Case Assessment

1. Which of the following is a symptom of major depressive disorder?
   a. Expansive mood
   b. Flight of ideas
   c. Diminished concentration
   d. Excessive worry
   **Justification:** Diminished ability to think or concentrate or indecisiveness is one of the nine diagnostic criteria for major depressive disorder in the DSM-5. Expansive mood and flight of ideas are symptoms of bipolar disorder while excessive worry is a symptom of generalized anxiety disorder.

2. Which of the following are first-line agents for major depressive disorder?
   a. **Serotonin norepinephrine reuptake inhibitors**
   b. Tricyclic antidepressants
   c. Monoamine oxidase inhibitors
   d. Atypical antipsychotics
   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, bupropion, or mirtazapine are appropriate first-line pharmacologic agents for major depressive disorder. Tricyclic antidepressants, monoamine oxidase inhibitors, and atypical antipsychotics are reserved for situations where first-line agents are not efficacious or are associated with adverse events.

3. Which of the following should be monitored in a patient prescribed venlafaxine?
   a. Respiratory rate
   b. **Blood pressure**
   c. Hemoglobin
   d. Potassium
   **Justification:** According to the prescribing information for venlafaxine, venlafaxine treatment is associated with a sustained increase in blood pressure in some patients. It is recommended that patients receiving venlafaxine have regular blood pressure monitoring. Monitoring is not necessary for respiratory rate, hemoglobin, or potassium according to the manufacturer prescribing information.

4. Which of the following side effects commonly occurs and should be discussed when counseling about amitriptyline?
   a. Urinary incontinence
   b. Hirsutism
   c. Hypothyroidism
   d. **Orthostatic hypotension**
   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, tricyclic antidepressants may cause orthostatic hypotension through their alpha adrenergic blockade. Amitriptyline has not been associated with urinary incontinence, hirsutism, or hypothyroidism.

5. Of the DSM-5 diagnostic criteria for major depressive disorder, how many symptoms of depression is this patient presenting with?
   a. Ten
   b. **Eight**
   c. Five
   d. Three
   **Justification:** According to the DSM-5 diagnostic criteria for major depressive disorder, the patient is demonstrating: 1. depressed mood most of the day through patient admission, 2. diminished interest or pleasure in all or most activities as patient does not leave home and stopped mountain biking and playing billiards, 3. significant unintentional weight loss demonstrated by a 26 lb weight loss over one year while not dieting, 4. insomnia demonstrated by chief complaint, 5. psychomotor retardation as noted on the mental status examination, 6. fatigue by admission of the patient, 7. excessive guilt demonstrated by feeling guilty about his coworkers having to pick up for his decreased efficiency, and 8. diminished ability to concentrate demonstrated by decreased focus and efficiency at work.

6. Which of the following is an appropriate first-line pharmacologic recommendation for this patient?
   a. Venlafaxine XR 37.5 mg po TID
   b. Bupropion SR 75 mg po daily
   c. **Sertraline 50 mg po daily**
   d. Mirtazapine 10 mg po qHS
   **Justification:** According to prescribing recommendations made by the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, sertraline 50 mg daily is an acceptable starting dose for major depressive disorder. The other options are incorrect despite being first-line medications because venlafaxine XR is not dosed three times a day, bupropion SR's starting dose is 150 mg daily, and mirtazapine does not come in a 10 mg dose.

7. The patient should be counseled about which Black Box Warning when initiated on an antidepressant?
   a. **Suicidal thinking and behavior**
   b. Myocarditis
   c. Decreased seizure threshold
   d. Hepatotoxicity
   **Justification:** According to the FDA, sertraline possesses a Black Box Warning indicating antidepressants increase the risk of suicidal thinking or behavior in children, adolescents, and young adults with major depressive disorder. Although sertraline does not have a Black Box Warning for the other conditions listed, it may lower seizure threshold and should be used with caution in individuals having hepatic impairment.


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8. The patient is concerned with how long it will take the medication to work. He is worried his girlfriend will leave before he “gets better.” What length of time would he likely begin to see a relief of sadness?
   a. Less than 1 week
   b. 2-4 weeks
   c. 5-8 weeks
   d. 9-12 weeks

   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, a patient may see improvement in depressive symptoms such as return of experiencing pleasure or relief of sadness within 2-4 weeks or 14-24 days of beginning treatment. Physical symptoms may start to improve within the first 1-2 weeks of therapy while emotional symptoms such as relief of sadness may take longer to improve.

9. While discussing timeframes for the antidepressant to work, the patient asks what will likely change first in his depressive presentation. He would like to let his girlfriend know what to look for so they know the medication is working. Which symptom is likely to improve first after beginning antidepressive therapy?
   a. Sadness
   b. Guilt
   c. Concentration
   d. Sleep

   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, a patient may see improvement in physical symptoms such as appetite or sleep within the first week of treatment. Emotional symptoms such as relief of sadness and experience of pleasure may take 2-4 weeks or longer.

10. After a few days of taking escitalopram 20 mg a day, the patient calls the primary care physician’s office complaining of side effects. He reports he has been taking the medication as prescribed every morning but has been feeling “jittery” ever since he started the medication. Which common antidepressant side effect is the patient experiencing?
    a. Anxiety
    b. Hypertension
    c. Akathisia
    d. Nausea

   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, some patients may experience anxiety symptoms such as jitters when first initiating antidepressants. Although SSRIs have been associated with akathisia, it is a rare side effect and more common with antipsychotics.

11. Now that the patient is experiencing side effects from his antidepressant, he has begun expressing he might just stop taking the medication. Which of the following is the best option to minimize the “jitters” side effect and help the patient be adherent?
    a. Switch to amitriptyline 50 mg po qHS
    b. Decrease escitalopram to 10 mg po daily
    c. Add on alprazolam 2 mg po BID
    d. Discontinue all medications

   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, a lower starting dose may be beneficial for patients who experience anxiety when initiating antidepressant therapy.

12. The patient returns to his primary care physician’s office five weeks later for a follow-up visit. A lot has occurred in the mean time, and the physician decided to switch him to sertraline. He is now taking sertraline 50 mg po daily, and has been on it for about 4 weeks. He indicates his performance and energy at work have improved, is feeling less guilty about being a burden on his coworkers, and is sleeping better. However, he still feels sad most of the time, doesn’t experience pleasure, and his relationship with his girlfriend is still “on the rocks.” What is an appropriate next step for this patient?
    a. Augment with nefazodone 100 mg po BID
    b. Switch to citalopram 20 mg po daily
    c. Increase sertraline to 75 mg po daily
    d. Switch to aripiprazole 5 mg po daily

   **Justification:** The patient is reporting or showing improvement in four out of the eight DSM-5 diagnostic criteria for major depressive disorder he demonstrated originally which were insomnia demonstrated by chief complaint (improvement in sleep), fatigue by admission of the patient (more energy at work), excessive guilt demonstrated by feeling guilty about his coworkers having to pick up for his decreased efficiency (feeling less guilty about being a burden to coworkers by admission of the patient), and diminished ability to concentrate demonstrated by decreased focus and efficiency at work (performance at work has improved). This patient would be considered to be having a partial response to sertraline because he is experiencing a decrease in symptoms between 25-50%. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, patients who exhibit a partial response to treatment should maximize doses of antidepressant medications, side effects permitting, before changing to a different antidepressant medication.
13. During the patient’s eight week follow-up visit, he indicates he is feeling “much better” and feels his relationship with his girlfriend has really improved. However, he has noticed since he began his antidepressant he has been experiencing delayed ejaculation during sex. He feels at this point in their relationship, intimacy is very important to keep them “on the right track” and would like to try a different medication. Which medication would you recommend that the patient be switched to?
   a. Nortriptyline
   b. Phenelzine
   c. Venlafaxine
   d. Bupropion

   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, studies indicate patients prescribed bupropion experience a lower incidence of sexual dysfunction than other antidepressants.

14. The patient returns to his primary care physician’s office for a 6-month follow-up visit and indicates he is feeling “great.” He reports he is sleeping well and able to focus at work. His relationship with his girlfriend is back to “normal” and he discusses he will be proposing next week. Because he is feeling well at this point in time, he is wondering when he can stop antidepressant therapy. How long must the patient be symptom free before he may begin a trial to taper off antidepressant therapy?
   a. 1-3 months
   b. 6-12 months
   c. 18-24 months
   d. 56-60 months

   **Justification:** According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, to reduce the risk of relapse, patients who have been treated successfully with antidepressant medications in the acute phase should continue treatment with these agents for 6-12 months.
Case Key

MAJOR DEPRESSIVE DISORDER (MDD)

Epidemiology
A. The National Comorbidity Survey Replication (NCS-R) denotes the lifetime prevalence of MDD among 9,090 adult participants as 16.2% with a 12-month prevalence of 6.6%.1,2
B. Socioeconomic factors associated with increased prevalence for MDD include female sex, middle-aged, never or previously married, low income, unemployed, disabled, or Native-American ethnicity.1,2,3
C. MDD rarely occurs in isolation as the NCS-R found MDD to have at least one other DSM-IV disorder in two-thirds of those surveyed.1,2
D. MDD can significantly impair function in all facets of life, including occupational and social function.1

Pathophysiology
A. The actual mechanism of MDD is unknown, but there are many hypotheses.
B. The monoamine hypothesis was generated from early antidepressants that blocked the reuptake of norepinephrine and serotonin by the presynaptic neuron. This lead to the immediate effect seen by the stimulation of the postsynaptic neuron through increased availability of serotonin and norepinephrine in the synapse.1 However, direct measurement of monoamine neurotransmission does not directly correlate with depression, or antidepressant effect, so other mechanisms are hypothesized.4
C. The serotonin-1B receptor regulates the release of serotonin by feedback inhibition and is located on the presynaptic neuron. It works in conjunction with p11, which is a protein that enhances the efficiency of serotonin-1B receptor signaling. Postmortem studies show that the levels of p11 are decreased in the brains of patients with depression.4,5
D. The sensitivity reduction of the serotonin-1A receptor has been associated with MDD. The serotonin-1A receptor is located both pre- and post-synaptically to help regulate serotonin function.4,6
E. Stress and cortisol may also play a role. Studies have associated depressed patients with elevated cortisol levels in plasma, elevated central corticotropin releasing factor in cerebrospinal fluid, and increased levels of central corticotropin releasing factor messenger RNA and protein in the limbic brain regions.4,7,8,9
F. There is a suggested heritability of approximately 37% between monozygotic and dizygotic twins when comparing concordance rates of MDD.4,10

Case Assessment/Finding
A. The patient is currently exhibiting more than the required 5 diagnostic criteria for MDD for greater than 2 weeks according to the DSM-5:11
   1. Depressed mood most of the day through patient's own admission.
   2. Diminished interest or pleasure in all or most activities as patient does not leave home and stopped mountain biking and playing billiards.
   3. Significant unintentional weight loss demonstrated by a 26 lb weight loss over one year while not dieting.
   4. Insomnia demonstrated by chief complaint of difficulty falling and staying asleep.
   5. Psychomotor retardation as noted on the mental status examination.
   6. Fatigue by admission of the patient’s statement he feels “tired all the time” and has no motivation.
   7. Excessive guilt demonstrated by feeling guilty about his coworkers having to pick up for his decreased efficiency.
   8. Diminished ability to concentrate, demonstrated by decreased focus and efficiency at work.
B. The patient is also suffering from relationship stressors as he reported he and his girlfriend are arguing daily as well as occupational stressors as he is not able to maintain his previous level of efficiency at work.
C. The patient has identified his family as being worried about him and this may be a source of support for him. He has expressed he feels he is not being supported by his girlfriend.
D. He may have had a previously untreated depressive episode. History is not conclusive but there was indication of depressed mood, isolation, crying, and decreased personal hygiene care in his teenage years.
E. There is a family history of depression. His sister is currently treated in the past.
F. At the time of assessment, the patient is currently not prescribed any medication for MDD, nor has he been treated in the past.

SHORT-TERM GOALS
A. Increase patient's efficiency at work.
B. Mend patient's relationship with girlfriend.

LONG-TERM GOALS
A. Alleviate functional impairments and improve quality of life in addition to achieving symptom resolution and episode remission.1

TREATMENT
The patient is entering the acute phase of treatment that is defined by treatment that lasts a minimum of 6-12 weeks. Treatment should consist of pharmacotherapy or other somatic therapies such as light therapy or electroconvulsive...
therapy (ECT), depression-focused psychotherapy, or the combination of somatic and psychosocial therapies. Selection of initial treatment is influenced by several patient factors including symptom profile, co-morbid disorders, psychosocial stressors, prior treatment experience, adverse effect profile, cost, and patient preference.

Pharmacologic Treatment

A. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder (MDD), selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), bupropion, or mirtazapine are appropriate first-line pharmacologic agents for major depressive disorder (Figure 1). For most patients, the effectiveness of antidepressant medications is generally comparable between classes and within classes of medications. Therefore, initial selection of pharmacotherapy depends on side effect profile, safety, cost of the medication, patient preference, and history of prior medication treatment.

When selecting a medication for this patient, one must factor in that he has recently lost weight, and weight loss is a possible side effect of both SNRIs, fluoxetine, and bupropion. Mirtazapine and paroxetine may not be first choices either as they have a side effect of weight gain, and despite the weight loss, the patient’s BMI is within normal range. However, serotonergic agents such as SSRIs and SNRIs are associated with sexual dysfunction and the patient reported decreased libido during the review of systems. Despite the possibility of sexual dysfunction, SSRIs are often utilized as first-line. SSRIs are also a cost effective choice for the patient as they are all generic and are often low cost when paying without insurance.

B. Within the SSRI class, there is variability when choosing a medication and one is not preferred over the others in terms of efficacy. Choosing an SSRI often depends on the side effect profile (Figure 2) and the patient’s previous experience within this medication class. Both fluvoxamine and paroxetine have undesirable side effects such as anticholinergic side effects. Fluvoxamine is also not FDA-approved for MDD. The FDA has issued a safety announcement for citalopram indicating its association of QTc prolongation at higher doses. Although the patient is young and does not have any comorbid health conditions, the dose cap may be limiting if the patient’s MDD requires higher doses. The current maximum dose of citalopram is set at 40 mg a day. Fluoxetine inhibits CYP450 2C19 moderately and 2D6 strongly. Paroxetine also has strong inhibition of CYP450 2D6. However, fluvoxamine has inhibition of CYP450 1A2, 2C9, 3A4, and 2C19 (Figure 3). Although the patient is not on medications currently, this has the potential for drug interactions in the future. Escitalopram has recently become generic and is still relatively expensive compared to sertraline. When the cost of escitalopram equals that of sertraline, it would be another viable option. Given the patient has no health insurance, the cheaper option would be appropriate to help encourage adherence. Sertraline would be an acceptable choice for the patient at this point. The recommended starting dose is 50 mg daily.

C. Given the patient’s concern over his relationship discourse, which he attributes to his depressive symptoms, it is important to discuss with the patient a timeframe for seeing improvement in depressive symptoms. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, a patient may see improvement in depressive symptoms such as return of experiencing pleasure or relief of sadness within 2-4 weeks or 14-24 days of beginning treatment. Physical symptoms such as appetite and sleep may start to improve within the first 1-2 weeks of therapy, while emotional symptoms such as relief of sadness may take longer to improve.

D. After about one week, the patient contacted his primary care physician to report “jitteriness” after initiating sertraline. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, some patients may experience anxiety symptoms such as jitteriness when first initiating antidepressants. To help ensure adherence, a lower starting dose may be beneficial for patients who experience anxiety when initiating antidepressant therapy.

E. When the patient returns to his primary care physician’s office after four weeks for a follow-up visit, the patient is reporting or showing improvement in four out of the eight DSM-5 diagnostic criteria for MDD he demonstrated 4 weeks previously. These can be compared to his chief complaints at the initial visit, such as insomnia (improvement in sleep at four weeks), fatigue by admission of the patient (more energy at work), excessive guilt demonstrated by feeling guilty about his coworkers having to pick up for his decreased efficiency (feeling less guilty about being a burden to coworkers by admission of the patient), and diminished ability to concentrate demonstrated by decreased focus and efficiency at work (performance at work has improved).

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Down in the Dumps: Developing a Depression Treatment Plan

F. During the patient’s eight week follow-up visit, he indicates he is feeling better and his relationship with his girlfriend has improved. However, he reports experiencing delayed ejaculation during sex. The patient requests to switch medications, as intimacy is important in his recovering relationship with his girlfriend. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, studies indicate patients prescribed bupropion and mirtazapine experience a lower incidence of sexual dysfunction than other antidepressants. At this time, bupropion would be the best choice given it would be optimal to avoid weight gain, given it is a common side effect of mirtazapine. Bupropion would be a weight neutral option (Figure 2). It is recommended to initiate bupropion IR 100 mg twice daily for three days then increase to 100 mg three times daily. Bupropion XL would also be a suitable choice. It would be initiated at 150 mg daily.

G. When the patient returns for a 6-month follow-up visit, he indicates he is feeling “great”, sleeping well, and able to focus at work. He also indicates his relationship with his girlfriend is going well and he plans to propose next week. Because he is feeling well at this point in time, the patient inquires about a timeline to stop antidepressant therapy. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, to reduce the risk of relapse, patients who have been treated successfully with antidepressant medications in the acute phase should continue treatment with these agents for 6-12 months. Now that the patient is stable and improved, it would be appropriate to begin discussing treatment discontinuation in 6-12 months.

Non-pharmacologic Therapy

A. Patient may also consider psychotherapy in conjunction with pharmacotherapy. Psychotherapy is particularly useful in addressing psychosocial stressors influencing MDD. Given the patient is experiencing relationship stressors with his girlfriend as well as occupational stressors, this would be an acceptable option if the patient chose to initiate this treatment. Couples therapy might also be useful given the extent of the relationship stressors the patient discussed. However, since the patient does not have health insurance, this may be an expensive option. He may be referred to a therapist who bills based on income or to a free clinic.

MONITORING

Major depressive disorder

A. Frequency of patient monitoring of symptoms is determined by symptom severity and suicidality as well as comorbid psychiatric or medical disorders, patient cooperation, patient’s social support, and occurrence of medication side effects. The patient should have a follow-up to assess symptoms of his MDD in four weeks as he is demonstrating at least moderate MDD and initiating a new medication. The patient’s vitals would also be assessed to monitor for possible weight gain. A telephone follow-up with the patient in 1-2 weeks would be appropriate to assess side effects and suicidality. Physical symptoms such as appetite and sleep may start to improve within the first 1-2 weeks of therapy while emotional symptoms such as relief of sadness may take 2-4 weeks or longer to improve.

B. Screen for comorbid psychiatric or medical disorders during each interaction with the patient.

C. Monitor for mania or hypomania. Undiagnosed bipolar disorder may present itself as a depressive episode first. Initiating an antidepressive agent may induce a switch into mania. This should be done at each interaction with the patient.

D. Monitoring psychotherapy for non-response or difficulty tolerating this form of treatment at each session.

E. To reduce the risk of relapse, patients who have been treated successfully with antidepressant medications in the acute phase should continue treatment with these agents for 6-12 months.

EDUCATION

A. Initiating an antidepressant may increase the risk for suicidal thinking or behavior in children, adolescents, and young adults with major depressive disorder. Contact your prescriber or proceed to the local emergency department if thoughts of self harm develop.

B. Medications involving serotonin put the patient at risk for developing serotonin syndrome. Serotonin syndrome is a potentially life-threatening disorder that may present as tremor, diarrhea, increased heart rate or blood pressure, sweating, altered mental status, muscle jerks, increased temperature, or muscle rigidity. Call 911 or proceed to the nearest emergency department if these symptoms develop.

C. Some common side effects of sertraline the patient may experience include dry mouth, sweating, nausea, dyspepsia, changes in sleep, diarrhea, headache, restlessness, and anxiety (Figure 2). These side effects are often transient and usually resolve with continued adherence after 7-10 days. A side effect that is not usually self-limiting is sexual dysfunction and may require a change in medication. The patient should be encouraged to contact their prescriber if any adverse events develop.

D. Some common bupropion side effects include headache, insomnia, nausea, and dry mouth (Figure 2). These side effects are also often transient and usually resolve with continued adherence after 7-10 days. Bupropion is also associated with decreasing the seizure threshold, which is not transient, and patient should use caution when combining with other seizure threshold decreasing medications.


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F. During the patient’s eight week follow-up visit, he indicates he is feeling better and his relationship with his girlfriend has improved. However, he reports experiencing delayed ejaculation during sex. The patient requests to switch medications, as intimacy is important in his recovering relationship with his girlfriend. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, studies indicate patients prescribed bupropion and mirtazapine experience a lower incidence of sexual dysfunction than other antidepressants. At this time, bupropion would be the best choice given it would be optimal to avoid weight gain, given it is a common side effect of mirtazapine. Bupropion would be a weight neutral option (Figure 2). It is recommended to initiate bupropion IR 100 mg twice daily for three days then increase to 100 mg three times daily. Bupropion XL would also be a suitable choice. It would be initiated at 150 mg daily.

G. When the patient returns for a 6-month follow-up visit, he indicates he is feeling “great”, sleeping well, and able to focus at work. He also indicates his relationship with his girlfriend is going well and he plans to propose next week. Because he is feeling well at this point in time, the patient inquires about a timeline to stop antidepressant therapy. According to the 2010 APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, to reduce the risk of relapse, patients who have been treated successfully with antidepressant medications in the acute phase should continue treatment with these agents for 6-12 months. Now that the patient is stable and improved, it would be appropriate to begin discussing treatment discontinuation in 6-12 months.

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B. Screen for comorbid psychiatric or medical disorders during each interaction with the patient.

C. Monitor for mania or hypomania. Undiagnosed bipolar disorder may present itself as a depressive episode first. Initiating an antidepressive agent may induce a switch into mania. This should be done at each interaction with the patient.

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D. Some common bupropion side effects include headache, insomnia, nausea, and dry mouth (Figure 2). These side effects are also often transient and usually resolve with continued adherence after 7-10 days. Bupropion is also associated with decreasing the seizure threshold, which is not transient, and patient should use caution when combining with other seizure threshold decreasing medications.
### Figure 1. First-line agent antidepressant dosing adapted from 2014 CPNP Psychiatric Pharmacotherapy Review Course Depression Module and Lexi Drugs®. Lexicomp®, Hudson, OH, USA.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Initial Dose (mg/day)</th>
<th>Titration Increments (mg)</th>
<th>Usual Daily Adult Dose (mg/day)</th>
<th>Renal Dose Adjustment Necessary</th>
<th>Hepatic Dose Adjustment Necessary</th>
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<td><strong>Selective Serotonin Reuptake Inhibitors</strong></td>
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<td>Citalopram</td>
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<td>Escitalopram</td>
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<td>10</td>
<td>10 - 20</td>
<td>CrCl &lt; 20 mL/min Use with caution</td>
<td>Maximum of 10 mg/day</td>
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<td>Fluoxetine</td>
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<td>Maximum of 40 mg/day</td>
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<td>50 - 200</td>
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<td>Desvenlafaxine</td>
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<td>50-100</td>
<td>Maximum of 50 mg/day (50 mg/every other day in ESRD)</td>
<td>Maximum dose of 100 mg/day</td>
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<td>20</td>
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<td>Levomilnacipran</td>
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<td>20-40</td>
<td>40-120</td>
<td>CrCl 30-59 mL/min maximum of 80 mg/day CrCl &lt; 15-29 mL/min maximum of 40 mg/day Not recommended in ESRD</td>
<td>No</td>
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<td>Milnacipran</td>
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<td>12.5-25</td>
<td>100-200</td>
<td>CrCl &lt; 30 mL/min maximum of 100 mg/day Not recommended in ESRD</td>
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<td>Venlafaxine</td>
<td>37.5</td>
<td>37.5-75</td>
<td>75-225</td>
<td>CrCl 10-70 mL/min reduce by 25-50% CrCl &lt; 10 mL/min reduce by 50%</td>
<td>Reduce by 50%</td>
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<td><strong>Dopamine Norepinephrine Reuptake Inhibitor</strong></td>
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<td>Buproprion</td>
<td>200</td>
<td>50-100</td>
<td>200-450</td>
<td>Reduce dose/frequency</td>
<td>Reduce dose/frequency</td>
</tr>
<tr>
<td><strong>Alpha₂ Antagonist</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>7.5</td>
<td>7.5-15</td>
<td>15-45</td>
<td>Use with caution</td>
<td>Use with caution</td>
</tr>
</tbody>
</table>

ESRD- End stage renal disease

This educational product is not designed to be comprehensive. Please see full prescribing information for products discussed in this case and key.
Figure 2. First-line agent antidepressant adverse effects adapted from 2014 CPNP Psychiatric Pharmacotherapy Review Course Depression Module and Lexi Drugs’. Lexicomp®, Hudson, OH, USA.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>GI Distress</th>
<th>Weight Gain</th>
<th>Drowsiness</th>
<th>Anti-cholinergic</th>
<th>Orthostasis</th>
<th>Cardiac Changes</th>
<th>Additional Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective Serotonin Reuptake Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Sertraline</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Serotonin Norepinephrine Reuptake Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desvenlafaxine</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Diaphoresis, lipid changes, headache, insomnia, sexual dysfunction, serotonin syndrome</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Levomilnacipran</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Milnacipran</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Dopamine Norepinephrine Reuptake Inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>-</td>
<td>++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Headache, insomnia, decrease seizure threshold</td>
</tr>
<tr>
<td>Alpha₂ Antagonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Sedation</td>
</tr>
</tbody>
</table>

- to +++ = absent to common

Figure 3. First-line agent antidepressant CYP450 interactions adapted from 2014 CPNP Psychiatric Pharmacotherapy Review Course Depression Module and Lexi Drugs’. Lexicomp®, Hudson, OH, USA.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>CYP1A2</th>
<th>CYP2C19</th>
<th>CYP2D6</th>
<th>CYP3A4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective Serotonin Reuptake Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>+</td>
<td>+</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>-</td>
<td></td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>-/+</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Sertraline</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Serotonin Norepinephrine Reuptake Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desvenlafaxine</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Levomilnacipran</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dopamine Norepinephrine Reuptake Inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>-</td>
<td>+++</td>
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<td>-</td>
</tr>
<tr>
<td>Alpha₂ Antagonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

+ = inhibitory potential, - no interaction
REFERENCES