

APPENDIX C:
PRESCRIBING ANTIDEPRESSANT
MEDICATION FOR ADULTS

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The following information has been adapted from clinical guidelines developed by the American Psychiatric Association (APA), the American College of Physicians, Brigham and Women’s Hospital, the MacArthur Initiative on Depression in Primary Care, and the Department of Veterans Affairs (VA).

■ **Should I prescribe antidepressant medication, refer patients for psychotherapy, or both?**

- Medication, psychotherapy or a combination of both have all been shown effective in treating depression.
- The selection of a treatment modality should be influenced by clinical factors, such as symptom severity, and patient factors, such as preference.

Antidepressant Medication:

- Antidepressant medication alone may be provided as an initial primary treatment for mild major depressive disorder, if preferred by the patient.
- Antidepressant medication should be provided for moderate to severe major depressive disorder.

Should Receive Medication	Strong Indications for Medication
Moderate to severe depressive symptoms are present.	Past history of a positive response to medications.
Significant impairment in social/occupational functioning.	Negative response to psychotherapeutic interventions.
Suicidal ideation is present.	Recurrent depressive episodes.
	Family history of depression.
	Patient preference for drug therapy.

Psychotherapy

- Psychotherapy alone may be considered for patients with mild to moderate major depressive disorder, if therapy alone is preferred by the patient.
- Clinical features that may suggest the need for psychotherapeutic interventions include the presence of psychosocial stressors, interpersonal problems, intrapsychic conflict, or a comorbid personality disorder.

Antidepressant Medication and Psychotherapy

- The combination of medication and therapy may be a useful initial treatment choice for patients with moderate to severe depression, particularly when psychosocial stressors, interpersonal problems, intrapsychic conflict, or comorbid personality disorders are present.
- Patients who previously have demonstrated inadequate responses to mono-therapy may be good candidates for combined medication and psychotherapy treatment.

Adding psychotherapy to medication may also be helpful when concerns for patient adherence to medication are present. In these cases, it is helpful to discuss these concerns with the therapist if possible.

■ In which situations should I consider referring the patient to a psychiatric specialist?

- A physician should refer any patient he or she does not feel comfortable treating for depression to a psychiatric specialist.
- Guidelines created by the VA recommend that physicians consider referring a patient to a specialist under the following conditions:
 - Extensive history of abuse/trauma.
 - Frequent nightmares or flashbacks suggestive of post-traumatic stress disorder.
 - Extreme weight loss suggestive of anorexia nervosa.
 - A pattern of bingeing and/or purging.
 - Bipolar disorder.
 - Schizophrenia.
 - Psychotic symptoms.
 - Suspected need for hospitalization.
 - Concerns about patient adherence to medication.
 - History of poor treatment response.
 - Patient preference for seeing a specialist.
 - Diagnostic clarification is needed.
 - Other major mental disorders, which are likely to significantly complicate the treatment of depression in primary care setting, are present.
- Patients whose depression is not remitting following treatment in the primary care setting should be referred to a specialist. (The VA guideline suggests that after two or more attempts at medication treatment with partial or no response, a specialist should be consulted.)
- Physician collaboration with mental health specialists can increase the effectiveness of care.

■ Which class of antidepressant medication should I prescribe?

- The effectiveness of antidepressant medications is generally comparable between classes of medication.
- Patient factors and drug side effect profiles may favor one class of antidepressants over another for any given patient. For example, a physician should consider which class of medication has been successful or unsuccessful for the patient in the past.

- SSRIs or venlafaxine are commonly prescribed in the primary care setting because of their lower level of toxicity and ease of administration, as compared to other antidepressant medications.
- The physician should consider the medical condition of the patient. For example, for patients with certain gastrointestinal disorders (such as chronic diarrhea or peptic ulcers), a TCA may be a better choice.

■ Which antidepressant medication should I prescribe?

- At this time, no antidepressant medication has been shown to be clearly more effective than another.
- Any antidepressant medication that has been effective for the patient in the past should be considered first choice when prescribing a new medication protocol.
- The selection of an antidepressant medication should be made based on:
 - Patient's past experience with antidepressant medication.
 - Anticipated side effects.
 - Safety or tolerability of the side effects for the individual patient.
 - Safety in overdose.
 - Concomitant medical conditions.
 - Patient preference.
 - Cost to the patient.
- Based on these considerations, the APA reports that the following antidepressant medications are likely to be optimal for most patients: SSRIs, desipramine, nortriptyline, bupropion and venlafaxine.
- Lower starting doses are recommended for elderly patients and for patients with panic disorder, significant anxiety, hepatic disease and general comorbidity.

■ What side effects might there be?

- The following table, adapted from the MacArthur Initiative on Depression and Primary Care displays common side effects and management strategies:

Side Effects	SSRIs & Effexor	Tricyclics (nortriptyline, amitriptyline, imipramine)	Bupropion	Mirtazapine	Management Strategy
Sedation	Uncommon	Moderate	Very Unlikely	Mild	<ul style="list-style-type: none"> • Give med at bedtime • Increase Remeron dose • Try caffeine
Anti-Cholinergic: Dry mouth, dry eyes, constipation, urinary retention, tachycardia	Uncommon	Severe	Very Unlikely	Uncommon	<ul style="list-style-type: none"> • Increase hydration • Sugarless gum/candy • Dietary fiber • Artificial tears • Consider switching
GI distress or nausea	Moderate	Very Unlikely	Mild	Uncommon	<ul style="list-style-type: none"> • Often improves in 1 to 2 weeks • Take with meals • Consider antacids or H2 blockers
Restlessness, jitters or tremors	Mild	Uncommon	Moderate	Very Unlikely	<ul style="list-style-type: none"> • Start with small doses, especially with anxiety disorder • Reduce dose temporarily • Add beta-blocker
Headache	Mild	Very Unlikely	Mild	Very Unlikely	<ul style="list-style-type: none"> • Lower dose • Acetaminophen
Insomnia	Mild	Very Unlikely	Mild	Very Unlikely	<ul style="list-style-type: none"> • Trazadone 25-100mg poqhs (can cause orthostatic hypotension and priapism) • Take medication in AM
Sexual Dysfunction	Moderate	Very Unlikely	Very Unlikely	Very Unlikely	<ul style="list-style-type: none"> • May be part of depression or medical disorder • Decrease dose • Consider trial of Viagra • Try adding Bupropion 100mg qhs or bid • Try adding Buspirone 10-20mg bid/tid • Try adding Cyproheptadine 4mg 1-2 hrs before sex

Side Effects	SSRIs & Effexor	Tricyclics	Bupropion	Mirtazapine	Management Strategy
Seizures	Very Unlikely	Very Unlikely	Mild	Uncommon	<ul style="list-style-type: none"> • Discontinue antidepressant
Weight Gain	Uncommon	Uncommon	Uncommon	Moderate	<ul style="list-style-type: none"> • Exercise • Diet • Consider changing med
Agranulocytosis	Very Unlikely	Very Unlikely	Very Unlikely	Uncommon	<ul style="list-style-type: none"> • Monitor for signs of infection, flu-like symptoms • Stop drug, check WBC

- Initiating medication at low doses may reduce the severity of side effects.
- A qam regimen may ease complaints of insomnia.
- Trazodone is sometimes added to SSRIs to manage insomnia.
- Bupropion may counteract sexual side effects.

Generic name (Trade name)	Pros	Cons
Fluoxetine (continued from page 16-7) Class: SSRI	<ul style="list-style-type: none"> • Has the most data suggesting no significant teratogenic effects. • Sarafem approved for PMDD 	<ul style="list-style-type: none"> • Found in breast milk though no concerning negative effects on child cited
Sertraline (Zoloft) Class: SSRI	<ul style="list-style-type: none"> • FDA-approved for depression, obsessive compulsive disease, panic and PTSD • FDA-approved for anxiety disorders • Mild DA reuptake inhibition • Fewer drug interactions than other SSRIs • Safety shown post MI • A good choice for breastfeeding women (very little found in breast milk) 	<ul style="list-style-type: none"> • May be agitating • Insomnia • Discontinuation effects
Paroxetine (Paxil) Class: SSRI	<ul style="list-style-type: none"> • FDA-approved for depression, general anxiety disorder, social anxiety disorder and panic • May be less agitating • More anxiolytic 	<ul style="list-style-type: none"> • May be more sedating • Possibly more weight gain • Mild anticholinergic effects • Discontinuation effects • Drug interactions
Fluvoxamine (Luvox) Class: SSRI	<ul style="list-style-type: none"> • FDA-approved for obsessive compulsive disease • Also effective for depression, other anxiety disorders • Usually less agitating 	<ul style="list-style-type: none"> • BID dosing usually necessary • Diarrhea • Drug interactions
Citalopram (Celexa/Lexipro) Class: SSRI	<ul style="list-style-type: none"> • FDA-approved for depression • 10mg dose usually effective for most • Usually less agitating • May be less disruptive to sleep • Least expensive SSRI • Fewer drug interactions • Well tolerated by elderly 	<ul style="list-style-type: none"> • May be too sedating
Trazodone (Desyrel) Class: Serotonin-2A blocker	<ul style="list-style-type: none"> • FDA-approved for depression • Very helpful for sleep • Low rate of sexual side effects (except priapism) 	<ul style="list-style-type: none"> • Antidepressant efficacy requires high dosing and at least bid dosing • Sedating • Priapism • Orthostasis

Generic name (Trade name)	Pros	Cons
<p>Bupropion (Wellbutrin, Wellbutrin SR, Zyban)</p> <p>Class: Dopamine & Norepinephrine Reuptake Inhibitor</p>	<ul style="list-style-type: none"> • Wellbutrin approved for depression, Zyban approved for smoking cessation • Helpful in ADHD and restless legs • Most stimulating • Very low risk of sexual side effects • Least likely to induce rapid-cycling/mixed states • No weight gain • No cardiotoxicity 	<ul style="list-style-type: none"> • Bid or tid dosing necessary above 200mg • Contraindicated in epilepsy and eating disorders due to increased risk of seizures (although SR form probably safer) • May aggravate anxiety
<p>Venlafaxine (Effexor, Effexor XR)</p> <p>Class: Serotonin & Norepinephrine Reuptake Inhibitor</p>	<ul style="list-style-type: none"> • Possibly more effective than SSRIs in severe depression • No drug interactions • Helpful with anxiety and at higher doses, concentration, attention • No cardiotoxicity • Safe in overdose • Less weight gain than SSRIs 	<ul style="list-style-type: none"> • Tachycardia and hypertension above 200mg/d may occur • Discontinuation effects • IR form requires divided dosing • Sexual side effects • Nausea
<p>Mirtazapine (Remeron)</p> <p>Class: Specific Serotonin & Adrenergic Receptor Blocker</p>	<ul style="list-style-type: none"> • Little nausea or diarrhea • Little agitation • May benefit sleep • Appetite stimulating (good choice for low weight elderly or medically ill patients) • No drug interactions • May have fewer sexual side effects • No cardiotoxicity • Safe in overdose 	<ul style="list-style-type: none"> • Can be sedating • Weight gain • Rare cases of reversible agranulocytosis (1.1/1000)
<p>Nefazodone (Serzone)</p> <p>Class: Serotonin-2A blocker Inhibitor</p>	<ul style="list-style-type: none"> • Particularly calming • Good for panic • Benefits insomnia • No sexual side effects • No weight gain 	<ul style="list-style-type: none"> • Bid dosing • Hard to titrate

■ What information should I get from my patient before prescribing antidepressant medication?

- Prior to prescribing antidepressant medication, assessments for the following conditions should occur:
 - Mania or hypomania, as antidepressant medication could trigger a manic episode in someone with bipolar disorder (see bipolar disorder section of the Depression chapter). If bipolar disorder is suspected, patient should be referred to a psychiatrist.
 - Psychosis.
 - Substance abuse.

■ What information should I give my patient when prescribing an antidepressant medication?

- Information on the nature and course of depression:
 1. Depression and anxiety are treatable.
 2. It is recommended that antidepressant medication be taken for at least six months.
 3. The medication is safe and is not addictive.
- Treatment information:
 1. When and how often to take the medication.
 2. Make a follow-up appointment in two to four weeks.
 3. Do not stop taking the medication without talking to your doctor.
 4. It may take several weeks before you begin to feel better.
 5. Even when you start to feel better, it is important to keep taking the medication.
- Potential side effects:
 1. Explain that side effects may be worse in the beginning.
 2. Side effects may occur before you begin to feel better.
 3. Abruptly stopping the medication may result in adverse withdrawal symptoms or a return of depressive symptoms.

■ When should I schedule a follow-up visit after prescribing an antidepressant medication?

- Guidelines vary slightly as to when the first follow-up appointment should be scheduled. The physician will need to make this decision based on clinical and patient factors. However, recommendations range from one to two weeks to three to four weeks for the first follow-up appointment.
- It is a good idea to make a follow-up appointment within two weeks to assess adherence and possible side effects. An assessment of patient response to the medication in terms of depressive symptoms should occur within weeks four to six.
- NCQA guidelines have set a minimum standard of three follow-up visits with a provider within three months for any depressed patient being prescribed an antidepressant.

- **What should I ask/assess the patient during the follow-up visits?**
 - Emergence of side effects.
 - Adherence to medication.
 - Assess response to medication.
 - Concurrent medical illness that may impede clinical response.
 - Clinical condition.
 - Safety (see Suicide chapter).
 - Signs of a switch to mania (see bipolar disorder section of Depression chapter).
 - Symptom status.
 - Substance abuse (see Substance Abuse chapter).
 - Comorbid psychiatric disorders.
 - Exacerbating psychosocial stressors.
 - Accuracy of diagnosis.
 - Developing rapport with the patient.

- **When should I consider increasing the dosage or changing the medication?**
 - Titration to full therapeutic dose can generally be accomplished over the initial weeks of treatment but vary by side effects, patient age and presence of comorbid illness.
 - Before assessing the efficacy of an antidepressant medication, the patient should have been on the medication at a therapeutic dose for a minimum of four to six weeks.
 - Depressed patients showing no improvement by week four typically will do no better than placebo if the treatment regimen is not changed. A change in the treatment regimen (e.g., increased dose, medication change, adding psychotherapy, etc.) is indicated if no improvement is seen after four weeks of proper medication adherence.
 - If moderate improvement is not seen within four to eight weeks of medication, a reappraisal of the treatment should be conducted and an increase in dosage may be considered.
 - If no improvement is seen after four to eight weeks of medication, a change in medication may be warranted.
 - Following any change, the patient should be closely monitored.

- **When should I discontinue the medication?**
 - Unless otherwise indicated, antidepressant medication should not be discontinued for patients who show an incomplete response, even if a substantial response has been noted, as stopping after only a partial response has been associated with poor outcomes.
 - The APA recommends continuing the antidepressant medication (on the current dose) for 16-20 weeks following remission of symptoms.
 - Patients who have had three or more episodes of major depression should remain on prophylactic antidepressant medication for one or more years after remission of depressive symptoms.
 - The decision to discontinue antidepressant treatment should be based on the probability of reoccurrence,

the frequency and severity of past episodes, the persistence of symptoms, the presence of comorbid disorders and patient preference.

- Discontinuation of an antidepressant medication following maintenance therapy should be done with a slow taper, guided by the elimination half-life of the parent compound and metabolites, with close monitoring of depressive symptoms.
- Use caution when tapering one medication or when substituting another, particularly when stopping SSRIs and venlafaxine, as the following symptoms may develop: dizziness, nausea, chills, anxiety, irritability, crying spells and depression.
- When discontinuing an antidepressant medication, it is a good idea to discuss ways of reducing the risk of relapse and to identify early warning signs of a return of depressive symptoms.

■ Important Definitions:

- Remission – a return to premorbid functioning accompanied by a substantial reduction in depressive symptoms. A PHQ score < 5 is often considered remission.
- Response – a 50 percent reduction in depressive symptoms is often considered “response” or “partial remission.” It is very important to treat to full remission.

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