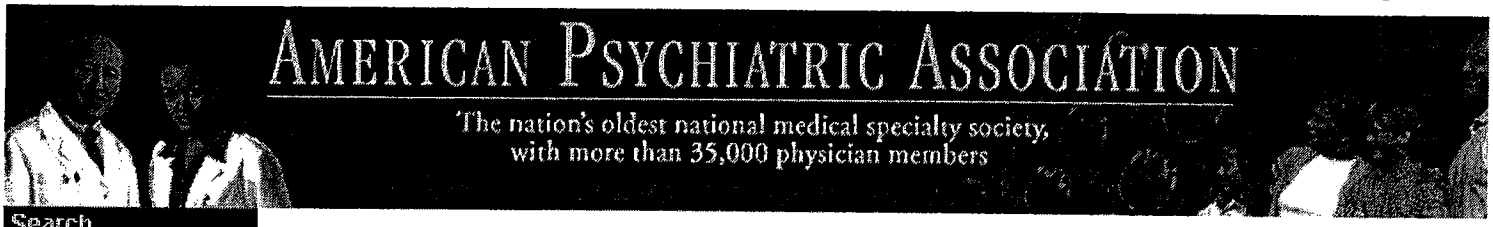

Practice Guideline for the Treatment of Patients With Bipolar Disorder (Revision)

PART A:
Treatment Recommendations for Patients With Bipolar Disorder

I. EXECUTIVE SUMMARY OF 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.

A. Psychiatric Management

At this time, there is no cure for bipolar disorder; however, treatment can decrease the associated morbidity and mortality [I]. Initially, the psychiatrist should perform a diagnost evaluation and assess the patient's safety and level of functioning to arrive at a decision about the optimum treatment setting [I]. Subsequently, specific goals of psychiatric management include establishing and maintaining a therapeutic alliance, monitoring the patient's psychiatric status, providing education regarding bipolar disorder, enhancing treatment compliance, promoting regular patterns of activity and of sleep, anticipating stressors, identifying new episodes early, and minimizing functional impairments [I].

B. Acute Treatment

1. Manic or mixed episodes

The first-line pharmacological treatment for more severe manic or mixed episodes is the initiation of either lithium plus an antipsychotic or valproate plus an antipsychotic [I]. For less ill patients, monotherapy with lithium, valproate, or an antipsychotic such as olanzapir may be sufficient [I]. Short-term adjunctive treatment with a benzodiazepine may also be helpful [II]. For mixed episodes, valproate may be preferred over lithium [II]. Atypical antipsychotics are preferred over typical antipsychotics because of their more benign side effect profile [I], with most of the evidence supporting the use of olanzapine or risperidone [II]. Alternatives include carbamazepine or oxcarbazepine in lieu of lithium or valproate [II Antidepressants should be tapered and discontinued if possible [I]. If psychosocial therapy approaches are used, they should be combined with pharmacotherapy [I].

For patients who, despite receiving maintenance medication treatment, experience a mani or mixed episode (i.e., a "breakthrough" episode), the first-line intervention should be to optimize the medication dose [I]. Introduction or resumption of an antipsychotic is sometimes necessary [II]. Severely ill or agitated patients may also require short-term adjunctive treatment with a benzodiazepine [I].

When first-line medication treatment at optimal doses fails to control symptoms, recommended treatment options include addition of another first-line medication [I]. Alternative treatment options include adding carbamazepine or oxcarbazepine in lieu of an additional first-line medication [II], adding an antipsychotic if not already prescribed [I], o changing from one antipsychotic to another [III]. Clozapine may be particularly effective ir the treatment of refractory illness [II]. ECT may also be considered for patients with sever or treatment-resistant mania or if preferred by the patient in consultation with the psychiatrist [I]. In addition, ECT is a potential treatment for patients experiencing mixed episodes or for patients experiencing severe mania during pregnancy [II].

Manic or mixed episodes with psychotic features usually require treatment with an antipsychotic medication [II].

2. Depressive episodes

The first-line pharmacological treatment for bipolar depression is the initiation of either lithium [I] or lamotrigine [II]. Antidepressant monotherapy is not recommended [I]. As an alternative, especially for more severely ill patients, some clinicians will initiate simultaneo treatment with lithium and an antidepressant [III]. In patients with life-threatening inaniti suicidality, or psychosis, ECT also represents a reasonable alternative [I]. ECT is also a potential treatment for severe depression during pregnancy [II].

A large body of evidence supports the efficacy of psychotherapy in the treatment of unipol depression [I]. In bipolar depression, interpersonal therapy and cognitive behavior therapy may be useful when added to pharmacotherapy [II]. While psychodynamic psychotherapy has not been empirically studied in patients with bipolar depression, it is widely used in addition to medication [III].

For patients who, despite receiving maintenance medication treatment, suffer a breakthrough depressive episode, the first-line intervention should be to optimize the dose maintenance medication [II].

When an acute depressive episode of bipolar disorder does not respond to first-line medication treatment at optimal doses, next steps include adding lamotrigine [I], bupropic [II], or paroxetine [II]. Alternative next steps include adding other newer antidepressants (e.g., a selective serotonin reuptake inhibitor [SSRI] or venlafaxine) [II] or a monoamine oxidase inhibitor (MAOI) [II]. For patients with severe or treatment-resistant depression o depression with psychotic or catatonic features, ECT should be considered [I].

The likelihood of antidepressant treatment precipitating a switch into a hypomanic episode probably lower in patients with bipolar II depression than in patients with bipolar I depression. Therefore, clinicians may elect to recommend antidepressant treatment earlier patients with bipolar II disorder [II].

Depressive episodes with psychotic features usually require adjunctive treatment with an antipsychotic medication [I]. ECT represents a reasonable alternative [I].

3. Rapid cycling

As defined in DSM-IV-TR (1) and applied in this guideline, rapid cycling refers to the occurrence of four or more mood disturbances within a single year that meet criteria for a major depressive, mixed, manic, or hypomanic episode. These episodes are demarcated either by partial or full remission for at least 2 months or a switch to an episode of opposit

polarity (e.g., from a major depressive to a manic episode). The initial intervention in patients who experience rapid cycling is to identify and treat medical conditions, such as hypothyroidism or drug or alcohol use, that may contribute to cycling [I]. Certain medications, particularly antidepressants, may also contribute to cycling and should be tapered if possible [II]. The initial treatment for patients who experience rapid cycling shou include lithium or valproate [I]; an alternative treatment is lamotrigine [I]. For many patients, combinations of medications are required [II].

C. Maintenance Treatment

Following remission of an acute episode, patients may remain at particularly high risk of relapse for a period of up to 6 months; this phase of treatment, sometimes referred to as continuation treatment, is considered in this guideline to be part of the maintenance phase Maintenance regimens of medication are recommended following a manic episode [I]. Although few studies involving patients with bipolar II disorder have been conducted, consideration of maintenance treatment for this form of the illness is also strongly warrant [II]. The medications with the best empirical evidence to support their use in maintenance treatment include lithium [I] and valproate [I]; possible alternatives include lamotrigine [I or carba-mazepine or oxcarbazepine [II]. If one of these medications was used to achieve remission from the most recent depressive or manic episode, it generally should be continued [I]. Maintenance sessions of ECT may also be considered for patients whose acu episode responded to ECT [II].

For patients treated with an antipsychotic medication during the preceding acute episode, the need for ongoing antipsychotic treatment should be reassessed upon entering maintenance treatment [I]; antipsychotics should be discontinued unless they are required for control of persistent psychosis [I] or prophylaxis against recurrence [III]. While maintenance therapy with atypical antipsychotics may be considered [III], there is as yet r definitive evidence that their efficacy in maintenance treatment is comparable to that of agents such as lithium or valproate.

During maintenance treatment, patients with bipolar disorder are likely to benefit from a concomitant psychosocial intervention-including psychotherapy-that addresses illness management (i.e., adherence, lifestyle changes, and early detection of prodromal symptoms) and interpersonal difficulties [II].

Group psychotherapy may also help patients address such issues as adherence to a treatment plan, adaptation to a chronic illness, regulation of self-esteem, and managemen of marital and other psychosocial issues [II]. Support groups provide useful information about bipolar disorder and its treatment [I].

Patients who continue to experience subthreshold symptoms or breakthrough mood episod may require the addition of another maintenance medication [II], an atypical antipsychotic [III], or an antidepressant [III]. There are currently insufficient data to support one combination over another. Maintenance sessions of ECT may also be considered for patient whose acute episode responded to ECT [II].

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