Management of Major Depressive Disorder (MDD) in Adults
Primary Care Initial Assessment and Diagnosis

1. Patient age > 18 with suspected depression presenting to primary care

2. Brief assessment of initial presentation to assess for dangerousness

3. Unstable urgent condition? [C]
   - Y: Provide appropriate care or refer to stabilize and follow legal mandates [D]
   - N: Obtain relevant history, physical examination, and lab tests [E]

4. Obtain symptoms score using PHQ-9
   Determine and document DSM IV-TR criteria for MDD [E]

5. Do medication(s) or comorbid medical condition(s) contribute to symptoms? [F]
   - Y: Provide medical treatment and follow-up as indicated
   - N: Continue medical follow-up as indicated

6. Presumptive diagnosis of MDD?
   - Y: History of MDD?
     - Y: Are there symptoms of depression or functional impairment that do not meet DSM IV-TR criteria for MDD? [H]
     - N: Assess for manic or hypomanic symptoms or family history of bipolar or other psychiatric comorbidities [G]
   - N: Are there concerns about functional ability or patient’s mental health?
     - Y: Provide psychoeducation for self management [I]
     - N: Repeat screening annually

7. Follow up within 4-6 weeks

8. Suspected bipolar disorder?
   - Y: Consider management of Bipolar Disorder
   - N: Occurrence of other major medical illness?
     - Y: Continue on page 2 Initial Treatment
     - N: Referred/consult to specialty care

Sidebar 1: Assessment
- Medical history
- Physical examination
- Mental Status Exam
- Relevant lab tests
- Drug inventory (including over the counter and herbal)
- Psychosocial history
Management of Major Depressive Disorder in Adults
Primary Care Initial Treatment

24. Patient with presumptive diagnosis or history of MDD, meets DSM IV-TR diagnostic criteria for MDD

25. Determine level of severity of MDD symptoms and functional impairment (J)

26. Discuss treatment options and patient’s preferences
   Arrive at shared decision regarding treatment goals and plan (K)

27. Is there indication for referral to mental health specialty? (L)
   Y: Refer to Mental Health Specialty Care
   N:

29. Initiate treatment strategies effective for depression (See Sidebar 4) (M)

30. Address psychosocial needs (N)

31. Schedule follow-up in 4-6 weeks

Continued on page 3

Sidebar 2: DSM-IV-TR Diagnostic Criteria for MDD
MDD diagnosis requires the presence of symptom 1, 2, or both; and at least 5 of 9 symptoms that persist for at least 2 weeks:
1. Depressed mood nearly every day for most of the day, based on self report or observation of others.
2. Marked reduction or loss of interest or pleasure in all, or nearly all, activities for most of the day, nearly every day.
3. Significant non-dieting weight loss or weight gain (>5% change in body weight)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation (should be observable by others).
6. Fatigue/loss of energy nearly every day.
7. Feelings of worthlessness or excessive/inappropriate guilt nearly every day.
8. Diminished cognitive function (reduced ability to think or concentrate) nearly every day.
9. Recurrent thoughts of death and/or suicide, suicide planning, or a suicide attempt.

Sidebar 3: Indications for Referral to Mental Health
- Unclear diagnosis
- Evidence of psychotic features, past mania, or hypomania
- Signs of comorbid psychiatric conditions
- Unable to treat patient in primary care
- Need for psychosocial interventions
- Patient preference

Sidebar 4: Initial Treatment Strategies for MDD

<table>
<thead>
<tr>
<th>SEVERITY</th>
<th>PHQ-9 Score</th>
<th>FUNCTIONAL IMPAIRMENT</th>
<th>INITIAL STRATEGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>10-14</td>
<td>Mild</td>
<td>Monotherapy — antidepressants or psychotherapy — or, possibly combination</td>
</tr>
<tr>
<td>Moderate</td>
<td>15-19</td>
<td>Moderate</td>
<td>Antidepressants or psychotherapy, or combination</td>
</tr>
<tr>
<td>Severe</td>
<td>≥20</td>
<td>Severe</td>
<td>May start with antidepressants or psychotherapy but should prefer combination or multiple antidepressants</td>
</tr>
</tbody>
</table>

Psychoeducation and self-management should be provided for all severity levels.
Management of Major Depressive Disorder in Adults
Primary Care Treatment Strategy and Follow-Up

Sidebar 5: Assessment of Treatment Response
- Symptom Severity (PHQ-9) and risk for suicide
- Tolerability to treatment (Adverse effects)
- Adherence to treatment
- Medical problems influencing recovery
- Psychosocial barriers to therapy
- Reevaluate diagnosis and appropriate treatment

Sidebar 6: Treatment Strategies
- Mono (Psych. Or Drugs)
- Combine psych and pharmacotherapy
- Complex psychopharmacology
- Somatic interventions
- Inpatient/residential

Sidebar 7: Indication for Consultation or Referral to Mental Health Specialty Care
- Primary care out of comfort zone
- Complicated depression with comorbidity
- Lack of resources
- Treatment resistance
- Patient request

32. Patient with a diagnosis of MDD on treatment

33. Complete assessment (see Sidebar 5)
   Review current medication
   Assess for dangerousness

34. Unstable or dangerous condition? [C]

35. Provide appropriate care or refer to stabilize and follow legal mandates [D]

36. Is patient condition improving and current treatment strategy tolerable? [P]

37. Continue current treatment strategy
   Reassess by 4-6 weeks [Q]

38. Full remission? [R]

39. Continue treatment to prevent relapse [S]

40. Sustained remission?

41. Continue maintenance therapy in Primary Care [T]

42. Sustained remission?

43. Screen annually

44. Adjust/modify treatment:
   - Consider longer duration
   - Consider increasing dose
   - Consider augmentation
   - Consider switching to another agent
   - Consider modifying treatment strategy (see Sidebar 6, 7)

45. Schedule follow-up

Return to Box 32
**VA / DoD DEPRESSION PRACTICE GUIDELINE PROVIDER CARE CARD**  
**Identification and Assessment**

### Depression Risk Factors

- Prior Episodes of Depression
- Family History of Depressive D/O
- Prior Suicide Attempt
- Female Gender
- Age of Onset Under 40
- Postpartum Period
- Medical Comorbidity
- Lack of Social Support
- Stressful Life Events
- Current Substance Abuse

### Screening Using the Patient Health Questionnaire 2 (PHQ-2)

(see 2009 MDD CPG pp. 17-21)

Screening with PHQ-2 should be completed annually by all patients seen in primary care settings.

Over the past two weeks, how often have you been bothered by either of the following problems?

A) Little interest or pleasure in doing things. (0-3)
B) Feeling down, depressed, or hopeless. (0-3)

<table>
<thead>
<tr>
<th>Not at All</th>
<th>Several Days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Patients with a score of 3 or more should be followed up with the PHQ-9.

### Assessment Using the Patient Health Questionnaire 9 (PHQ-9)

(see 2009 MDD CPG Appendix B pp. 149-153)

**Purpose:** The Patient Health Questionnaire (PHQ) is designed to facilitate the recognition and diagnosis of depressive disorders in primary care patients. For patients with a depressive disorder, a PHQ Depression Severity Index score can be calculated and repeated over time to monitor change.

**Making a Diagnosis:** Since the questionnaire relies on patient self-report, definitive diagnoses must be followed up on and verified by the clinician, taking into account any presenting functional impairments and/or the patient’s understanding of the questions. The clinician should also consider relevant information obtained from the patient, their family, and other sources.

Over the last two weeks, how often have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th>Not at All</th>
<th>Several Days</th>
<th>More Than Half the Days</th>
<th>Nearly Every Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

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 of hurting yourself in some way

Add Columns: + +

Total:

10. If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not Difficult at All
- Somewhat Difficult
- Very Difficult
- Extremely Difficult
Assessment Using the Patient Health Questionnaire 9 (PHQ-9) (cont.)

Interpreting the PHQ to Make a Provisional Diagnosis: To facilitate interpretation of patient responses, all clinically significant responses are found in the columns farthest to the right. Any symptom endorsed as being present at least “more than half the days” counts toward a DSM-IV-TR diagnosis. (The only exception is for suicidal ideation which counts toward a DSM-IV-TR diagnosis if endorsed as being present “several days” or more.)

Major Depressive Disorder is suggested if Q#1 or 2 and five or more of Q#1-9 are at least “more than half the days” (count Q#9 if present at all). Other Depressive Disorder is suggested if: Q#1 or 2 and two, three, or four of Q#1-9 are at least “more than half the days” (count Q#9 if present at all). To score the instrument, tally each response by the number value under the answer headings. Add the numbers together to total the score on the bottom of the questionnaire. Interpret the score by using the following guide:

<table>
<thead>
<tr>
<th>PHQ-9 Score</th>
<th>DSM-IV-TR Criterion Symptoms</th>
<th>Depression Severity</th>
<th>Proposed Treatment Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–4</td>
<td>Few</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5–9</td>
<td>&lt; 5</td>
<td>Mild Depressive Symptoms</td>
<td>Watchful waiting; repeat PHQ-9 at follow-up</td>
</tr>
<tr>
<td>10–14</td>
<td>5–6</td>
<td>Mild Major Depression</td>
<td>Treatment plan; Consider counseling, follow-up, and/or pharmacotherapy</td>
</tr>
<tr>
<td>15–19</td>
<td>6–7</td>
<td>Moderate Major Depression</td>
<td>Immediate initiation of pharmacotherapy and/or psychotherapy</td>
</tr>
<tr>
<td>20–27</td>
<td>&gt; 7</td>
<td>Severe Major Depression</td>
<td>Immediate initiation of pharmacotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management</td>
</tr>
</tbody>
</table>

Note: The diagnoses of Major Depressive Disorder and Other Depressive Disorder require ruling out normal bereavement (mild symptoms, duration less than two months), a history of a manic episode (Bipolar Disorder) and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

Additional Clinical Considerations

(see 2009 MDD CPG Appendix B pp. 149-153)

After making a provisional diagnosis with the PHQ, there are additional clinical considerations that may affect decisions about management and treatment:

- Have current symptoms been triggered by psychosocial stressor(s)?
- What is the duration of the current disturbance and has the patient received any treatment for it?
- To what extent are the patient’s symptoms impairing his or her usual work and activities?
- Is there a history of similar episodes, and were they treated?
- Is there a family history of similar conditions?
### Assessing Homicidal Ideation

(see 2009 MDD CPG pp. 26-27)

Risk of violence towards others should be assessed by asking directly whether or not the patient has thoughts of harming anyone.

- Assess whether the patient has an active plan and method/means (e.g., weapons in the home)
- Assess whom the patient wishes to harm
- Assess whether the patient has ever lost control and acted violently
- Assess seriousness/severity of past violent behavior.

In the event of expressed dangerousness to self or others by a person with possible MDD, steps must be taken to ensure patient safety until further evaluation and a referral or consultation with a mental health professional has taken place.

### Eliciting Suicidal Ideation, Intent, and/or Planning

(see 2009 MDD CPG Appendix C pp. 154-155)

Eliciting suicidal ideation, intent, and/or planning involves a free and honest exchange of information between the patient and clinician. Familiarity with the existing epidemiological and demographic data concerning suicide is useful in generating an index of suspicion. From there, direct questioning regarding suicidal ideation/intent/planning may be initiated. There are no data demonstrating an increased rate of suicide attempts or deaths following questioning about suicide.

Despite the lack of reliable measures of suicide risk among individuals, a basic assessment should:

1. Determine presence/absence of depression, delirium, and/or psychosis
2. Elicit patient’s statements about his/her suicidal ideation
3. Elicit patient’s own ideas concerning what would help attenuate or eliminate suicidal ideation/intent/planning
4. Attempt to gather collateral data from a third party in order to confirm the patient’s story
5. A suggested sequence of suicide questions to ask is:
   - Are you discouraged about your medical condition (or social situation, etc.)?
   - Are there times when you think about your situation and feel like crying?
   - During those times, what sorts of thoughts go through your head?
   - Have you ever felt that if the situation did not change, it would not be worth living?
   - Have you reached a point that you’ve devised a specific plan to end your life?
   - Do you have the necessary items for completion of that plan readily available?
6. Formulate an acute and chronic management plan. Encourage active patient participation in negotiating a plan for follow-up:
   - What epidemiological risk factors are present (may have to inquire about each one individually)?
   - What other psychiatric conditions are present (besides the ones mentioned above)?
   - What is the level of psychological defense functioning?
   - Has there been a will made recently?
   - Is there talk of plans for the future?
   - What is the makeup and condition of the patient’s social support system? How can the patient be contacted?
   - Is there active suicidal ideation? “How strong is (your) intent to do this?”
   - “Can you resist the impulse to do this?” “Do you tend to be impulsive?”
   - “Have you ever rehearsed how you would kill yourself?”
   - “Have any family members or people close to you ever killed themselves?”
Gathering Data on Risk Factors for Suicide

(see 2009 MDD CPG Appendix C pp. 155-156)
The causes of suicide are multifactorial. The risk for suicide increases with the accumulation of risk factors in an individual. Clinician should be alert for suicide risk in patients with a sad or depressed mood, suicidal ideation and one or more of the following risk factors:

- History of previous suicide attempts
- Family history of completed suicide or suicide behavior
- Presence of psychiatric illness
- Psychosocial disruption
- Means for suicide completion readily available
- Active substance abuse and/or dependence

There is no accepted standard screening instrument for suicidal risk. Recent publications including the VA Education Module, “Prevention of Suicide: Everyone's Concern,” and the article by Hirschfeld and Russell provide examples of brief, thorough screening tools (Hirschfeld & Russell, 1997). Patients with evidence of intent for suicide should be offered mental health counseling and possibly hospitalization (U.S. PSTF, 1996).

Evaluating the Available Data to Make Clinical Decisions About Safety

(see 2009 MDD CPG Appendix C pp. 156-157)
If suicide risk is present, a stratification system is useful in terms of formulating a strategy for intervention. One such system includes the following divisions: imminent (suicide may be attempted within the next two days); short-term (days to weeks); and long-term.

**Imminent Risk** – Suspect if patient endorses suicidal intent, an organized plan is presented, lethal means are available, signs of psychosis (especially command hallucinations) are present, extreme pessimism is expressed (despair, hopelessness, etc.), or several additional risk factors for suicide are present.

**Management suggestions:**

a. Immediate action is required. Hospitalize or commit. DO NOT leave the patient alone.

**Short-Term Risk** – Suspect if several risk factors for suicide are present, but no suicidal behaviors are present.

**Management suggestions:**

a. With patient’s permission, involve family member or other person close to patient and advise them of the situation.

b. If potentially lethal means of suicide completion are available, initiate steps to make these items inaccessible.

c. Collaboratively generate a safety plan with the patient and/or family member (after obtaining patient consent).

The plan should include emergency contact numbers for the national suicide hotline (1-800-SUICIDE) as well as information for local hospital(s) or emergency center(s).

d. Stay in contact with the patient (telephone calls, more frequent office visits, etc.). Frequently reevaluate risk. Document all contact and explain decision-making process for management.

e. Treat psychiatric conditions as appropriate, including substance abuse/dependence (may require consultation from mental health professional). Close follow-up will help to improve compliance and continue risk assessment.

f. Consider hospitalization as appropriate.

**Long-Term Risk** – The therapeutic goal is to eliminate or improve modifiable suicide risk factors. This may involve treatment of psychiatric illness (through pharmacotherapy or psychotherapy), treatment of substance abuse, etc. Frequent reassessment is still a useful guideline, and acute situations mandating psychiatric referral or hospitalization may arise. Thus, all of the aforementioned management suggestions should be considered even here.

Providing Appropriate Care or Referring to Stabilize and Follow Legal Mandates

(see 2009 MDD CPG p. 29)
Initial steps in assessing and caring for dangerous conditions in patients with MDD include the provision of appropriate care to stabilize the situation. Depending on the seriousness of the condition and the resources at hand, this will be accomplished on-site or through urgent/emergent referral to mental health. However, it is also essential that providers and their administrative staffs have an understanding of, and ability to access local, state and federal regulations/policies/procedures and guidelines relating to danger to self or others. If patients represent a risk to others, additional notifications may be required by state or federal laws and/or regulations. When making notifications, it is wise to consult a peer and/or medical law consultant on the legal and ethical requirements.

For VA patients, these procedures should also reflect the opinion and guidance of the VHA District Council. For DoD patients, these procedures are directed by DoD Directive 6490.1, “Mental Health Evaluation of Members of the Armed Forces,” DoD Instruction 6490.4, “Requirements for Mental Health Evaluations of Members of the Armed Forces,” and related Service regulations/instructions. These regulations/instructions may require a number of notifications (e.g., commanders) which would not be made in a civilian practice.
Common Presentations of Depression in Primary Care

- **Multiple Organ Systems** - Symptoms from multiple organ systems, especially neurologic, gastrointestinal, and cardiac that are difficult if not impossible to ascribe to a single medical condition.
- **Emotions** - Patients who are emotionally flat and verbally unproductive, tearful or who are worried or upset out of proportion to the apparent severity of the problem.
- **Visits** - Frequent, often unscheduled, patient-initiated visits to the physician or the emergency room for unclear reasons.
- **Sleep** - Sleep disturbance.
- **Dysfunction** - Patients who have cognitive or emotional dysfunction such as forgetfulness, irritability and loss of motivation or energy.
- **Family History** - A family history of psychiatric illness, suicide or abuse of any kind (sexual, physical, or substance).
- **Recurrence** - Past history of similar episodes or unspecified “breakdowns.”
- **“Difficult”** - Patients labeled by health care providers as “difficult” or a “problem.”
- **Chronic Pain Syndromes**

Pathologies Related to Depression

(see 2009 MDD CPG pp. 36-38).

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Coronary Artery Disease, Congestive Heart Failure, Stroke, Vascular Dementia</td>
</tr>
<tr>
<td>Chronic Pain Syndrome</td>
<td>Fibromyalgia, Reflex Sympathetic Dystrophy, Low Back Pain (LBP), Chronic Pelvic Pain, Bone or Disease Related Pain</td>
</tr>
<tr>
<td>Degenerative</td>
<td>Hearing Loss, Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Other Neurodegenerative Diseases</td>
</tr>
<tr>
<td>Immune</td>
<td>HIV (both primary and infection-related), Multiple Sclerosis, Systemic Lupus Erythematosus (SLE), Sarcoidosis</td>
</tr>
<tr>
<td>Metabolic/Endocrine Conditions</td>
<td>Malnutrition, Vitamin Deficiencies, Hypo/Hyperthyroidism, Addison's Disease, Diabetes Mellitus, Hepatic Disease (Cirrhosis), Chronic Obstructive Pulmonary Disease (COPD) or Asthma, Kidney Disease</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>Of any kind, especially pancreatic or central nervous system (CNS)</td>
</tr>
<tr>
<td>Trauma</td>
<td>Traumatic Brain Injury, Amputation, Burn Injuries</td>
</tr>
</tbody>
</table>

Depression Diagnostic Considerations in Primary Care

(see 2009 MDD CPG pp. 30-33, 40-41)

- **Symptom–Sign Mismatch** - Suspect depression in cases of many seemingly severe symptoms, a negative physical exam, and an increasingly long list of normal laboratory tests. Caution: maintain the usual vigilance for undiagnosed medical disease.
- **History** - Establish duration of illness, history of prior episodes, family history, history of prior manic/hypomanic episodes, substance abuse and/or other comorbid disorders.
- **Physical Examination** - Screen for anemia, liver/renal dysfunction and thyroid disease, if indicated.
- **Evaluate** - the severity of depressed symptoms, suicidal tendencies and psychotic features (if present).
- **Laboratory Testing** - Laboratory tests have value in ruling out medical conditions that might mimic the symptoms of depression.
- **General Medical Illnesses Associated with Depression** - Myocardial infarction, stroke (particularly left frontal lobe), cancer, major trauma, multiple sclerosis, or any major new diagnosis, particularly if hospitalization is involved.
- **Unexplained Treatment Failure** - Clinical depression can interfere with effective treatment of the primary medical condition, delay recovery and significantly increase morbidity.
Signs of Comorbid Psychiatric Conditions

(see 2009 MDD CPG pp. 38-39)
Other common psychiatric conditions may complicate treatment or put the patient at increased risk for adverse outcomes. It is recommended that patients presenting to primary care with evidence or suspicion of a co-occurring psychiatric disorder be referred to a mental health specialty for evaluation and treatment. Conditions that should prompt the provider to consider referral may include, but is not limited to:

- Dangerousness to self and/or others.
- Frequent and disabling nightmares or flashbacks suggestive of Post-Traumatic Stress Disorder (PTSD).
- Frequent use or binging of alcohol and/or other drugs despite negative consequences (Substance Use Disorder).
- An extensive history of childhood abuse, unstable or broken relationships, or criminal behavior starting before or during adolescence, that is suggestive of a personality disorder.
- Extreme weight loss suggestive of Anorexia Nervosa or a pattern of binge-eating and purging, suggestive of Bulimia Nervosa.
- The presence of a psychotic disorder (e.g., Schizophrenia) which is likely to significantly complicate the primary care management of depression symptoms.
- The presence of unexplained physical symptoms suggestive of a Somatoform Disorder.
- The presence of Bipolar Disorder, since initiating or titrating routine antidepressant medication can precipitate a manic episode.

Screening for Alcohol Dependence Using AUDIT-C

The Alcohol Use Disorders Test—Consumption (AUDIT-C) is a shorter version of the AUDIT test designed to measure consumption. Only three questions, it differs from other tests in that it is not yes/no but a multiple-choice test (with scoring for each response).

<table>
<thead>
<tr>
<th>Questions</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How often do you have a drink containing alcohol?</td>
<td>Never</td>
<td>Monthly or less</td>
<td>2–4 times per month</td>
<td>2–3 times per week</td>
<td>4 or more times per week</td>
<td></td>
</tr>
<tr>
<td>2. How many drinks containing alcohol do you have on a typical day of drinking?</td>
<td>1 or 2</td>
<td>3 or 4</td>
<td>5 or 6</td>
<td>7 to 9</td>
<td>10+</td>
<td></td>
</tr>
<tr>
<td>3. How often do you have five or more drinks on one occasion?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
<td></td>
</tr>
</tbody>
</table>

AUDIT-C Score (add items 1-3)

In men, a score of 4 or more is considered positive; in women, a score of 3 or more is considered positive. Generally, the higher the AUDIT-C score, the more likely it is that the patient’s drinking is affecting his/her health and safety.

Differentiating Mania from Major Depression

(see 2009 MDD CPG pp. 39-40)
Some depressed patients manifest periods of mania. A past history of mania (lasting at least one week) or hypomania (lasting at least four days) excludes a patient from a diagnosis of MDD.

According to DSM-IV-TR, a manic episode is a distinct period of persistently elevated, expansive, or irritable mood, lasting at least four days (hypomanic episode) or at least one week (manic episode), that is clearly different from the usual nondepressed mood and is observable by others.

During this period of abnormal mood, at least three of the following symptoms need to be present and persistent to a significant degree.

- Inflated Self-Esteem or Grandiosity
- Decreased Need for Sleep
- Pressure to Keep Talking
- Excessive Involvement in Pleasurable Activities that Have a High Potential for Painful Consequences
- Flight of Ideas or Subjective Experience that Thoughts are Racing
- Increase in Goal-Directed Activity or Psychomotor Agitation
- Distractibility

These symptoms need to be severe enough to cause marked impairment in social or occupational functioning or require hospitalization. The clinician also needs to determine that symptoms are not secondary to a substance use or general medical condition. Hypomania is characterized by a manic episode without accompanying impairment or psychosis.

These patients may require referral to a mental health professional. These patients often need a specialist’s treatment and follow-up, since initiating or titrating routine antidepressant medication can precipitate a manic episode.
Evidence of Psychosis

(see 2009 MDD CPG pp. 27-28)

Psychosis is defined as a mental state in which the patient is significantly out of touch with reality to the extent that it impairs functioning. Patients with psychotic symptoms may present in an acutely agitated state with a recent onset of disturbing symptoms. However, patients may also present with enduring, chronic symptoms which are long-standing and to which patients have made a reasonably comfortable adaptation.

In particular, paranoid concerns that others wish to harm the patient and voices (especially command hallucinations) telling the patient to hurt him or herself or someone else, are indications for an immediate mental health consultation or referral. Patients who have longstanding psychotic illness and who are able to attend to present circumstances without responding to their psychosis may be evaluated and treated for a comorbid depression in the primary care setting.

It is important to bear in mind that psychotic symptoms may be the direct result of an underlying medical condition, toxic state, alcohol or substance use disorder, or may be associated with a mental health condition such as schizophrenia or affective illness.

Patients with a possible diagnosis of MDD who exhibit any of the following characteristics related to psychosis need to be referred for urgent/emergent mental health intervention as these are inappropriate for care in the primary care setting:

- Serious Delusions (fixed false beliefs)
- Visual or (typically) Auditory Hallucinations
- Incoherence
- Confusion
- Catatonic Behavior (motor immobility or excessive agitation)
- Extreme Negativism or Mutism or Peculiar Voluntary Movement
- Inappropriate Affect of a Bizarre or Odd Quality
- Paranoia

Overview of Appropriate Conditions for Consultation or Referral

A. Refer to an intensive outpatient recovery program for persistent substance abuse.
B. Refer to Behavioral Health for suicidal ideation, plan or intent, or depression with vegetative symptoms (insomnia, fatigue, or impaired attention).
C. Refer to Behavioral Health for psychotic disorders.
D. Refer to Behavioral Health for non-compliance with or abuse of psychopharmacological medication.
E. Refer to Behavioral Health for persistent or disabling psychiatric conditions or dysfunction without resolution of symptoms.
F. Refer to Behavioral Health for personality disorders or dissociative identity disorders.
G. Refer to Behavioral Health for patient request for consultation.
H. Refer to Behavioral Health for the presence of mania indicative of Bipolar Disorder.

** For additional information on Bipolar Disorder please refer to the VA/DoD Clinical Practice Guidelines for Bipolar Disorder.

*Consultations and/or referrals should be made based upon provider experience and expertise.

**Consult Behavioral Health for hospitalization considerations, psychological testing, medication issues, psychotherapy, etc.
# Criteria for Inpatient Admission

## I-Dangerousness / Severity of Illness

**A.** A DSM-IV-TR diagnosis or diagnoses are present and complete on all five axes and there is evidence of significant associated social impairment, occupational impairment or subjective suffering.

**B.** The patient is a danger to him/herself such as might be indicated by one or more of the following:
- High lethality or high-intent suicide attempt in past two weeks
- Recent suicide gesture in patient with history of high lethality or high intent suicide attempt
- Suicidal ideation with a plan, in the presence of command hallucinations, delusions of guilt or impending death, intractable pain, feelings of depression or hopelessness or other known precipitant of suicide
- Persistent acts of self-mutilation
- Medical emergencies influenced by mental illness
- Inability to provide for own basic needs of food, shelter or medical care as the result of a mental illness
- Bizarre behavior due to a psychotic disorder that endangers patient, his/her reputation, assets or relationships

**C.** The patient is a danger to others as a result of a mental disorder that is likely to improve by hospitalization, as evidenced by one or more of the following:
- Threats of harm against a specific individual associated with a delusional thought pattern or persistent anger/agitation
- Threats of harm against an unidentified person(s)
- Threatening behavior with a lethal weapon or possession of a lethal weapon in a state of emotional disturbance
- Escalating threatening language or behavior in a patient with a history of assaultive or aggressive behavior
- Significant damage to property

**D.** The patient has a serious mental disorder causing significant impairment of social, familial, vocational or educational functioning that would benefit from the intensity of acute treatment, such as:
- Depressed mood with disabling vegetative symptoms
- Exacerbation of acute schizophrenia with severe disordered thinking and perception
- Marked deterioration in personal hygiene as a result of an acute psychiatric disorder
- Complete withdrawal from work, school or social situations due to an acute psychiatric disorder
- Adequate trial of outpatient treatment resulting in failure. Examples of outpatient failures are:
  - six weeks of outpatient therapy, including medication and psychotherapy, for an affective or psychotic disorder
  - non-compliance with treatment as a complication of affective or psychotic disorder
  - socially disruptive behavior that alienates the social support necessary for outpatient treatment success
  - severe primary psychiatric illness worsened by substance abuse
  - unstable, unsupportive or hostile living situation that significantly interferes with outpatient treatment success
  - medical condition or physical disability that prevents regular participation in outpatient treatment

## II-Treatment Needs

**A.** Non-Inpatient Intensive Services:
- Crisis stabilization is required to avert hospitalization
- Transitional treatment following a period of acute inpatient care is required because the patient cannot safely be maintained in the community with outpatient treatment
- The patient requires more intensive services than outpatient treatment to increase his/her level of independent functioning, but does not require acute inpatient treatment

**B.** Hospitalization:
- Electroconvulsive therapy (ECT)
- Closely monitoring and daily titration of medication with disabling side effects or toxicity
- Constant staff observation as part of an intensive behavioral modification program
- Close monitoring of behavior in an episodic disorder
- Close monitoring of vital signs or need for multiple daily laboratory or electrophysiological tests
### Overview of Treatment Strategies

#### Treatment Strategies (see 2009 MDD CPG p. 51-60)

<table>
<thead>
<tr>
<th>Severity</th>
<th>LEVEL</th>
<th>PHQ TOTAL SCORE</th>
<th>FUNCTIONAL IMPAIRMENT</th>
<th>INITIAL TREATMENT STRATEGIES*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td></td>
<td>5-14</td>
<td>Mild</td>
<td>Watchful waiting, supportive counseling, self-management (e.g., exercise – see self-management worksheet on cards 14 and 15); if no improvement after one or more months, consider use of an antidepressant or brief psychological counseling.</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>15-19</td>
<td>Moderate</td>
<td>Start with combination of medications and psychotherapy.</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td>≥20</td>
<td>Severe</td>
<td>Combination of antidepressants and psychotherapy, or multiple drug therapy.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Modifiers</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated</td>
<td>Co-occurring PTSD, SUD, mania, or significant social stressors</td>
<td>Start with combination of medications and somatic interventions.</td>
<td></td>
</tr>
<tr>
<td>Chronicity</td>
<td>&gt; 2 years of symptomatology despite treatment</td>
<td>For mild – start with monotherapy of either antidepressants or psychotherapy, or a combination of both. For Mod/Severe - combination of antidepressants and psychotherapy or multiple drug therapy.</td>
<td></td>
</tr>
</tbody>
</table>

*Initial Treatment strategy options include:
1. Psychoeducation and self-management (provided to all MDD patients)
2. Watchful waiting
3. Monotherapy (psychotherapy or pharmacotherapy)
4. Combination psychotherapy and antidepressants
5. Treatment of complex patients
6. Somatic treatment
7. Inpatient and residential

### Psychoeducation

**Psychoeducation**

(see 2009 MDD CPG pp. 51–55)

- Psychoeducation should be provided for individuals with depression at all levels of severity and in all care settings and should be provided both verbally and with written educational materials.
- There should be education on the nature of depression and its treatment options and should include the following:
  a. Depression is a medical illness, not a character defect
  b. Education on the causes, symptoms, and natural history of major depression
  c. Treatment is often effective and is the rule rather than the exception
  d. The goal of treatment is complete remission; this may require several treatment trials
  e. Treatment of depression can lead to decreased physical disability and longer life
  f. Education about various treatment options, including the advantages and disadvantages of each, side effects, what to expect during treatment, and the length of treatment
- When antidepressant pharmacotherapy is used, the following key messages should be given to enhance adherence to medication: [B]
  a. Side effects often precede therapeutic benefit, but typically recede over time while benefits increase
  b. A slight increase in suicidal ideation in the first month may occur and patients should contact their provider if this does occur.
  c. Successful treatment often entails medication and/or dosage adjustments in order to maximize response while minimizing side effects
  d. Most people need to be on medication for at least six to 12 months after adequate response
  e. It usually takes two to six weeks before improvements are seen
  f. Continue to take the medication even after feeling better
  g. Do not discontinue taking medications without first discussing with your provider
- Education focused on treatment adherence should focus on the following:
  a. Education on the risk of relapse in general; essentially, that relapse risk is high, particularly as the frequency of prior episodes increases
  b. Education on how to monitor symptoms and side effects
  c. Education on early signs and symptoms of relapse or recurrence, along with encouragement to seek treatment early in the event these signs or symptoms occur.
- Psychoeducational strategies should be incorporated into structured and organized treatment protocols, which entail structured systematic monitoring of treatment adherence and response and self-management strategies.
Depression Education - What Every Patient and Family Should Be Told

- **What is Major Depression?** - An illness, characterized by depression that is believed to be associated with biochemical changes in brain function. More than just a feeling of sadness, it affects day-to-day thoughts, feelings, actions, and physical well-being.
- **Myths** - Major depression is not a trivial disorder, may not go away on its own and is not the result of personal weakness, laziness or lack of will power.
- **Incidence** - Depression is one of the most common illnesses treated by health care professionals.
- **Risk Factors** - Females, people with a first-degree relative with depression, a history of drug or alcohol misuse or a history of anxiety or eating disorders have an increased chance of having depression.
- **Treatment Response** - Depression is very responsive to treatment through antidepressant medication, psychotherapy or a combination. People do get better.
- **Medications** - All antidepressant medications take several weeks to produce their full effect. They are not addicting.
- **Medication Side Effects** - Discuss medication side effects or other problems with your primary care manager. Most problems can be resolved.
- **Don’t** - Drink alcohol, self-medicate, or blame yourself. Talk with your provider before making major life decisions or changes during treatment.
- **Do** - Get plenty of rest, exercise, eat regularly, and socialize.
- **Outpatient vs Inpatient Care** - Most patients with depression are successfully treated in the outpatient setting. Inpatient hospitalization is generally reserved for patients who have delusions or hallucinations or are a danger to themselves or others.
- **Consultation/Referral** - Sometimes a second opinion is required because a combination of treatments might work best, or the depression is severe or lasts a long time or the first treatment did not work well.
- **Treatment Compliance** - Take medication as directed, including dosage, frequency and length of time prescribed. Follow-up appointments with your provider, a mental health specialist or others need to be kept.
- **Suicide** - Thoughts of death often accompany depression. If you are thinking about hurting yourself, discuss these thoughts with your provider. If not available, seek immediate emergency care or tell a trusted friend or relative who can get you professional help right away.
- **Communication** - Discuss feelings, activity, sleep and eating patterns, as well as unusual symptoms or physical problems with your provider.
- **Recurrence** - Depression is often recurrent. Long-term use of antidepressant medication or more frequent therapy sessions are sometimes indicated.

Self-Management

**Self-Management**  
(see 2009 MDD CPG pp. 53–55)

- A major goal for the use of self-management strategies is to enhance the patient's active engagement in treatment. A common strategy is for a patient to collaboratively select one or two self-management goals at a time to pursue during treatment. Education should incorporate principles of self-management and may include information and goals related to:
  
a. **Nutrition** – Often patients with MDD do not have a balanced diet. Expert opinion suggests that diet should be included in the therapeutic content. However, there is not a robust evidence base that improving diet impacts treatment outcomes.

- **Exercise** – MDD is associated with low levels of exercise. There is fairly strong evidence that exercise often has significant antidepressant effects.
  
c. **Bibliotherapy** – Bibliotherapy (the use of self-help texts) maybe helpful to patients for understanding their illness and developing self-management skills. Guided self-help programs which entails a cognitive behavioral focus and intermittent monitoring and over sight by a healthcare professional are significantly more effective than no treatment control and as effective as more traditionally delivered modes (e.g., individual or group cognitive behavioral therapy).

  
  
d. **Sleep hygiene** – Patients with MDD often have substantial sleep problems including insomnia, hypersomnia, and disturbances of sleep maintenance. Education regarding appropriate sleep hygiene should be included for patients exhibiting any sleep disturbances.

  
e. **Tobacco use** – Tobacco use has been demonstrated to impact on the recovery of depression; therefore, patients being treated for depression should be advised to abstain until their symptoms remit. Referral or treatment of nicotine dependence should be considered in patients treated for depression.

  
f. **Caffeine use** – Expert opinion suggests that excessive caffeine use may exacerbate some symptoms of depression such as sleep problems or anxiety symptoms.

  
g. **Alcohol use and abuse** – Even low levels of alcohol use have been demonstrated to impact on the recovery of depression; therefore, patients being treated for depression should be advised to abstain until their symptoms remit.

  
h. **Pleasurable Activities** – Depression has been conceptualized by behavioral theorists as the loss or significant decrement of reinforcing activities. Behavioral activation (the systematic scheduling and monitoring of pleasurable or reinforcing activities) has been shown to have significant antidepressant effects.

**Please see Cards 14 and 15 for a sample Self Management Plan for patient use.**
### Self-Management Worksheet

1. **Make time for fun physical activities and exercise.**
   Exercise can improve your mood. Even taking a short walk may help you feel a little better.
   For ___ days next week, I'll spend at least ____ minutes doing ______
   __________________________________________________________
   __________________________________________________________

2. **Find time for pleasurable activities.**
   Even though you may not feel as motivated or happy as you used to, commit to scheduling a fun activity (such as a favorite hobby) at least a few times a week.
   For ___ days next week, I'll spend at least ____ minutes doing ______
   __________________________________________________________
   __________________________________________________________
   (Remember to make your goal both easy and reasonable.)

3. **Spend time with people who can support you.**
   It's easy to avoid contact with people when you're feeling down. But it's during these times that you actually need the support of friends and family. Try explaining to them what you are feeling. If you don't feel comfortable talking about it, that's all right. Just asking them to be with you, maybe during an activity, is a good first step. Suggestions: Meet a friend for coffee or to play cards, take a walk with a neighbor, or work in the garden with your spouse.
   During the next week, I'll make contact at least___________times with ____________________________________________
   __________________________________________________________
   __________________________________________________________

4. **Practice relaxing.**
   For many people, the changes that come with depression be stressful. Since physical relaxation can lead to mental relaxation, try deep breathing, taking a hot shower, or just finding a quiet, comfortable, and peaceful place. Say comforting things to yourself like “It’s going to get better.”
   For _____________ days next week, I’ll practice physical relaxation at least ___________times for at least _____________ minutes each time.
   __________________________________________________________
   __________________________________________________________

5. **Avoid making major life decisions when you are feeling depressed.**
   Major decisions might include changing jobs, making a financial investment, moving, divorcing, or making a major purchase. If you feel you must make a major decision about your life, ask your care provider or someone you trust to help you.
   If I need to make a major life decision, I will reach out to ________________
   __________________________________________________________

6. **Pace yourself. Set simple goals and take small steps.**
   It's easy to feel overwhelmed by problems and decisions, and it can be hard to deal with them when you're feeling sad, have little energy, or aren’t thinking as clearly as usual. Some problems and decisions can be delayed, but others can’t. Try breaking down a large problem into smaller ones and then taking one small step at a time to solve it.
   Give yourself credit for each step you take.
   The problem is: ___________________________________________
   My goal is: _______________________________________________
   Step 1: __________________________________________________
   Step 2: __________________________________________________
   Step 3: __________________________________________________

7. **Eat nutritious, balanced meals.**
   Many people find that when they eat more nutritious, balanced meals, they not only feel better physically, but also emotionally and mentally.
   During the next week, I will improve my diet by: _________________
   __________________________________________________________
   __________________________________________________________
   (Example: “Strive for five.” Eat at least five fruits and vegetables a day.)

8. **Avoid or minimize use of alcohol.**
   Alcohol is a depressant and can add to feeling down and alone. It can also interfere with the help you may receive from antidepressant medication.
   ________I will restrict my alcohol intake to no more than two drinks on no more than two days per week.
Self-Management Worksheet (cont.)

9. Develop healthy sleep habits.
Sleep problems are common for those with depression. Getting enough sleep can help you feel better and more energetic.
__________I will create a plan for improving my sleep, using the Sleep Hygiene Improvement Plan on the following pages.

10. Follow your care provider’s instructions about your treatment and communicate openly.
It is very important to take your medicine as prescribed each day and to keep your appointments with your provider, even when you begin to feel better. Ask your provider if you have any questions or concerns about your treatment. Tell your provider about your feelings, activities, sleep and eating patterns, unusual symptoms, or physical problems.
I will take my medication each day at ____________ (time), even when I begin to feel better.
__________I will keep my appointments with my provider and be honest about how I am feeling.

11. Tell someone if you are thinking about death or hurting yourself.
Thoughts of death may accompany depression. Always discuss this symptom with your care provider or tell a trusted friend, your spouse, or a relative who can get you immediate emergency professional help.
If I am thinking about death or hurting myself, I will call ____________

12. Practice positive thinking.
With treatment, most people with depression can begin to feel better, but it may take some time. Remember that negative thinking (blaming yourself, feeling hopeless, expecting failure, and other similar thoughts) is part of depression. As the depression lifts, the negative thinking will also.
When I have negative thoughts, I will tell myself ____________

Sleep Hygiene Improvement Plan

Use this worksheet to develop a plan for improving your sleep. It will take time for your sleep to improve, so stick with your plan for at least six to eight weeks.

1. Ensure that your bedroom is quiet, dark, and has a comfortable temperature, and that your mattress and pillow are in good condition.
I will make the following changes to my bedroom:
_________________________________________________________
_________________________________________________________
_________________________________________________________

2. Stay on a regular sleep schedule.
I will get up at _______ a.m., seven days a week, no matter how poorly I slept overnight.

3. Limit time in bed.
I have been sleeping an average ________ hours per night. Therefore, I will limit my time in bed to _______ hours (same number).
If I am not asleep in 15 to 20 minutes, I will get up and not return to bed until I am sleepy.

4. Exercise regularly, but not within two hours of bedtime.
I will do __________ for ______________ minutes on the following days each week: ____________________________________________
_________________________________________________________
_________________________________________________________

5. Take a hot shower or bath one to two hours before bedtime.
I will take a hot shower or bath at _______ p.m.

6. Eat a light snack at bedtime but avoid large amounts or foods that can create indigestion.
I will eat ______________________ or _____________________ or ____________________________________________ before bed.

7. Cautiously use sleeping pills.
If you are currently using sleeping pills regularly, your care provider should medically supervise any changes.

8. Avoid caffeine, nicotine, and alcohol six to eight hours before bedtime.
I will not have caffeine after _______ p.m.
I will not have a cigarette or other tobacco after _______ p.m.
I will not have more than _______ drinks in the evening.
Overview of Treatment Interventions

Watchful Waiting
(see 2009 MDD CPG pp. 55–56)
- Watchful Waiting (WW) is defined as prospective monitoring (i.e., four to eight weeks) of symptoms and disability and is a strategy to be used in mild cases of depression to differentiate a diagnosis of major depression from an adjustment disorder, uncomplicated bereavement, or minor depression.
- In patients with relatively few depressive symptoms, the diagnosis of major depression or dysthymia may not be self evident.
- In patients with likely adjustment disorder, bereavement or subsyndromal depression rather than major depression, a period of WW should be initiated. WW should only be considered when systematic follow-up assessments can be conducted.
- WW should incorporate psychoeducation, general support, and prospective symptom monitoring over a four to eight week period.
- There is an evidence base that a substantial number of patients with minor or subsyndromal depression will improve without formal treatments such as antidepressants or psychotherapy. Therefore, it is important not to expose patients to the expense or burden of treatments that are not recommended.

Psychotherapy
(see 2009 MDD CPG pp. 101–107)
- Evidence-based psychotherapies and antidepressant medication are effective for most patients across the spectrum of depressive patients seen in outpatient settings. Generally, medication, an evidence-based psychotherapy, or a combination of both, should be considered as first-line treatment in most cases.
- Evidence-based psychotherapies for depression are usually brief (six to 12 sessions), are focused on current concerns, and assist the patient in altering their thought patterns and behavior.
- In order for psychotherapy to be most effective, patients should be active participants who attend sessions consistently and follow through with agreed upon action plans.
- If the patient is not engaged in therapy after six weeks or is worse, consider antidepressant medication in addition or if already receiving medications, adjust accordingly.
- A combination of psychotherapy and medication should be tried for patients who have not responded to either approach alone during the current episode or who have responded well to combination therapy in prior episodes.

Types of Short-Term Psychotherapy
(see 2009 MDD CPG pp. 108–129)
- Cognitive Behavioral Therapy – Should be considered as a first-line treatment.
- Interpersonal Psychotherapy – Should be considered as a first-line treatment.
- Behavioral Therapy – Found most effective for the geriatric patient population.
- Problem Solving Therapy – Found most effective for teens and young adults.
- Client-Centered Counseling.
- Acceptance and Mindfulness.
- Short-Term Psychodynamic Psychotherapy.
- Computer-Based Cognitive Behavioral Therapy.
- Guided Self-Help.

Monotherapy
(see 2009 MDD CPG pp. 56–57)
- MDD or mild-moderate MDD, necessitates the initiation of treatment in order to prevent further disability, psychic pain, and mortality. A thorough and heartfelt discussion with the patient may delineate the proper therapy (either the use of an antidepressant or psychotherapeutic intervention).
- Patients who are diagnosed with mild-moderate MDD should receive an initial trial of monotherapy that incorporates either an antidepressant medication or psychotherapy.
- Patient preferences, resources, and tolerability of treatment should be considered in determining the choice between an antidepressant and psychotherapy.
- Monotherapy should be optimized before proceeding to subsequent strategies by monitoring outcomes, maximizing dosage (medication or psychotherapy), and allowing sufficient response time (eight to 12 weeks).

Combination Therapy
(see 2009 MDD CPG pp. 57–58)
- In the initial treatment of moderate to severe MDD, the concurrent use of psychotherapy and antidepressant medication demonstrated statistically significant improvements in outcomes relative to monotherapy. Combining psychotherapy and antidepressant medication is also one of several legitimate alternative strategies to partial response or treatment non-response.
- In patients with moderate to severe MDD, the initial treatment strategy should include both empirically validated psychotherapy and an antidepressant medication.
- Patient preferences, resources, and tolerability of treatment may override this recommendation in certain circumstances. In these circumstances, more aggressive monotherapy should be considered as well as adapting treatment when response is not robust.

Pharmacotherapy
(see 2009 MDD CPG p. 83)
- There is insufficient evidence to recommend one antidepressant medication over another for all patients.
- The choice of medication is based on side effect profiles, history of prior response, family history of response, type of depression, concurrent medical illnesses, concurrently prescribed medications, and cost of medication.
- Selective Serotonin Reuptake Inhibitors (SSRIs) along with Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), Bupropion and Mirtazapine are considered a first-line treatment option for adults with MDD.
- Generally, SSRIs or Venlafaxine are first-line antidepressants for patients in the primary care setting because of their low toxicity and ease of administration relative to other antidepressants.
- Generally, initial doses used for the elderly should be lower than in healthy adults.
- Prior to discontinuing an antidepressant for nonresponse, providers should ensure that an appropriate dose titration and target dose range has been achieved and an adequate response period allowed (a minimum of four to six weeks).
**Overview of Treatment Interventions (cont.)**

**Pharmacotherapy (cont.)**
(see 2009 MDD CPG p. 83)
- Discontinuation of antidepressant maintenance therapy should be done with a slow taper, as it may result in adverse withdrawal symptoms or return of original depressive symptoms. Tapering should be guided by the elimination half-life of the parent compound and metabolites, and by close monitoring of depressive symptoms.

**Managing Medication Side Effects**
- Insomnia – Confirm time of dosing is daytime hours, decrease dose or change antidepressants.
- Sexual Dysfunction – Common with all SSRIs, SNRIs and others. Change antidepressant to Bupropion or Mirtazapine since these two medications are considered an alternative for patients who have experienced sexual side effects with other antidepressants.

**Treatment of Complex Patients**
(see 2009 MDD CPG p. 58)

**Refractory Depression**
(see 2009 MDD CPG pp. 78-80, 97-99)
If partial response to one antidepressant after six weeks then you may consider the following:
- Increase dose of the current antidepressant.
- Change medication to another antidepressant in the same class or switch classes of antidepressants.
- Augment current medication with another medication or combine with psychotherapy.
- Bupropion SR (initial dose of 100mg BID) or Buspirone (initial dose of 7.5mg BID) are the preferred initial augmentation strategies.
- Another option is to add as augmentation for first-line and TCAs: Lithium carbonate, 300 mg or 450mg as a single daily dose or in divided doses or Liothyronine (Cytomel, T3), 25 micrograms initial daily dose. Baseline T4 or TSH are not predictive of response but useful to monitor TSH suppression during T3 therapy.
- ECT may be used but should be followed by maintenance treatment with antidepressant or repeat treatment with ECT.

**Second Opinion or Referral**
Consider for the following:
- Suicidal patients
- Patients who need hospitalization
- Patient request or need for psychotherapy
- Psychosis
- Bipolar Disorder
- PTSD
- Somatoform Disorder
- Patients who require specialized treatment (MAOIs, ECT, light therapy)
- Need for involuntary commitment

**Somatic Treatments**
(see 2009 MDD CPG p.p. 58-59)
- There is evidence to support the efficacy of ECT for patients with refractory MDD. While ECT is efficacious in MDD in general, it is often reserved for more severe cases based on patient preference, safety, residual side effects and stigma. Vagus nerve stimulation (VNS) is a relatively novel treatment and lacks a strong evidence base that allows recommendations in specific patients.
- Somatic treatment strategies should be prescribed and monitored only by physicians who have specific training and expertise in the management of treatment-resistant depression and the use of these devices.
  a. ECT is a recommended treatment strategy for patients who have failed multiple other treatment strategies.
  b. ECT may be a first-line treatment for pregnant women, patients with psychotic depression, catatonic patients, or patients who have severe self-neglect issues.
  c. VNS is currently FDA approved only for treatment of resistant depression for patients who have failed to respond to at least four adequate medications and/or ECT trials.

**Inpatient and Residential Treatments**
(see 2009 MDD CPG p.p. 59-60)
- Inpatient and residential settings are used to provide acute stabilization and to provide a safe environment. Inpatient care usually lasts no more than two weeks and should be linked to ongoing outpatient or residential care. Residential care can last up to six to 12 months and provide a therapeutic environment in which the patient can develop a social network, work toward independence, and learn sufficient coping skills.
- Patients who express suicidal or homicidal thoughts or who are unable to provide basic self-care should be considered for admission to an inpatient psychiatric unit.
- Patients with unstable social networks or who lack significant support in the community may require sub-acute care in a residential setting.
- Residential settings may be particularly warranted for patients who are homeless.
### Treatment of Depression

#### Treatment Response and Follow-up (see 2009 MDD CPG p. 80)

<table>
<thead>
<tr>
<th>STEP</th>
<th>PATIENT CONDITION</th>
<th>OPTIONS</th>
<th>REASSESS AT:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Initial Treatment</td>
<td>• Initiate low dose antidepressant</td>
<td>2 Weeks*</td>
</tr>
</tbody>
</table>
| 2    | No response to initial low dose antidepressant | • Increase dose  
• Consider longer duration  
• Switch  
• Consider referral to specialty care | 4 to 6 Weeks |
| 3    | Failed 2nd trial of antidepressant | • Switch  
• Augment or combine  
• Consider referral to specialty care | 8 to 12 Weeks |
| 4    | Failed 3rd trial, including augmentation | • Reevaluate diagnosis and treatment  
• Consider referral to specialty care | 12 to 18 Weeks |

*If treatment is not tolerable, switch to another antidepressant.

#### Ongoing Clinical Assessment
- Initially, see patients frequently (every one to two weeks for four to six weeks) to assess treatment compliance and the patient’s response. Assess/reassure the patient regarding side effects, adjust medication, evaluate risk factors for suicide, answer questions, rule out comorbid disorders and/or refer for counseling.
- When a therapeutic response has been reached (within about four to six weeks) continue dosage. Reassess at 12 weeks. If patient in symptom remission, continue medication at the same dosage for up to nine months. Conduct office visits or telephonic communication monthly following symptom remission.
- Maintenance phase treatment is recommended for patients with three or more episodes of major depression or two or more episodes in combination with another risk factor for recurrence, or those in professions that involve safety (pilots, boat captains, etc.). In these cases, the patient should remain on prophylactic anti-depressant medication for one or more years after remission of the acute episode at the continuation phase dosage.

#### Assess Depressive Symptoms, Functional Status and Suicide Risk
- The PHQ-9 should be used to monitor treatment response at four to six weeks after initiation of treatment, after each change in treatment, and periodically until full remission is achieved.
- In patients who reach full remission, assessment of symptoms should be continued periodically to monitor for relapse or recurrence.
- Patients with suicidal ideation should have a careful evaluation of suicide risk.

#### Tolerability of Treatment
- Using a clinical interview, assess for treatment burden (e.g., medication side effects or adverse effects, attending appointments) after initiating or changing treatment, when the patient is non-adherent to treatment, or when the patient is not responding to treatment.
- Identified side effects should be managed to minimize or alleviate the side effects.

#### Adherence to Treatment
- Adherence should be assessed directly and routinely, targeting common reasons for nonadherence (e.g., side effects, lack of efficacy, feeling better).
- Providers should give simple educational messages regarding antidepressants in order to increase adherence to treatment in the acute phase of treatment.
- In primary care, utilize collaborative care personnel (e.g., nurses, social workers, psychologists) and systems strategies to enhance adherence to treatment beyond the acute phase.
- Collaborative care strategies used by mental health specialists focus on patient education via systematic in-person or telephonic follow-up/monitoring to address adherence, relapse prevention issues and self-management strategies.
- For patients who are at high risk for non-adherence to antidepressant medication, refer for psychotherapy to increase medication adherence and decrease the chance of treatment discontinuation.

#### Reevaluate Diagnoses and Treatment Strategy for Non-Response
- In treatment of non-responders, the diagnosis of MDD should be reconfirmed and the patient should be assessed for factors that may contribute to non-response. Referral to mental health specialty for a comprehensive assessment may be considered. Evaluation should include:
  - Assessment for existence of psychiatric conditions that may present initially with depressive symptoms or adversely affect treatment response, including bipolar disorder, substance abuse, post-traumatic stress disorder, generalized anxiety or panic disorder and in older adults, dementia.
  - Assessment for medical conditions that may present with depressive symptoms. This may require additional history, physical examination, and laboratory testing. Poorly controlled medical conditions (e.g., chronic pain, congestive heart failure [CHF]) that may potentiate depression should be treated aggressively.
  - Assessment for psychosocial problems that may contribute to treatment unresponsiveness. Domains assessed may include financial, legal, relationship, work, or negative life events.
This card summarizes the Primary Care Manager’s depression assessment and treatment documentation requirements.

Recognition - Vital Signs, Visit Information, and Depression Self Assessment

Patient presents with depressive symptoms and/or complaints, or the clinician suspects depression. Ask the patient to complete your facility’s designated outpatient forms for depression. Ancillary staff can assist in this process.

Review the following information with the patient: reason for visit, vital signs, tobacco, alcohol or drug use, pain assessment, deployment-related visit, allergies, medications, and total score on the PRIME-MD PHQ and the AUDIT-C screening.

Assessment - Medical, Physical, and Mental Status Exam

Complete the Medical History and Physical Assessment. Rule out medical problems, especially thyroid disorders, substance abuse/dependence (especially alcohol or cocaine use), occult malignancies and the use of some cardiovascular drugs, antihypertensives, sedative/hypnotic agents, anti-inflammatory/analgesic agents, steroids, and other medications that may contribute to depression.

Complete a Mental Status Assessment.

Diagnosis & Risk Factors - DSM-IV Diagnosis and Risk Assessment

Provide a Diagnosis.

• Establish a DSM-IV Diagnosis.

Review Red Flag Risk Factors. Check all that apply.

Does the patient need emergency treatment?

• Suicidal thoughts and/or plans which make you uncertain of the patient’s safety.
• Assaultive/homicidal thoughts and/or plans which make you uncertain about the safety of the patient or others.
• Inability to care for self.
• Psychotic thinking.
• Mania.
• Serious mental/medical disorder causing significant impairment of social, familial, vocational or educational functioning.
• Delirium.

If any of these conditions are present, consider referral/consultation to Behavioral Health and/or hospitalization.

Is active chemical abuse/dependency present?

If present or suspected, consider referral for a chemical dependency assessment.

Is there a history of non-compliance with or abuse of psychopharmacological medication?

If present or suspected, refer to Behavioral Health.

Is there a strong suggestion of a personality disorder?

If present or suspected, refer to Behavioral Health.

Treatment - Treatment Plan

Complete a Treatment Plan. Involve patient and family. Review and obtain concurrence and response to plan.

• Supportive Counseling with Watchful Waiting.
• Antidepressant Medication.
• Psychotherapy and Medication Combined.
• Standard Laboratory Work-up with more specific tests ordered as indicated by patient’s condition.
• Referral to Behavioral Health.
• Referral to Other Services (Nutrition, Substance Abuse Program, Case Management, etc.).

Education - Patient & Family Education and Instruction

Provide Patient and Family Education and Instruction. (Videos, Brochures, Handouts)

• VA / DoD or Other MTF-Approved Self-Management Materials.
• VA / DoD or Other MTF-Approved Depression Brochure.
• VA / DoD or Other MTF-Approved Antidepressant Medication Handouts.
• VA / DoD or Other MTF-Approved Depression Management Videos.
• Continuity of Care Appointments/Safety Plan/Special Instructions/Other Disease Management Considerations.

Monitoring & Follow-Up Documentation

Monitor response to medication and side effects, improvement (or lack of) in symptoms and function, treatment compliance or non-compliance, referral care progress (if applicable), complications, medical issues, other outcomes, etc. Modify treatment as appropriate and refer or consult to Behavioral Health for complicated issues.
### System Level Performance Metrics

#### Aspect of Care - Detection

**Purpose** - To determine if providers are screening for depression in their patients.
**Measure** - Percent of patients seen in a general medicine, primary care, women's primary care clinic who were screened for depression during the previous 12 months.

#### Aspect of Care - Assessment / Diagnosis

**Purpose** - A means to evaluate the prevalence of depressive disorders in a primary care population as compared to expected rates.
**Measure** - Percent of patients diagnosed with a depressive disorder during the previous 12 months.

#### Aspect of Care - Assessment / Diagnosis

**Purpose** - To measure the adherence in the guideline regarding adequacy of treatments.
**Measure** - Percent of patients newly diagnosed with and treated for a major depressive disorder during the past 12 months who continue on prescribed medication for at least 90 days in the next 120 days or at least eight psychotherapy sessions in the next 180 days.

#### Aspect of Care - Effectiveness / Outcomes

**Purpose** - To measure whether clinicians are assessing the outcomes of depression treatment.
**Measure** - Percent of patients who were seen during the past 12 months with a diagnosis of major depression who have a systematic symptom assessment 12 weeks following diagnosis, or if in remission by week 12, then a systematic symptom assessment is performed at the time of remission.

#### Additional System Level Performance Metrics

**Criteria #1 - Mental Status Examination**

**Purpose** - To measure assessment of depression.
**Measure** - Medical record documentation supports a mental status assessment was performed that specifically address mood and affect, sensorium, and suicidal ideation.

**Criteria #2 - Red Flag Risk Factors**

**Purpose** - To measure assessment and recognition of symptoms that warrant consultation or referral to behavioral health (or other service).
**Measure** - Medical record documentation supports assessment of Red Flag Risk Factors (danger to self or others, psychosis, delirium, personality disorder, substance abuse, manic symptoms, and other mental disorder causing significant impairment).

**Criteria #3 - Consultation / Referral**

**Purpose** - To measure appropriate consultation or referral to behavioral health (Red Flag Risk Factors, medication failure, medication noncompliance or abuse, unclear diagnosis, psychotherapy, or patient request) or other services (based on medical or social services need).
**Measure** - Medical record documentation supports appropriate referral to behavioral health or other services.

**Criteria #4 - Treatment Plan**

**Purpose** - To measure the formulation of a treatment plan based on current assessment.
**Measure** - Medical record documentation supports treatment planning (medication, treatment monitoring, referrals if required, clinic follow-up, general instructions, review with patient, and patient’s response to treatment plan).

**Criteria #5 - Education / Instruction**

**Purpose** - To measure education issues with patient and/or family as they relate to the patient’s illness.
**Measure** - Medical record documentation supports educational information is provided (medication, continuity of care, disease management, special instructions, etc.).
### Selective Serotonin Reuptake Inhibitors (SSRIs)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram (Celexa)</td>
<td>Initial adult dose = 20mg QD. Max dose/day = 60mg. Max geriatric dose/day = 40mg QD</td>
<td>May be used for diabetic neuropathy, Generic. Possibly fewer cytochrome P450 (CYP450) Interactions. May be taken without regard to meals.</td>
<td>No evidence of increased efficacy by dose escalation within the first 4 weeks. Dose escalation after 6 weeks appeared less effective than continuing the same dose.</td>
<td>C</td>
<td>Serious systemic toxicity has occurred with overdose. Taper dose slowly to prevent clinically significant discontinuation symptoms. Drug interactions may include MAOIs, Tricyclic Antidepressants, Carbamazepine, Warfarin, Nilotinib, Pimozide, Sibutramine, Tamoxifen, Tetrabenazine, Thioridazine and Ziprasidone.</td>
<td>Response rate: Mild depression = 4-8 weeks. Moderate depression = 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>Initial adult dose = 10mg QD. Max adult dose/day = 20mg. Initial geriatric dose = 10mg QD. S-enantiomer more potent than racemic (Citalopram).</td>
<td>10mg dose often effective. Once daily dosing without regard to meals.</td>
<td>No evidence of increased efficacy by dose escalation within the first 4 weeks. Dose escalation after 6 weeks appeared less effective than continuing the same dose.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>Initial adult dose = 20mg QD. Max adult dose/day = 80mg QD. Initial geriatric dose = 10mg QD. User lower doses in the elderly.</td>
<td>Long half-life good for poor adherence, missed doses. FDA approved for OCD use in children &gt;=7 and MDD in children &gt;=8. AM daily dosing.</td>
<td>Slower to reach steady state. Sometimes too stimulating. Possibly more CYP450 interactions. Should not be taken at night in the elderly unless for sedation. Associated with rash and allergic events.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine (Prozac) Weekly</td>
<td>90mg Q week</td>
<td>Once weekly dosing in the maintenance therapy for patients who have responded to daily administration.</td>
<td>If a satisfactory response is not maintained with once weekly dosing, consider re-establishing a daily dosing regimen. Possibly more CYP450 interactions.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine (Paxil)</td>
<td>Initial adult dose = 20mg QD. Max adult dose/day = 50mg QD. Initial geriatric dose = 10mg QD. Max geriatric dose = 40mg QD.</td>
<td>May be taken with or without food. Am daily dosing. Generic.</td>
<td>Of the SSRIs, highest reported d/c rate, highest rate of sexual dysfunction and weight gain. Sometimes sedating and more anti-cholinergic symptoms. Possibly more CYP450 interactions. Avoid in pregnancy.</td>
<td>D</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Selective Serotonin Reuptake Inhibitors (SSRIs) (cont.)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Paroxetine CR</strong> (Paxil CR)</td>
<td>Initial adult dose = 25mg QD. Max adult dose/day = 62.5mg QD. Initial geriatric dose = 12.5mg QD. Max geriatric dose = 50mg QD.</td>
<td>Generic. May be taken with or without food.1,2,3 AM daily dosing.</td>
<td>Of the SSRIs, highest reported dc rate, highest rate of sexual dysfunction and weight gain. Sometimes sedating and more anti-cholinergic symptoms.4 Possibly more CYP450 interactions.4 Avoid in pregnancy. Do not crush or chew CR tab.</td>
<td></td>
<td>Serious systemic toxicity has occurred with overdose.1,2,3 Taper dose slowly to prevent clinically significant discontinuation symptoms.7 Drug interactions may include MAOIs, Tricyclic Antidepressants, Carbamazepine, Warfarin, Nilotinib, Pimozide, Sibutramine, Tamoxifen, Tetrabenzazine, Thioridazine and Ziprasidone.1</td>
<td></td>
</tr>
<tr>
<td><strong>Sertraline</strong> (Zoloft)</td>
<td>Initial adult dose = 50mg QD. Max dose/day = 200mg QD. Initial geriatric dose = 25mg QD.</td>
<td>Safety shown post MI.4 FDA approved for use in OCD in children ≥6.1,2,3 Generic. AM daily dosing.</td>
<td>Higher rate of diarrhea than other SSRIs. Monitor for weight and nutritional intake.4,5</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### First Line Antidepressant Medication

Drugs of this class differ substantially in safety, tolerability and simplicity from other classes of antidepressants. Can work in Tricyclic Antidepressant (TCA) non-responders. Other possible uses are in Anxiety disorders, Post-Traumatic Stress Disorder (PTSD), Obsessive Compulsive Disorder (OCD), Panic Disorder and Premenstrual Dysphoric Disorder (PMDD).1,2,3 SSRIs, Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), Bupropion, Mirtazapine are first line therapy for adults with Major Depressive Disorder (MDD). Reduce dose in the elderly. See specific literature for hepatic, renal dosing. Monitor patients for symptom resolution, depression, suicidal ideation, anxiety, panic attacks and mania.1,2,3
### Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>Initial adult dose = 20-30mg BID. Max adult dose/day = 60mg. Initial geriatric dose = 10-20mg BID.</td>
<td>Also used for anxiety, peripheral neuropathy, fibromyalgia or stress urinary incontinence. May take without regards to meals.</td>
<td>BID dosing. May increase BP. Avoid in patients with substantial alcohol use or evidence of chronic liver disease. Avoid if CRCL &lt; 30ml/min and in hepatic impairment. Monitor BUN, CR, glucose. Do not chew or crush capsules, swallow whole.</td>
<td>C</td>
<td>Serious systemic toxicity has occurred with overdose. Taper dose slowly to prevent clinically significant discontinuation symptoms. Avoid concomitant use with MAOIs, Sibutramine, alcohol, Valerian, St. John's Wort, SAMe, Kava Kava for Duloxetine and Venlafaxine. Avoid concomitant use of Duloxetine with Thioridazine. Use with caution with either Warfarin or NSAID with Duloxetine.</td>
<td>Response rate: Mild depression = 4-8 weeks. Moderate depression = 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
<tr>
<td>Venlafaxine IR (Effexor IR)</td>
<td>Initial adult dose is 25mg TID or 37.5mg BID. Max adult dose/day = 375mg. Initial geriatric dose = 25mg QD.</td>
<td>Also used in Anxiety or Panic disorder. Possibly fewer CYP450 interactions. Generic.</td>
<td>Take with food. May increase BP at higher doses. More lethal in overdose (with other drugs &amp; alcohol) than SSRIs but not TCAs. Reduce dose by 50% if hepatic impairment or if CRCL = 10-70 ml/min. Monitor height and weight in children. Monitor cholesterol.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine XR (Effexor XR)</td>
<td>Initial adult dose = 75mg QD. Max adult dose/day = 225mg. Initial geriatric dose = 37.5mg QD.</td>
<td>XR version administered QD. Used in Anxiety or Panic disorder. Possibly fewer CYP450 interactions. XR capsule dose may be swallowed whole or opened and sprinkled on apple sauce followed by a glass of water.</td>
<td>Take with food. May increase BP at higher doses. Expensive. More lethal in overdose (with other drugs &amp; alcohol) than SSRIs but not TCAs. Reduce dose by 50% if hepatic impairment or if CRCL = 10-70 ml/min. Monitor height and weight in children. Monitor cholesterol.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### First Line Antidepressant Medication

Dual action drugs which are Serotonin and Norepinephrine Reuptake inhibitors. SSRIs, SNRIs, Bupropion, Mirtazapine are first line therapy for adults with MDD. Possible efficacy in cases not responsive to TCAs or SSRIs. Reduce dose for the elderly. Monitor blood pressure regularly especially when initiating and titrating the dose. Monitor depression, suicidal ideation, anxiety, mania and panic attacks.
## Dopamine and Norepinephrine Reuptake Inhibitors (DNRIs)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion IR (Wellbutrin IR)</td>
<td>Initial adult dose = 100mg BID. Max adult dose/day = 450mg. Initial geriatric dose = 37.5mg BID.</td>
<td>Used as an alternative for patients who have experienced intolerable sexual side effects or weight gain from other antidepressants. Generic. May be taken without regard to meals.</td>
<td>Avoid bedtime dosing. May be stimulating. At higher doses, may induce seizures in persons with seizure disorder.</td>
<td>C</td>
<td>Seizure risk is dose dependent and increased when used in combination with other drugs that lower the seizure threshold. In higher doses may induce seizures in persons with seizure disorders, eating disorders or in diabetics treated with oral hypoglycemic or insulin. Avoid concomitant use with MAOIs, alcohol, Valerian, St. John’s Wort, SAMe, Kava Kava.</td>
<td>Response rate: Mild depression = 4-8 weeks. Moderate depression = 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
<tr>
<td>Bupropion SR (Wellbutrin SR)</td>
<td>Initial adult dose = 150mg QD. Max adult dose/day = 400mg. Initial geriatric dose = 100mg QD.</td>
<td>Used as an alternative for patients who have experienced intolerable sexual side effects or weight gain from other antidepressants. Generic. May be taken without regard to meals.</td>
<td>Avoid bedtime dosing. May be stimulating. At higher doses, may induce seizures in persons with seizure disorder.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion XL (Wellbutrin XL)</td>
<td>Initial adult dose = 150mg QD. Max adult dose/day = 450mg.</td>
<td>Used as an alternative for patients who have experienced intolerable sexual side effects or weight gain from other antidepressants. Generic. May be taken without regard to meals.</td>
<td>Avoid bedtime dosing. May be stimulating. At higher doses, may induce seizures in persons with seizure disorder.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**First Line Antidepressant Medication**

SSRIs, SNRIs, Bupropion, Mirtazapine are first line therapy for adults with MDD. Bupropion may also be used for smoking cessation and Seasonal Affective Disorder. Do not use if there is a history of seizure disorder, head trauma, bulimia or anorexia. Increase dose gradually to decrease risk of seizures. Requires dose titration. Can work in TCA non-responders. Reduce dose for the elderly and hepatic impairment. Monitor weight. Monitor BP and HR when administering concomitantly with transdermal nicotine. Monitor depression, suicidal ideation, anxiety, mania and panic attacks. Use with caution in patients with cardiovascular disease, hepatic or renal insufficiency and in the elderly.
### Serotonin 2A Antagonist Reuptake Inhibitors (SARIs)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nefazodone</strong> (formerly known as Serzone)</td>
<td>Initial adult dose = 100mg BID. Max adult dose/day = 600mg. Initial geriatric dose = 50mg BID. Max geriatric dose/day = 400mg.</td>
<td>Avoid using in hepatic disease. Monitor for signs and symptoms of liver dysfunction and consider routine LFT monitoring. Black box warning for hepatic failure.¹ ² ³</td>
<td>No serious systemic toxicity from OD. Monitor Digoxin levels with Nefazodone. Nefazodone contraindicated with MAOIs, Pimozide, Carbamazepine, alcohol, Eplerenone, Benzodiazepines including Alprazolam, Triazolam.¹ ²</td>
<td>C</td>
<td>Response rate: Mild depression = 4–8 weeks. Moderate depression = 8–12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
<td></td>
</tr>
<tr>
<td><strong>Trazodone</strong> (formerly known as Desyrel)</td>
<td>Initial adult dose = 50mg TID. Max adult dose/day = 600mg. Initial geriatric dose = 25–50mg QHS.</td>
<td>Generic. Causes fewer anticholinergic effects than TCAs.² May also be used for insomnia.¹ ³</td>
<td>May cause priapism.¹ ² ³ Use with caution in cardiovascular patients, seizure disorder and the elderly.¹ ³ Administer after meals to prevent lightheadedness and postural hypotension.¹ ² ³</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Taper dose slowly to prevent clinically significant discontinuation symptoms.⁷ Monitor for signs of suicidal ideation.¹ ² ³ Reduce dose for the elderly.
### Antidepressant Medication Table

#### Noradrenergic & Specific Serotonin Antidepressant (NaSSAs)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>Initial adult dose = 15mg QHS. Max adult dose/day = 45mg. Initial geriatric dose = 7.5mg QHS.</td>
<td>QHS dosing. May be taken without regard to meals. Used as a treatment option for patients who have experienced intolerable sexual side effects from other antidepressants.</td>
<td>SolTab contains Aspartame which should be avoided by Phenylketonurics. Moderate to high sedation as compared to other antidepressants. Should be avoided in patients for whom weight gain is a problem.</td>
<td>C</td>
<td>Avoid concomitant use with MAOIs, Sibutramine.</td>
<td>Response rate: Mild depression = 4-8 weeks. Moderate = depression 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
</tbody>
</table>

**First Line Antidepressant Medication**

Use with caution in seizure disorder, elderly patients, hepatic or renal impairment. Adjust dose in CRCL < 40ml/min. Use with caution in hepatic impairment. Monitor Mirtazapine for signs of agranulocytosis, neutropenia, sore throat, infection, depression, suicidal thoughts, anxiety, panic attacks, lipid profile.  

---

1. [1]
2. [2]
3. [3]
## Antidepressant Medication Table

### Tricyclic Antidepressants (TCAs)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN FOR TCAs</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amitriptyline</strong> (formerly known as Endep, Elavil)</td>
<td>Initial adult dose = 50mg QHS up to TID. Max adult dose/day = 300mg. Initial geriatric dose = 10-25mg QHS.</td>
<td>Used in neuropathic pain, prophylaxis for migraine headaches.(^1,2,3) FDA approved for use in children &gt; 12.(^1,2,3) Generic.</td>
<td>Side effects include anticholinergic, cardiovascular, CNS, weight gain, sexual dysfunction and decreased seizure threshold. Higher doses may be required for smokers taking Amitriptyline due to increased metabolism.(^1)</td>
<td>C</td>
<td>Lethal on OD. Slow system clearance. Avoid concomitant use with MAOIs, alcohol, Valerian, St. John’s Wort, Kava Kava, Nilotinib, Sibutramine, Tetrabenazine, Thoridazine, and Ziprasidone.(^1) Bupropion, Haloperidol and SSRIs may increase the TCA’s level which may increase the pharmacologic and adverse effects. Wait 5 weeks after discontinuing fluoxetine before starting a TCA.(^2,3)</td>
<td>Response rate: Mild depression = 4-8 weeks. Moderate depression = 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
<tr>
<td><strong>Imipramine</strong> (Tofranil)</td>
<td>Initial adult dose = 25mg QD to QID. Max adult dose/day = 300mg. Initial geriatric dose = 10mg-25mg QHS.</td>
<td>Therapeutic plasma concentrations can be used to guide treatment. Monitor serum levels after one week of treatment. Therapeutic Levels: 200-350 ng/mL. Also used for Neuropathic Pain or Panic Disorder.(^1,2,3) Generic.</td>
<td>Side effects include anticholinergic, cardiovascular, CNS, weight gain, sexual dysfunction and decreased seizure threshold.</td>
<td>D</td>
<td>Quinolones (Gatifloxacin, Moxifloxacin) if used with TCAs may cause QT prolongation and may increase the risk of life-threatening cardiac arrhythmias. Quinolones (Grepafloxacin, Sparfloxacin) if used with TCAs have an increased risk of life-threatening arrhythmias including torsades de pointes.(^3)</td>
<td></td>
</tr>
<tr>
<td><strong>Nortriptyline</strong> (Pamelor)</td>
<td>Initial adult dose = 25mg TID – QID. Max adult dose/day = 150mg. Initial geriatric dose = 10-25mg QHS.</td>
<td>Secondary amine – lower orthostatic hypotension and sedation than other TCAs.(^5) Equal efficacy and fewer side effects than the parent tertiary amines (Amitriptyline and Imipramine). Therapeutic plasma concentrations can be used to guide treatment. Monitor serum levels after one week of treatment. Therapeutic Levels: 50-175 ng/mL. Generic.</td>
<td>Side effects include anticholinergic, cardiovascular, CNS, weight gain, sexual dysfunction and decreased seizure threshold.</td>
<td>D</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Antidepressant Medication Table (cont.)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN FOR TCAs</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Desipramine</strong> (Norpramin)</td>
<td>Initial adult dose = 25mg TID or 75mg QD. Max adult dose/day = 300mg. Initial geriatric dose = 10mg-25mg QHS.</td>
<td>Secondary amine – lower orthostatic hypotension and sedation than other TCAs. Equal efficacy and fewer side effects than the parent tertiary amines (Amitriptyline and Imipramine). Therapeutic plasma concentrations can be used to guide treatment.</td>
<td>Side effects include anticholinergic, cardiovascular, CNS, weight gain, sexual dysfunction and decreased seizure threshold.</td>
<td>C</td>
<td>Lethal on OD. Slow system clearance. Avoid concomitant use with MAOIs, alcohol, Valerian, St. John's Wort, Kava Kava, Nilotinib, Sibutramine, Tetrabenazine, Thoridazine, and Ziprasidone. Bupropion, Haloperidol and SSRIs may increase the TCA's level which may increase the pharmacologic and adverse effects. Wait 5 weeks after discontinuing fluoxetine before starting a TCA. Quinolones (Gatifloxacin, Moxifloxacin) if used with TCAs may cause QT prolongation and may increase the risk of life-threatening cardiac arrhythmias. Quinolones (Grepafloxacin, Sparfloxacin) if used with TCAs have an increased risk of life-threatening arrhythmias including torsades de pointes.</td>
<td>Response rate: Mild depression = 4-8 weeks. Moderate depression = 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
<tr>
<td><strong>Doxepin</strong> (Sinequan)</td>
<td>Initial adult dose = 25-75mg QHS or BID. Max adult dose/day = 300mg. Use lower dose in the elderly and increase gradually.</td>
<td>May also be used for Anxiety. Can be used in adolescents. Generic.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Tricyclic Antidepressants (TCAs)**

- **Desipramine** (Norpramin): Initial adult dose = 25mg TID or 75mg QD. Max adult dose/day = 300mg. Initial geriatric dose = 10mg-25mg QHS. Secondary amine – lower orthostatic hypotension and sedation than other TCAs. Equal efficacy and fewer side effects than the parent tertiary amines (Amitriptyline and Imipramine). Therapeutic plasma concentrations can be used to guide treatment. Monitor serum levels after one week of treatment. Therapeutic Levels: 125-300 ng/mL. Generic. Can be used in adolescents.

- **Doxepin** (Sinequan): Initial adult dose = 25-75mg QHS or BID. Max adult dose/day = 300mg. Use lower dose in the elderly and increase gradually. May also be used for Anxiety. Can be used in adolescents. Therapeutic Levels: 125-300 ng/mL. Generic. Can be used in adolescents.
### Tricyclic Antidepressants (TCAs) (cont.)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN FOR TCAs</th>
<th>EFFICACY</th>
</tr>
</thead>
</table>

May lower seizure threshold. Administer at bedtime to reduce daytime sedation. Therapy should not be abruptly discontinued in patients receiving high doses for prolonged periods of time. Use with caution in the elderly and use Nortriptyline or Desipramine first. Avoid Amitriptyline, Imipramine and Doxepin in the elderly. Do not use in the acute recovery phase following MI. Avoid use in glaucoma, urinary retention, cardiovascular disease, patients at risk for suicide and patients with cognitive impairment. Taper if patient is on high doses for prolonged periods. Use a lower dose and slower titration for hepatic disease. If combining SSRIs and TCAs then add TCAs to SSRIs and not vice-versa. Obtain an ECG before starting a TCA. Obtain blood levels for compliance. Monitor weight, BP, pulse, prior to and during initial therapy. Evaluate mental status, suicidal ideation. Monitor ECG in older adults and those with cardiac disease.
### Monoamine Oxidase Inhibitors (MAOIs)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isocarboxazid (Marplan)</td>
<td>Initial adult dose = 10mg BID to TID. Max daily adult dose = 60mg. Initial geriatric dose = 10mg BID.</td>
<td>Treatment option for those who have not achieved remission on other antidepressants.</td>
<td>Patient education must include dietary and drug restrictions including a tyramine-restricted diet to avoid a hypertensive crisis. Allow adequate wash-out periods following treatment with other antidepressants or other drugs that interact with MAOIs.</td>
<td>C</td>
<td>Avoid concurrent use with other medications with serotonergic effects (other Antidepressants, Meperidine, Tramadol, Propoxyphene, Dextromethorphan) due to risk of Serotonin Sickness. Also avoid concurrent use with stimulants, vasoconstrictors, other medications with adrenergic effects due to the potential for a hypertensive crisis.</td>
<td>Response rate = Mild depression 4-8 weeks. Moderate depression = 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
<tr>
<td>Phenelzine (Nardil)</td>
<td>Initial adult dose = 15mg TID. Max adult daily dose is 90mg. Initial geriatric dose = 7.5mg QD.</td>
<td>Treatment option for those who have not achieved remission on other antidepressants.</td>
<td>Patient education must include dietary and drug restrictions including a tyramine-restricted diet to avoid a hypertensive crisis. Allow adequate wash-out periods following treatment with other antidepressants or other drugs that interact with MAOIs.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Antidepressant Medication Table

#### Monoamine Oxidase Inhibitors (MAOIs) (cont.)

<table>
<thead>
<tr>
<th>GENERIC (BRAND NAME)</th>
<th>ADULT STARTING DOSE (MAX PER DAY)</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>PREGNANCY CATEGORY</th>
<th>SAFETY MARGIN</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selegiline patch (Emsam)</td>
<td>Initial adult dose = 6mg patch per 24 hours. Max adult daily dose = 12mg.</td>
<td>Treatment option for those who have not achieved remission on other antidepressants. Apply QD.</td>
<td>Patient education must include dietary and drug restrictions including a tyramine-restricted diet to avoid a hypertensive crisis. Allow adequate wash-out periods following treatment with other antidepressants or other drugs that interact with MAOIs.</td>
<td>C</td>
<td>Avoid concurrent use with other medications with serotonergic effects (other Antidepressants, Meperidine, Tramadol, Propoxyphene, Dextromethorphan) due to risk of Serotonin Sickness. Also avoid concurrent use with stimulants, vasoconstrictors, other medications with adrenergic effects due to the potential for a hypertensive crisis.</td>
<td>Response rate = Mild depression 4-8 weeks. Moderate depression = 8-12 weeks. Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist).</td>
</tr>
<tr>
<td>Tranylcypromine (Parnate)</td>
<td>Initial adult dose = 10mg BID. Max adult dose/day = 60mg.</td>
<td>Treatment option for those who have not achieved remission on other antidepressants.</td>
<td>Patient education must include dietary and drug restrictions including a tyramine-restricted diet to avoid a hypertensive crisis. Allow adequate wash-out periods following treatment with other antidepressants or other drugs that interact with MAOIs.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

These medications are a treatment option for those who have not achieved remission on other antidepressants. MAOIs may be effective in patients who do not respond to treatment with other antidepressants, but their requirement for dietary restrictions, adverse effect profile and propensity for drug interactions limit their use. No dosage change in renal or hepatic impairment. Reduce dose for the elderly. Notify MD if severe headache, palpitation, tachycardia, sweating, dizziness, stiff neck, nausea or vomiting occur.³
**Black Box Warning for all Antidepressants:** Antidepressants increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders.\(^{1,2,3}\) Appropriately monitor and closely observe for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments.\(^{1,2,3}\) Short-term studies did not show an increase in the risk of suicidality with Antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with Antidepressants compared to placebo in adults aged 65 and older.\(^{1,2,3}\)

**Medications That Can Cause Depression**

<table>
<thead>
<tr>
<th>MEDICATION/CLASS</th>
<th>ASSOCIATION</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Blockers</td>
<td>+/-</td>
<td>Recent, better designed investigations have not supported earlier findings that beta-blockers increase the risk of depression. Propranolol and Sotalol have side effects labeled as depression.</td>
</tr>
<tr>
<td>Calcium-Channel Blockers (CCBs)</td>
<td>+/-</td>
<td>An association between CCBs and depression or suicide has been reported in some studies; other studies have not found an association.</td>
</tr>
<tr>
<td>ACE-inhibitors</td>
<td>+/-</td>
<td>Conflicting reports of an association; some trials have reported an improvement in mood.</td>
</tr>
<tr>
<td>Lipid-lowering agents</td>
<td>+/-</td>
<td>A meta-analysis reported an association between cholesterol lowering and suicide, violent, and accidental deaths. It is not clear whether the increased risk of mortality was secondary to the lowered cholesterol or the intervention(s). No such association has been found with the newer lipid-lowering agents (i.e., the statins).</td>
</tr>
<tr>
<td>Reserpine, Clonidine, Methyldopa</td>
<td>+</td>
<td>Reserpine and the other rauwolfia alkaloids have long been associated with depression. The frequency and strength of association may have been exaggerated by the high doses used in the past. Clonidine and methyldopa may also cause sedation and symptoms of depression.</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>+</td>
<td>The majority of studies support an association. Corticosteroids, particularly higher doses, are associated with psychosis and mania.</td>
</tr>
<tr>
<td>Selective estrogen receptor modulators (SERM)</td>
<td>+/-</td>
<td>Data primarily suggest a lack of relationship between SERMs and depression. Confounding by diagnosis (usually breast cancer) may account for positive links.</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>+</td>
<td>Rare psychiatric symptoms, not limited to depression, have been seen.</td>
</tr>
<tr>
<td>H2-antagonists</td>
<td>-</td>
<td>No association found in small studies.</td>
</tr>
<tr>
<td>Benzodiazepines and Barbiturates</td>
<td>+</td>
<td>Primarily a concern in older patients who use chronically or those who abuse. Toxicity, namely sedation, may be mistaken for depressive symptoms.</td>
</tr>
<tr>
<td>Topiramate</td>
<td>+</td>
<td>Known to have CNS effects (confusion and poor concentration) which may be mistaken for depressive symptoms.</td>
</tr>
<tr>
<td>Progesterone implants</td>
<td>+/-</td>
<td>Levonorgestrel has been associated with depression. Medroxyprogesterone acetate has been reported to slightly increase the risk for depression in one study.</td>
</tr>
</tbody>
</table>
# Antidepressant Medication Table

## Medications That Can Cause Depression (cont.)

<table>
<thead>
<tr>
<th>MEDICATION/CLASS</th>
<th>ASSOCIATION</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon-a</td>
<td>+</td>
<td>Interferon has been associated with depression.1,2,3</td>
</tr>
<tr>
<td>Interferon-beta</td>
<td>+</td>
<td>Interferon has been associated with depression.1,2,3</td>
</tr>
<tr>
<td>Interleukin-2</td>
<td>+</td>
<td>Depressive symptoms along with cognitive problems, fatigue and appetite changes have been observed and usually appear early in the course of treatment.</td>
</tr>
<tr>
<td>Isotretinoin</td>
<td>+</td>
<td>iPledge program for patients on Isotretinoin requires the patients and clinicians to register for the program.1,2,3 Patients are instructed to immediately report depression symptoms and clinicians evaluate for depression at every visit.1,2,3</td>
</tr>
<tr>
<td>Vareniciline (Chantix)</td>
<td>+++</td>
<td>Chantix is a medicine used to help patients stop smoking. Chantix may cause worsening of a current psychiatric illness. Symptoms may include anxiety, nervousness, tension, depressed mood, unusual behaviors and thinking about or attempting suicide. Black Box warning: Patients should stop taking Chantix and contact a healthcare provider immediately if agitation, hostility, depressed mood, or changes in behavior or thinking that are not typical for the patient are observed, or if the patient develops suicidal ideation or suicidal behavior while taking Chantix or shortly after discontinuing Chantix.8</td>
</tr>
</tbody>
</table>

### References:
<table>
<thead>
<tr>
<th>MEDICATION NAME</th>
<th>ANTICHOLINERGIC ACTIVITY (MUSCARINIC)</th>
<th>SEDATION (H1)</th>
<th>ORTHOSTATIC HYPOTENSION (ALPHA1)</th>
<th>CARDIAC EFFECTS</th>
<th>GI EFFECTS</th>
<th>SEIZURES</th>
<th>WEIGHT GAIN</th>
<th>SEXUAL DYSFUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0/+</td>
<td>0/+</td>
<td>+++</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>0/+</td>
<td>0/+</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0/+</td>
<td>+++</td>
</tr>
<tr>
<td>Sertraline</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>0</td>
<td>0/+</td>
<td>0/+</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0/+</td>
<td>+++</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Bupropion</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>+++</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>0/+</td>
<td>0/+</td>
<td>0/+</td>
</tr>
<tr>
<td>Trazodone</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>0</td>
<td>+++</td>
<td>0/+</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>0/+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Imipramine</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>0/+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>0/+</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Desipramine</td>
<td>+</td>
<td>0/+</td>
<td>+</td>
<td>++</td>
<td>0/+</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Doxepin</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>0/+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>
### Antidepressant Adverse Drug Effects: Relative Comparisons\(^5\) (cont.)

<table>
<thead>
<tr>
<th>MEDICATION NAME</th>
<th>ANTICHOLINERGIC ACTIVITY (MUSCARINIC)</th>
<th>SEDATION (H(_1))</th>
<th>ORTHOSTATIC HYPOTENSION (ALPHA(_1))</th>
<th>CARDIAC EFFECTS</th>
<th>GI EFFECTS</th>
<th>SEIZURES</th>
<th>WEIGHT GAIN</th>
<th>SEXUAL DYSFUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenelzine</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Selegiline</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Tranylcypromine</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0/+</td>
<td>0</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

**CAUTION:** Use of antidepressants with MAOIs is contraindicated. Patients treated with Antidepressants should be closely observed for worsening of depression or suicidality especially at the beginning of therapy or when the dose increases or decreases. SSRIs and SNRIs have the possibility of serotonin syndrome.\(^1,2\) Augmentation with another antidepressant may be considered for patients who have had a partial response to antidepressant monotherapy at therapeutic doses for at least 6 weeks. The augmenting medication selected should be based on the patient's current medications, co-morbid conditions, and adverse effect profile. St. John’s Wort may be used for patients with mild major depression who have a strong preference for herbal therapy. Psychostimulants are not appropriate as monotherapy for treatment of MDD. Psychostimulants may have a role in augmentation of therapy.

**NOTE:** Antidepressant Medication Information current as of May 2010. May become outdated.