Complete Summary

GUIDELINE TITLE

Practice guideline for the treatment of patients with bipolar disorder (revision).

BIBLIOGRAPHIC SOURCE(S)

Practice guideline for the treatment of patients with bipolar disorder (revision). Am J Psychiatry 2002 Apr;159(4 Suppl):1-50. [472 references] PubMed

GUIDELINE STATUS

According to the guideline developer, this guideline is still considered to be current as of November 2005. A Guideline Watch, which summarizes significant developments in practice since the publication of the original guideline, was published in November 2005 and is available from the American Psychiatric Association Web site (see also the "Availability of Companion Documents" field below).

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse (NGC): This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 12, 2007, Carbamazepine: The U.S. Food and Drug Administration (FDA) has provided recommendations for screening that should be performed on specific patient populations before starting treatment with carbamazepine.
- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
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METHODOLOGY - including Rating Scheme and Cost Analysis
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IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Bipolar disorder, including:

- Bipolar I disorder
- Bipolar II disorder
- Cyclothymic disorder
- Bipolar disorder not otherwise specified (NOS)

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Psychiatry

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To assist the clinician faced with the task of implementing a specific regimen for the treatment of a patient with bipolar disorder

TARGET POPULATION

Primarily adults (18 years of age or older) with bipolar disorder

INTERVENTIONS AND PRACTICES CONSIDERED

Psychiatric management

1. Diagnostic evaluation
2. Evaluation of the safety of the patients and others and determination of a treatment setting
3. Establishment and maintenance of a therapeutic alliance
4. Monitoring of treatment response

5. Patient and family education
6. Measures to enhance treatment compliance
7. Promotion of awareness of stressors and regular patterns of activity and sleep
8. Work with patient to anticipate and address early signs of relapse
9. Evaluation and management of functional impairments

Somatic treatments

1. Pharmacologic agents:

   Classes of medications:

   - Antidepressants
     - Monoamine oxidase inhibitors (MAOIs)
     - Selective serotonin reuptake inhibitor (SSRI)
   - Antipsychotics
   - Benzodiazepines

   Specific medications:

   - Bupropion
   - Olanzapine
   - Carbamazepine
   - Clozapine
   - Lamotrigine
   - Lithium
   - Oxcarbazepine
   - Paroxetine
   - Risperidone
   - Valproate
   - Venlafaxine
2. Electroconvulsive therapy (ECT)
3. Combination therapies

Concomitant psychosocial interventions (psychoeducational, interpersonal, family, group, social rhythm, psychodynamic, and cognitive behavior therapies)

MAJOR OUTCOMES CONSIDERED

- Efficacy of treatment as evidenced by morbidity and mortality associated with bipolar disorder
- Adverse effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A computerized search of the relevant literature from MEDLINE and PsycINFO was conducted. Sources of funding were not considered when reviewing the literature.

The first literature search was conducted by searching MEDLINE and PsycINFO for the period from 1992 to 2000. Key words used were "bipolar disorder," "bipolar depression," "mania," "mixed states," "mixed episodes," "mixed mania," "antimanic," "hypomanic," "hypomania," "manic depression," "prophylactic," "pharmacotherapy," "mood stabilizers," "mood-stabilizing," "rapid cycling," "maintenance," "continuation," "child and adolescent," "antidepressants," "valproate," "lithium," "carbamazepine," "olanzapine," "risperidone," "gabapentin," "topiramate," "lamotrigine," "clonazepam," "divalproex," "psychotherapy," "family therapy," "psychoeducation," "course," "epidemiology," "comorbidity," "anxiety," "anxiety disorders," "attention deficit," "catatonia," "elderly," "family history," "gender," "general medical conditions," "life events," "personality disorders," "pregnancy," "psychosis," "stress," "substance-related disorders," "suicide," "homicide," and "violence."

An additional MEDLINE search for the period from 1992 to 2001 used the key words "genetic counseling," "family functioning," "cross-cultural issues," and "pharmacokinetics." A search on PubMed was also conducted through 2001 that used the search terms "electroconvulsive," "intravenous drug abuse," "treatment response," "pharmacogenetic," "attention deficit disorder," "violence," "aggression," "aggressive," "suicidal," "cognitive impairment," "sleep," "postpartum," "ethnic," "racial," "metabolism," "hyperparathyroidism," "overdose," "toxicity," "intoxication," "pregnancy," "breast-feeding," and "lactation."

Additional, less formal, literature searches were conducted by American Psychiatric Association (APA) staff and individual members of the work group on bipolar disorder.

NUMBER OF SOURCE DOCUMENTS

The first literature search yielded 3,382 citations

The additional MEDLINE search yielded 122 citations.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Once a topic is chosen for guideline development, a work group is formed to draft the guideline. By design, the work group consists of psychiatrists in active clinical practice with diverse expertise and practice experience relevant to the topic. Policies established by the Steering Committee guide the work of systematically reviewing data in the literature and forging consensus on the implications of those data, as well as describing a clinical consensus. These policies, in turn, stem from criteria formulated by the American Medical Association to promote the development of guidelines that have a strong evidence base and that make optimal use of clinical consensus.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Each recommendation is identified at 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.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This practice guideline was developed under the auspices of the American Psychiatric Association Steering Committee on Practice Guidelines. The development process is detailed in a document available from the American Psychiatric Association Department of Quality Improvement and Psychiatric

Services: the "American Psychiatric Association Guideline Development Process" (see "Companion Documents").

Key features of this process, relevant to review methodology, include the following:

- The production of multiple drafts with widespread review; seven organizations and more than 40 individuals (named in the original guideline document) submitted significant comments.
- Approval by the American Psychiatric Association Assembly and Board of Trustees. This guideline was approved in December 2001.

RECOMMENDATIONS

MAJOR 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.

Definition of grades of recommendation [I-III] are presented at the end of the "Major Recommendations" field.

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 diagnostic 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]**.

Acute Treatment

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 olanzapine 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 manic 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]**, or changing from one antipsychotic to another **[III]**. Clozapine may be particularly effective in the treatment of refractory illness **[II]**. Electroconvulsive therapy may also be considered for patients with severe or treatment-resistant mania or if preferred by the patient in consultation with the psychiatrist **[I]**. In addition, electroconvulsive therapy 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]**.

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 simultaneous treatment with lithium and an antidepressant **[III]**. In patients with life-threatening inanition, suicidality, or psychosis, electroconvulsive therapy also represents a reasonable alternative **[I]**. Electroconvulsive therapy 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 unipolar 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 of 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]**, bupropion **[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 or depression with psychotic or catatonic features, electroconvulsive therapy should be considered **[I]**.

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

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

Rapid Cycling

As defined in DSM-IV-TR 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 opposite 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 should include lithium or valproate **[I]**; an alternative treatment is lamotrigine **[I]**. For many patients, combinations of medications are required **[II]**.

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 warranted **[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 **[II]** or carbamazepine 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 electroconvulsive therapy may also be considered for patients whose acute episode responded to electroconvulsive therapy **[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 no 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 management 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 episodes 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 electroconvulsive therapy may also be considered for patients whose acute episode responded to electroconvulsive therapy **[II]**.

Refer to the original guideline document for a discussion of special clinical features influencing the treatment plan.

Definitions:

Grades of Recommendations:

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

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on the best available data and clinical consensus with regard to a particular clinical decision. The summary of treatment recommendations is keyed according to the level of confidence with which each recommendation is made (see the "Major Recommendations" field). In addition, the following coding system is used to indicate the nature of the supporting evidence in the references:

[A] Randomized clinical trial
[B] Clinical trial
[C] Cohort or longitudinal study
[D] Case-control study
[E] Review of secondary analysis
[F] Review
[G] Other

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Benefits of treatment in general include decreased frequency, severity, and psychosocial consequences of episodes; and improved psychosocial functioning between episodes.
- Potential benefits of psychiatric management include treatment of acute exacerbations; prevention of recurrences; improved interepisode functioning; the provision of assistance, insight, and support to the patient and family; and the reduction of the morbidity and sequelae of bipolar disorder.
- Potential benefits of pharmacologic treatments include the effective treatment of acute episodes; decreased symptoms of mania or depression; the prevention of future episodes; and mood-stabilizing effects.
- Electroconvulsive therapy (ECT) is efficacious in the treatment of both phases of bipolar disorder.

POTENTIAL HARMS

Side effects and toxicities of medications

- *Lithium*. Dose-related side effects of lithium include polyuria, polydipsia, weight gain, cognitive problems (e.g., dulling, impaired memory, poor concentration, confusion, mental slowness), tremor, sedation or lethargy, impaired coordination, gastrointestinal distress (e.g., nausea, vomiting, dyspepsia, diarrhea), hair loss, benign leukocytosis, acne, and edema. Lithium may cause benign electrocardiogram (ECG) changes associated with repolarization. Less commonly, cardiac conduction abnormalities have been associated with lithium treatment. The most common renal effect of lithium is impaired concentrating capacity caused by reduced renal response to antidiuretic hormone (ADH), manifested as polyuria, polydipsia, or both. Although the polyuria associated with early lithium treatment may resolve, persistent polyuria (ranging from mild and well tolerated to severe nephrogenic diabetes insipidus) may occur. In addition to the other signs and symptoms of hypothyroidism, patients with bipolar disorder are at risk of developing depression or rapid cycling. Hyperparathyroidism has also been noted with lithium treatment. A small number of case reports have described exacerbation or first occurrences of psoriasis associated with lithium treatment. Approximately 10% to 20% of patients receiving long-term lithium treatment (i.e., for more than 10 years) display morphological kidney changes, usually interstitial fibrosis, tubular atrophy, and sometimes glomerular sclerosis. Additionally, several studies have shown that a small percentage of patients treated with lithium may develop rising serum creatinine concentrations after 10 years or more of treatment.

  Signs and symptoms of early lithium intoxication (with levels above 1.5 meq/liter) include marked tremor, nausea and diarrhea, blurred vision, vertigo, confusion, and increased deep tendon reflexes. With lithium levels above 2.5 meq/liter, patients may experience more severe neurological complications and eventually experience seizures, coma, cardiac dysrhythmia, and permanent neurological impairment.

- *Valproate*. Common dose-related side effects of valproate include gastrointestinal distress (e.g., anorexia, nausea, dyspepsia, vomiting, diarrhea), benign hepatic transaminase elevations, osteoporosis, tremor, and sedation. Mild, asymptomatic leukopenia and thrombocytopenia occur less frequently and are reversible upon drug discontinuation. Other side effects that are often bothersome to the patient include hair loss, increased appetite, and weight gain. Polycystic ovarian syndrome may be possible with valproate treatment. Rare, idiosyncratic, but potentially fatal adverse events with valproate include irreversible hepatic failure, hemorrhagic pancreatitis, and agranulocytosis. Signs of overdose include somnolence, heart block, and eventually coma. Deaths have been reported. Overdose can be treated with hemodialysis.
- *Carbamazepine*. The most common dose-related side effects of carbamazepine include neurological symptoms, such as diplopia, blurred vision, fatigue, nausea, and ataxia. These effects are usually transient and often reversible with dose reduction. Less frequent side effects include skin rashes, mild leukopenia, mild thrombocytopenia, hyponatremia, and (less commonly) hypo-osmolality. Mild liver enzyme elevations occur in 5% to 15% of patients. Hyponatremia occurs in 6% to 31% of patients, is rare in children but probably more common in the elderly, occasionally develops many months after the initiation of carbamazepine treatment, and sometimes necessitates carbamazepine discontinuation. In addition, carbamazepine may decrease total and free thyroxine levels and increase free cortisol levels, but these effects are rarely clinically significant. Weight gain is also a common side effect of carbamazepine. Rare, idiosyncratic, but serious and potentially fatal side effects of carbamazepine include agranulocytosis, aplastic anemia, thrombocytopenia, hepatic failure, exfoliative dermatitis (e.g., Stevens-Johnson syndrome), and pancreatitis. Although these side effects usually occur within 3 to 6 months of carbamazepine initiation, they have also occurred after more extended periods of treatment. Other rare side effects include systemic hypersensitivity reactions, cardiac conduction disturbances, psychiatric symptoms (including sporadic cases of psychosis), and, very rarely, renal effects (including renal failure, oliguria, hematuria, and proteinuria). Carbamazepine may be fatal in overdose; deaths have been reported with ingestions of more than 6 grams. Signs of impending carbamazepine toxicity include dizziness, ataxia, sedation, and diplopia. Acute intoxication can result in hyperirritability, stupor, or coma. The most common symptoms of carbamazepine overdose are nystagmus, ophthalmoplegia, cerebellar and extrapyramidal signs, impaired consciousness, convulsions, and respiratory dysfunction. Cardiac symptoms may include tachycardia, arrhythmia, conduction disturbances, and hypotension. Gastrointestinal and anticholinergic symptoms may also occur.
- *Olanzapine*. In placebo-controlled clinical trials, somnolence was the most common side effect associated with olanzapine. Other common side effects included constipation, dry mouth, increased appetite, and weight gain. Especially during initial dose titration, olanzapine may induce orthostatic hypotension associated with dizziness, tachycardia, and, in some patients, syncope. Syncope was reported in 0.6% of olanzapine-treated patients in phase II and III trials. In clinical trials, seizures occurred in 0.9% of olanzapine-treated patients. Transient elevations in plasma prolactin concentrations were also observed in short-term trials. Clinically significant hepatic transaminase elevations (Â³ 3 times the upper limit of the normal range) were observed in 2% of olanzapine-treated patients.

- *Lamotrigine*. The most common side effects of lamotrigine in the treatment of depression are headache, nausea, infection, and xerostomia. The risk of serious rash, including Stevens-Johnson syndrome and toxic epidermal necrolysis, was approximately 0.3% in adults and approximately 1% in children in clinical trials for epilepsy. However, with a slow titration schedule, the risk of serious rash was reduced to 0.01% in adults, which is comparable to that of other anticonvulsant medications. Rash can occur at any time during treatment but is more likely to occur early in treatment. It may also be more likely if lamotrigine and valproate are administered concomitantly. Whenever lamotrigine is prescribed, patients should be apprised of the risk of rash and urged to contact the psychiatrist or primary care physician immediately if a rash occurs. At rash onset, it is difficult to distinguish between a serious and a more benign rash. Particularly worrisome are rashes accompanied by fever or sore throat, those that are diffuse and widespread, and those with prominent facial or mucosal involvement. In such circumstances lamotrigine (and concurrent valproate) should be discontinued. With concurrent valproate treatment, pharmacokinetic interactions lead to lamotrigine levels that are approximately twice normal. To minimize the risk of potentially serious rash in patients who are receiving valproate, the dose schedule should be cut in half (i.e., 12.5 mg/day or 25 mg every other day for 2 weeks, then 25 mg/day for weeks 3 and 4). Similarly, concurrent carbamazepine treatment leads to an increase in lamotrigine metabolism and requires dosing to be doubled.

Note: For information on side effects of electroconvulsive therapy (ECT), refer to the American Psychiatric Association Task Force Report on ECT (The practice of electroconvulsive therapy: recommendations for treatment, training, and privileging: a Task Force report of the American Psychiatric Association, 2nd ed. Washington [DC]: American Psychiatric Press, 2001; Available from the American Psychiatric Association Web site).

For information on side effects of antidepressants, see the related National Guideline Clearinghouse (NGC) summary of the American Psychiatric Association guideline Practice Guideline for the Treatment of Patients With Major Depressive Disorder.

Subgroups Most Likely to be Harmed:

- Women taking lithium are more likely to experience hypothyroidism than men.
- Patients taking valproate who have had or currently have hepatic disease may be at greater risk for hepatotoxicity when taking valproate.
- Elderly patients may be more sensitive to side effects of carbamazepine.
- Patients with a history of seizure disorder or in clinical conditions associated with lowered seizure threshold are more likely to experience seizures when taking olanzapine.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and practice patterns evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the psychiatrist in light of the clinical data presented by the patient and the diagnostic and treatment options available.

This practice guideline has been developed by psychiatrists who are in active clinical practice. In addition, some contributors are primarily involved in research or other academic endeavors. It is possible that through such activities some contributors have received income related to treatments discussed in this guideline. A number of mechanisms are in place to minimize the potential for producing biased recommendations due to conflicts of interest. The guideline has been extensively reviewed by members of American Psychiatric Association as well as by representatives from related fields. Contributors and reviewers have all been asked to base their recommendations on an objective evaluation of available evidence. Any contributor or reviewer who has a potential conflict of interest that may bias (or appear to bias) his or her work has been asked to notify the American Psychiatric Association Department of Quality Improvement and Psychiatric Services. This potential bias is then discussed with the work group chair and the chair of the Steering Committee on Practice Guidelines. Further action depends on the assessment of the potential bias.

The cross-sectional (i.e., current clinical status) and longitudinal (i.e., frequency, severity, and consequences of past episodes) context of the treatment decision should guide the psychiatrist and bipolar disorder patient in choosing from among various possible treatments and treatment settings. Such treatment decisions must be based on knowledge of the potential beneficial and adverse effects of available options along with information about patient preferences. In addition, treatment decisions should be continually reassessed as new information becomes available, the patient´s clinical status changes, or both.

Distinctions in Types of Bipolar Disorder

Every effort has been made to identify and highlight distinctions between bipolar I and bipolar II disorder in terms of patient response to treatment. However, with few exceptions, data from large trials have been presented in such a way that making such distinctions is difficult. For the treatment of patients with major depressive disorder, see the related National Guideline Clearinghouse (NGC) summary of the American Psychiatric Association guideline Practice Guideline for the Treatment of Patients With Major Depressive Disorder.

Psychotherapy

There have been no definitive studies to date of psychotherapy in lieu of antidepressant treatment for bipolar depression.

Treatment of Adolescents with Bipolar Disorder

To date, there has been only one double-blind, placebo-controlled, randomized study of pharmacotherapy in the treatment of adolescents with bipolar disorder. The majority of information available about pharmacological treatments for bipolar disorder in youth relies upon open studies, case series, and case reports.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The American Psychiatric Association develops derivative products including patient guides, quick reference guides, and quality of care indicators with research studies to evaluate the effectiveness of the guideline.

IMPLEMENTATION TOOLS

Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Practice guideline for the treatment of patients with bipolar disorder (revision). Am J Psychiatry 2002 Apr;159(4 Suppl):1-50. [472 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1994 Dec (revised 2002 Apr; reviewed 2005 Nov)

GUIDELINE DEVELOPER(S)

American Psychiatric Association - Medical Specialty Society

SOURCE(S) OF FUNDING

American Psychiatric Association (APA)

GUIDELINE COMMITTEE

Work Group on Bipolar Disorder

Steering Committee on Practice Guidelines

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

This practice guideline has been developed by psychiatrists who are in active clinical practice. In addition, some contributors are primarily involved in research or other academic endeavors. It is possible that through such activities many contributors have received income related to treatments discussed in this guideline. A number of mechanisms are in place to minimize the potential for producing biased recommendations due to conflicts of interest. The guideline has been extensively reviewed by members of American Psychiatric Association (APA) as well as by representatives from related fields. Contributors and reviewers have all been asked to base their recommendations on an objective evaluation of the available evidence. Any contributor or reviewer who has a potential conflict of interest that may bias (or appear to bias) his or her work has been asked to notify the APA Office of Research. This potential bias is then discussed with the work

group chair and the chair of the Steering Committee on Practice Guidelines. Further action depends on the assessment of the potential bias.

GUIDELINE STATUS

According to the guideline developer, this guideline is still considered to be current as of November 2005. A Guideline Watch, which summarizes significant developments in practice since the publication of the original guideline, was published in November 2005 and is available from the American Psychiatric Association Web site (see also the "Availability of Companion Documents" field below).

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Psychiatric Association Web site.

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; Fax (703) 907-1091.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- American Psychiatric Association practice guideline development process. In: practice guidelines for the treatment of psychiatric disorders: compendium 2000. Washington (DC): American Psychiatric Press, Inc (APPI), 2000.
- Hirschfeld RMA. Guideline watch: practice guideline for the treatment of patients with bipolar disorder, 2nd edition. Arlington (VA): American Psychiatric Association; 2005 Nov. 9 p. Electronic copies available in Portable Document Format (PDF) from the American Psychiatric Association Web site.

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; Fax (703) 907-1091.

Additionally, a continuing medical education (CME) course is available online at the American Psychiatric Association Web site.

PATIENT RESOURCES

None available

NGC STATUS

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