GERIATRIC PHARMACIST

BOOT CAMP

Psychiatric Disorders in the Older Adult

Marketa Marvanova, PharmD, PhD, BCGP, BCPP, FASCP

Dean and Professor

Pacific University School of Pharmacy, Hillsboro, Oregon

Supported in part by an educational grant from the ASCP Foundation.

1

1

Meet the Speaker

Dr. Marvanova serves as the Professor and Dean of the Pacific University School of Pharmacy in Hillsboro, Oregon. She is a Board-Certified Psychiatric and Geriatric Pharmacist, as well as a Fellow of the American Society of Consultant Pharmacists (ASCP). She holds an M.S. (Pharm), Pharm.D., and a Ph.D. in Pathological Neurobiochemistry from Charles University in the Czech Republic, along with a Ph.D. in Neuropharmacology from the University of Eastern Finland. She also completed a medical research fellowship in neuropharmacology at Vanderbilt University School of Medicine and a Parkinson's disease traineeship at Northwestern University.

Her clinical expertise lies in geriatrics and neuropsychiatry, and she has extensive experience practicing in both inpatient and outpatient team-based clinical settings. Since 2013, she has served on the editorial board of *Continuum: Lifelong Learning in Neurology* (published by the American Academy of Neurology) and acts as a clinical pharmacy specialist consultant in neurology and psychiatry for Lexicomp, Wolters Kluwer. As a clinician, educator, and scholar, Dr. Marvanova is deeply committed to advancing training in geriatrics and neuropsychiatry while working to improve health outcomes for older adults.

GERIATRIC PHARMACIST BOOT CAMP

2

2

Disclosure

Marketa Marvanova does not have relevant financial relationships with ineligible companies.

None of the planners for this activity have relevant financial relationships to disclose with ineligible companies.

This presentation will include discussion of off-label, experimental, and/or investigational use of drugs or devices.

3

Learning Objectives

1. Determine therapeutic options for depression, anxiety, sleep disturbances and substance abuse in the older adult.
2. Interpret psychiatric clinical findings and incorporate functional status into therapeutic decision-making.
3. Resolve and/or prevent psychiatric medication-related problems.
4. Apply psychiatric therapy recommendations and person-specific goals to senior patient cases.

4

GERIATRIC PHARMACIST

BOOT CAMP

MAJOR DEPRESSIVE DISORDER (MDD)

Supported in part by an educational grant from the ASCP Foundation.

5

5

Major Depression Disorder (MDD) in Older Adults: Prevalence

- Not a normal part of aging
- Prevalence of major depression is lower than in community dwelling elderly than in younger adult population
  - Prevalence about 1-5% in healthy older adults
  - More common in medically ill: chronic illness: 5-10%
  - 80% are treated in primary care clinics
- Up to 42% prevalence in long-term care residents

Centers for Disease Control and Prevention, "Depression is Not a Normal Part of Growing Older," Division of Population Health, updates January 31, 2017. Available at https://www.cdc.gov/aging/depression/index.html. Accessed on January 5, 2025; Kok RB, Reynolds CF. *JAMA.* 2017;317(20):2114-2122; Fiske A, Wetherell JL, Gatz M. *Annu Rev Clin Psychol.* 2009; 5 363–389.

6

Major Depression Disorder (MDD) in Older Adults: Complications

- Co-occurrence with medical illnesses and disabilities
- Commonly misdiagnosed or undertreated in older adults
- Suicide rates in older adults are the highest of any age group
- Less likely remission and high relapse rate

Centers for Disease Control and Prevention, "Depression is Not a Normal Part of Growing Older," Division of Population Health, updates January 31, 2017. Available at https://www.cdc.gov/aging/depression/index.html. Accessed on January 5, 2025; Kok RB, Reynolds CF. *JAMA*. 2017;317(20):2114-2122; Fiske A, Wetherell JL, Gatz M. *Annu Rev Clin Psychol*. 2009; 5 363–389.

GERIATRIC PHARMACIST BOOT CAMP 7

7

MDD Diagnostic Criteria (DSM-5-TR)

- **≥ 5** of the following **most days** for at least **2 weeks and one of them needs to be depressed mood or anhedonia** (Markedly diminished interest in pleasurable activities)*

S: changes in **Sleep**
I: decreased **Interest** (anhedonia)
G: excessive **Guilt**
E: decreased **Energy**
C: decreased **Concentration**
A: **Appetite** change
P: **Psychomotor** change
S: **Suicidal** thoughts & behavior

- **Not due to effects of substances or general medical conditions**

* Older adults and African American men are more likely to express anhedonia than feelings of sadness or low mood

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022

GERIATRIC PHARMACIST BOOT CAMP 8

8

Depressive Symptoms in Older Adults

VEGETATIVE SYMPTOMS:

appetite/weight change, disturbed sleep, psychomotor agitation or retardation, low energy

Less useful in medically ill persons

AFFECTIVE/COGNITIVE SYMPTOMS:

depressed mood, anhedonia, guilt/worthlessness, poor concentration, suicidal ideation of thoughts of death

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022

GERIATRIC PHARMACIST BOOT CAMP

9

9

MDD Clinical Presentation in Older Adults vs in Younger Counterparts

- Less likely to report feeling depressed (especially the oldest old)
- Often present with
  - Physical complaints: headache, fatigue, dizziness, muscle pain, low energy
  - Pain and somatic complaints
  - Anhedonia
  - Memory complaints and confusion
  - Insomnia
  - Decreased appetite/weight loss
  - Increased irritability

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022, Kaplan M, Huguet N, McFarland B, et al. *Psychology of Men & Masculinity.* 2012;13:65-74; Kok RB, Reynolds CF. *JAMA.* 2017; 17(20):2114-2122.

GERIATRIC PHARMACIST BOOT CAMP

10

10

Depression Evaluation/Diagnosis

MDD is a clinical diagnosis and need to rule out other secondary causes (e.g., bipolar disorder, hypothyroidism, anemia, vitamin deficiency, medications)

- **Medical, family and social history** (substance use) review
- **Medication review**
- **Labs reviews**: CBC, CMP, TSH, B12 and folate level, & urine drug screen
- **Physical & mental state examination**
  - Depression rating scales (self- or clinician-administered)
    a) Presence of depression
    b) Severity of depression
    c) Response to therapy

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022..

11

Medications Associated with Depression

- Alpha and beta interferons
- Natalizumab
- Levetiracetam
- Corticosteroids (>80 mg/day prednisone equivalents)
- Progesterone
- Beta-blockers?

Botts S, Ryan M. Drug-induced Diseases: Prevention, Detection, and Management, 2010. Available at https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/medications-suicidality/drug-induced-diseases.ashx. Accessed on January 6, 2025.

12

The Patient Healthcare Questionnaire (PHQ-9)

Scoring:

0-4: No depression
5-9: Mild depression
10-14: Moderate depression
15-19: Moderately severe depression
≥20: Severe depression

Scores > 10 have 88% sensitivity and specificity

#	Question (Scoring 0-3)
1	Little interest or pleasure in doing things
2	Feeling down, depressed, or hopeless
3	Trouble falling or staying asleep, or sleeping too much
4	Feeling tired or having little energy
5	Poor appetite or overeating
6	Feeling bad about yourself—or that you are a failure or have let yourself or your family down
7	Trouble concentrating on things, such as reading the newspaper or watching television
8	Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual
9	Thoughts that you would be better off dead or hurting yourself in some way
0 = Not at all, 1 = Several days, 2 = More than half the days, 3 = Nearly every day	

~~PHQ-2~~

Maurer D, Raymond T, Davis B. Am Fam Physician 2018;98(8):508-515. http://www.integration.samhsa.gov/images/res/PHQ%20-%20Questions.pdf. Accessed on January 6, 2025.

GERIATRIC PHARMACIST BOOT CAMP

13

13

Bolded: 1st line antidepressants or most commonly used antidepressants for management of MDD

Classes of Antidepressants

SSRIs = selective serotonin reuptake inhibitors

SNRIs = serotonin norepinephrine reuptake inhibitors

SSRI + partial 5-HT_{1A} agonist (vilazodone)

SSRI + 5-HT_{1A} agonist, 5-HT_{1B} partial agonist, 5-HT_3, 5-HT_{1D} and 5-HT_7 antagonist (vortioxetine)

NDRI = norepinephrine dopamine reuptake inhibitor (bupropion)

TCAs = tricyclic antidepressants

MAOIs = monoamine-oxidase inhibitors

Serotonin modulator (mirtazapine)

5-HT_{2A} receptor antagonists & reuptake inhibitors (trazodone; nefazodone)

NMDA receptor antagonist (esketamine): for treatment resistant depression or MDD with suicides

NMDA receptor antagonist and sigma-1 receptor agonist (dextromethorphan/bupropion)

Lam RW, Kennedy SH, Adams C, et al. *Can J Psychiatry*. 2024;69(9):641-687; Veterans Health Administration and Department of Defense. VA/DoD practice guideline for the management of major depressive disorder, version 4.0. Washington, D.C.: Veterans Health Administration and the Department of Defense, 2022.

GERIATRIC PHARMACIST BOOT CAMP

14

14

How Do We Select The Best Initial Therapy?

Medication Factors

- Efficacy to treat comorbidities
- Pharmacokinetics (e.g., hepatic inhibition CYP2D6 and tamoxifen)
- Tolerability/Safety/Interactions
- Simplicity of use
- Cost/Formulary

Patient Factors

- Past experience/response
- Clinical guideline/1st line
- Comorbid conditions
- Patient preference
- Response & adverse effects (AEs) during previous use

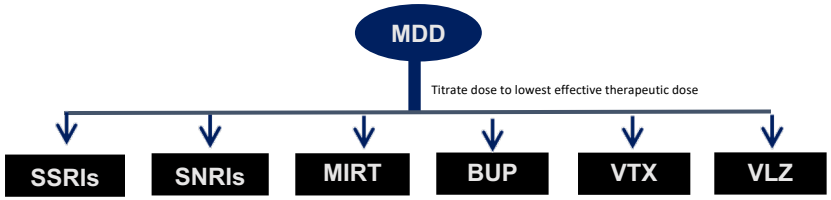
Marvanova M, McGrane I. *Sr Care Pharm* 2021; 36:11-21;
Lam RW, Kennedy SH, Adams C, et al., *Can J Psychiatry.* 2024;69(9):641-687.

GERIATRIC PHARMACIST BOOT CAMP

15

15

MDD First-Line Pharmacologic Treatment



MIRT = mirtazapine; BUP=bupropion; VTX=vortioxetine; VLZ=vilazodone

Lam RW, Kennedy SH, Adams C, et al., *Can J Psychiatry.* 2024;69(9):641-687; *Marvanova M, McGrane I. Sr Care Pharm. 2021;36:11-21.; American Psychiatric Association (APA). Practice guideline for the treatment of patients with major depressive disorder, 3rd ed. Arlington, Virginia: American Psychiatric Association, 2010.*

GERIATRIC PHARMACIST BOOT CAMP

16

16

Neurotransmitter-Specific Adverse Effects (AEs) Associated with Antidepressants

Serotonergic (5-HT)

- GI upset/decreased appetite
- Sexual dysfunction
- Irritability and jitteriness
- Headache
- Increased risk of bleeding/bruising*
- Serotonin syndrome
- Hyponatremia: syndrome of inappropriate antidiuretic hormone secretion, SIADH)

• Noradrenergic (NE)

- Increased BP
- Increased HR
- Hyperhidrosis
- Dry mouth and constipation
- Insomnia

• Dopaminergic (DA)

- Psychomotor activation
- Nervousness

GERIATRIC PHARMACIST BOOT CAMP

* Further increased if combined with NSAIDs, antiplatelets or anticoagulants

17

17

Possible Other Neurotransmitter-Specific Adverse Effects (AEs)

These pharmacologic effects can be seen with select antidepressants but also select sleep medications, anxiety medications, and antipsychotics

- **Block of muscarinic acetylcholine receptors = anticholinergic adverse effects (AEs)**: dry mouth, dry eyes, constipation, urinary retention, cognitive impairment (subchronic/chronic use)
- **Block of histamine 1 receptors=** sedation/somnolence and increased appetite/weight gain
- **Block of alpha-1 adrenergic receptors=** orthostatic hypotension

GERIATRIC PHARMACIST BOOT CAMP

18

18

Antidepressants and 2023 AGS Beers Criteria

- **SSRIs, SNRIs, TCAs:** Moderate evidence for falls and risk for fractures
- **TCAs and paroxetine**: anticholinergics, increased risk for cognitive decline, delirium, and falls or fractures
- **Tertiary TCAs** (amitriptyline, clomipramine, imipramine): avoid in syncope due to bradycardia and orthostatic hypotension
- **SSRIs, SNRIs, TCAs, mirtazapine**: May exacerbate or cause syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hyponatremia. Monitor sodium level closely when starting or changing dosages in older adults

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.

GERIATRIC PHARMACIST BOOT CAMP

19

19

Hyponatremia and SIADH

- A serum sodium level <135 mmol/L
- 2023 AGS Beers Criteria:
  - Antidepressants: **mirtazapine, SNRIs, SSRIs, TCAs**
  - Other: antipsychotics, carbamazepine, diuretics, oxcarbazepine, tramadol, dextromethorphan/quinidine
- **Risk Factors**
  - Advanced age
  - Female
  - Co-administration with diuretics and medications causing SIADH/hyponatremia
  - Low baseline sodium level
- **Time Course**
  - Average onset 13 days (range 3 – 120 days)
  - Resolution: average 2 weeks after discontinuation

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.
Jacob S, Spinler SA. *Ann Pharmacother* 2006; 40:1618-1622.

GERIATRIC PHARMACIST BOOT CAMP

20

20

Selective Serotonin Reuptake Inhibitors

AEs: appetite change, gastrointestinal (N/V/D), sexual dysfunction, falls, hyponatremia, risk of GI bleeds, serotonin syndrome (SS), tremor, and headache

Clinical indications: MDD, anxiety disorders, PTSD, OCD

Citalopram	Risk of QTc prolongation (Max dose of 20 mg/day in older adults)
Escitalopram	Risk of QTc prolongation (max dose 10 mg/day in older adults)
Fluoxetine	Long half-life (~72 hours) and active metabolite= does not require taper; Less weight gain; ↑↑drug interactions (CYP2D6, CYP3A4, CYP2C9/19)
Paroxetine	Anticholinergic adverse effects; ↑drug interactions (CYP2D6 inhibitor); short half-life, higher risk of discontinuation/withdrawal symptoms
Sertraline	Favorable AEs, Higher doses (> 150 mg start to inhibit CYP2D6)

Monitor: ECG; K^+; Mg^{2+}

Marvanova M, McGrane I. *Sr Care Pharm* 2021; 36:11-21.
Lam RW, Kennedy SH, Adams C,. et al., *Can J Psychiatry.* 2024;69(9):641-687.
Sanchez C, Reines EH, Montgomery SA. *Int Clin Psychopharmacol* 2014; 29:185-196.
Prescribing information. Available at http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm. Accessed on December 28, 2024.

21

Serotonin Norepinephrine Reuptake Inhibitors

AEs: Same as SSRIs plus risk of increased HR, BP, insomnia, sweating, and dry mouth

Clinical indications: MDD, anxiety disorders, PTSD, OCD, neuropathic pain

Venlafaxine	Highest risk of hypertension (dose-dependent) and nausea; norepinephrine reuptake begins at 150 mg/day; short $T_{1/2}$ for immediate release formulations and is associated with high risk of discontinuation/withdrawal symptoms
Desvenlafaxine	Active metabolite of venlafaxine; requires renal dosage adjustment; short half-life Higher cost = coverage issues
Duloxetine	Use in chronic neuropathy pain. Lower BP effects than venlafaxine in doses ≥150 mg/day).
Levomilnacipran	Higher cost = coverage issues; High impact on NE>5-HT
Milnacipran	Higher cost; FDA-approved for fibromyalgia

Marvanova M, McGrane I. *Sr Care Pharm* 2021; 36:11-21.
Lexicomp Online Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2019

22

Norepinephrine Dopamine Reuptake Inhibitor

Bupropion	Indications: MDD, smoking cessation AEs: Increased BP and HR, insomnia, activation, decreases appetite, and decrease seizure threshold (contraindicated in seizure and eating disorders) Lacking sexual dysfunction AEs

Serotonin Modulator

Mirtazapine

Useful for weight loss/decrease appetite and insomnia symptoms as AEs include: somnolence, increased appetite and weight gain.
Minimal/lack of sexual AEs

lower doses > high doses

Marvanova M, McGrane I. *Sr Care Pharm* 2021; 36:11-21.
Sanchez C, Reines EH, Montgomery SA. *Int Clin Psychopharmacol* 2014; 29:185-196.
Lexicomp Online Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2019

GERIATRIC PHARMACIST BOOT CAMP

23

23

Liver Enzyme Inhibition: Potential for Interactions

Moderate-Strong CYP2D6 Inhibition

Paroxetine Fluoxetine Bupropion Duloxetine Sertraline (doses >150 mg/day

Moderate-Strong CY3A4 Inhibition

Fluoxetine

Strong CY2C9/C19 Inhibition

Fluoxetine

Lam RW, Kennedy SH, Adams C. et al., *Can J Psychiatry*. 2024;69(9):641-687.
Low Y, Setia S, Lima G. *J Neuropsychiatric Disease and Treatment* 2018; 14:567-80.
Markowitz J, et al. *JAMA* 2003; 290(11):1500-4.

GERIATRIC PHARMACIST BOOT CAMP

24

24

Antidepressants and CYP2D6 Substrate

- **Pharmacokinetic interaction with select opioid analgesics and tamoxifen = inhibition of CYP2D6 enzyme by fluoxetine, paroxetine, duloxetine, bupropion**
  - Decreased analgesia or failure to achieve analgesia with co-administration with moderate to potent CYP2D6 antagonist
  - Reduced effectiveness of tamoxifen (breast cancer treatment)

Prodrug	Active Metabolite	Potency (Active Metabolite vs Prodrug)
Codeine	Morphine	300 x more potent
Tramadol	O-desmethyltramadol (M1 metabolite)	200 x more potent
Tamoxifen	Endoxifen	100 x more potent

Yiannakopoulou E. Int J Genomics 2015:368979. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4446490/. Accessed January 23, 2024.

GERIATRIC PHARMACIST BOOT CAMP

25

bps

25

Antidepressants and CYP2D6 Substrate

- Fluoxetine, paroxetine, duloxetine, bupropion are moderate/strong inhibitors of CYP2D6
  - ✓ Interactions with CYP2D6 substrates

Prodrug (CYP2D6 substrate)	Active Metabolite	Potency (Active Metabolite vs Prodrug)
Codeine	Morphine	300 x more potent
Tramadol	O-desmethyltramadol (M1 metabolite)	200 x more potent
Tamoxifen	Endoxifen	100 x more potent

1. **Decreased analgesia or failure to achieve analgesia**
2. **Reduced effectiveness of tamoxifen (breast cancer treatment)**

Yiannakopoulou E. Int J Genomics 2015:368979. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4446490/. Accessed January 23, 2024.

GERIATRIC PHARMACIST BOOT CAMP

26

bps

26

Other Antidepressants

SSRI, $5HT_{1a}$ agonist, $5HT_3$ antagonist	**Vortioxetine**	10-20 mg/day Higher cost; **Similar AEs as SSRI** **Higher cost; "studied" in older adults (age range 55-88 years; average 62 years)**
SSRI, $5HT_{1a}$ partial agonist	**Vilazodone**	10-40 mg/day Higher cost; **Same AEs as SSRIs**
$5HT_{2A}$ antagonist + serotonin reuptake inhibitor	**Trazodone**	Not routinely used for depression but if used then 200-400 mg/day is usual range More commonly used for insomnia: 50-100 mg/dose AEs: **Similar to SSRIs plus** • Block of histamine-1 receptors in the brain=weight gain and sedation/somnolence • Block of adrenergic-1 receptors=**priapism and orthostatic hypotension**

Marvanova M, McGrane I. *Sr Care Pharm* 2021, 36:11-21.
Stahl; SM. The Prescriber's Guide, 4th ed. Cambridge University Press, 2011.
Nomikos GG, Tomori D, Zhong W, eat al. *CNS Spect* 2017; 22(4):348-362.

27

Tricyclic Antidepressants (TCAs)

- **Clinical indications:** MDD and anxiety disorders (more as second- or third-line therapy), OCD (clomipramine), ADHD, and neuropathic pain
- Narrow therapeutic index medications with many AEs and complications
  - Serotonergic AEs: risk for bleeding, sexual dysfunction, SS, and hyponatremia (SIADH)
  - Anticholinergic AEs: constipation, dry mouth, dry eyes, urinary retention, cognitive impairment
  - Alpha 1-aderenergic receptor blockade: tachycardia, orthostatic hypotension
  - Histamine 1-receptor blockade: weight gain and sedation
  - Miscellaneous: risk for seizures and QTc prolongation

TCA Group	Generics	Notes
Tertiary Amines	Amitriptyline Imipramine Clomipramine Doxepin	**Most AEs and toxicities** Amitriptyline is the most anticholinergic Doxepin is not used in MDD; Low doses ≤ 6 mg used for insomnia (only histamine-1 receptor antagonism)
Secondary Amines	Nortriptyline Desipramine	Less adverse effects Nortriptyline is best tolerated

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.
Marvanova M, McGrane I. *Sr Care Pharm* 2021; 36:11-21.

28

Monoamine Oxidase Inhibitors (MAOIs)

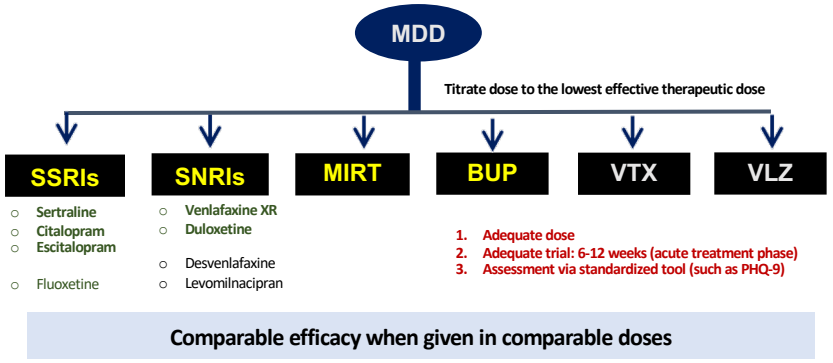
- Selegiline (patch formulation ONLY), tranylcypromine, phenelzine
- Usually used as third-line therapy for MDD and anxiety disorders
- AEs: orthostasis, weight gain, sexual dysfunction, and risk for hypertensive crisis due to consumption of tyramine
- Risk for hypertensive crisis
  - Need to adhere to **tyramine low diet** (exclude diet like beer, wine, aged cheese, smoked and cured meet, cold cuts)
    - Low dose of selegiline patch (6mg patch) does not require this diet
  - Also associated with combination of **sympathomimetics** (e.g., epinephrine, pseudoephedrine, amphetamines, methylphenidate)

GERIATRIC PHARMACIST BOOT CAMP

29

29

MDD First-Line Pharmacologic Treatment



Comparable efficacy when given in comparable doses

MIRT = mirtazapine; BUP=bupropion; VTX=vortioxetine; VLZ=vilazodone

Lam RW, Kennedy SH, Adams C. et al., *Can J Psychiatry. 2024;69(9):641-687; Marvanova M, McGrane I. Sr Care Pharm. 2021;36:11-21.; American Psychiatric Association (APA). Practice guideline for the treatment of patients with major depressive disorder, 3rd ed. Arlington, Virginia: American Psychiatric Association, 2010.*

GERIATRIC PHARMACIST BOOT CAMP

30

30

MDD Treatment Principles

- Antidepressant monotherapy is preferred in order to minimize side effects, cost, and enhance likelihood of adherence
- Start low and titrate slowly
  - Allow 4-6 weeks (up to 12 weeks) of treatment to elicit a full response
- Only 40-65% of patients will have an adequate response to any given antidepressant

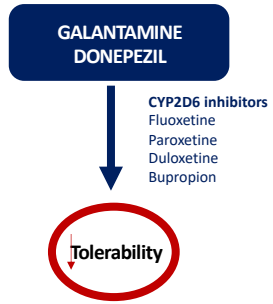
1. If no response, consider switching within class or out of class to a new 1st line antidepressant
2. If partial response, can consider:
   - SSRI/SNRI + atypical antipsychotic (aripiprazole, brexpiprazole, quetiapine)
   - SSRI/SNRI + bupropion, or SSRI/SNRI + buspirone
   - Or refer for psychotherapy

- Continue treatment 12 months to reduce risk of recurrence of depression

Management of Depression in Dementia

- Prevalence of depression in dementia is 32%

1. **Pharmacodynamic interactions** by anticholinergic antidepressants
   - Drug-Disease
   - Drug-Drug with all acetylcholinesterase inhibitors
2. **Pharmacokinetic interaction** with CYP2D6 inhibitors and donepezil and galantamine



Marvanova M, McGrane I. *Sr Care Pharm.* 2021;36:11-21; Pasqualetti G, et al. *Clin Interv Aging.* 2015;10:1457-1466.

MDD Treatment Principles Summary

- All traditional (impacting monoamines) antidepressants have the same efficacy in MDD but not the same safety
- Use the lowest effective dose and maximize use of 1 antidepressant
- Give adequate trial with antidepressant up to 12 weeks
- Ensure a 5-week washout period between fluoxetine and 2-week washout period between MAOIs and other antidepressant
- When using first-line therapy antidepressants, SSRI and SNRIs, monitor for increased risk for AEs in older adults such as hyponatremia, bleeding, and serotonin syndrome.
- When using antidepressant with moderate to strong CYP450 inhibitory properties watch/control for drug interactions

GERIATRIC PHARMACIST BOOT CAMP 33

33

Self Assessment Question #1: Clinical Vignette

72-year-old presents with symptoms including depression, anhedonia, excessive guilt, insomnia, and lack of concentration for the past 6 weeks. This is her first depressive episode.

PMH: low back pain due to inoperable spine compression (currently well controlled on tramadol after several medication trials), and hyperlipidemia

Medications: tramadol 100mg twice daily, atorvastatin 40mg daily

VS: 130/85 mm Hg; HR 78 bpm, RR 14 rpm, BMI 28 kg/m^2

Labs: CBC and CMP: within the normal limits; CrCl=80 mL/min

PE: pulmonary and cardiovascular exams: unremarkable; PHQ-9 score 13 with no suicidal thoughts or plan

GERIATRIC PHARMACIST BOOT CAMP 34

34

Self-Assessment Question #1:

Which of the following antidepressants would be the most appropriate at this time?

A. Amitriptyline
B. Bupropion
C. Escitalopram
D. Paroxetine

GERIATRIC PHARMACIST BOOT CAMP

35

35

GERIATRIC PHARMACIST

BOOT CAMP

POST-TRAUMATIC STRESS DISORDER (PTSD)

Supported in part by an educational grant from the ASCP Foundation.

36

36

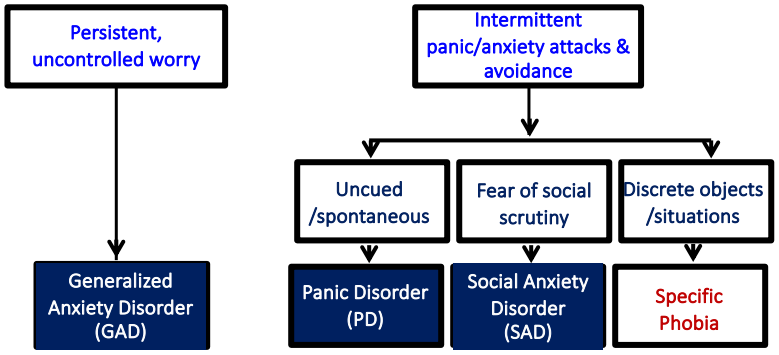
Anxiety Disorders in Older Adults

- Higher rates of anxiety complaints in older adults with medical illness, homebound and nursing home residents
- Estimated prevalence rates ranging from 1.2 to 15.0%
- Specific phobias and generalized anxiety disorder (GAD) are the most common
- Panic disorder less severe as sympathetic overdrive is reduced
- Comorbidity with MDD, sleep disorders, and substance use disorders
- Commonly underdiagnosed (complicated detection and diagnosis)

Pary R, Sarai SK, Micchelli A, Lippmann S. Prim Care Companion *CNS Disord.* 2019;31;21(1):18nr02335.S; Bower ES, et al. *Harvard Review of Psychiatry.* 2015;23(5):329-342; Mackenzie CS, El-Gabalawy R, Chou KL, et al. *Am J Geriatr Psychiatry.* 2014;22:854–865; Anxiety in Later life. https://focus.psychiatryonline.org/doi/epdf/10.1176/appi.focus.20160045. Accessed on January 6, 2025.

37

Anxiety Disorders (DSM-5-TR)



American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022.

38

Assessment

- Clinical diagnosis: **Rule out medical and medication condition as a cause of anxiety**

Medications	Medical Conditions
Stimulants: caffeine, pseudoephedrine, ginseng, ephedra, amphetamines, methylphenidate, PCP, cocaine, Ecstasy High dose of **levothyroxine**	**Withdrawal** of alcohol, benzodizepines, barbiturates, opioids **Endocrine:** Cushing's disease, hyperthyroidism, pheochromocytoma

- Vital signs: BP, HR, RR, weight (BMI)
- Labs (for all): CBC, CMP, TSH
- Labs (specific cases): urine drug screen, blood alcohol level, and serum drug levels
- Standardized rating scales (e.g., Generalized Anxiety Disorder 7-item scale, GAD-7)

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022.

39

Screening Standardized Tool: GAD-7

- **Generalized Anxiety Disorder 7-item scale (GAD-7)**
  - Self-rated and brief (2 min)
  - Utility: Screens for GAD and severity assessment
  - Can also be used for screening for other anxiety disorders: panic disorder, social anxiety disorders, and post-traumatic stress disorder
  - If positive (≥10 score), further anxiety evaluation is recommended

GAD-7 Score	Anxiety Severity
0 - 4	None-minimal
5 - 9	**Mild**
10 - 14	**Moderate**
15 - 21	**Severe**

Spitzer RL. *Arch Intern Med.* 2006. Available at http://austintmsclinic.com/blog/wp-content/uploads/2015/09/Scoring-the-GAD-7-Dr-Vache.pdf . Accessed on January 6, 2025; GAD=7 Scale. https://www.crossroadscounselingcenters.com/pdf/Generalized%20Anxiety%20Disorder.pdf. Accessed on January 6, 2025..

40

Avoid medication and substance triggers (e.g., caffeine, nicotine, stimulants, decongestant, diet pills, excessive use of alcohol)

First-line Pharmacotherapy for Anxiety Disorders

Psychotherapy (cognitive behavioral therapy; CBT) is also first-line

Generalized Anxiety Disorder	Panic Disorder
SSRIs: **escitalopram, sertraline**, ~~paroxetine~~ (avoid due to AGS Beers Criteria)	**SSRIs**: all (except for ~~paroxetine~~: AGS Beers Criteria)
SNRIs: venlafaxine XR, duloxetine	**SNRIs**: venlafaxine XR
Response time is in 4-12 weeks	Response time is in 4-12 weeks
NOTE: SSRIs should be initiated at lower doses (1/2 dose for depression) and titrated more slowly than MDD	***NOTE: SSRIs should be initiated at lower doses (1/2 dose for depression) and titrated more slowly than MDD***
After failure of initial therapy start other 1st line therapy	***After failure of initial therapy start other 1st line therapy***

Acute Treatment (only if needed): Benzodiazepines for first 2-4 weeks

GERIATRIC PHARMACIST BOOT CAMP

41

41

Benzodiazepine (BZD) Considerations In Anxiety

- MOA: Acts on GABA-A receptor (allosteric modulator) and increases its activity (increases frequency of opening Cl^- channel)
- Not effective for depression and depression can worsen
- Usually only used for **acute treatment of anxiety** but also available as second-line therapy if first-line therapy fails or cannot be tolerated
  - **Rapid relief of anxiety symptoms (30-60 min)**
  - **Only use for about 2-4 weeks** as bridge therapy for SSRIs/SNRIs
- Use carefully and ONLY if needed
- Use lowest effective dose and use for the shortest time

GERIATRIC PHARMACIST BOOT CAMP

42

42

Benzodiazepine Considerations: Treatment

- Control substance CIV: risk for psychological and physiological dependence (withdrawal and rebound anxiety)
- Contraindication in myasthenia gravis
- AEs: Drowsiness, sedation, fatigue, confusion, misuse and physical dependence, decreased breathing, and risk for falls, risk for withdrawal symptoms
- Careful use in older adults, dementia, history of falls, respiratory insufficiency, combination with opioids (box warning: respiratory depression, coma, death), hepatic insufficiency, and history of substance use
- BZD for anxiety: lorazepam, oxazepam, alprazolam, clonazepam, diazepam

GERIATRIC PHARMACIST BOOT CAMP 43

43

Benzodiazepine (BZD) Considerations in Older Ad(AGS Beers Criteria)

- Increased sensitivity and decreased metabolism of log-acting agents due to pharmacokinetic and pharmacodynamic changes of aging
- All benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults
- When combined with opioids: increased risk for sedation, respiratory depression, coma, and death
- May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder (RBD), benzodiazepine withdrawal, ethanol withdrawal, or severe generalized anxiety disorder, and periprocedural anesthesia

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.

GERIATRIC PHARMACIST BOOT CAMP 44

44

Benzodiazepines Characteristics

L: **L**orazepam (Ativan)

O: **O**xazepam (Serax)

T: **T**emazepam (Restoril)*

- In general, "LOT" is preferred in older adults and people with hepatic disease/insufficiency
- Short or intermediate acting
- Undergoes only phase II metabolism and no active metabolite(s)

Alprazolam, clonazepam, diazepam

- Alprazolam (Xanax) metabolized by CYP3A4
- Clonazepam (Klonopin)**
  - Longer duration
  - Undergoes Phase I metabolism with no active metabolites
- Diazepam (Valium)**/***
  - Long duration
  - undergoes Phase I metabolism (CYP3A4) and has active metabolite
  - Risk for accumulation

* Temazepam only FDA-approved for insomnia but not anxiety
** Clonazepam and diazepam not appropriate in significant hepatic insufficiency, narrow angle glaucoma
*** Diazepam not appropriate in respiratory insufficiency (COPD, obstructive sleep apnea)

GERIATRIC PHARMACIST BOOT CAMP

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.
Lexicomp Online Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2019.

45

45

The Second-line Pharmacotherapy for Anxiety Disorders

Generalized Anxiety Disorder	Panic Disorder
Buspirone (FDA-approved for GAD)	Mirtazapine
Pregabalin	BZD: clonazepam, alprazolam, lorazepam
Hydroxyzine (AGS Beers Criteria)	TCAs: clomipramine, imipramine (AGS Beers Criteria)
Bupropion	Augmentation: aripiprazole, olanzapine
Augmentation: quetiapine XR, olanzapine or risperidone	
Andrews G, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of panic disorder, social anxiety disorder and generalised anxiety disorder. *Aust N Z J Psychiatry.* 2018;52(12):1109-1172; Katzman MA, et al., Canadian clinical practice guideline for the management of anxiety, posttraumatic stress, and obsessive-compulsive disorders. *BMC Psychiatry.* 2014;14(Suppl 1):S1; Abejuela HR, et al. The Psychopharmacology Algorithm Project at Harvard South Shore Program: An algorithm for generalized anxiety disorder. *Harv Rev Psychiatry.* 2016; 4(4):243-256.	Andrews G, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of panic disorder, social anxiety disorder and generalised anxiety disorder. *Aust N Z J Psychiatry.* 2018;52(12):1109-1172; Katzman MA, et al., Canadian clinical practice guideline for the management of anxiety, posttraumatic stress, and obsessive-compulsive disorders. *BMC Psychiatry.* 2014;14(Suppl 1):S1.

GERIATRIC PHARMACIST BOOT CAMP

46

46

Medication	Comments and Highlights
Pregabalin	- Off-label use for GAD but effective treatment for GAD; Onset of action in 1 week - Effective in a short- or long-term treatment of GAD; Anxiolytic effect similar to BZD in acute efficacy studies with lorazepam and alprazolam - Switching to pregabalin from BZD is a possible way to manage withdrawal symptoms
Buspirone	- FDA-approved for GAD; MOA=5-HT_{1A} partial agonist - Delayed onset of effectiveness (4-6 weeks) - Lack of efficacy for comorbid depression or other anxiety disorder - AEs: dizziness, nausea, headache, and risk of serotonin syndrome
Hydroxyzine	- FDA-approved for GAD: relief of anxiety and tension - Mild anticholinergic and strong antihistaminic effect, AGS Beers Criteria - Sedative/calming effect within 30 min - Lack of efficacy for comorbid depression
Atypical Antipsychotics	- Off-label use ; MOA= 5HT1A receptor agonism; Monotherapy has sparse data - Anticholinergic, orthostatic, and metabolic AEs (olanzapine >quetiapine>risperidone >>aripiprazole)

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023; 71(7): 2052-2081; Katzman MA, et al., Canadian clinical practice guideline for the management of anxiety, posttraumatic stress, and obsessive-compulsive disorders. *BMC Psychiatry.* 2014;14(Suppl 1):S1; Abejuela HR, et al. The Psychopharmacology Algorithm Project at Harvard South Shore Program: An algorithm for generalized anxiety disorder. *Harv Rev Psychiatry.* 2016;4(4):243-256.

47

Principles of Anxiety Disorders Treatment

- Begin SSRI/SNRI with lower starting dose (50% of initial dose for MDD) to avoid jitteriness syndrome and then titrate
- Use BZD as bridge therapy ONLY if needed for 2-4 weeks
- If first line therapy does not work, switch to other SSRI or venlafaxine XR or duloxetine (GAD only)
- Other options:
  - Buspirone is ONLY effective for GAD and can be used as monotherapy if needed
  - BZD: augmentation or used for treatment of residual anxiety/attacks
  - TCAs (imipramine, clomipramine) if therapy trials of first-line therapy fails for GAD, panic disorder
  - MOAI (phenelzine): reserved for treatment resistant GAD or panic disorder
- Treat for at least 12 months after response

48

Self-Assessment Question #2:

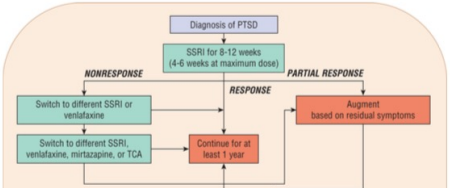
Which of the following is TRUE regarding SSRIs used in the treatment of generalized anxiety disorder versus their use in major depression?

A. SSRIs should be initiated at lower doses and titrated more slowly
B. SSRIs are less effective as monotherapy
C. SSRIs are more likely to cause suicidal ideation
D. SSRIs are used for a shorter duration

49

Principles of PTSD Treatment

- Initial therapy with trauma-focused psychotherapy or medications or combination



Add-on treatment for nightmares: prazosin
Initial dose prazosin 1-2 mg/qhs with increase 1 mg week.
Usual dose 2-13 mg/day

- Alternatives: TCAs, phenelzine (MAOI), and weak recommendation against SGAs
- Do not use benzodiazepines and cannabis (strong recommendations against)
- Treat for at least 12 months (many patients choose to continue indefinitely)

2023 VA/DoD PTSD Guideline. https://www.healthquality.va.gov/guidelines/MH/ptsd/, Forman-Hoffman V, et al. Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder: A Systematic Review Update [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2018 May. Report No.: 18-EHC011-EFReport No.: 2018-SR-01; National Institute for Health and Care Excellence. *Guideline 116.* Post-traumatic Stress Disorder. 2018. Available at https://www.nice.org.uk/guidance/ng116.

50

PTSD Guidelines Examples

	VA/DoD (2023)[1]	AHRQ (2018)[2]	NICE (2018)[3]
FIRST-LINE	Trauma-focused psychotherapy: Cognitive processing therapy, Eye Movement Desensitization and Reprocessing (EMDR), and Prolong exposure	CBT SSRIs: fluoxetine, paroxetine SNRI: venlafaxine	Individual trauma-focused CBT SSRIs SNRI: venlafaxine
SECOND-LINE	SSRI: paroxetine, sertraline SNRI: venlafaxine	Cognitive processing therapy, Eye Movement Desensitization and Reprocessing (EMDR), narrative exposure therapy	EMDR, CBT for sleep or anger
Other	Prazosin for nightmares (weak recommendation)	Sertraline; olanzapine, risperidone; prazosin (mixed results for nightmares)	SGAs

GERIATRIC PHARMACIST BOOT CAMP

[1] 2023 VA/DoD PTSD Guideline. https://www.healthquality.va.gov/guidelines/MH/ptsd/. [2] Forman-Hoffman V, et al. Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder: A Systematic Review Update [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2018 May. Report No.: 18-EHC011-EFReport No.: 2018-SR-01; [3] National Institute for Health and Care Excellence. *Guideline 116.* Post-traumatic Stress Disorder. 2018. Available at https://www.nice.org.uk/guidance/ng116.

51

51

GERIATRIC PHARMACIST

BOOT CAMP

SLEEP DISORDERS

Supported in part by an educational grant from the ASCP Foundation.

52

52

Sleep Disorders in Older Adults

Sleep Disorder	Prevalence
Insomnia	Up to 1/3 of the population have complaints of insomnia 6-10% meet criteria for insomnia disorder
REM Sleep Behavior Disorder (RBD)	40-70% patients with Parkinson's disease and Lewy body dementia (vs 0.5% in adult population)
Restless Legs Syndrome (RLS)	4% of older adults aged 70-89 years

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022; Zdanys KF, Steffens DC. *Psychiatr. Clin N Am.* 2015;38:723-741.

53

Management of Insomnia

1. **Complaints of unsatisfactory sleep quality or quantity**
   - Difficulty with sleep initiation (sleep latency)
   - Difficulty with sleep maintenance
   - Early-morning awakening
2. **Daytime fatigue or impaired daytime functioning**
3. **Causing significant distress or impaired social, occupational or other areas of functioning**

(A) Insomnia as a SYMPTOM **(B) Insomnia as a DISORDER**

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022

54

Insomnia as a SYMPTOM

Medication/Substance-Induced

- **Stimulating medications**
  - Decongestants
    - Pseudoephedrine, epinephrine
  - Stimulants
    - Selegiline tablets/capsules (BID dosing: last dose before 3 pm)
    - ADHD/narcolepsy meds
    - Caffeine and nicotine
    - Illegal substances
  - Stimulating antidepressants and antiseizure medications (ASMs)
- **High dose of levothyroxine**
- **Diuretics**

Conditions/Illnesses

- Hyperthyroidism
- Pain and breathing difficulty
- Depression
- Hypomania/mania
- Restless leg syndrome
- Increased urination urges

Dopp JM, et al. Pharmacotherapy: A Pathophysiologic Approach, 2014.

55

Medication Classes for Insomnia (DISORDER)

Medication/Drug Class	Mechanism of Action	
Benzodizepines	GABAA receptor modulators	AGS Beers Criteria
Non-benzodiazepine receptor agonists (NBRAs) or "Z-hypnotics"	GABAA receptor modulators	AGS Beers Criteria
Melatonin (exogenous)	Stimulation of melatonin (MT) receptors	
Melatonin receptor agonists	MT1 and MT2 receptors agonism	
Orexin antagonists	Orexin 1 and orexin 2 receptors antagonism	
Diphenhydramine	Histamine 1 receptor antagonism	AGS Beers Criteria
Doxepin (≤6 mg/dose) and other TCAs	Histamine 1 receptor antagonism	AGS Beers Criteria
Mirtazapine, trazodone	Histamine 1 receptor antagonism	

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.

56

Medication Used in Management of Insomnia: Preferred in Older Adults

Class	Medications	Comments and Highlights
Antihistamine/ Sedative antidepressants	Doxepin (Silenor®)	Doxepin ≤ 6 mg dose; Administer on empty stomach (do not take within 3 hours of meal). Max effect: during the 1st night
	Trazodone (Desyrel®)	Off-label use but seems effective
	Mirtazapine (Remeron®)	Mirtazapine: lower doses are sedative 7.5-15 mg/day. Might be beneficial in insomnia with comorbid depression
Melatonin agonists	Ramelteon (Rozerem®)	Take up to 3 weeks for maximal effect on sleep. Non-control substance; Less likely to cause dizziness, impair balance or memory. Administer on empty stomach.
Supplement	Melatonin	Conflicting efficacy data but may be a safer option especially in older adults. Prolonged-release melatonin improves sleep quality and sleep latency in patients > 55 years (high level evidence)

GERIATRIC PHARMACIST BOOT CAMP

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081; Lexicomp Online Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2019

57

57

Class	Medications	Considerations
BZDs C-IV AGS Beers Criteria	Estazolam (Prosom®) Flurazepam (Dalmane®) Quazepam (Doral®) Temazepam (Restoril®) Triazolam (Halcion®)	Abuse potential Avoid those with long $t_{1/2}$ in older adults (estazolam, flurazepam, quazepam) If indicated, **temazepam** and triazolam are preferred in older adults (shorter $t_{1/2}$) but triazolam more associated with rebound insomnia
NBRA/"Z" hypnotics C-IV AGS Beers Criteria	Eszopiclone (Lunesta®) Zolpidem (Ambiem®) Zaleplon (Sonata®)	Abuse potential Zaleplon has the shortest half-life (sleep onset) Zolpidem has a specific gender dosing (max 5 mg/dose for female and 10 mg/dose for male) and comes in many dosage forms
Orexin Antagonists C-IV	**Suvorexant (Belsomra®)** Lemborexant (Dayvigo®) Daridorexant (Quviviq®)	Newer medications, CYP3A4 substrates; Food/Fat delays onset of action; Suvorexant was shown to be safe and effective in mild-moderate Alzheimer's (AD)
Antihistamines (OTC products) AGS Beers Criteria	Diphenhydramine (Benadryl®) Doxylamine (Unisom®)	Tolerance may develop and strongly anticholinergic Avoid in older adults or those with issues of anticholinergic AEs (e.g., constipation, BPH)

GERIATRIC PHARMACIST BOOT CAMP

2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081; Lexicomp Online Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2019

58

58

Self-Assessment Question #3:

A 72-year-old female presents to the clinic with complaints of early morning awakening several days per week. She completed several weeks of cognitive behavioral therapy for insomnia and has made recommended changes in her sleep hygiene and lifestyle modifications. **Which of the following would be the most appropriate at this time?**

A. Diphenhydramine 25 mg at bedtime
B. Doxepin 3 mg at bedtime
C. Temazepam 15 mg at bedtime
D. Zolpidem 5 mg at bedtime

59

Key Points in Management of Insomnia in Older Adults

- Rule out medication- or medical condition-induced insomnia
- Low dose doxepin, ramelteon, trazodone or melatonin is preferred
- If coexisting depression, also consider mirtazapine
- Suvorexant was found to be safe and effective in mild-moderate AD
- NBRAs have a better safety than BZDs
- Fat content or food can delay onset of action of orexin antagonists, doxepin, ramelteon
- Medication is usually administered 30 min prior to bedtime and takes between 15-30 min to onset of action

American Academy of Sleep Medicine. *J Clin Sleep Med.* 2017;13:307-349.

60

REM Sleep Behavior Disorder (RBD) Management

- **A parasomnia characterized by dream-enactment behaviors that emerge during loss of REM sleep atonia during sleep**
- Management:
- Separate bed for spouses
- Padding of bed railing(s)
- Adjustment of physical environment of area around the bed
- Melatonin 3-15 mg one hour before sleep
  - No evidence that long-acting melatonin is more useful than short-acting
- Clonazepam 0.5-2 mg before sleep

Roguski A, Rayment D, Whone AL, et al. *Front Neurol*. 202011:610.

Restless Legs Syndrome (RLS) Management

1. **Assess iron status in all patients with RLS and in all new or worsening cases with serum ferritin level <75 mcg/L:**
   - Initiate ferrous sulfate 325 mg BID to TID with 100-200 mg vitamin C
   - Repeat ferritin levels after 12 weeks post treatment
2. **Avoidance or reduction of triggers/aggerating factors is cornerstone**
   - Medications (serotonergic antidepressants, antihistamines, dopamine antagonists)
   - Alcohol, nicotine, caffeine
3. **Initiate Pharmacotherapy for moderate-severe RLS**
   - **Gabapentinoids**: gabapentin and pregabalin
   - **Dopamine D2 agonists**: pramipexole, rotigotine, ropinirole

Silber MH, Buchfuhrer MJ, Earley CL. et al. *Mayo Clin Proc*. 2021;96(7):1921-1937.
Winkelman JW, Armstrong MJ, Allen RP, et al. *Neurology*. 2016;87(24):2585-2593.
Allen RP, Picchietti DL, Auerbach M, et al. *Sleep Med*. 2018;41:27-44.

GERIATRIC PHARMACIST

BOOT CAMP

ALCOHOL USE DISORDER (AUD)
OPIOID USE DISORDER (OUD)

Supported in part by an educational grant from the ASCP Foundation.

63

63

Clinical Presentation of OUD

Opioid Intoxication

Recent ingestion of opioid and clinically significant maladaptive behavior of psychological changes during or shortly thereafter. **Constriction of pupils** plus one of the following:

- Drowsiness or coma
- Shallow breathing or respiratory depression
- Slurred speech
- Impaired attention or memory

Opioid Withdrawal

≥ 3 signs after termination (or administration of opioid antagonist):

- Dysphoria
- Nausea/vomiting
- Myalgias
- Lacrimation, Rhinorrhea, Diarrhea
- Mydriasis
- Piloerection
- Sweating
- Yawning
- Fever
- Insomnia

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022

GERIATRIC PHARMACIST BOOT CAMP

64

64

Management of OUD: Intoxication

	APA (2006, 2018)[1,2]	ASAM (2015, 2020)[3,4]
FIRST-LINE	Intoxication: naloxone	Intoxication: naloxone

[1] American Psychiatric Association: Practice guideline for the treatment of patients with substance use disorders. 2nd ed; 2006.
[2] American Psychiatric Association Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder. *Am J Psychiatry*. 2018;175(1):86-90.
[3] American Society of Addiction Medicine. Kampman K, et al. *J Addict Med*. 2015;9(5):358-367.
[4] American Society of Addiction Medicine National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. J Addict Med. 2020 Mar/Apr;14(2S Suppl 1):1-91.

- Naloxone=selective **mu opioid receptor antagonist**
- Very short half life (~90 min)
- Depending on opioid intoxication, might have to repeat
- Variety of dosage forms: intranasal, IM and intravenous
- Recommended for all patients on opioids especially those at higher risk for overdose/respiratory depression (e.g., older age, coadministration with antidepressants, BZDs, and other CNS antidepressants)

65

Management of OUD: Withdrawal & Maintenance

	APA (2006, 2018)[1,2]	ASAM (2015, 2020)[2,3]
FIRST-LINE	Acute Withdrawal/Detox: buprenorphine, methadone Maintenance treatment: buprenorphine, methadone	Acute Withdrawal/Detox: buprenorphine, methadone Maintenance treatment: buprenorphine, methadone, naltrexone

[1] American Psychiatric Association: Practice guideline for the treatment of patients with substance use disorders. 2nd ed; 2006.
[2] American Psychiatric Association Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder. *Am J Psychiatry*. 2018;175(1):86-90.
[3] American Society of Addiction Medicine. Kampman K, et al. *J Addict Med*. 2015;9(5):358-367.
[4] American Society of Addiction Medicine National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. J Addict Med. 2020;14(2S Suppl 1):1-91.

- **Clinical Opiate Withdrawal Scale (COWS)**
  - Follow the course of withdrawal symptoms and medication effectiveness
  - 11 symptoms (max. 48 points)
  - Higher score = higher withdrawal severity (e.g., severe > 36)

66

OUD Medication-Assisted Treatment (MAT)

Buprenorphine	**Partial mu receptor agonist**. Available in many dosage forms (e.g., oral, SL tabs and films). Filled in a pharmacy and managed independently. Risk for QT interval prolongation.
Buprenorphine /naloxone	Combo preferred as it is abuse-deterrent formulation; Preferred in older adults, Available SL tabs and film and other formulations.
Methadone	**Full mu receptor agonist and also serotonin reuptake inhibitor**. Dispensed from a Methadone Maintenance Program (typically liquid formulation with daily dosing and administration under supervision of a practitioner) Monitoring: vital signs, LFT, and ECG (QT interval prolongation), SS (if co-administered with serotonergic drugs) Drug interactions : substrate for CYP3A4, CYP2D6 with narrow therapeutic index
Naltrexone (Vivitrol)	**Opioid mu-receptor antagonist**. Need to be opioid free for 7-10 days before initiation. Available as PO and IM formulation (IM formulation preferred as PO has poor compliance). AEs: transaminitis and more severe AEs such as acute hepatitis and severe liver impairment (LFT> 5 UNL). Monitor: LFT (baseline, 1 month, 6 months, then annually) Useful for co-morbid AUD and OUD. **Offered after opioid agonists in older adults**

GERIATRIC PHARMACIST BOOT CAMP

[a] American Society of Addiction Medicine National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. J Addict Med. 2020;14(2S Suppl 1):1-91; Canadian Research Initiative in Substance Misuse. Bruneau J, et al. *CMAJ*. 2018;190(9):E247-E257.

67

67

Clinical Presentation: Alcohol Use Disorder (AUD)

Alcohol INTOXICATION

Recent ingestion of alcohol with clinically significant maladaptive behavior or psychological changes during or shortly thereafter with **≥ 1 signs:**

- Slurred speech
- Incoordination
- Unsteady gait
- Nystagmus
- Inattention
- Memory impairment
- Stupor or unconsciousness

Alcohol WITHDRAWAL

≥ 2 signs after cessation or reduction of alcohol consumption:

- Autonomic hyperactivity
- Hand tremor
- Insomnia
- Hallucinations
- Psychomotor agitation
- Nervousness
- Seizure activity

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Text Revision Arlington, VA: American Psychiatric Association. 2022

GERIATRIC PHARMACIST BOOT CAMP

68

68

Management of AUD

	WFSBP (2017)[2]	APA (2018)[1]
First-line	Withdrawal: BZD* AUD: naltrexone or acamprosate	Withdrawal: BZD* AUD: naltrexone or acamprosate
Second-line	AUD: disulfiram, baclofen	AUD: disulfiram, topiramate, gabapentin

[1] American Psychiatric Association : Reus VI et al. *Am J Psychiatry.* 2018;175(1):86-90.
[2] World Federation of Societies of Biological Psychiatry: Soyka M, et al. *World J Biol Psychiatry.* 2017;18(2):86-119.

- For maintenance treatment of AUD: best when pharmacotherapy is combined with psychosocial interventions (e.g., CBT, 12-steps programs)

69

Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar)

Scoring of level of withdrawal:
<15=- mild
10-18= Moderate
≥ 10 = Severe

CIWA-Ar ≥ 10 BZD is indicated

https://nida.nih.gov/sites/default/files/ClinicalOpiateWithdrawalScale.pdf

Treatment usually lasts 3-5 days (some need up to 10 days)

- Chlordiazepoxide (25-100 mg)
- Diazepam (2.5-10 mg)
- Oxazepam (15-30 mg)
- Lorazepam (0.5-2 mg)

The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management. *J Addict Med.*. 2020 ;14(3S Suppl 1):1-72
Sullivan JT, Sykora K, Schneiderman J, et al. *Br J Addict.* 1989;84:1353-1357.
https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf. Accessed on January 6, 2025.

70

AUD Medication-Assisted Treatment (MAT)

Acamprosate (Campral®)	**NMDA receptor antagonist enhancing GABAergic activation and GABA/glutamate balance** Oral formulation dosed three times daily Monitor: renal function; Contraindication: CrCl ≤ 30 mL/min Therapy goals: decrease drinking and craving
Naltrexone (Vivitrol®)	Opioid mu-receptor antagonist. Needs to be opioid free for 7-10 days before initiation. Available as PO and IM formulation (IM is preferred). AEs: transaminitis and more severe AEs such as acute hepatitis and severe liver impairment (LFT> 5 UNL). Monitor: LFT (baseline, 1 month, 6 months, then annually) Useful for co-morbid AUD and OUD Therapy goals: decrease drinking and craving
Disulfiram (Antabuse®)	AVERSIVE THERAPY (SECOND-LINE THERAPY) Blocks irreversibly aldehyde dehydrogenase, effect lasts 1-2 weeks (disulfiram reaction with accumulation of aldehyde). Contraindicated in severe cardiac disease and coronary occlusion. Caution in hepatic insufficiency; Interaction with metronidazole (psychosis) and alcohol (need to abstain from all forms of alcohol); Monitor LFT

Reus VI, Fochtmann LJ, Bukstein O, et al. *Am J Psych.* 2018;175:86-90.
Lexicomp Online Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2019

71

Self-Assessment Question #4:

A 68-year-old male is safely treated for alcohol withdrawal. He was found to have a broken wrist and ankle and has been receiving oxycodone for his severe pain. At discharge he asks if there is a medication to help him remain abstinent from alcohol. His liver function tests are elevated, and renal function is within normal limits. **Which of the following would be the most appropriate at this time?**

A. Acamprosate
B. Disulfiram
C. Naloxone
D. Naltrexone

72