OPTUM

# Hospice Pharmacotherapy 101:
## Management of Psychiatric Symptoms

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## Disclosure

- I have 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.

## Objectives

- Review pathophysiology and assessment of common psychiatric symptoms at the end of life: anxiety, depression, agitation/delirium, and insomnia
- Discuss non-pharmacologic and pharmacologic treatment of common psychiatric symptoms at the end of life
- Develop a plan for addressing psychiatric symptoms based on clinical presentation and patient-specific goals of care

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## The LTC Mega-Rule: Unnecessary Drugs (F757)

- Inadequate indication for use
- Inadequate monitoring
- Excessive dose
- Excessive duration
- Adverse consequences

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## The LTC Mega Rule: Psychotropic Drugs (F758)

- Psychotropic medication: any drug that affects brain activities associated with mental processes and behavior, including, but not limited to:
  - Antidepressants
  - Anxiolytics
  - Hypnotics
  - Antipsychotics
  - Other
    - Not specifically listed, but could potentially include antihistamines, antiepileptic drugs, anti-Parkinson's drugs, muscle relaxants

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## The LTC Mega-Rule: Psychotropic Drugs (F758)

- 14 day limit on as-needed (PRN) orders
- For psychotropics that are *not* antipsychotics, PRN orders may be extended if:
  - Prescriber or attending physician believes it to be appropriate
  - Rationale for extending the time period is documented in the medical record
  - A specific time duration of the extension is indicated
- For antipsychotics, PRN orders may only be re-ordered if:
  - Prescriber or attending physician directly evaluates the resident (face-to-face or telemedicine) and documents:
    - If the medication is still needed on a PRN basis
    - The benefit of the medication to the patient
    - If the medication has improved the patient's expressions or indications of distress
  - Rationale for extending the time period is documented in the medical record
  - A specific time duration of the extension is indicated

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## Patient Case: Amanda Anderson

45 year old female admitted to hospice with recurrent breast cancer and lung metastases. The tumor in her breast can be palpated inside her right axilla. Patient is the primary care provider for 2 children under the age of 10, and has a supportive husband who works full time outside of their home.

PMH: diabetes, tobacco use

Allergies: codeine

Medications:

-Glucophage (Metformin®) 1000mg by mouth twice daily

-Glucotrol (Glipizide XL®) 10mg by mouth every morning

-Dexamethasone (Decadron®) 4mg by mouth qAM

-Morphine ER (MS Contin®) 15mg by mouth q8h ATC

-Morphine sulfate 20mg/mL solution (Roxanol®) 5mg by mouth q4h PRN breakthrough pain

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## Anxiety

## Anxiety: Prevalence and Background

- Prevalence not well studied, but reported to be 21-23% in palliative care patients
- Many conditions and medications can precipitate anxiety

| Conditions | Medications |
|---|---|
| • Impaired physical activity | • Albuterol |
| • Decreased social life | • Caffeine |
| • Loss of independence | • Pseudoephedrine |
| • Uncontrolled symptoms | • Amphetamines |
| • Depression | |
| • Drug withdrawal states | |

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## Anxiety: Characteristics

- Exaggerated worry, tension, and irritability that appears to have no cause or is more intense than the situation warrants
- Physical signs:
  - Restlessness
  - Headaches
  - Sweating
  - Trembling
  - Muscle twitching or tension
  - Dyspnea
  - Insomnia

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## Anxiety: Non-Pharmacologic Treatment

- Treat underlying cause if appropriate
  - e.g. decreased social interactions
- Psychotherapeutic support
  - Incorporate interdisciplinary team including social workers, spiritual care counselors, and psychologists
  - Techniques:
    - Simple relaxation exercises
    - Distraction strategies

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## Anxiety: Pharmacological Treatment

- History of effective treatments?
- Aim to prevent anxiety, not just treat flare-ups
- Pain management analogy:
  - Scheduled medication + PRN orders
- Start low and titrate up as needed
- Assess for underlying depression
  - If life expectancy > 2-3 months, add serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI)?

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## Benzodiazepines for Anxiety

| Medication | Approximate Equivalent Dose (mg) | Usual Dosing Regimen | Peak Effect (PO) | Available Routes of Administration |
|---|---|---|---|---|
| Lorazepam (Ativan®) | 1 | 0.5mg q6h | 2-4 hours | PO, SL, PR, IV, SQ, IM |
| Alprazolam (Xanax®) | 0.5 | 0.25mg q6h | 1-2 hours | PO, SL, PR |
| Diazepam (Valium®) | 5 | 5mg q8h | 0.5-2 hours | PO, SL, PR, IV, IM |

**Doses should be individualized based on patient-specific factors*

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## Benzodiazepines for Anxiety

- Short-acting benzodiazepines are preferred
- When possible, avoid agents with active metabolites
  - Alprazolam
  - Diazepam
- Consider an agent that may be beneficial for other symptoms
  - Seizures
  - Insomnia
- Consider other disease states
  - Liver disease – avoid benzodiazepines undergoing oxidative metabolism
    - Alprazolam
    - Clonazepam
    - Diazepam

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## Benzodiazepines: Adverse Events

- Excessive sedation
- Lack of coordination
- Dizziness
- Falls and fractures
- Worsened cognition
- Delirium
- Respiratory depression
- Paradoxical worsening of anxiety or agitation
- Dependency and withdrawal

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## Considerations for Amanda Anderson

1. **Would you be concerned about anxiety in this patient?**
   A. Yes
   B. No

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## Considerations for Amanda Anderson

1. **Would you be concerned about anxiety in this patient?**
   - **A. Yes**
   - B. No

2. **What, if any, therapies would you initiate for the patient?**
   - A. Lorazepam 0.25mg PO Q4H prn anxiety
   - B. Diazepam 10mg PO BID and Q4H prn anxiety
   - C. Citalopram 20mg daily
   - D. None at this time

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## Considerations for Amanda Anderson

1. **Would you be concerned about anxiety in this patient?**
   - **A. Yes**
   - B. No

2. **What, if any, therapies would you initiate for the patient?**
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   - C. Citalopram 20mg daily
   - D. None at this time

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# Depression

## Depression: Prevalence and Background

- Clinical depression prevalence is estimated between 20-50%
- Clinical depression is a complication of life-limiting illness and extends beyond the phase of adaptation to loss in the grieving process
- Potential causes or contributors to depression symptoms include:
  - Untreated symptoms (pain, anxiety, nausea, etc)
  - Spiritual concerns
  - Sudden loss or receiving bad news

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## Depression: Characteristics

- Clinical features of a depression episode include **depressed mood** and the following symptoms (SIG-E-CAPS):
  - **S**leep disturbance
  - **I**nterest/pleasure reduction
  - **G**uilty feeling or thoughts of worthlessness
  - **E**nergy change/fatigue
  - **C**oncentration impairment
  - **A**ppetite/weight change
  - **P**sychomotor retardation or agitation
  - **S**uicidal thoughts
- Asking **"Are you depressed?"** may be a sufficient depression screening
- Inquire about presence of suicidal thoughts or intent in patient with signs or symptoms of depression

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## Depression: Non-Pharmacologic Treatment

- Semi-psychotherapeutic techniques
  - Incorporate interdisciplinary team including social workers, spiritual care counselors and psychologists
  - Examples: dignity therapy, short-term life review, life completion discussions
- Cognitive-behavioral techniques
  - Relaxation
  - Music therapy
  - Art therapy

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## Depression: Pharmacological Treatment

- Treatment regimens based on the patient's prognosis
  - **Shorter prognosis** (less than 4-6 weeks)
    - Drug of choice: stimulants (off-label indication)

| Medication | Starting Dose | Dosage Forms |
|---|---|---|
| Methylphenidate (Ritalin®) | 2.5-10mg PO BID (usually 8AM and 12PM) | Tablets, chewable tablets, oral solution |

  - **Longer prognosis** (greater than 4-6 weeks)
    - Drugs of choice: **selective serotonin reuptake inhibitors (SSRIs)**
      - Less risk of side effects compared to tricyclic antidepressants (TCAs)
      - Onset of action generally 4-6 weeks
      - All can lower seizure threshold

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## SSRIs and SNRIs

| Medication | Starting Dose | Dosage Forms | Notes |
|---|---|---|---|
| Fluoxetine (Prozac®) | 10-20mg PO daily | Tablets, capsules, oral solution | • Long half-life (4-6 days)<br>• Dose adjustment in liver disease |
| Sertraline (Zoloft®) | 25-50mg PO daily | Tablets, oral solution | • Caution in liver disease |
| Citalopram (Celexa®) | 10-20mg PO daily | Tablets, oral solution | • > 60 y/o: max dose 20mg/day<br>• Caution in liver disease |
| Escitalopram (Lexapro®) | 5-10mg PO daily | Tablets, oral liquid | • > 60 y/o: max dose 10mg/day<br>• Caution in liver disease |
| Paroxetine (Paxil®) | 10mg PO daily | Tablets, oral suspension | • Highest risk of anticholinergic effects<br>• Withdrawal symptoms due to short half-life |
| **SNRI**<br>Duloxetine (Cymbalta®) | 30-60mg PO daily | Capsules | • Indication for depression and neuropathy |

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## Antidepressant SSRIs: Adverse Events

- Cautions:
  - Increased rate of fracture and decrease bone mineral density
  - Dose-dependent QT prolongation – citalopram, escitalopram
- Side effects:
  - Anxiety, insomnia
  - Nausea, diarrhea, anorexia
  - Hyponatremia and SIADH
  - Lethargy, mental status changes
  - Serotonin syndrome
    - GI distress, tremor, hyperreflexia, agitation, hypertension, tachycardia, diaphoresis, hyperthermia
  - Withdrawal symptoms

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## Depression: Monitoring

- Monitor depressed patients for development of suicidal ideation or intent
  - FDA boxed warning for antidepressants
- Symptom improvement:
  - Week 1: decreased agitation/anxiety, improved sleep and appetite
  - Week 1-3: improved activity, concentration, thinking and self-care
  - Week 2-4: improved mood, return of pleasure, decreased hopelessness

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## Depression: Suboptimal Treatment Response

| | |
|---|---|
| **Patient tolerating and below therapeutic dose range** | • Consider increasing dose of antidepressant (AD) |
| **Within therapeutic dose range of newly initiated AD** | • Assess patient safety and prognosis<br>• Monitor response over 6-8 weeks<br>• Maintain current dose |
| **Adequate trial (6-8 weeks) on current regimen** | • Changing medication within same/different AD class<br>• Obtain psychiatric consult for combination/augmentation therapies |

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## Considerations for Amanda Anderson

1. **Would you be concerned about depression in this patient?**
   A. Yes
   B. No

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## Considerations for Amanda Anderson

1. **Would you be concerned about depression in this patient?**
   - **A. Yes**
   - B. No

2. **What, if any, therapies would you initiate for the patient?**
   - A. Fluoxetine 10mg by mouth daily
   - B. Psychosocial support
   - C. None

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## Considerations for Amanda Anderson

1. **Would you be concerned about depression in this patient?**
   - **A. Yes**
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2. **What, if any, therapies would you initiate for the patient?**
   - A. Fluoxetine 10mg by mouth daily
   - **B. Psychosocial support**
   - C. None

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# Agitation and Delirium

## Agitation and Delirium: Prevalence and Background

- Delirium is estimated to occur in more than 80% of all terminally ill patients prior to death
- Agitation is a component of delirium in approximately 46% of patients
- Etiology is multifactorial

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## Potentially Reversible Causes of Delirium

- Urinary retention
- Constipation
- Hypoxemia
- Infection
- Metabolic abnormalities
  - ↑ or ↓ sodium
  - ↑ calcium
  - Altered blood glucose
- Brain tumors, metastases
- Dehydration
- Fatigue, sleep deprivation, altered circadian rhythms
- Severe anemia
- Nutritional deficiencies
  - Thiamine, folate, B12
- Drug and alcohol withdrawal
- Pain (especially uncontrolled)

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## Agitation and Delirium: Characteristics

### Agitation

- An unpleasant state of extreme arousal, increased tension, irritability
- Extreme agitation can lead to confusion, hyperactivity, and hostility
- Agitation can have a **gradual or sudden onset**
  - May last minutes, weeks, or months
- Pain, stress and fever can all increase agitation

### Delirium

- **Alterations in consciousness and attention** associated with:
  - Cognitive (e.g. amnesia), behavioral (e.g. agitation), perceptual disturbances (e.g. hallucinations)
- Other clinical features:
  - Sleep-wake cycle disturbance (diurnal disruptions)
  - Delusions
  - Emotional lability
    - Psychomotor activity disturbances

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## Take Note!

Assess for and, if appropriate, treat reversible causes of delirium and agitation.

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## Agitation and Delirium: Non-Pharmacologic Treatment

- Environmental control:
  - Sound, lighting, stimuli
  - Frequent reorientation
- Psychosocial support:
  - Family, friends, counselors
- Distraction:
  - Relaxation, massage, music
- Adequate sleep

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## Agitation and Delirium: Treatment

- If appropriate, treat reversible causes
  - Individualized approach based on patient's goals of care
- Reduce, eliminate, or change drugs that may be contributing to delirium
- Where appropriate, use hypnotic medication to provide adequate sleep
- Consider antipsychotic drugs to treat confusion
  - Neuroleptics (antipsychotics): off label use
    - Haloperidol (Haldol®), chlorpromazine (Thorazine®)
    - Olanzapine (Zyprexa®), quetiapine (Seroquel®), risperidone (Risperdal®)
- Add benzodiazepines only if needed for anxiety and/or restlessness

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## Antipsychotic Agents

- May help with agitation, hallucinations, and aggression
- FDA Black Box warning in elderly patients with dementia
  - Increased risk of mortality compared to placebo
    - Meta-analysis showed 60-70% increased risk of death
  - Most deaths are cardiovascular or infectious in nature
- Always start at low end of dosing range and titrate cautiously
  - Do not usually need high doses indicated for psychiatric disorders for agitation/delirium

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## Antipsychotic Agents: Adverse Events

- Extrapyramidal side effects (EPS)
  - Risperidone > ziprasidone > olanzapine > quetiapine
  - Higher risk of EPS with haloperidol
- Anticholinergic side effects
  - Olanzapine ≥ quetiapine > risperidone = ziprasidone = aripiprazole
  - Minimal to no anticholinergic effect with haloperidol
- Orthostatic hypotension
  - Quetiapine > risperidone > olanzapine = ziprasidone = aripiprazole
  - No orthostatic hypotension with haloperidol
- Sedation
  - Quetiapine ≥ olanzapine > risperidone = ziprasidone = aripiprazole
  - Minimal to no sedation with haloperidol at lower doses

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## Antipsychotic Agents: Special Populations

- Lewy body dementia (LBD)
  - Patients are at an increased risk of adverse effects with antipsychotics
  - Response is often worse than with other types of dementia
- Parkinson's disease (PD)
  - Patients are at an increased risk of extrapyramidal symptoms with antipsychotics
- Quetiapine
  - Preferred antipsychotic for patients with LBD and PD

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## Antipsychotic Agents

| Medication | Approximate Equivalent Dose (mg) | Usual Dosage Regimen | Available Routes of Administration |
|---|---|---|---|
| Haloperidol (Haldol®) | 1 | 0.5mg PO BID | PO, SL, PR, IM, SQ, IV |
| Chlorpromazine (Thorazine®) | 50 | 25mg PO BID | PO, SL, PR, IM, IV |
| Olanzapine (Zyprexa®) | 2.5 | 2.5mg PO Daily | PO, SL, IM |
| Quetiapine (Seroquel®) | 50 | 50mg PO Daily | PO |
| Risperidone (Risperdal®) | 1 | 0.5mg PO BID | PO, SL |

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## Antipsychotic Agents

| Antipsychotic Agent | Comments |
|---|---|
| Haloperidol (Haldol®) | Least sedating antipsychotic; treats nausea/vomiting; AVOID in Parkinson's Disease and Lewy Body Dementia |
| Chlorpromazine (Thorazine®) | FDA indication for hiccups; other uses: headache in brain cancer; tenesmus; nausea/vomiting; may cause orthostatic hypotension in ambulatory patients; AVOID in Parkinson's Disease and Lewy Body Dementia |
| Olanzapine (Zyprexa®) | Potential for lipid and glucose abnormalities; sedating |
| Quetiapine (Seroquel®) | Potential for lipid and glucose abnormalities; sedating; PREFERRED in Parkinson's Disease and Lewy Body Dementia |
| Risperidone (Risperdal®) | Potential for lipid and glucose abnormalities; sedating |

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## Considerations for Amanda Anderson

1. **Which of the following could contribute to the development of delirium in this patient?**
   - A. Opioid regimen
   - B. Continuation of medications for diabetes
   - C. Brain metastases
   - D. All of the above

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## Considerations for Amanda Anderson

1. **Which of the following could contribute to the development of delirium in this patient?**
   - A. Opioid regimen
   - B. Continuation of medications for diabetes
   - C. Brain metastases
   - **D. All of the above**

2. **What actions can we ensure are occurring for the patient to reduce risk of delirium?**
   - A. Regularly monitor blood glucose levels, discontinue therapy when no longer indicated
   - B. Prevent and treat constipation
   - C. Monitor pain control
   - D. All of the above

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## Considerations for Amanda Anderson

1. **Which of the following could contribute to the development of delirium in this patient?**
   - A. Opioid regimen
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   - C. Monitor pain control
   - **D. All of the above**

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## Insomnia

## Insomnia: Prevalence and Background

- Prevalence not well studied, but reported to be as high as 70%
- Insomnia is the occurrence of difficulty with initiating or maintaining sleep 3 or more days per week that results in impaired daytime function
- Potential causes or contributors to insomnia include:
  - Untreated physical symptoms (pain, anxiety, nausea, etc)
  - Other psychological disorders include insomnia in diagnostic criteria
  - Medications (caffeine, corticosteroids, diuretics, nicotine)

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## Insomnia: Characteristics

- Insomnia symptoms:
  - Difficulty with sleep initiation
  - Decreased duration of sleep intervals
  - Early morning wakening
- Patient may appear to sleep an adequate duration but sleep may not be restful or restorative
- Assess for barriers to sleep:
  - New location/caregiver
  - Noise
  - Uncontrolled symptoms
  - Fearful of dying/loneliness
  - Sleep apnea
  - Restless leg
  - Medications
  - Depression

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## Insomnia: Non-Pharmacologic Treatment

| | |
|---|---|
| **Sleep hygiene** | • Appropriate surroundings<br>• Quiet atmosphere<br>• Limit caffeine/alcohol |
| **Sleep restriction** | • Limit daytime naps<br>• Set realistic bedtimes |
| **Stimulus control** | • Reducing time spent in bed awake |
| **Cognitive therapy** | • Control pre-sleep thoughts<br>• Relaxation strategies |

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## Insomnia: Pharmacological Treatment

- Assessment of sleep disturbance can be helpful to choose therapy

**Sleep onset**
(falling asleep) difficulty

- May benefit from shorter-acting agent
  - e.g. lorazepam

**Maintenance**
(staying asleep) difficulty

- Evaluate for possible causes of wakening
- May benefit from a longer acting agent
  - e.g. trazodone

**Circadian rhythm dysfunction**
(biological daily cycle)

- Common in neurocognitive disorders or blindness
- May benefit from melatonin

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## Benzodiazepines for Insomnia

| Medication | Approximate Equivalent Dose (mg) | Usual Dosing Regimen | Available Routes of Administration |
|---|---|---|---|
| Lorazepam (Ativan®) | 1 | 0.5mg QHS | PO, SL, PR, IV, SQ, IM |
| Temazepam (Restoril®) | 30 | 15mg QHS | PO |

- Avoid duplications of therapy (multi-symptom therapy)
- May worsen symptoms of delirium

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## Benzodiazepine-Like Medications

- The Zs
  - Produce hypnotic effects similar to benzodiazepines
    - No clear advantage over benzodiazepines
  - Less anxiolytic and anticonvulsant effects
  - Short duration of action of 4 to 6 hours
  - More effective for sleep onset

| Medication | Usual Dosing Regimen | Dosage Forms |
|---|---|---|
| Zolpidem (Ambien®) | 5-10mg PO QHS | Tablets |
| Zaleplon (Sonata®) | 5-10mg PO QHS | Capsules |
| Eszopiclone (Lunesta®) | 1mg PO QHS | Tablets |

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## Antidepressants for Insomnia

| Medication | Usual Dosing Regimen | Comments |
|---|---|---|
| Trazodone (Desyrel®) | 25-100mg PO QHS | • Lower doses for sleep than depression |
| Mirtazapine (Remeron®) | 7.5-15mg PO QHS | • Useful for appetite stimulation<br>• Less sedating at higher doses |
| Doxepin (Silenor®) | 3-6mg PO QHS | • Also useful for itching |

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## Melatonin for Insomnia

- Available over-the-counter
- Potentially useful in reducing sleep onset latency in sleep-related disorders
  - Evidence is less clear for improvements in sleep duration or quality
- Drowsiness may occur within 30 minutes of taking dose
- Possible adverse reactions:
  - Dizziness
  - Excessive daytime sedation
  - Headache
  - Nausea
  - Nightmares

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## Diphenhydramine for Insomnia

- Sedating agent in several over-the-counter sleep aids
  - Tylenol PM®, Advil PM®, Aleve PM®
- Use as a sedative in the elderly is not recommended
- Disease-related cautions:
  - Cardiovascular disease
  - Glaucoma
  - Prostatic hyperplasia
  - Thyroid dysfunction
- Anticholinergic risks:
  - Urinary retention
  - Dry mouth
  - Constipation
  - Blurred vision

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## Take Note!

Pay attention to side effect profiles of medications and use them to your advantage

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## Antipsychotics for Insomnia

- Typical/atypical antipsychotics
  - Off-label use
  - Not first line agents, unless psychiatric condition or symptoms present
- Quetiapine
  - Commonly prescribed for sleep disturbances
    - Depression, bipolar, schizophrenia FDA indications
    - Modest improvement in total sleep time (TST) ~20-40min
    - Side effects: daytime sleepiness, agitation, dry mouth, CVA
    - Not enough evidence to recommend first line unless also treating psychiatric symptoms
      - Insomnia not an acceptable use of quetiapine for patients in LTC facilities
      - Citation risk F329

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## Patient Case: Amanda Anderson

45 year old female on hospice with recurrent breast cancer and lung metastases. Patient is primary care provider for 2 children under the age of 10, and has a supportive husband who works full time outside of their home.

**Current complaint: patient is complaining of difficulty sleeping at night – occurring for about a week. Pain is controlled well.**

Medications:

-Glucophage (Metformin®) 1000mg PO BID

-Glucotrol (Glipizide XL®) 10mg PO qam

-Dexamethasone (Decadron®) 4mg PO qam

-Morphine ER (MS Contin®) 15mg PO q8h ATC

-Morphine sulfate 20mg/ml solution (Roxanol®) 5mg PO q4h PRN breakthrough pain

-Lorazepam (Ativan®) 0.25mg PO q4h PRN anxiety

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## Patient Case: Amanda Anderson

- Goals: to remain as alert as possible during the day, sleep well at night, have energy to interact with children and husband
- What information would be beneficial to determine appropriate **medication** therapy for treating insomnia?

A. Are you having trouble falling asleep or staying asleep?
B. What is causing your anxiety?
C. Are you feeling depressed?

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## Patient Case: Amanda Anderson

- Goals: to remain as alert as possible during the day, sleep well at night, have energy to interact with children and husband
- What information would be beneficial to determine appropriate **medication** therapy for treating insomnia?

**A. Are you having trouble falling asleep or staying asleep?**
B. What is causing your anxiety?
C. Are you feeling depressed?

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## Patient Case: Amanda Anderson

- The patient states she is having trouble falling asleep because she feels overwhelmed and anxious before bed.
- What medication regimen would you initiate?

A. Trazodone 50mg QHS
B. Lorazepam 0.5mg QHS
C. Zolpidem 5mg QHS

- What non-pharmacologic treatment options would you suggest?

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## Patient Case: Amanda Anderson

- The patient states she is having trouble falling asleep because she feels overwhelmed and anxious before bed.
- What medication regimen would you initiate?

A. Trazodone 50mg QHS
**B. Lorazepam 0.5mg QHS**
C. Zolpidem 5mg QHS

- What non-pharmacologic treatment options would you suggest?

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## Key Points

- Aim to prevent anxiety, which may require scheduling medication doses throughout the day
- The pharmacologic treatment regimen for depression should depend on the patient's prognosis
- Assess for, and if appropriate, treat reversible causes of delirium and agitation
- Determine if patient is having trouble falling asleep or staying asleep to choose appropriate regimen for relieving insomnia

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OPTUM

# Questions?

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Hospice Pharmacy Services

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