

Search
Home
Join APA
Members Corner
About APA
District Branches & State Associations
Advocacy
Education
Ethics
Research
Psychiatric Practice
Public Information
Career Corner
Interest Groups
News Room
Calendar
Media
Publishing (APPI)
Foundation (APF)
Research & Education (APIRE)
Resource Links

## **PART A:**

# **TREATMENT RECOMMENDATIONS FOR PATIENTS WITH MAJOR DEPRESSIVE DISORDER**

### **I. SUMMARY OF TREATMENT RECOMMENDATIONS**

Each recommendation is identified as falling into one of three categories of endorsement, indicated by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence regarding the recommendation:

- [I] Recommended with substantial clinical confidence.
- [II] Recommended with moderate clinical confidence.
- [III] May be recommended on the basis of individual circumstances.

Successful treatment of patients with major depressive disorder is promoted by a thorough assessment of the patient [I]. Treatment consists of an acute phase, during which remission is induced; a continuation phase, during which remission is preserved; and a maintenance phase, during which the susceptible patient is protected against the recurrence of subsequent major depressive episodes. Psychiatrists initiating treatment for major depressive disorder have at their disposal a number of medications, a variety of psychotherapeutic approaches, electroconvulsive therapy (ECT), and other treatment modalities (e.g., light therapy) that may be used alone or in combination. The psychiatrist must determine the setting that will most likely ensure the patient's safety as well as promote improvement in the patient's condition [I].

#### **A. Psychiatric Management**

Psychiatric management consists of a broad array of interventions and activities that should be instituted by psychiatrists for all patients with major depressive disorder [I]. Regardless of the specific treatment modalities selected, it is important to continue providing psychiatric management through all phases of treatment. The specific components of psychiatric management that must be addressed for all patients include performing a diagnostic evaluation, evaluating safety of the patient and others, evaluating the level of functional impairments, determining a treatment setting, establishing and maintaining a therapeutic alliance, monitoring the patient's psychiatric status and safety, providing education to patients and families, enhancing treatment adherence, and working with patients to address early signs of relapse.

#### **B. Acute Phase**

##### **1. Choice of an initial treatment modality**

In the acute phase, in addition to psychiatric management, the psychiatrist may choose between several initial treatment modalities, including pharmacotherapy, psychotherapy, a combination of medications plus psychotherapy, or ECT [I]. Selection of an initial treatment

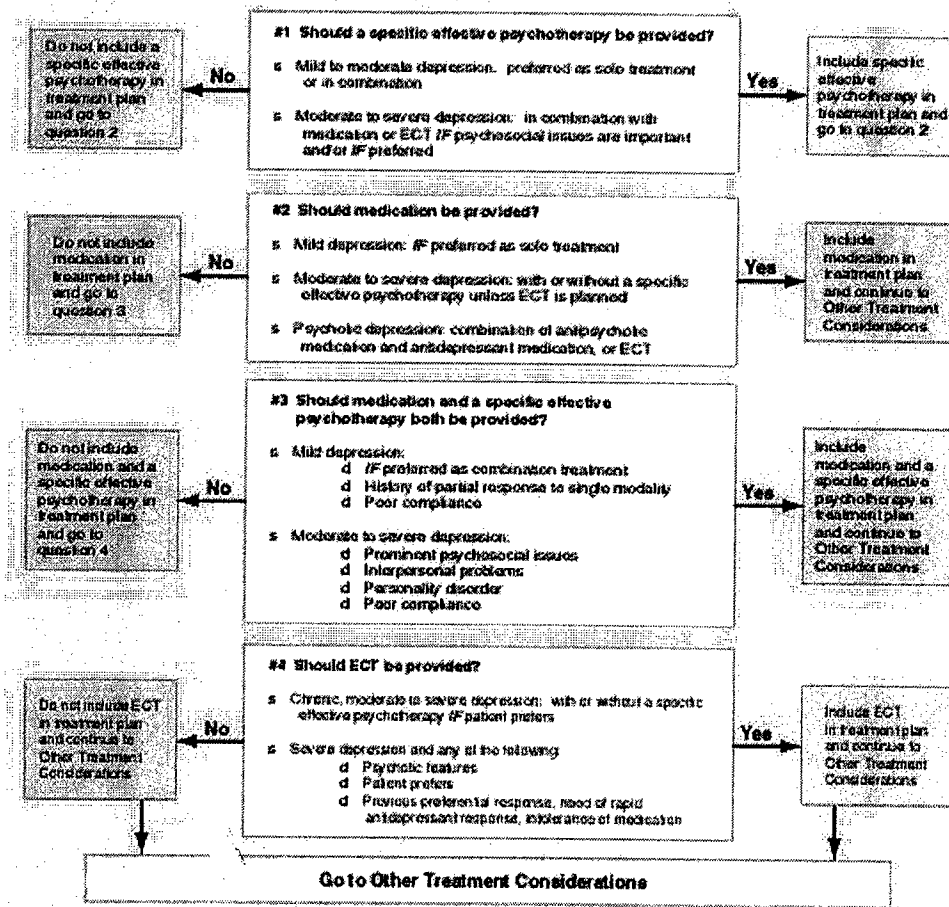


modality should be influenced by both clinical (e.g., severity of symptoms) and other factors (e.g., patient preference) (figure 1) (See Choice of Treatment Modalities for Major Depressive Disorder).

*a. Antidepressant medication*

If preferred by the patient, antidepressant medications may be provided as an initial primary treatment modality for mild major depressive disorder [I]. Antidepressant medications should be provided for moderate to severe major depressive disorder unless ECT is planned [I]. A combination of antipsychotic and antidepressant medications or ECT should be used for psychotic depression [I].

**FIGURE 1. Choice of Treatment Modalities for Major Depressive Disorder.**



*b. Psychotherapy*

A specific, effective psychotherapy alone as an initial treatment modality may be considered for patients with mild to moderate major depressive disorder [II]. Patient preference for psychotherapeutic approaches is an important factor that should be considered in the decision. Clinical features that may suggest the use of psychotherapeutic interventions include the presence of significant psychosocial stressors, intrapsychic conflict, interpersonal difficulties, or a comorbid axis II disorder [I].

*c. Psychotherapy plus antidepressant medications*

The combination of a specific effective psychotherapy and medication may be a useful initial treatment choice for patients with psychosocial issues, interpersonal problems, or a comorbid axis II disorder together with moderate to severe major depressive disorder [I]. In addition, patients who have had a history of only partial response to adequate trials of single treatment modalities may benefit from combined treatment. Poor adherence with treatment

may also warrant combined treatment modalities.

*d. Electroconvulsive therapy*

ECT should be considered for patients with major depressive disorder with a high degree of symptom severity and functional impairment or for cases in which psychotic symptoms or catatonia are present [I]. ECT may also be the treatment modality of choice for patients in whom there is an urgent need for response, such as patients who are suicidal or refusing food and nutritionally compromised [II].

**2. Choice of specific pharmacologic treatment**

Antidepressant medications that have been shown to be effective are listed in Table 1 "Commonly Used Antidepressant Medications:[II]. The effectiveness of antidepressant medications is generally comparable between classes and within classes of medications. Therefore, the initial selection of an antidepressant medication will largely be based on the anticipated side effects, the safety or tolerability of these side effects for individual patient: patient preference, quantity and quality of clinical trial data regarding the medication, and cost (see Section V.A.1.) [I]. On the basis of these considerations, the following medications are likely to be optimal for most patients: selective serotonin reuptake inhibitors (SSRIs), desipramine, nortriptyline, bupropion, and venlafaxine. In general, monoamine oxidase inhibitors (MAOIs) should be restricted to patients who do not respond to other treatments because of their potential for serious side effects and the necessity of dietary restrictions. Patients with major depressive disorder with atypical features are one group for whom several studies suggest MAOIs may be particularly effective; however, in clinical practice, many psychiatrists start with SSRIs in such patients because of the more favorable adverse effect profile.

**TABLE 1.** Commonly Used Antidepressant Medications

Generic Name Usual Dose	Starting Dose (mg/day)	
<b>Tricyclics and tetracyclics</b>		
<i>Tertiary amine tricyclics</i>		
Amitriptyline	25-50	100-300
Clomipramine	25	100-250
Doxepin	25-50	100-300
Imipramine	25-50	100-300
Trimipramine	25-50	100-300
<i>Secondary amine tricyclics</i>		
Desipramine <sup>b</sup>	25-50	100-300
Nortriptyline <sup>b</sup>	25	50-200

Protriptyline	10	15-6
<i>Tetracyclics</i>		
Amoxapine	50	100-400
Maprotiline	50	100-225
<b>SSRIs<sup>b</sup></b>		
Citalopram	20	20-60c
Fluoxetine	20	20-60c
Fluvoxamine	50	50-300c
Paroxetine	20	20-60c
Sertraline	50	50-200c
<b>Dopamine-norepinephrine reuptake inhibitors</b>		
Bupropion <sup>b</sup>	150	300
Bupropion, sustained release	150	300
<b>Serotonin-norepinephrine reuptake inhibitors</b>		
Venlafaxine <sup>b</sup>	37.5	75-225
Venlafaxine, extended release	37.5	75-225
<b>Serotonin modulators</b>		
Nefazodone	50	150-300
Trazodone	50	75-300
<b>Norepinephrine-serotonin modulator</b>		
Mirtazapine	15	15-4
<b>MAOIs</b>		
<i>Irreversible, nonselective</i>		
Phenelzine	15	15-9
Tranylcypromine	10	30-6
<i>Reversible MAOI-A</i>		
		300-

Moclobemide	150	600
<b>Selective noradrenaline reuptake inhibitor</b>		
Reboxetine	-d	-d

<sup>a</sup>Lower starting doses are recommended for elderly patients and for patients with panic disorder, significant anxiety or hepatic disease, and general comorbidity.

<sup>b</sup>These medications are likely to be optimal medications in terms of the patient's acceptance of side effects, safety, and quantity and quality of clinical trial data.

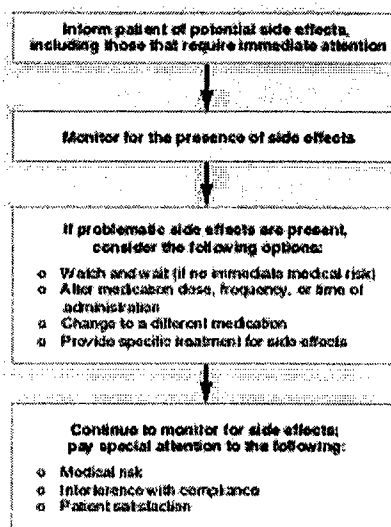
<sup>c</sup>Dose varies with diagnosis; see text for specific guidelines.

<sup>d</sup>FDA approval is anticipated. When available, consult manufacturer's package insert or the Physician's Desk Reference for recommended starting and usual doses.

#### a. Implementation

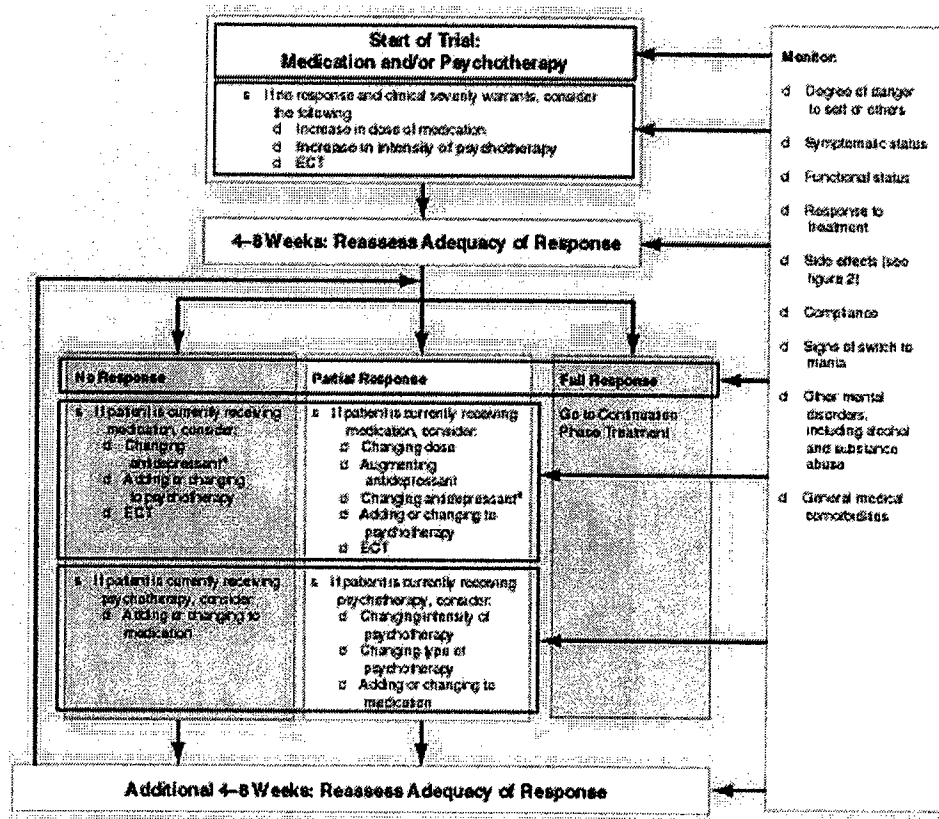
When pharmacotherapy is part of the treatment plan, it must be integrated with the psychiatric management and any other treatments that are being provided (e.g., psychotherapy) [I]. Once an antidepressant medication has been selected, it can be started at the dose levels suggested in Table 1 "Commonly Used Antidepressant Medications" [I]. Titration to full therapeutic doses generally can be accomplished over the initial week(s) of treatment but may vary depending on the development of side effects, the patient's age, and the presence of comorbid illnesses. Patients who have started taking an antidepressant medication should be carefully monitored to assess their response to pharmacotherapy as well as the emergence of side effects, clinical condition, and safety [I] (see figure 2 Management of Medication Side Effects). Factors to consider in determining the frequency of patient monitoring include the severity of illness, the patient's cooperation with treatment, the availability of social supports, and the presence of comorbid general medical problems. Visits should also be frequent enough to monitor and address suicidality and to promote treatment adherence. In practice, the frequency of monitoring during the acute phase of pharmacotherapy can vary from once a week in routine cases to multiple times per week in more complex cases.

**FIGURE 2. Management of Medication Side Effects.**



**b. Failure to respond**

If at least moderate improvement is not observed following 6-8 weeks of pharmacotherapy a reappraisal of the treatment regimen should be conducted [I]. Section II.B.2.b. reviews options for adjusting the treatment regimen when necessary. Following any change in treatment, the patient should continue to be closely monitored. If there is not at least a moderate improvement in major depressive disorder symptoms after an additional 6-8 weeks of treatment, the psychiatrist should conduct another thorough review. An algorithm depicting the sequence of subsequent steps that can be taken for patients who fail to respond fully to treatment is provided in figure 3 Acute Phase Treatment of Major Depressive Disorder.



**FIGURE 3. Acute Phase Treatment of Major Depressive Disorder.**

<sup>a</sup>Choose either another antidepressant from the same class or, if two previous medication trials from the same class were ineffective, an antidepressant from a different class.

**3. Choice of specific psychotherapy**

Cognitive behavioral therapy and interpersonal therapy are the psychotherapeutic approaches that have the best documented efficacy in the literature for the specific treatment of major depressive disorder, although rigorous studies evaluating the efficacy of psychodynamic psychotherapy have not been published [II]. When psychodynamic psychotherapy is used as a specific treatment, in addition to symptom relief, it is frequently associated with broader long-term goals. Patient preference and the availability of clinician with appropriate training and expertise in the specific approach are also factors in the choice of a particular form of psychotherapy.

**a. Implementation**

When psychotherapy is part of the treatment plan, it must be integrated with the psychiatric management and any other treatments that are being provided (e.g., medication treatment [I]). The optimal frequency of psychotherapy has not been rigorously studied in controlled

trials. The psychiatrist should take into account multiple factors when determining the frequency for individual patients, including the specific type and goals of psychotherapy, the frequency necessary to create and maintain a therapeutic relationship, the frequency of visits required to ensure treatment adherence, and the frequency necessary to monitor and address suicidality. The frequency of outpatient visits during the acute phase generally varies from once a week in routine cases to as often as several times a week.

Regardless of the type of psychotherapy selected, the patient's response to treatment should be carefully monitored [I].

If more than one clinician is involved in providing the care, it is essential that all treating clinicians have sufficient ongoing contact with the patient and with each other to ensure that relevant information is available to guide treatment decisions [I].

#### *b. Failure to respond*

If after 4-8 weeks of treatment at least a moderate improvement is not observed, then a thorough review and reappraisal of the diagnosis, complicating conditions and issues, and treatment plan should be conducted [I]. Figure 3 and section II.B.3.b. review the options to consider.

### **4. Choice of medications plus psychotherapy**

In general, the same issues that influence the specific choice of medication or psychotherapy when used alone should be considered when choosing treatments for patients receiving combined modalities [I].

### **5. Assessing the adequacy of response**

It is not uncommon for patients to have a substantial but incomplete response in terms of symptom reduction or improvement in functioning during acute phase treatments. It is important not to conclude the acute phase of treatment for such patients, as a partial response is often associated with poor functional outcomes. When patients are found to have not fully responded to an acute phase treatment, a change in treatment should be considered as outlined in figure 3 Acute Phase Treatment of Major Depressive Disorder [II]

### **C. Continuation Phase**

During the 16-20 weeks following remission, patients who have been treated with antidepressant medications in the acute phase should be maintained on these agents to prevent relapse [I]. In general, the dose used in the acute phase is also used in the continuation phase. Although there has been less study of the use of psychotherapy in the continuation phase to prevent relapse, there is growing evidence to support the use of a specific effective psychotherapy during the continuation phase [I]. Use of ECT in the continuation phase has received little formal study but may be useful in patients for whom medication or psychotherapy has not been effective in maintaining stability during the continuation phase [II]. The frequency of visits must be determined by the patient's clinical condition as well as the specific treatments being provided.

### **D. Maintenance Phase**

Following the continuation phase, maintenance-phase treatment should be considered for patients to prevent recurrences of major depressive disorder [I]. Factors to consider are discussed in Table 2 Consideration in the Decision to Use Maintenance Treatment and in section II.D.

In general, the treatment that was effective in the acute and continuation phases should be used in the maintenance phase [II]. In general, the same full antidepressant medication doses are employed as were used in prior phases of treatment; use of lower doses of antidepressant medication in the maintenance phase has not been well studied. For cognitive behavioral therapy and interpersonal therapy, maintenance phase treatments usually involve a decreased frequency of visits (e.g., once a month).

The frequency of visits in the maintenance phase must be determined by the patient's clinical condition as well as the specific treatments being provided. The frequency required

could range from as low as once every 2-3 months for stable patients who require only psychiatric management and medication monitoring to as high as multiple times a week for those in whom psychodynamic psychotherapy is being conducted.

**TABLE 2.** Considerations in the Decision to Use Maintenance Treatment

Factor	Component
Risk of recurrence	Number of prior episodes; presence of comorbid conditions; residual symptoms between episodes
Severity of episodes	Suicidality; psychotic features; severe functional impairments
Side effects experienced with continuous treatment	
Patient preferences	

#### **E. Discontinuation of Active Treatment**

The decision to discontinue active treatment should be based on the same factors considered in the decision to initiate maintenance treatment, including the probability of recurrence, the frequency and severity of past episodes, the persistence of dysthymic symptoms after recovery, the presence of comorbid disorders, and patient preferences [I]. In addition to the factors listed in Table 2 "Considerations in the Decision to Use Maintenance Treatment" and Table 3 "Risk Factors for Recurrence of Major Depressive Disorder", patients and their psychiatrists should consider the patient's response, in terms of both beneficial and adverse effects, to maintenance treatments.

Specific clinical features that will influence the general treatment are discussed in Section 1

**TABLE 3. Risk Factors for Recurrence of Major Depressive Disorder**

- Prior history of multiple episodes of major depressive disorder
- Persistence of dysthymic symptoms after recovery from an episode of major depressive disorder
- Presence of an additional, nonaffective psychiatric diagnosis
- Presence of a chronic general medical disorder