalsis	PO: 5-15mg x1 dose PR: 10mg x1 dose	PO: 6-10 hours PR: 15 min–1 hour	30mg
Senna	Colon; stimulates myenteric plexus, alters water and electrolyte secretion	2 tabs (8.6mg/each) qHS	6-10 hours	68.8mg
Osmotic Laxatives		•	•	•
Polyethylene Glycol	GI tract; osmotic effect	17g (1 capful) q24 hours in 8 ounces of water	48-96 hours	As tolerated by patient
Lactulose	Colon, osmotic effect	15-30mL q12-24 hours	24-48 hours	60mL (or 40g)
Sorbitol	Colon; delivers osmotically active molecules to the colon	15-30mL q12-24 hours	24-48 hours	27-40g
Saline Laxative		•	•	•
Magnesium Citrate ∞	Small and large bowel; attracts and retains water in the bowel lumen	6.5-10 ounces once daily	30 min–3 hours	6.5-10 ounces
Magnesium Hydroxide (MoM) ∞	Colon; osmotic effect & increased peristalsis	30mL q12-24 hours	30 min–3 hours	60mL

• Goal is for patient to have a bowel movement every 3 days. If no bowel movement after 4 or more days, consider enema or high colonic tap water enema.

Other medications that can exacerbate constipation: ondansetron (Zofran®), anticholinergics (tricyclic antidepressants, scopolamine, oxybutynin, promethazine, diphenhydramine), lithium, verapamil, bismuth, iron, aluminum, calcium salts. Constipation can occur with even 1 dose of IV morphine, and patient will never become tolerant to this adverse reaction

· Oral docusate capsules (alone) will not increase frequency of bowel movements

• ∞: Avoid use of MoM and related products in patients with renal dysfunction because of risk of electrolyte imbalances

10

Agents for Refractory Opioid Induced Constipation

OIC Definition: those receiving opioids, with less than 3 spontaneous bowel movements per week despite treatment with maximum doses of two first-line laxatives (found on slide 8)

Preferred, Formulary Agent: 1st line: Naloxegol (PO)

Dosing:	Administration:
Initial dose: 25mg once daily Reduce in patients with CrCl <60 mL/min to 12.5mg once daily Avoid in severe hepatic impairment Use with strong CYP3A4 inhibitors is contraindicated; avoid if	All other laxatives should be held for at least 3 days at initiation of naloxegol therapy. Other laxatives can be initiated after 3 days if inadequate results with naloxegol alone
possible with moderate CYP3A4 inhibitors	Naloxegol should be taken on an empty stomach

11

Formulary-Restricted Agents (Restricted to: Pain Service, Oncology, Critical Care, GI Services, Palliative Care): 2nd line: Naldemedine (PO) and 3rd line: Methylnaltrexone (PO and SC)

aldemedine dosing: 0.2mg PO daily with or ethylnaltrexone PO Dosing: 450mg once da CrCl <60mL/min) Methylnaltrexone SC Dosing:			Administration: Not recommended for the following: - Use >4 months - Treatment of post-operative ileus	
Patien	t Weight	Dose (Administer once	*In patients with renal impairment (CrCl <60 mL/min), reduce dose by ½	 Patients with known or suspected mechanical gastrointestinal obstruction
Pounds	Kilograms	daily or every other day)		Discontinue all maintenance laxatives before starting, may
<84	<38	0.15mg/kg		resume if suboptimal response after 3 days
84-136	38-62	8mg		Methylnaltrexone administration recommendations:
136-251	62-114	12mg		PO: take 30 minutes before first meal of day
>251	>114	0.15mg/kg		SC: inject into upper arm, abdomen, or thigh

References: Product Information: RELISTOR(R) subcutaneous injection, methylnaltrexone bromide subcutaneous injection. Salix Pharmaceuticals, Inc. (per FDA), Raleigh, NC, 2014. 9/2015. Product Information: MOVANTIK(TM) oral tablets, naloxegol oral tablets. AstraZeneca Pharmaceuticals. Wilmington, DE. 1/2015. Product Information: SYMPROIC(R) oral tablets, naloxegol oral tablets, naloxegol, NC. 5/2020.

Prescribing of Take-Home Intranasal Naloxone Kits

Patients who should be considered for take-home intranasal naloxone kits at discharge (any of the following):

- 1) Currently prescribed >50mg OME/day
- 2) Currently prescribed long-acting or extended release opioids (especially Oxycontin® and methadone)
- 3) Concurrently prescribed sedating medications (especially benzodiazepines and gabapentin)
- 4) Known history of opioid use disorder or history of overdose
- 5) Prescribed opioids and carries a diagnosis of pulmonary disease (e.g. OSA, COPD, etc.)

	Narcan® Nasal Spray
Dosing	Administer a single spray/dose into one nostril. May repeat dose q2-3 minutes until patient is responsive or EMS arrives.
Notes	FDA approved formulation. Kit contains 2 doses

In 2015, Pennsylvania issued a **state-wide standing order** for naloxone kits such that any Pennsylvania resident can obtain these kits from participating pharmacies without a prescription from a prescriber.

• To find a local pharmacy that carries intranasal naloxone visit: http://www.overdosefreepa.pitt.edu/find-naloxone/

References: Zedler B, Xie L, Wang L, Joyce A, et al. Development of a risk index for serious prescription opioid-induced respiratory depression or overdose in Veterans' Health Administration patients. Pain Med. 2015 Aug;16(8):1566-1579.

Interventional Pain Management

Interventions that minimize systemic opioids and help with pain relief in a targeted fashion can be considered for a wide spectrum of patients. At UPMC, the chronic pain and palliative care services collaborate to identify patients who are most likely to benefit from such interventions.

Examples of available interventions which are best supported by evidence are listed below:

	Common Nerve Blocks					
Block Type:	Indications:					
Celiac Plexus Block	Abdominal visceral pain from: pancreatic cancer and other upper abdominal tumors					
Superior Hypogastric Block	Pelvic visceral pain from gynecological, colorectal or GU cancers					
Lumbar Sympathetic Block	Intractable LE pain from PVD or Chronic Regional Pain Syndrome					
Pudendal Nerve Block	Vaginal pain, penile/scrotal pain, perineal pain					
Sphenopalatine/Trigeminal Nerve Block	Facial pain					
Epidural Steroid Injection	Low back pain – often for non-malignant pain					
	Centrally Implanted Pumps					
Hardware Type:	Indications:					
Intrathecal Pump	Pain refractory to systemic opioids with a prognosis of >3 months					
Tunneled Epidural Catheter	Pain refractory to systemic opioids with a prognosis of <3 months					
Spinal Cord Stimulator	Most helpful in refractory neuropathic limb pain (especially ischemic limb)					
Exclude patients who are:						
Neutropenic/Septic	Coagulopathic (INR >1.4 or platelets <100K)					

Infection in the region of the proposed	Coagulopathic (INR >1.4 or platelets <100K) On anticoagulants/antiplatelet agents that are not safe to hold or reverse
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13

Medical Cannabinoids

Medical cannabinoids include: 1. Single molecular compounds (e.g. dronabinol – *contains tetrahydrocannabinol (THC) only*); 2. Liquid extracts (e.g. nabiximols - *not yet approved in the US*); and 3. Botanicals (i.e. medical marijuana).

FAQs: Medical Marijuana

- 1. What medical marijuana formulations are approved in PA? Pill, oil, topical forms, tinctures and liquids, and dry leaf formulations for vaporization or nebulization only. <u>No</u> smoking or plant forms are allowed.
- 2. How can patients obtain medical marijuana? There is a 4 step process. 1. Patient registers for program through medical marijuana registry; 2. State-approved physician certifies patient has a medical condition that qualifies for medical marijuana (copay usually included); 3. Patient pays for medical marijuana card (up to \$50); 4. Patient gets medical marijuana from approved dispensary.
- 3. What serious medical conditions qualify a patient for medical marijuana? The list is constantly updated. *Some* of the approved conditions are: ALS, autism, cancer, Crohn's disease, epilepsy, glaucoma, HIV/AIDS, Huntington's disease, IBS, MS, Parkinson's Disease, PTSD, severe chronic or intractable pain, anxiety disorder, and sickle cell anemia.
- **4.** How much does medical marijuana cost? Varies. A month supply can cost anywhere from \$30-200 depending on formulation and route. Costs are determined by individual dispensaries. Insurances do <u>not</u> cover medical marijuana. The hospice benefit does <u>not</u> cover medical marijuana.
- 5. Can the patient use medical marijuana in the hospital? Potentially. Per UPMC policy, attending physicians may approve requests for patients enrolled in the medical marijuana program with a designated caregiver who can assist with administration during the hospitalization. Attending physician must review and sign consent forms completed by patient and caregiver (linked in the policy below). However, clinical staff will <u>not</u> under any circumstances handle medical marijuana, including obtaining, storing or administering.

To learn more, visit the PA medical marijuana website: https://www.pa.gov/guides/pennsylvania-medical-marijuana-program/

Assessment of Dyspnea

For Patients Who Can Communicate: Ask about Severity (cannot rely on RR or pO2 alone):

		0	1	2	3	4	5	6	7	8	9	10
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No Shortness of Breath

Worst Shortness of Breath Imaginable

For Patients Who Cannot Communicate: e.g.: Respiratory Distress Observation Scale (RDOS):

	0 Points	1 Point	2 Points
Heart Rate	<90 bpm	90-109 bpm	≥110 bpm
Respiratory Rate	≤18 breaths/min	19-30 breaths/min	>30 breaths/min
Restlessness (non purposeful movements)	None	Occasional, slight movements	Frequent movements
Paradoxical Breathing Pattern (abdomen moves on inspiration)	None		Present
Accessory Respiratory Muscle Use (rise in clavicle during inspiration)	None	Slight rise	Pronounced rise
Grunting at End-Expiration (guttural sound)	None		Present
Nasal Flaring (involuntary movements in nares)	None		Present
Look of Fear	None		Eyes wide open, muscle tense, etc.
		TOTAL:	

A score of 3 or more (indicating moderate) should prompt the administration of medication for dyspnea. A score of 7 (indicating severe) or higher should prompt a call to primary provider or palliative and supportive care team.

References: Campbell ML, Templin T, Walch J. A Respiratory Distress Observation Scale for patients unable to self-report dyspnea. J Palliat Med. 2010 Mar;13(3):285-90.

Treatment of Dyspnea

- Address potential underlying etiologies: respiratory disease (e.g. COPD), cardiovascular diseases (e.g. CHF), infection, anemia, chronic kidney disease (CKD)
- Treat utilizing both nonpharmacological interventions and medications

Nonpharmacological Interventions: Handheld fan, pulmonary rehab, oxygen (with input from pulmonologist)

Medications: First line therapy: low-dose opioids. Include PRN reason: dyspnea for low-dose opioid orders to be used for dyspnea and NOT for pain or NOT only for pain).

- Consider benzodiazepines (BZDs), only if anxiety component exists. BZDs will not improve dyspnea alone

	Starting Doses	Other Dosing Considerations				
Opioid Naïve	 For Non End of Life Patients: Consider oxycodone 2.5-5mg PO q4h PRN or morphine 2mg IV q3h PRN For End of Life Patients: Morphine 3-5mg IV q2h PRN Opioid doses exceeding 30mg OME/day are not recommended in opioid naïve patients 	 If distress not relieved in 15 minutes after starting dose, give bolus equal to the loading dose increased by 50%. If severe distress persists repeat the dose every 15 minutes until comfortable For increased pain/distress give extra bolus dose(s) equal to the last given bolus dose every 30 minutes as needed If using more than 2 bolus doses over a 6-hour period, consider starting a continuous infusion 				
Opioid Tolerant	 Calculate the equianalgesic parenteral dose of morphine for the last 24 hours (see page 7 for more information), and consider dosing strategies as listed Increase PRN dose by 50% Opioid doses should not exceed more than a 25% increase in opioid tolerant patients 	 Divide the total 24 hour IV morphine dose by 24 to determine initial hourly infusion rate (mg/hour). Start continuous infusion at this rate If patient in pain/distress use loading dose = hourly infusion rate If distress not relieved in 15 minutes after initial loading dose or the patient is in increased pain/distress, administer the loading dose increased by 50% and repeat every 15 minutes until comfortable If using more than two bolus doses over 6-hour period, determine new continuous infusion rate by recalculating total dose given over last 6 hours and dividing it by 6 				

References: Kamal AH[,] Maguire JM, Wheeler JL, Currow DC, et al. Dyspnea review for the palliative care professional: assessment, burdens, and etiologies. J Palliat Med. 2011 Oct;14(10):1167-72.

Medications should be selected based on perceived etiology and pathophysiology.

	Drug	Starting Dose/Route	MDD	Comments
apies	Metoclopramide*	5-20mg PO/SC/IV AC and HS	60mg	Dopamine antagonist Contraindicated in bowel obstruction Risk of EPS with prolonged use (>12 weeks)
First Line Therapies	Haloperidol	0.5-4mg PO/SC/IV q6h	5mg	Dopamine antagonist IV has higher risk of EPS and QTc prolongation than PO. Risk may not be significant with lower doses for emesis
First Li	Olanzapine	2.5-5mg PO once daily	20mg	Dopamine, histamine, serotonin, alpha-1 and acetylcholine antagonist Risk of QTc prolongation although may not be significant with lower doses used for nausea; Common ADRs: sedation, dry mouth, headache, dizziness, increased appetite
s or ns	Prochlorperazine	5-10mg PO/IV q6h or 25mg PR q6h	40mg	Dopamine and histamine antagonist Risk of EPS; Common ADR: sedation
e Therapies o g Indications	Ondansetron	4-8mg PO/IV q4-8h	32mg	Serotonin antagonist Risk of QTc prolongation Helpful for chemotherapy induced nausea only Common ADRs: headache, fatigue and constipation
econd Line Compelling	Dexamethasone	4-8mg PO/IV qAM or BID	8-16mg	Helpful for nausea due to raised ICP Common ADRs: agitation, insomnia, and hyperglycemia
Second Compe	Scopolamine	1.5mg patch q72h	1 patch q72h	Acetylcholine antagonist Common ADRs: dry mouth, blurred vision, ileus, urinary retention. Considered a higher cost agent

*Metoclopramide is considered first line for empiric therapy; MDD: maximum daily dose (for nausea); ICP: intracranial pressure

References: Glare P, Miller J, Nikolova T, Tickoo R. Treating nausea and vomiting in palliative care: a review. Clin Interv Aging. 2011;6:243-59. Wood GJ, Shega JW, Lynch B, Von Roenn JH. Management of intractable nausea and vomiting in patients at the end of life: "I was feeling nauseous all of the time . . . nothing was working". JAMA. 2007 Sep 12;298(10):1196-207.

17

Diagnosis of Delirium

- Delirium is conceptualized as a reversible illness, except in the last 24-48 hours of life
- Delirium occurs in at least 25-50% of hospitalized cancer patients, and in a higher percentage of patients who are terminally ill
- · Delirium increases the risk of in-hospital and six month mortality

	D: Drugs	Opioids, anticholinergics, sedatives, benzodiazepines, steroids, chemo - and immunotherapies, some antibiotics				
SS:	E: Eyes and Ears	Poor vision, hearing, isolation				
Etiologies:	L: Low flow states	Hypoxia, MI, CHF, COPD, shock				
Etiol	I: Infections					
	R: Retention (of urine or stool)					
Potential	I: Intracranial	CNS metastases, seizures, CVA, hypertensive encephalopathy				
	U: Under hydration/nutrition/sleep/pain					
	M: Metabolic disorders Sodium, glucose, thyroid, hepatic, deficiencies of Vitamin B12, folate, niacin, and thiamine and toxic levels of lead, manganese, mercury, alcohol					

DSM-V Criteria for delirium includes five components:

- A. A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment)
- **B.** The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day
- C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception)
- **D.** The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma
- E. There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin, or is due to multiple etiologies

References: American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

3D CAM (Confusion Assessment Method)

Diagnosis is positive with presence of: 1 AND 2; and either 3 OR 4

Feature	Questions Asked	Observations at Bedside	Positive Answers			
1. Acute Onset or Fluctuation not really in the hospital?		 Fluctuation in level of consciousness Fluctuation in attention during interview Fluctuation in speech or thinking 	Any answer other than 'no' is positive Any positive observation is a yes			
		- AND -				
 Can you tell me the days of the week backwards, starting with Saturday? Can you tell me the months of the year backwards, starting with December? 		 Did the patient have trouble keeping track of what was being said during the interview? Did the patient appear inappropriately distracted by environmental stimuli? 	Anything other than 'correct' is coded as positive Either observation is positive			
	· · ·	ND EITHER -				
3. Disorganized Thinking	 Can you tell me the year we are in right now? Can you tell me the day of the week? Can you tell me what type of place this is? 	 Was the patient's flow of ideas unclear or illogical, for example: did the patient tell a story unrelated to the interview (tangential)? Was the patient's conversation rambling, for example did he/she give inappropriately verbose and off target responses? Was the patient's speech unusually limited or sparse? (i.e. yes/no answers)? 	Any answer other than 'correct' is coded as positive Answer is 'yes'			
		- OR-				
4. Altered Level of Consciousness		Was the patient's speech unusually limited or sparse? (i.e. yes/no answers)	Either observation is positive			

References: Confusion Assessment Method. © 1988, 2003, Hospital Elder Life Program. All rights reserved. Adapted from: Inouye SK et al. Ann Intern Medicine. 1990;113:941-8.

Treatment of Delirium

- Always consider nonpharmacological interventions
- Always look for and treatment underlying causes of delirium (see Page 16)
- Benzodiazepines are NOT effective in treating delirium not associated with alcohol withdrawal, may worsen delirium, and should be used cautiously
- Although evidence is mixed, neuroleptics can be considered for the treatment of <u>agitated</u> delirium[®]. Haloperidol is considered first line agent

			Adverse Drug Reactions				
Medication	Starting Dose	MDD	EPS	Anti- cholinergic	Sedation	QTc Prolongation	
Haloperidol	0.5-1mg (2mg in ICUΔ) BID to q8h	20mg	PO: ++ IV: +++	+	0/-	PO: + IV: ++	
Risperidone	0.25-1mg BID, up to q6h	6mg	++	+	++	++	
Olanzapine	2.5-10mg daily	20mg	+	++	+++	+	
Quetiapine	12.5-50mg BID	800mg	+	++	+++	++	
Aripiprazole	5-15mg qAM	30mg	++	+	++	0/-	
Thioridazine	50-100mg TID	800mg	+	+++	+++	+	

MDD: maximum daily dose

The FDA has determined that the use of antipsychotic medications in the treatment of behavioral disorders in elderly patients with dementia is associated with increased mortality. This risk appears to be highest during the first two weeks of use.

References: Grassi L, Caraceni A, Mitchell AJ, Nanni MG. Management of delirium in palliative care: a review. Curr Psychiatry Rep. 2015 Mar;17(3):550. 20

Treatment of Depression and Anxiety

Commonly prescribed antidepressants:

Category		Starting Dose	Torrat Doily	Adverse Drug Reactions		
	Medication		Target Daily Dose	Anti- cholinergic	Insomnia	GI Distress
SSRIs	Citalopram	10-20mg daily	10-40mg	+	+	++
	Escitalopram	5-10mg daily	10-20mg	+	+++	++
	Sertraline	25-50mg daily	50-200mg	-	+	+++
	Fluoxetine	10mg daily	40mg	-	+	+
	Paroxetine	10mg daily	40mg	++	+	+
SNRIs	Venlafaxine (IR and XR)*	75mg/day (either qAM (XR) or divided TID (IR)	150-375mg	+	++++	++
	Duloxetines	20mg BID	30-60mg	+	++	++
Stimulants	Methylphenidateo	2.5-5mg BID (at 08:00/12:00)	5-40mg		++++	+
Other	Mirtazapine	7.5-15mg daily	30-45mg	+	-	+

* Dual serotonin/norepinephrine action at doses of 150-225mg which is effective in neuropathic pain and is mildly activating. On switching from the venlafaxine XR to venlafaxine, the shorter half life of venlafaxine requires frequent dosing to reach the same dose of venlafaxine XR. Use with caution in patients with hypertension **b** Do not use in patients with liver dysfunction

 $\pmb{\sigma}$ Energizing, will see effect of medication after first dose

- Tricyclic antidepressants (TCAs) are not recommended first-line for treatment of depression or anxiety; for more information on this class utilize drug information resources like Micromedex®

References: Rodin G, Katz M, Lloyd N, Green E, et al. Treatment of depression in cancer patients. Curr Oncol. 2007 Oct; 14(5): 180–188.

Treatment of Oral Secretions at the End of Life

- As the level of consciousness decreases in the dying process, patients lose their ability to swallow and clear oral secretions. As air
 moves over the secretions, the resulting turbulence produces noisy ventilation with each breath, described as gurgling or rattling
 noises (also referred to as the "death rattle")
- These sounds are good predictors of near death; one study indicated the median time from the onset of death rattle to death was 16 hours¹
- Families may feel distress when hearing sounds produced by secretions at the end of life. It is important to discuss this with them and talk about how certain therapies can be helpful
- It may be helpful to discuss the role of oral and pharyngeal suctioning with family and nursing staff. While suctioning can help clear secretions initially, ongoing suctioning can cause discomfort at the end of life

Nonpharmacological Interventions: Position the patient on their side or in a semi-prone position (30-45° angle) to facilitate postural drainage

Medications: Standard of care are muscarinic receptor blockers (anticholinergic drugs). Note these agents will only address future secretions - will not dry up present secretions

Medication (Route)	Starting Dose	Onset of Action	Maximum Daily Dose
Glycopyrrolate (PO)*	1mg q4-6h PRN	30 min	8mg
Glycopyrrolate (SC/IV)*	0.2mg q4-6h PRN	1 min	8mg
Atropine (IV)	0.1mg q4-6h PRN	1 min	2mg
Atropine (SL drops)	1gtt (1%) q4-6h PRN	30 min	48gtts
Scopolamine (Transdermal Patch)	1mg patch q72h	12 hrs	1 patch q72 hrs
Hyoscyamine (Tabs, and SL Tabs)	0.125mg TID-QID PRN	30 min	1.5mg

* Glycopyrrolate will not cross the blood-brain-barrier, reducing the risk of CNS toxicity (sedation, delirium)

ightarrow Use atropine ophthalmic drops

References: 1. Bickel K, Arnold RM. Death rattle and oral secretions--second edition #109. J Palliat Med. 2008 Sep;11(7):1040-1.

Spirituality Pearls

Spirituality consists of cognitive, emotional, and behavioral components that contribute to defining a person and to the way life is experienced. It is important to realize just how dynamic the concept of spirituality is, especially in patients with serious illness.

Incorporating Spirituality into Patient Care:

HOPE Talking Map (to ask patients about their spirituality)

Н: Норе	Sources of hope, strength, comfort, meaning, peace, love and connection
O: Organized Religion	Role of organized religion in the patient's life
P: Personal	Personal spiritual practices
E: Effects	Effects of patient's spiritual and/or religious values on care

Principles of Spiritual Care:

- Combination: Professionalism with compassion
- **Presence:** To be maximally useful to patients and their experiences, we must be fully aware of our own biases and distortions
- Listening: Listening attentively with genuineness and acceptance
- Facilitate Exploration: Meaning cannot be given by another, it must be found by the person him/herself
- Allow for Paradox: Conflicting priorities in the care of patients may mean that some questions are difficult to answer. The emotional pain of this needs to be recognized and supported
 Easter Pacification Hence: To give uprediction hence that life will be
- Foster Realistic Hope: To give unrealistic hope that life will be prolonged is unethical but there is always something more that can be done to bolster hope in a realistic way
- **Create 'Space' for Patients:** Patients need to feel that they still have some choice and control
- Allow for Mystery: Some issues will always defy explanation

Inquiring Patients Regarding Formal Chaplain Consult:

- <u>Referral by Inclusion</u>: "Our treatment team consists of a variety of professionals to assist you during this stressful time. In addition to your physicians and nurses, you may meet social workers, chaplains and others. We all work together on your behalf."
- <u>Referral by Exclusion:</u> "Would it be helpful for a chaplain to see you?

References: Puchalski CM, Ferrell B, Viriani R, et al. Improving the quality of spiritual care as a dimension of palliative care: Consensus conference report. J Palliat Med. 2009;12(10): 885-903. Watson, Max S. et al Oxford Handbook of Palliative Care 2005.

UPMC Palliative Care and Pain Treatment Resources

Inpatient Supportive and Palliative Care Services				
PUH/MUH Supportive & Palliative Care Service	412-647-7243; pager: 8511			
Shadyside Supportive & Palliative Care Service	412-647-7243; pager: 8513			
Magee Womens Hospital of UPMC Supportive and Palliative Care Service	412-647-7243; pager: 8510			
Children's Hospital of Pittsburgh of UPMC Supportive Care Program	412-692-3234			
VA Palliative Care Program Outpatient and Oncology	412-360-6242			
UPMC Altoona Supportive and Palliative Care Service (Altoona Family Practice)	814-889-2701			
UPMC East Supportive and Palliative Care Service	412-858-9565			
UPMC Hamot Supportive and Palliative Care Service	814-877-5987			
UPMC McKeesport Supportive and Palliative Care Service	412-664-2717			
UPMC Mercy Supportive and Palliative Care Service	412-232-7549			
UPMC Northwest Supportive and Palliative Care Service	814-677-7440			
UPMC Passavant Supportive and Palliative Care Service	412-367-6700			
UPMC St Margaret Supportive and Palliative Care Service	412-784-5484			
Inpatient Medical Ethio	s Services			
PUH/MUH Medical Ethics	412-647-2345 (call operator, ask for Medical Ethics)			
Shadyside Medical Ethics	412-623-2121 (call operator, ask for Medical Ethics)			
Inpatient Pain Treatment Services				
PUH/MUH Chronic Pain Service	412-692-2234			
Shadyside Chronic Pain Service (Center Commons)	412-665-8030; after hours call: 412-665-8031			
PUH/MUH Acute Interventional Perioperative Pain Service (AIPPS)	412-647-7243; pager: 7246 (PAIN)			
Shadyside Acute Interventional Perioperative Pain Service (AIPPS)	412-692-2333			

UPMC Palliative Care and Pain Treatment Resources

Outpatient Services			
Palliative Care at Benedum Clinic	412-692-4200		
Palliative Care at Hillman Cancer Center	412-692-4724		
Palliative Care at Falk Cystic Fibrosis Clinic	412-648-6161		
Palliative Care at Presbyterian Heart Failure Clinic	412-647-7061		
Palliative Care at the Kidney Clinic	412-802-3043		
Palliative Care at Magee in the GynOnc Clinic	412-641-5411		
Palliative Care at St. Margaret Clinic	412-784-5050		
Palliative Care at Passavant Clinic	412-748-5790		
Palliative Care at Mercy Oncology Clinic	412-232-7328		
Advanced Illness Care (AIC) Program	833-876-2242 (833-UPMC-AIC)		
Family Hospice	Administration: 412-572-8800 Info/Referrals: 1-800-513-2148		
Internal Medicine Recovery Engagement Program	412-232-6275		
St Margaret Pain Medicine	412-784-5119		
UPMC Presbyterian Pain Medicine	412-692-2234		

UPMC Spiritual Care Resources

Inpatient Hospital Spiritual or Pastoral Care Offices		
UPMC Magee-Women's Hospital	412-641-4525	
UPMC Presbyterian/Montefiore	412-647-7560	
UPMC Shadyside	412-623-1692	
UPMC St. Margaret	412-784-4749	
UPMC Mercy	412-232-8198	
UPMC McKeesport	412-664-2057	
UPMC East	412-357-3151	
UPMC Passavant	412-367-6700	
Children's Hospital of Pittsburgh	412-692-5349	
VA Hospital Oakland campus	412-822-1551	

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Indications for Palliative Care Referral:

- Pain in patients with life-limiting illness
- Management of other symptoms such as nausea, vomiting, shortness of breath, delirium
- Negotiating goals of treatment or end-of-life decision making
- Family support for a patient with a life-limiting illness

- Psychological or spiritual counseling for patients and their families
- Discharge planning and interface with local hospices
- · Bereavement services in the event of death
- Outpatient palliative care follow up

Questions or comments regarding this information, contact Robert Arnold, MD (<u>rabob@pitt.edu</u>). This information provided by the UPMC Supportive and Palliative Care Programs are merely in the form of recommendations and do not replace the service of a provider. Authors: Mamta Bhatnagar, MD and Maria Lowry, PharmD, with contributions from Julie Childers, MD and Jessie Merlin, MD. This guide was made possible with the assistance of Kelly Prilla and the generous support of the UPMC Palliative and Supportive Institute. Produced in cooperation with the University of Pittsburgh.

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