UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

Palliative Care Symptom Guide

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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 speech with negative or disapproving quality	Repeated troubled calling out. Loud moaning or groaning. Crying
Facial Expression	Smiling or inexpressive	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
		TOTAL:	*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	
Nociceptive Pain	APAP	650mg PO/PR q4h 1000mg IV q6h	• MDD: 3-4,000mg; 2,000mg/day for those with alcohol abuse and elderly • IV Duration: ≤2 doses per UPMC policy	• Lacks anti-inflammatory effects of NSAIDs • Avoid in severe hepatic disease	
	NSAIDs	**Ibuprofen** 400mg PO q8h	• MDD: 3,200mg	• Caution in patients with gastric disease, renal impairment or at risk for bleeding	• Avoid use in severe hepatic and renal impairment
		Naproxen 250mg PO q12h	• MDD: 1,250mg		• CrCl <30mL/min: use is not recommended • Use lowest possible dose in advanced liver disease
		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		• Use caution in hepatic impairment
Neuropathic Pain	Anti-epileptics	**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	
	SNRIs	**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	
		Duloxetine 30mg PO once daily	• MDD: 90mg.day	• Avoid in severe renal insufficiency • Contraindicated in hepatic insufficiency	

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

Principles of Opioid Therapy

Initiating Opioids:

Appropriate?	Are opioids appropriate for the patient's specific pain(s)? *Some types of pains do not respond well to opioids* Always screen patients for risk factors for opioid misuse upon initiation of opioid therapy. *Must check PA PDMP** 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: https://pennsylvania.pmpaware.net/login

References: Katz NP, Adams EH, Benneyan JC, et al. Foundations of opioid risk management. Clin J Pain. 2007 Feb;23(2):103-18.
Passik SD. Issues in long-term opioid therapy: Unmet needs, risks and solutions. Mayo Clin Proc. 2009 Jul; 84(7): 593–601.

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 66% of total OME as long-acting. Give 5-15% of total daily long-acting agents as short acting breakthrough agent (PRN) every 3-6 hours

Rotating Opioids:

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

Converting Opioids:

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

$$\frac{\text{mg of } \textbf{current} \text{ opioid (\& form)}}{\text{Equivalent mg } \textbf{current} \text{ opioid (\& form)}} = \frac{\text{“X” mg of } \textbf{new} \text{ opioid (\& form)}}{\text{Equivalent mg } \textbf{new} \text{ opioid (\& form)}}$$

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

Tapering Opioids:

Reduce opioid dose by 10% each week for patients who have been on opioids for more than one year

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 severe withdrawal symptoms

Select Opioid Products

COMMONLY AVAILABLE ORAL OPIOID FORMULATIONS*

*Not all inclusive. 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) **Kadian®** Caps (10, 20, 30, 40, 50, 60, 80, 100, 200) **Avinza®** Caps (30, 45, 60, 75, 90, 120) **MorphaBond ER®** Tabs (15, 30, 60, 100) **Arymo ER®** Tabs (15, 30, 60)
Oxycodone	**Roxicodone®**, **RoxyBond®** Tabs (5, 10, 15, 20, 30) **Oxaydo®** Tabs (5, 7.5) **Roxicodone®** Oral Solution (5mg/mL); **OxyFAST®**, **Oxydose®**, **Roxicodone® Intensol** Oral Concentrate (20mg/mL) § **Endocet®, Percocet®** Tabs (oxycodone/APAP) (2.5/325, 5/325, 7.5/325, 10/325); **Primlev®** Tabs (5/300, 7.5/300, 10/300)	**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	⊘	**Duragesic®** Transdermal Patch (12, 25, 37.5, 50, 75, 100mcg/hr)
Codeine	Tabs (15, 30, 60)	
Tramadol	**Ultram®** Tabs (50)	**Ultram ER®** Tabs (100, 150, 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

Opioid Analgesic Equivalencies*

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; Note: 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

Note on Buprenorphine Patches:

- Buprenorphine is a partial mu-agonist (ceiling dose for analgesia)
- Buprenorphine 20mcg patch is approximately equivalent to 15mcg fentanyl patch (or 30mg OME)
- Consider major interactions with CYP 3A4 inhibitors or inducers

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	Age, Opioid Status	**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	8-20	1	When indicated, calculate based on intermittent PCA use or previous opioid requirements
	Elderly (>70 years old)	2mg q20 min	0.5	8-20	0.5	
Hydromorphone	*Opioid Naïve*	0.2-0.3mg q15 mins	0.2	8-20	0.2	
	Elderly (>70 years old)	0.2mg q20 mins	0.1	8-20	0.1	

- Morphine is the opioid of choice (except for true drug allergy and renal failure)
- Capnography ($EtCO_2$) 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.

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	34g
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 small doses of short acting opioids, and patient will never become tolerant to this adverse reaction
- Oral docusate capsules (alone) will not increase frequency of bowel movements and are not recommended as first line therapy for laxation in this setting.
- ∞: Avoid use of MoM and related products in patients with renal dysfunction because of risk of electrolyte imbalances

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-Restricted Agent: **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 possible with moderate CYP3A4 inhibitors	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 Naloxegol should be taken on an empty stomach

Formulary-Restricted Agent: **Methylnaltrexone (PO and SC)**

PO Dosing: 450mg once daily (150mg if CrCl <60mL/min)

SC Dosing:

Patient Weight		Dose (Administer once daily or every other day)
Pounds	Kilograms	
<84	<38	0.15mg/kg
84-136	38-62	8mg
136-251	62-114	12mg
>251	>114	0.15mg/kg

*In patients with renal impairment (CrCl <60 mL/min), reduce dose by ½

Administration:

Not recommended for the following:
- Use >4 months
- Treatment of post-operative ileus
- Patients with known or suspected mechanical gastrointestinal obstruction

Discontinue all maintenance laxatives before starting, may resume if suboptimal response after 3 days
PO: take 30 minutes before first meal of day
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.

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

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. No 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 suffers from 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, 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 not cover medical marijuana. The hospice benefit does not 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. However, clinical staff will not 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/

References: Medical Marijuana During Hospitalization at UPMC Presbyterian-Shadyside: Summary of Policy CP-75: https://infonet.upmc.com/UPMCPolicies/PRSHPolicyDocuments/CP75.pdf

Assessment of Dyspnea

For Patients Who Can Communicate: Ask about Severity (cannot rely on RR or pO_2 alone):

0	1	2	3	4	5	6	7	8	9	10

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	90-109bpm	>110bpm
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
- Use IV opioids for actively dying patients and oral opioids for patients with longer prognosis who can take PO. USE LOW DOSES.

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

Medications: First line therapy: low-dose opioids. Educate team and RN that opioid is being used for dyspnea (NOT for pain or NOT only for pain). Administration of opioids based on the RDOS in an EOL setting has not been shown to result in an expedited death. The purpose of opioid administration for dyspnea at the EOL is to relieve suffering, and not to shorten life.

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

	Starting Doses	Other Dosing Considerations
Opioid Naïve	• Oral Regimen: Consider oxycodone 2.5-5mg PO q4-6h PRN or morphine ER 10-20mg/day • IV Regimen: Morphine 2-5mg IV q4-6h PRN • Opioid doses exceeding 30mg OME/day are not recommended in opioid naïve patients	• If distress not relieved in 15 minutes after starting IV dose or an hour after an oral dose, give bolus equal to the loading dose increased by 50%. If severe distress persists repeat the dose every 15 minutes for IV or every 2 hours for PO 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 of IV opioids over a 6-hour period, consider starting a continuous infusion or a long acting opioid
Opioid Tolerant	• Calculate the equianalgesic parenteral dose of morphine for the last 24 hours *(see slides 6 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 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.

Nausea and Vomiting Treatment

Medications should be selected based on perceived etiology and pathophysiology.

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

*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.

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

Potential Etiologies:

D: Drugs	Opioids, anticholinergics, sedatives, benzodiazepines, steroids, chemo - and immunotherapies, some antibiotics
E: Eyes and Ears	Poor vision, hearing, isolation
L: Low flow states	Hypoxia, MI, CHF, COPD, shock
I: Infections	
R: Retention (of urine or stool)	
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.

Diagnosis of Delirium

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	• During the past day have you felt confused? • During the past day did you think you were not really in the hospital? • During the past day did you see things that were not really there?	○ 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 -			
2. Inattention	• 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
- AND 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 which are the most beneficial** to prevent and reduce delirium. Can include frequent orientation, treatment of hearing and vision problems, treatment of incontinence
- Benzodiazepines are NOT effective in treating delirium, may worsen delirium, and should be used cautiously
- **Evidence suggests that neuroleptics don't alter the symptoms or duration of delirium꩜. If need they can be used for hyperactive delirium. Haloperidol is considered first line agent**

Medication	Starting Dose	MDD	Adverse Drug Reactions			
			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

꩜N Engl J Med 2018;379:2506-16. JAMA Intern Med. 2017;177(1):34-42 Curr Psychiatry Rep. 2015 Mar;17(3):550.
Δ Refer to the UPMC Presbyterian Shadyside "Acute Agitation Management" order set

Treatment of Depression and Anxiety

Commonly prescribed antidepressants:

Category	Medication	Starting Dose	Target Daily Dose	Adverse Drug Reactions		
				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	+	++++	++
	Duloxetineϐ	20mg BID	30-60mg	+	++	++
Stimulants	**Methylphenidateω**	2.5-5mg BID (at 08:00/12:00)	5-40mg	--	++++	+

* 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

ϐ Do not use in patients with liver dysfunction

ω Energizing, may increase appetite

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 hours[1]
- 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)
⌂ 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, behavioral, and ritual components that contributes to understanding the whole person and to the way life is experienced. Chaplains are "healers of the soul" and help persons understand the existential reality of themselves in the world. It is important to realize just how dynamic the concept of spirituality is, especially in persons who experience the disruption of serious illness.

How to ask about spirituality: HOPE Talking Map

H: Hope	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:

Presence: To allow for empathy, compassion, and to serve as a spiritual exemplar for all faiths and non-believers
Build coping skills : The objective of spiritual care is to guide the seriously ill patient to cope with pain, existential and spiritual distress, alienation, and isolation. Coping skills are acquired by self-reflection with the help of an attentive chaplain.
Listening: Listening attentively with genuineness and acceptance
Allow for Mystery: Some questions are difficult to answer. Unresolved emotional and spiritual pain is recognized and supported.
Facilitate Exploration: Meaning cannot be given by another. Through psycho-dynamic conversation and guiding questions, it is found by the person him or herself.

Strength exceptions: Chaplains listen to the life narrative of the person and understands how illness disruption fits into the narrative. A positive way toward coping skills is underscoring strength exceptions towards good health and behavior in a life filled with pain and distress.
Hope: Even if illness will shorten a life, there is always hope for the last chapter of life and even into the beyond (depending upon belief). The chaplain coaches this hope and does not make unrealistic claims.
Intervention of the spirit (optional): Lastly, the chaplain prays with the person and the family tailoring the prayer to that person's uniqueness, his or her unique life, hope, love, faith, and the eternity of a Sovereign Authority who brings life in the world.

Inquiring Patients Regarding Formal Chaplain Consult:

- Referral by Inclusion (recommended): "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."

References: Puchalski CM, Ferrell B, Viriani R, et al. Improving the quality of spiritual care as a dimension of palliative care:
De Jong, Kim Berg, Insoo, Interviewing for Solutions, Brooks/Cole/Thompson Learning, 2002
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 Inpatient 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	412-784-5111
Inpatient Medical Ethics 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	
Benedum Geriatric Center Supportive Care Clinic	412-692-4200
Hillman Cancer Center's Cancer Pain and Supportive Care Program	412-692-4724
UPMC Heart and Vascular Institute's Advanced Heart Failure Clinic	412-647-6000
Comprehensive Lung Center	412-648-6161
Renal Supportive Clinic (Kidney Clinic at University Center)	412-802-3043
UPMC Presbyterian Pain Medicine	412-692-2234
Magee Women's Cancer Center	412-641-4530
Magee Gynecological Cancer Program	412-641-5411
St Margaret Geropalliative Care Clinic	412-784-5050
St Margaret Pain Medicine	412-784-5119
East Pain and Supportive Care Clinic	412-380-5775
Passavant Pain and Supportive Care Clinic	412-748-5790
Family Hospice	Administration: 412-572-8800 Info/Referrals: 1-800-513-2148

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	412-459-8377/412-623-1692
UPMC St. Margaret	412-784-4749
UPMC Mercy	412-232-8198
UPMC McKeesport	412-664-2057
UPMC East	412-357-3151
UPMC Passavant	412-367-6700/412-297-6865
Children's Hospital of Pittsburgh	412-692-5349
VA Hospital Oakland campus	412-822-1551

Notes

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 (rabob@pitt.edu). 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 Jennifer Pruskowski, PharmD, with contributions from Julie Childers, MD; Scott Freeman, MD; Amar Bansal, MD; Rebecca Sands MD; Linda King MD, Jonathan Perlman BCC. This guide was made possible with the assistance of Colleen Kosky and the generous support of the UPMC Palliative and Supportive Institute. Produced in cooperation with the University of Pittsburgh.
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