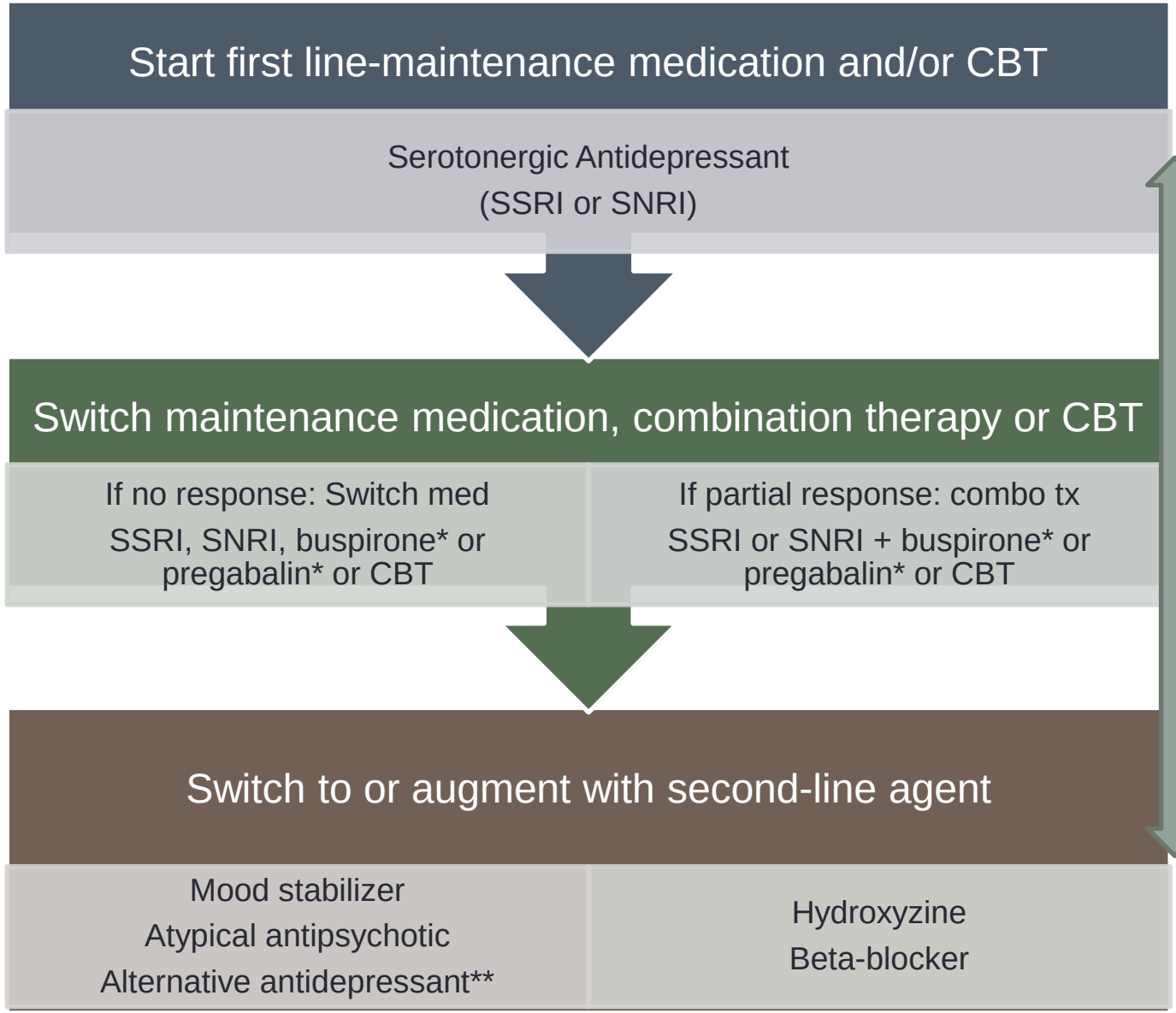
MAINTENANCE MEDICATIONS FOR ANXIETY

Casey Gallimore, Pharm.D., M.S.

Learning Objectives

1. Identify first- and second-line medication used for maintenance treatment of anxiety disorders
2. List common/serious adverse effects of buspirone, and pregabalin
3. Describe how the risk of paradoxical anxiety can be minimized when starting antidepressants or buspirone for anxiety treatment
4. Compare and contrast the pros and cons of maintenance medication options for treating anxiety disorders (considering indication, ADE profile, time to benefit, dosing frequency, use in co-morbid conditions)
5. Recommend a maintenance medication for treating anxiety in an individual patient



Bridge therapy if high degree of functional impairment

*pregabalin and buspirone for generalized anxiety disorder (GAD) only

**alternative antidepressants include mirtazapine or TCAs; avoid bupropion

**Guidelines available from: American Psychiatric Association (APA), World Federation of Societies of Biological Psychiatry (WFSBP), and British Association for Psychopharmacology.[1-4]

Buspirone (Buspar®)

- Non benzodiazepine anxiolytic
- 5HT1A receptor partial agonist

- Dosing for GAD
  - Initial: 5mg po BID or TID, may titrate Q 5 days
  - Maintenance: 20 – 30 mg/day (2-3 divided doses)
- Takes 2 – 3 weeks to see effect
- Patients treated previously with benzodiazepines less likely to respond

Pregabalin (Lyrica®)

- GABA analog- binds alpha(2)-delta site of voltage gated calcium channels in CNS
- Use in GAD supported by several randomized controlled trials, not FDA-approved for this indication however
- 150 to 600 mg/day in 2-3 divided doses (uncertain if increased efficacy in doses >300 mg/day)
- Onset of efficacy possible after several days
- Requires taper to prevent withdrawal

Maintenance Medication Adverse Effects

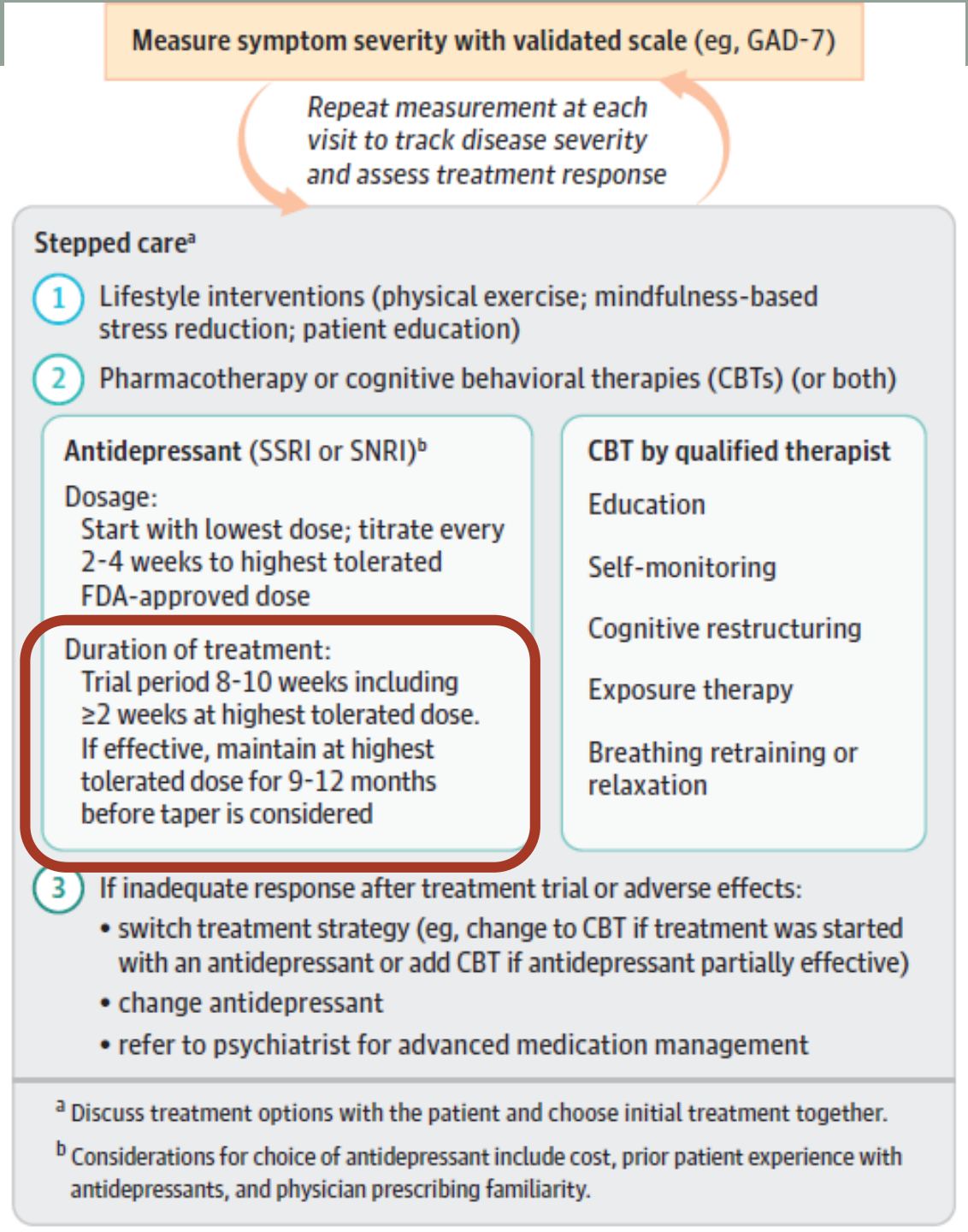
Buspirone (Buspar®)	Pregabalin (Lyrica®)
Sedation Agitation Weakness Dizziness Insomnia Headache GI distress No sexual side effects	Sedation Dizziness Edema Weight gain Abuse potential

Paradoxical anxiety

- Overstimulation related to activating effects of antidepressants and buspirone
- Patients with underlying anxiety most susceptible
- Jitteriness, shakiness, ↑ anxiety, insomnia
- Improvement usually experienced within 7-10 days

- Start low (possibly subtherapeutic dose)
- Titrate by increasing dose Q 2-4 weeks to target dose

	SSRIs and SNRIs	Buspirone (Buspar®)	Pregabalin (Lyrica®)
MOA	5HT reuptake inhibition	5HT1A receptor partial agonist	GABA analog
Indication	Varies by agent, but generally PD, OCD, GAD, SAD	GAD	GAD
Dosing frequency	Usually once daily	BID or TID	BID or TID
Titration on	Yes	Yes	No
Taper off	Yes	Yes	Yes
Onset of efficacy	4-6 weeks (once at therapeutic dose)	2-4 weeks (once at therapeutic dose)	Several days to a week
Adverse effects	paradoxical anxiety (see depression lecture)	sedation, agitation, weakness, paradoxical anxiety, dizziness, HA, GI distress	sedation, dizziness, edema, weight gain, abuse potential
Co-morbid conditions	Depression, pain (SNRIs)	Depression augmentation	Neuropathic pain


Measure symptom severity with validated scale (eg, GAD-7)
Repeat measurement at each visit to track disease severity and assess treatment response
Stepped care[a]
1 Lifestyle interventions (physical exercise; mindfulness-based stress reduction; patient education)
2 Pharmacotherapy or cognitive behavioral therapies (CBTs) (or both)
Antidepressant (SSRI or SNRI)[b]
Dosage:
Start with lowest dose; titrate every 2-4 weeks to highest tolerated FDA-approved dose
Duration of treatment:
Trial period 8-10 weeks including ≥2 weeks at highest tolerated dose.
If effective, maintain at highest tolerated dose for 9-12 months before taper is considered
CBT by qualified therapist
Education
Self-monitoring
Cognitive restructuring
Exposure therapy
Breathing retraining or relaxation
3 If inadequate response after treatment trial or adverse effects:
• switch treatment strategy (eg, change to CBT if treatment was started with an antidepressant or add CBT if antidepressant partially effective)
• change antidepressant
• refer to psychiatrist for advanced medication management
[a] Discuss treatment options with the patient and choose initial treatment together.
[b] Considerations for choice of antidepressant include cost, prior patient experience with antidepressants, and physician prescribing familiarity.

Practice Case

Scenario: A patient presents to the pharmacy to pickup a refill of Flovent. When reviewing the patient profile you notice the patient was prescribed fluoxetine 20mg ~4 weeks ago and you figure he must almost be out of that medication too. However, when you ask if he would like you to also refill the fluoxetine he says “no”. When you probe further you find out he was prescribed the medication for depression and generalized anxiety disorder. He took the medication for 1 week and then stopped. When asked why, he states he hadn’t noticed much benefit on his anxiety or mood. Shortly after starting the fluoxetine he reported feeling really restless and on edge, “I think it made my anxiety worse…”

Practice Case

Based on the information you have been provided, which of the following is the most appropriate education to provide the patient with today?

A. He should refill and restart the fluoxetine today, and within a few weeks the restless/edgy feelings should subside and he should start to see some improvement in his mood and anxiety.
B. He should schedule an appointment to talk with his prescriber about switching to an alternative antidepressant that is less likely to cause those side effects.
C. He should schedule an appointment to talk with his prescriber about switching to pregabalin.
D. He should schedule an appointment to talk with his provider about increasing the fluoxetine since a higher dose might be more effective for his depression and anxiety.

- Options A or B would be appropriate choices in this patient.
- Option A: Fluoxetine could be restarted in this patient with appropriate education on expected time to benefit and timeline for improvement in anxiety as a side effect of fluoxetine. However, instead of starting at the 20mg dose again, would consider starting at 10mg daily dose to minimize paradoxical anxiety which is a common dose-related ADE of SSRIs in patients with underlying anxiety. Lower doses are often more tolerable.
- Option B: This is also a valid option, especially if the patient is hesitant to restart fluoxetine given the ADEs he experienced. Fluoxetine tends to be a pretty activating SSRI, so selecting an alternative SSRI (such as sertraline) may be more tolerable. Any alternative SSRI that is started should be started very low dose as this patient appears to be sensitive to paradoxical anxiety as a SE.
- Option C: pregabalin is a valid option for treating GAD, however this patient was prescribed fluoxetine for both mood and anxiety symptoms. Pregabalin would not be appropriate as monotherapy because it is not effect for depression in addition to anxiety.
- Option D: This is not a recommended option given the ADEs the patient was experiencing that resulted in him stopping the fluoxetine prematurely. Higher doses of fluoxetine (or any antidepressant) are more likely to precipitate dose-dependent ADEs such as paradoxical anxiety.

Questions??

- Casey.Gallimore@wisc.edu