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Essential Medications in Hospice: Why We Use What We Use

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Disclosure

- The presenter has no relevant financial relationships with manufacturers of any commercial products and/or providers of commercial services discussed in this presentation.
- This discussion will include the use of medications for off-label indications.

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Objectives

1. Explain factors that drive medication choice in hospice.
2. Identify appropriate medications for end-of-life symptom management.
3. Recognize initial doses of medications for management of symptoms.

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The Hospice Medicine Toolkit

Acetaminophen	Alprazolam	Atropine	Bisacodyl	Chlorpromazine
Dexamethasone	Haloperidol	Hydromorphone	Lorazepam	Methadone
Morphine	Oxycodone	Phenobarbital	Prednisone	Senna

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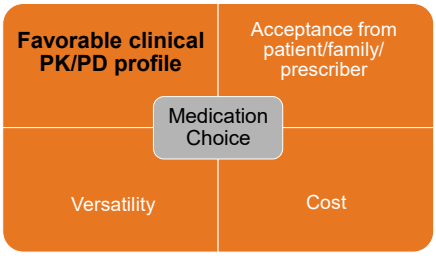
What Factors Drive Medication Choice?



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Pharmacokinetic and Pharmacodynamic Considerations

- Pharmacokinetics (PK)
  - What the body does to the drug
  - Absorption, distribution, metabolism, elimination
- Pharmacodynamics (PD)
  - What the drug does to the body
  - Therapeutic effects, adverse effects, duration and intensity of effects

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Pharmacokinetic Considerations

- Sublingual/buccal drug delivery
  - Sublingual surface highly permeable, buccal surface less permeable
  - Favorable drug properties: lipophilic, small molecular size, non-ionized
  - Rapidly-dissolving tablets or liquids preferred
    - Higher concentration liquids are preferred when using a liquid preparation
- Rectal drug delivery
  - Absorption of most drugs is delayed/prolonged or unpredictable
  - Favorable drug properties: alkaline pH, passive diffusion
  - Aqueous solutions preferred over solids or suspensions

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Pharmacokinetic Considerations

- Metabolism
  - Ideal drugs have no active metabolites, or metabolites that do not put patients at high risk of adverse effects
- Elimination/Excretion
  - Renal impairment common in the hospice population
    - Slows elimination of the drug (prolonged effect)
    - Slows elimination of metabolites (increased or toxic effect)
    - Proper dose adjustment for renal function helps prevent adverse effects

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Pharmacodynamic Considerations

- Therapeutic Effect
  - Ideal drug → effective for the therapeutic intent + minimal side effects
  - Even better → multiple desired therapeutic effects!
    - Example: oral corticosteroid (prednisone) for pain, breathing, appetite stimulation

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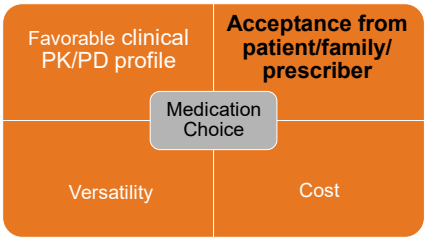
What Factors Drive Medication Choice?



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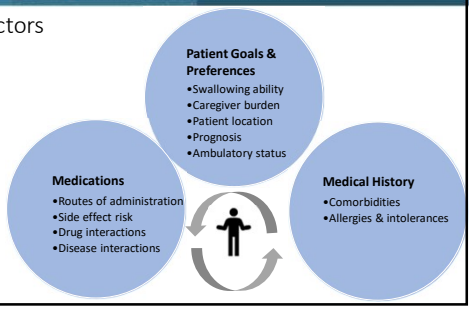
Patient Specific Factors



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Patient Specific Factors

- What are the patient's goals and expectations?
- What are the patient's comorbidities? Medication allergies?
- What medications is the patients already taking?
- What is the patient's expected prognosis? Swallowing capabilities? Ambulatory status?
- What is the patient's caregiver situation?

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Assessment of the patient's symptoms

- When did the symptom start?
- What makes it better or worse?
- What treatments has the patient already tried?
- Are there any potentially reversible underlying causes?
  - Side effects from a medication?
  - Acute changes in patient condition?

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Prescriber Concerns

- Familiarity with medication
  - Non-hospice prescribers may not be used to managing symptoms at end-of-life
  - Some medications are used more prevalently in hospice than other outpatient settings
- Prescribing preferences

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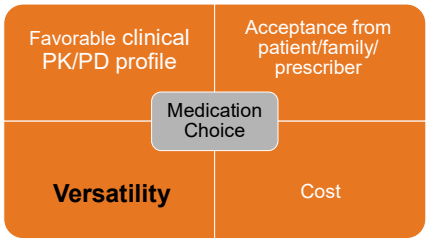
What Factors Drive Medication Choice?



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Versatility

What makes a drug versatile?

a) Easy for patient/caregiver to administer
b) Treats multiple symptoms
c) Able to be given via multiple routes of administration
d) All of the above

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Versatility

What makes a drug versatile?

a) Easy for patient/caregiver to administer
b) Treats multiple symptoms
c) Able to be given via multiple routes of administration
d) **All of the above**

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Versatility

- Multi-Symptom Treatment (MST)
  - Drug that can manage 2 or more symptoms with the same dose
    - Ex: morphine for pain and shortness of breath
- Multiple Routes of Administration
  - Oral dosage forms that can be given SL or PR
  - Injection forms that can be given IV, IM, subQ

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Versatility

- Dosage Form Preferences
  - Tablet
    - Small, easy to crush
  - Capsule
    - Able to be opened for easier swallowing
  - Oral liquid
    - High concentration/small volume for easier swallowing or sublingual administration near end of life
  - Injectable solution
    - Can be given subQ so that IV access or painful IM injection is not necessary

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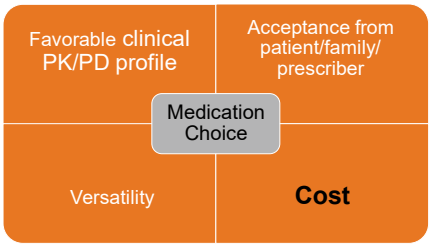

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Cost

Why it matters

- Payment/reimbursement for hospice services
  - Medicare reimbursement is on a per diem model
    - Hospice employee salaries
    - DME
    - Bereavement
    - Medical testing
    - Medications
    - Any service deemed part of the patient's plan of care

Where is there flexibility in controlling costs?

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Cost

- What does cost effectiveness mean?
  - Not only affordable, but also *effective*
- Cost-effectiveness analysis
  - Compares both cost and health outcomes of a treatment to alternative treatments
- Cost-effectiveness research
  - Conducted alongside efficacy, safety, tolerability research
  - Assigns value to medications
  - Determines the least costly and most effective way to achieve positive health outcome
  - Goal = efficient use of healthcare resources

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Take Note!

Cost alone should not prohibit the patient from receiving the most beneficial drug for his or her condition.

*Formularies aren't designed to provide patient-centered clinical decisions. They're structured to be a list of cost-effective medications for **most** patients. The medication selection process should account for specific patient parameters.*

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Medication Appropriateness Index

1. Is there an indication for the drug?
2. Is the medication effective for the condition?
3. Is the dosage correct?
4. Are the directions correct and understandable?
5. Are the directions practical?
6. Are there clinically significant drug-drug interactions?
7. Are there clinically significant drug-disease/condition interactions?
8. Is there unnecessary duplication with other drugs?
9. Is the duration of therapy acceptable?
10. Is this drug the least expensive alternative compared with others of equal usefulness?

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Keys to Managing Symptoms and Using Medications Effectively

- Minimize the number of drugs
- Consider alternatives for drugs that are ineffective, causing adverse events, are difficult to give or may cause harm in patient's disease state
- Start low and go slow with medications for symptom management
  - Titrate therapy as needed
- Educate the patient and caregivers on appropriate use of the medication
  - Explain the difference in PRN vs. scheduled medications
- Regularly review medications and appropriate use

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Essential Medications in Hospice Care

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Common Symptoms for Hospice Patients

Agitation	Anorexia	Anxiety
Constipation	Depression	Dyspnea
Edema	Fatigue	Nausea/vomiting
Fever	GERD	Hiccups
Insomnia	Pain	Muscle spasms
Secretions	Seizures	

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What are the Goals of Symptom Management?

- Improve patient quality of life
- Use medications efficiently
- Minimize medication side effects
- Keep medication dosing regimens simple
- Anticipate disease progression
- Provide information and choices to the patient and caregivers

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Commonly used Comfort Medications

- Analgesics
- Anticholinergics
- Antiemetics
- Antipsychotics
- Anxiolytics
- Laxatives

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Common Analgesics in Hospice Care

- Acetaminophen
- Morphine
- Hydromorphone
- Oxycodone
- Methadone

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Acetaminophen

- Pharmacologic Category: Analgesic
- Uses: Pain, Fever
- Starting Dose: 325 mg PO/PR q4h PRN
- Maximum Daily Dose: 3,000 mg for most hospice patients; 2,000 mg for patients with liver disease or malnutrition
- Adverse Effects
  - Generally well tolerated; liver & renal toxicity with chronic overdose
  - Boxed Warnings: rare but serious skin reactions: toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome (SJS)
- Monitoring Parameters
  - Symptom improvement
- Drug Interactions
  - Avoid multiple acetaminophen-containing medications to reduce accidental overdose
  - Avoid excessive alcohol use

Protus, 2015; LexiComp, 2021

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Morphine

- Pharmacologic Category: Opioid
- Uses: Pain, dyspnea, cough
- Starting Dose
  - Immediate-release: 2.5-5 mg PO/SL/PR q4h PRN
  - Extended-release: 15 mg PO/PR q12h
- Adverse Effects
  - Boxed Warnings: addiction, abuse and misuse; respiratory depression; accidental injection; risk of medication errors (oral solution); concomitant CNS depressants
  - Somnolence, constipation, nausea, hypotension, vomiting, dry mouth, urinary retention, pruritis, respiratory depression, opioid-induced neurotoxicity
- Monitoring Parameters
  - CNS side effects, vitals (including respiratory rate)

Protus, 2015; LexiComp, 2021

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Morphine

- Drug-Drug Interactions
  - CNS depressants, alcohol
- Clinical Pearls
  - Use caution in renal impairment; high risk for opioid-induced neurotoxicity
  - Inexpensive and versatile
  - Duration of action for immediate-release morphine is approximately 3-5 hours
    - Onset of action: approximately 30 minutes for oral medications
    - Peak dose effects: approximately 1 hour

Protus, 2015; LexiComp, 2021

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Short-Acting Opioids

Opioid	Initial Dosing	Clinical Pearls
Morphine	2.5-5 mg PO/SL/PR q4h PRN for pain or shortness of breath	• Versatile and cost-effective • Concentrated oral solution allows for easy administration in patients with difficulty swallowing • Use caution in patients with renal impairment • Lowest-dose of immediate-release tablets is 15 mg
Oxycodone	2.5 mg PO/SL/PR q4h PRN for pain or shortness of breath	• Preferred immediate-release opioid in patients with renal impairment • Concentrated oral solution is costly • Frequency of combination products (oxycodone/acetaminophen) are limited due to maximum daily doses of acetaminophen
Hydromorphone	1 mg PO/SL/PR q4h PRN for pain or shortness of breath	• Oral solution (1 mg/mL) is not concentrated • Use caution in patients with renal impairment

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Patient Case: Susan

Mrs. Elliot is 84 years old with end stage COPD, CVA, dysphagia, diabetes, and Stage IV CKD. She has decided to elect hospice care at home. She is too short of breath to ambulate and says her breathing is not controlled despite optimal inhaler use. She is hesitant to use morphine because she received it in the hospital and it made her feel loopy. She is opioid-naïve. What is the best choice for Mrs. Elliot to palliate her shortness of breath?

a) Oxycodone 20mg/ml oral concentrate 2.5 mg (0.125 mL) PO/SL q4h PRN for shortness of breath or pain
b) Hydromorphone 1mg/ml oral solution 1 mg (1 mL) PO/SL q4h PRN for shortness of breath or pain
c) Oxycodone 5mg tablet 2.5 mg (1/2 tablet) PO/SL q4h PRN for shortness of breath or pain
d) Morphine 20mg/ml oral concentrate 5 mg PO/SL q4h PRN for shortness of breath or pain

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b) Hydromorphone 1mg/ml oral solution 1 mg (1 mL) PO/SL q4h PRN for shortness of breath or pain
c) Oxycodone 5mg tablet 2.5 mg (1/2 tablet) PO/SL q4h PRN for shortness of breath or pain
d) Morphine 20mg/ml oral concentrate 5 mg PO/SL q4h PRN for shortness of breath or pain

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Methadone

- Pharmacologic Category: Opioid
- Uses: Pain (somatic, visceral, and neuropathic pain)
- Starting Dose (opioid-naive)
  - 2.5 mg PO q12h or 2.5 mg PO q24h
- Adverse effects
  - Boxed Warnings: addiction, abuse, and misuse; respiratory depression; QT prolongation; accidental ingestion; concomitant CNS depressants
  - Dizziness, sedation, N/V, constipation, QT prolongation, arrhythmias, respiratory depression, urinary retention
- Monitoring parameters
  - Pain control, mental status, sedation level
  - Respiratory rate, heart rate & rhythm

Protus, 2015; LexiComp, 2021

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Methadone

- Drug-Drug Interactions
  - CYP 3A4 and 2B6 (inducers and inhibitors)
  - QTc Prolonging Medications
  - CNS Depressants
- Clinical Pearls
  - Methadone is not as commonly used outside of hospice and palliative care so prescribers may not be as comfortable with dosing
  - Methadone has a long half-life
    - Caution with initiation and dose titration
  - Avoid use for shortness of breath; reserve methadone for pain management
  - Available as an oral solution or an oral tablet (may be crushed)
    - Only 5 mg and 10 mg tablets may be used for pain management

Protus, 2015; LexiComp, 2021

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Long-Acting Opioids

- Extended-release dose preparations
  - Mechanism to slowly release drug over time
  - Duration of action: 12h, 24h, 72h, 1 week
  - Tablets, capsules, transdermal patches
  - Typically cannot be crushed or given SL/PR
- Morphine ER tablets
  - Least costly of the ER oral dose preparations
  - ER capsules are higher cost, but can be opened for easier swallowing
  - ER tablets may be given rectally at EOL
- Fentanyl transdermal patches
  - Easy to administer
  - Harder to titrate in patients having pain crisis
  - Newer patch strengths are more costly

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Common Anticholinergics in Hospice Care

- Atropine
- Hyoscyamine
- Glycopyrrolate
- Scopolamine

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Anticholinergics

Anticholinergics	Initial Dosing	Clinical Pearls
Atropine 1% ophthalmic solution	2 drops SL q4h PRN	• 1st line treatment for terminal secretions are non-pharmacologic interventions • 1% ophthalmic solution is given sublingually; educate caregivers about non-standard route • Easy dosage formulation for caregivers to administer
Hyoscyamine	0.125 mg SL q4h PRN	• 1st line treatment for terminal secretions are non-pharmacologic interventions • ODT are easier to administer than oral tablets
Glycopyrrolate	1 mg PO q8h PRN	• Bioavailability is low; poor choice to give orally for terminal secretions • May be useful for treating chronic sialorrhea • Fewer CNS adverse effects (sedation, confusion) • Oral solution is costly • Injectable preparation may be useful for management of bowel obstruction (oral dosing is not equivalent to IV)
Scopolamine	1 patch q72h TD	• Should not be used for terminal secretion management due to slow onset of action • If using for chronic sialorrhea, rotate patch site to avoid skin irritation

Protus, 2015; LexiComp, 2021

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Common Antiemetics in Hospice Care

- Haloperidol
- Promethazine
- Prochlorperazine

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Haloperidol

- Pharmacologic Category: typical antipsychotic
- Uses: agitation, nausea/vomiting
- Starting Dose: 0.5 mg PO/SL/PR q4h PRN
- Adverse Effects
  - Boxed Warming: Elderly patients with dementia-related psychosis treated with antipsychotics are at an increased risk of death compared to placebo
  - EPS, QTc prolongation, anticholinergic, insomnia, anxiety, seizures
- Monitoring Parameters
  - Vital signs, hyperglycemia
  - Abnormal involuntary movements

Protus, 2015; LexiComp, 2021

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Haloperidol

- Drug-Drug Interactions
  - CYP2D6 (inhibitors and inducers)
  - Anti-Parkinson Agents (dopamine agonists)
  - QTc Prolonging Medications
  - CNS depressants
- Clinical Pearls
  - Always assess for underlying causes of agitation/delirium prior to use of haloperidol
  - Use may be limited in nursing facilities due to regulations regarding PRN use of psychotropics

Protus, 2015; LexiComp, 2021

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Antiemetics

Antiemetic	Initial Dosing	Clinical Pearls
Haloperidol	0.5 mg PO/SL/PR q6h PRN	• Versatile; available as an oral concentrate (2 mg/mL), oral tablets or injectable • Useful for management of agitation • Avoid use in Parkinson's disease or Lewy Body Dementia • Cost-effective medication
Promethazine	25 mg PO/PR q6h PRN	• More sedating than haloperidol • Preferred agent for patients with Parkinson's disease or Lewy Body Dementia • Suppositories are high cost
Prochlorperazine	10 mg PO q6h PRN Or 25 mg PR q12h PRN	• More sedating than haloperidol • Avoid use in Parkinson's disease or Lewy Body Dementia • Suppositories are costly
Ondansetron	4 mg PO/SL q8h PRN	• Most efficacious when scheduled • Typically reserved for chemotherapy or post-op nausea/vomiting • Can cause constipation, which may worsen nausea in some patients

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Common Antipsychotics in Hospice Care

- Haloperidol
- Chlorpromazine
- Quetiapine
- Risperidone

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Antipsychotics

Antipsychotic	Initial Dosing	Clinical Pearls
Haloperidol	0.5 mg PO/SL/PR q6h PRN	• Versatile; available as an oral concentrate (2 mg/mL), oral tablets or injectable • Avoid use in Parkinson's disease or LBD • Also useful for nausea/vomiting • Cost-effective medication
Chlorpromazine	10 mg PO/SL q8h PRN or ATC	• More sedating than haloperidol • Use in caution in ambulatory patients due to risk of orthostatic hypotension • One of the antipsychotics with highest risk for seizure • Avoid use in Parkinson's disease or LBD
Quetiapine	25 mg PO BID	• Preferred antipsychotic in patients with Parkinson's disease or LBD • Most sedating of the atypical antipsychotics • Limited dosage formulations
Risperidone	0.25 mg PO BID	• Available as an oral solution, ODT, or oral tablet; ODT more expensive than traditional tablets • May have some benefits for nausea when haloperidol in shortage

Protus, 2015; LexiComp, 2021

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Common Anxiolytic in Hospice: Lorazepam

- Pharmacologic Category: Benzodiazepine
- Uses: Anxiety, shortness of breath related to anxiety, muscle spasms, seizure, insomnia
- Starting Dose
  - Lorazepam 0.5 mg PO/SL/PR q4h PRN for anxiety or shortness of breath
  - Dose may differ for other indications
- Adverse Effects
  - Boxed Warning: concomitant use with opioids; abuse, misuse and addiction; dependence and withdrawal reactions
  - Sedation, dizziness, weakness, ataxia, agitation
- Monitoring Parameters
  - Symptom control, respiratory rate, hypotension

Protus, 2015; LexiComp, 2021

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Lorazepam

- Drug-Drug Interactions
  - CNS depressants
- Clinical Pearls
  - Potential for paradoxical worsening of agitation
  - Preferred benzodiazepine in elderly patients due to lack of active metabolites
  - If using for insomnia related to anxiety, may require higher doses
  - Dose recommended for treatment of acute seizures:
    - Lorazepam 2 mg PR/SL every 15 minutes as needed for acute seizure activity
  - Approximate PO equivalence to other benzodiazepines:
    - Lorazepam 1 mg…alprazolam 0.5 mg…diazepam 5 mg

Protus, 2015; LexiComp, 2021

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Common Laxatives in Hospice Care

- Senna
- Docusate and Senna
- Bisacodyl

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Senna

- Pharmacologic Category: Stimulant Laxative
- Uses: constipation (opioid-induced)
- Starting Dose
  - Senna 8.6 mg tablets 2 tablets PO QHS
- Adverse Effects
  - Diarrhea, nausea, vomiting, abdominal cramps, electrolyte & fluid imbalance
- Clinical Pearls
  - May use in combination with a stool softener (docusate)
  - Dose may be titrated up to a maximum 8 tablets per day

Protus, 2015; LexiComp, 2021

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Laxatives

Laxative	Initial Dosing	Clinical Pearls
Bisacodyl	5 mg PO daily 10 mg PR daily as needed	• May combine with oral stool softener • Suppositories may not be effective if rectum is full of stool • Onset of action, 6-12 hours (oral)
Senna	8.6 mg tablets, 2 tablets PO daily	• Available as an oral solution (8.8 mg/5 mL) • May combine with oral stool softener • Onset of action, 6-12 hours (oral)
Docusate + Senna	2 tablets PO daily	• May not be more effective than single product • Poor taste when crushed • Onset of action, 6-12 hours (oral)

Protus, 2015; LexiComp, 2021

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Patient Case- Bobby

Bobby is a 72-year-old male on hospice with a primary diagnosis of lung cancer with metastases to the bone. Bobby is experiencing significant issues with shortness of breath, even at rest. Other past medical history includes hypertension and depression.

Current medications:
- Albuterol 1 unit via nebulizer q4h PRN
- Lisinopril 10 mg PO once daily
- Sertraline 100 mg PO once daily
- Prednisone 20 mg PO once daily

Which of the following initial medication orders would be most beneficial for treating Bobby's shortness of breath?

a) Morphine (20 mg/mL) 2.5 mg (0.125 mL) PO q4h PRN for shortness of breath
b) Lorazepam 0.5 mg PO q4h PRN for shortness of breath
c) Benzonatate 100 mg PO TID PRN for cough
d) Haloperidol 0.5 mg PO q4h PRN for agitation/shortness of breath

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- Albuterol 1 unit via nebulizer q4h PRN
- Lisinopril 10 mg PO once daily
- Sertraline 100 mg PO once daily
- Prednisone 20 mg PO once daily
- Morphine 2.5 mg PO q4h PRN dyspnea

What additional comfort medication should be added to Bobby's profile at this time?

a) Lorazepam 0.5 mg PO q4h PRN for nausea/vomiting

b) Haloperidol 0.5 mg PO q4h PRN for nausea/vomiting

c) Senna 8.6 mg tablets 2 tablets PO once daily at bedtime PRN for opioid-induced constipation

d) Atropine 1% ophthalmic solution 2 gtts SL q4h PRN for terminal secretions

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Patient Case- Bobby

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Key Points

- The key factors that affect why we use the medications we use include favorable clinical pharmacological properties, versatility, patient and provider acceptance, and cost.
- Ideal medications can treat multiple symptoms at the same dose, can be given via multiple routes of administration, and have minimal side effects at the therapeutic dose.
- Not all patients are candidates for these common medications. Medication selection and treatment for all symptoms should be patient-centered.

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Thank You

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