Treatment Guidelines: Current and Future Management of Bipolar Disorder

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The emergence of new treatments for bipolar disorder has coincided with a proliferation of published treatment algorithm recommendations and practice guidelines. Several guidelines derive from critical appraisals of current treatment literature and, as such, may serve as a critical reference resource to complement individual clinical judgment. This review describes points of overlap and discordance across currently available treatment guidelines for bipolar disorder and presents common clinical situations in which the consultation of treatment guidelines may provide clinicians with useful information and a rationale for making sequential treatment decisions.

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Recent years have witnessed the growth of an array of treatment options for all phases of bipolar disorder. Despite the availability of new anticonvulsants with possible mood-stabilizing properties, antidepressants, atypical antipsychotics, and diagnosis-specific psychotherapies, complex forms of bipolar disorder remain prevalent, and suboptimal treatment responses often necessitate serial pharmacotherapy trials. In managing complex forms of illness, clinicians often select from among diverse treatment options with little guidance from established criteria or systematic methodologies. Because sequential randomized drug trials for the same bipolar cohort have not, as yet, been reported in the literature, serial treatment strategies remain largely an area guided more by clinical judgment and opinion than empirical study. This article will review concepts about the use of current treatment guidelines for bipolar disorder, drawing especially on their value as resource documents for issues related to complex clinical management.

Treatment guidelines offer a frame of reference for choosing from among the myriad of clinical options now available for all phases of bipolar illness. Much as the strength of data to support specific treatments varies greatly—from anecdotal case reports to well-designed randomized controlled trials—so too do guidelines vary in the degree to which they specify and grade the evidence for their recommendations or follow other standard methods for guideline development.[1] To the extent that guidelines offer readers a critical distillation of published treatment studies, some authors have observed that the strength of their recommendations relies on how well they account for (1) study designs (i.e., randomized clinical trials versus observational studies), (2) heterogeneity of patients studied (greater heterogeneity across studies weakens their comparability), and (3) reporting of nonoverlapping confidence intervals around effect sizes (stronger recommendations are warranted when the smallest effect, or lower boundary of the confidence interval, remains above the threshold below which negative outcomes outweigh benefits).[2] At the same time, as noted by Kahn et al.,[3] published evidence for treatment outcomes may be incomplete or poorly applicable to usual practice circumstances; guidelines drawn from consensus-based expert opinions may then complement those that are solely evidence based and partly compensate for gaps in the empirical database.

While clinical decisions for an individual patient usually defy generic or formulaic procedures and complex situations often lack either definitive or generalizable advice, guidelines can augment individual clinical judgment by summarizing reasonable options for initial and successive treatments. In this sense, guidelines may be regarded as a resource document to consult in the course of medical decision making (Table 1). A guideline may provide useful recommendations and rationales for managing difficult clinical problems, for example by (1) formulating a treatment plan for bipolar prophylaxis during pregnancy (revised Expert Consensus Guidelines[4] advocate either conventional or atypical neuroleptics as first-line treatments during both conception and the first trimester), (2) advising patients on the longevity of mood stabilizer use after a single hypomanic episode (a decision often based on the severity of the episode and family history), (3) considering the role of antidepressants in mixed mania (Depart-

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Table 1. Common Clinical Problems as Addressed by Treatment Guidelines

When should a mood stabilizer be used indefinitely?
If bipolar I with > 2 manic episodes or 1 manic episode if especially severe or strong bipolar family history[4,14,25]
What is the optimal duration of antidepressant use after remission from bipolar depression?
2–6 months after euthymia, although 25% of experts recommended indefinite treatment[4]
Should antidepressants be used as monotherapy for bipolar depression?
Originally described as an "occasional consideration" for bipolar II depression,[14] but revised edition advises against the use of antidepressants without a mood stabilizer[4]
Is there a preferred mood stabilizer for rapid cycling?
Divalproex as first line,[4,24] although some guidelines advocate lithium with equal or greater endorsement[5]
Is there a preferred mood stabilizer for mixed mania?
Divalproex[4] or carbamazepine[24] may be a treatment of choice, although some guidelines advocate lithium as being at least comparable to divalproex, based on current data[5]
When is ECT indicated in bipolar disorder?
For depressions with psychotic or suicidal features,[31] especially after nonresponse to a mood stabilizer and 2 antidepressant trials,[4] or for depressions unresponsive to trials of ≥ 2 mood stabilizers + 2 antidepressants[4]
For rapid response[12]
For pure or mixed manias unresponsive to prior mood stabilizers[4,11,24]
As a later intervention for rapid cycling with current depression unresponsive to other pharmacotherapies[4]
When are 2 or more mood stabilizers indicated?
As 2nd- or 3rd-line treatment for acute euphoric mania after nonresponse to a single agent mood stabilizer[4,11,12,15,24] or after nonresponse to 2 different mood stabilizers, including lithium[5]
In mixed states, as next step if unresponsive to divalproex[4] or carbamazepine[11] or only partially responsive to a single mood stabilizer[4]
As 2nd-line for rapid cycling if no response to single agent mood stabilizers[4,5,12]
As next intervention for bipolar depression if nonresponse to single agent mood stabilizer,[5] especially if a breakthrough episode while on lithium or divalproex monotherapy[4]
When should atypical antipsychotic medications be used in bipolar disorder?
For psychosis associated with mania or depression[5,12,15,24,31]
As an alternative 2nd-line monotherapy for rapid cycling (after divalproex, lithium, or carbamazepine), especially for manic phase[4]
During the first trimester of pregnancy[4] (conventional antipsychotics considered first line[4])
What is the role in bipolar disorder for newer anticonvulsants such as lamotrigine, gabapentin, and topiramate?
Lamotrigine is considered an acceptable 1st-line mood stabilizer for bipolar depression or as augmentation for lithium or divalproex during breakthrough depressions with or without rapid cycling[4]
Lamotrigine and gabapentin are both viewed as reasonable experimental options for acute mania after nonresponses to standard mood stabilizers, atypical antipsychotics, and/or electroconvulsive therapy[5,11]; in revised Expert Consensus Guidelines,[4] lamotrigine is not recommended as a later intervention for acute mania except among patients with rapid cycling
Topiramate and gabapentin are both considered appropriate later options after nonresponses to lithium, divalproex, and/or carbamazepine for acute mania with or without rapid cycling[4]
Topiramate is considered an acceptable 2nd-line augmentation to promote weight loss when necessary (after diet and exercise counseling)[4]

ment of Veterans Affairs [VA] Practice Guidelines[5] recommend avoiding antidepressants in mixed states), (4) contemplating the safety and efficacy of an antidepressant when used unopposed by a mood stabilizer in bipolar II depression (revised Expert Consensus Guidelines[4] recommend initial therapy with a mood stabilizer in all phases of bipolar illness).

On a broader level, Rush and colleagues[6] have noted that guidelines may facilitate clinical decision making, reduce clinically inappropriate or cost-inefficient variation in practice patterns, provide consistent treatment across different environments, individualize treatment, and increase cost-efficiency of treatment. They further acknowledge risks associated with the use of guidelines. These include the potential for recommendations to be formulated on the basis of insufficient evidence or biased opinions, increased costs and service utilization related to training clinicians, the possibility that guidelines could be misused to substitute for clinical judgment, and the reality that complex cases often defy generalization in their treatment.

Potential barriers to the adoption of guidelines, as noted by Gilbert et al.,[7] involve physicians' perceptions about guidelines (e.g., being "told" what to do) coupled with additional training and work related to implementing guidelines, the potential "static" nature of guidelines set against constant change and advancement in new treatments or applications, and the potential for patient nonadherence to guideline-directed treatment (although studies of depression treatment in primary care settings suggest that longer-term patient compliance with pharmacotherapy may be higher during guideline-based interventions than with treatment as usual[8]).

Eddy[9] distinguished treatment *standards* from *guidelines* and *options*. *Standards* reflect recommendations that apply in nearly all instances and almost always result in the best possible outcome. In contrast, *guidelines* describe treatment interventions that produce the best outcome most of the time, but not in almost all instances. *Options* refer to multiple treatment alternatives that produce similar outcomes, but lack evidence that one is clearly superior to another. The importance of these distinctions becomes apparent when one considers the potential for misuse of treatment guidelines in legal or administrative settings should they be misconstrued as defining the standard of care within the field or the limits of reimbursable care in specific clinical situations.

Clinicians often must extrapolate from published studies when adapting their findings to ordinary practice conditions. For example, randomized clinical drug trials typically exclude patients with comorbid substance abuse, yet in community-based samples, 60% or more of bipolar patients have histories of a substance use disorder.[10] Reported outcomes for special subpopulations (e.g., bipolar patients with mixed mania or rapid cycling) sometimes derive from post hoc analyses of previously collected data sets, rather than the a priori randomization of unique patient groups to different treatment arms. Treatment studies also vary in the adequacy of statistical power and sample sizes and the inclusion of concomitant pharmacotherapies or psychosocial treatments. Individual treatment studies must further be contextualized by the scarcity of published negative results from clinical trials and the dearth of well-designed polypharmacotherapy trials in bipolar illness. Guidelines generally attempt to account for constraints such as these in their efforts to assimilate formal recommendations, although they may offer only a starting point for highly idiosyncratic clinical situations.

EXISTING PRACTICE GUIDELINES

Several published guidelines or algorithms have gained particular attention for their breadth and scope, the endorsement of major organizations (e.g., the American Psychiatric Association [APA]), their applicability to critical patient populations (e.g., individuals seen in the VA), or their implementation in empirical treatment studies (e.g., the Texas Medication Algorithm Project [TMAP][6,7,11]). The rationale and development of these guidelines may be summarized as follows:

- *The Practice Guideline for the Treatment of Patients With Bipolar Disorder*[12] was developed by the APA in 1994. As described by Zarin et al.,[13] the initial draft for this document was created by an expert work group, combined with a literature review and subsequent review by 120 individuals and 40 organizations.
- In 1996, *The Expert Consensus Guideline Series*[14] reported the aggregate opinions from survey results among 68 identified experts in the treatment of bipolar illness in response to specific clinical situations. A revision of these guidelines, involving a different expert cohort of 65 clinical investigators, was recently published.[4]
- The *Clinical Practice Guidelines for Bipolar Disorder From the Department of Veterans Affairs*[5] was developed by an initial literature review, followed by consumer input via focus groups. A 14-member work group summarized the initial recommendations, which were then critiqued by 10 non-VA experts along with input from other experts and general practitioners. Specific recommendations are annotated by supporting literature.
- The Texas Medication Algorithm Project[6,7,11] involved a Rand-style survey of academicians and clinicians, followed by a consensus conference that led to the formulation of a multistep algorithm, subsequently implemented at 16 sites.
- The Canadian Network for Mood and Anxiety Treatments (CANMAT)[15] was developed by a group of clinicians and clinical researchers from across Canada and methodologically incorporated a large-scale literature review and classification of the quality of existing evidence. Initial algorithm recommendations were reviewed by 206 psychiatrists and 91 family practitioners, with further critique by additional clinicians in both Canada and the United States.

Since the introduction of treatment guidelines, both within psychiatry and elsewhere in medicine, questions remain about how their availability affects clinicians' actual practice patterns. What factors affect clinician adherence to guidelines, and how do patients treated according to guideline recommendations differ in their treatment outcomes from those who receive treatment as usual?

Regarding clinicians' reactions to practice guidelines, Cabana et al.[16] identified several potential barriers to the use of practice guidelines for primary care medicine. Over half of physician survey respondents cited a number of obstacles to guideline use, including a lack of awareness of guidelines, a lack of familiarity with their use, and disagreement with guideline recommendations. Less frequently cited potential obstacles to guideline use included a lack of physician self-efficacy, lack of outcome expectancy, and external factors (e.g., guidelines perceived as inconvenient, cumbersome, or confusing). Extensive data on the outcome of patients treated by guideline recommendations versus treatment as usual are not yet available, although as noted previously, antidepressant pharmacotherapy compliance was found to be higher when guideline-based approaches for depression were used in primary care medical settings.[8] In addition, an open trial[17] of guideline-based treatment for severely and persistently mentally ill bipolar outpatients found that at least a 30% improvement from baseline levels of psychopathology was evident after 4 months in over half of patients.

SPECIFIC CLINICAL SITUATIONS

Acute Mania

As summarized in Table 2, first-line interventions for acute mania in most current practice guidelines involve the use of a mood stabilizer as monotherapy, typically either lithium or divalproex sodium. Guidelines vary in their elaboration of additional points for management consider-

Table 2. Treatments for Acute Euphoric/Classic Mania Across Practice Guidelines[a]

Guideline	1st-Line Treatment	Next Interventions	Later Interventions
APA	Lithium, divalproex, or carbamazepine; ECT for rapid response	If no response by 2–3 weeks, add 2nd mood stabilizer; ECT; adjunctive benzodiazepines or neuroleptics if needed	
Expert Consensus[4]	Lithium or divalproex	Benzodiazepine; atypical neuroleptic; divalproex + lithium; change atypical neuroleptic; lithium + divalproex + carbamazepine	ECT; gabapentin; topiramate
VA	Lithium; discontinue antidepressants; benzodiazepine for insomnia/agitation; neuroleptic if psychotic	If no response by 3 weeks, change mood stabilizers; combine 2 mood stabilizers if partial response	Consider clozapine, lamotrigine, gabapentin
TMAP	Divalproex or lithium	Anticonvulsant + lithium; different anticonvulsant plus lithium; divalproex + carbamazepine; atypical neuroleptic + mood stabilizer	ECT; lamotrigine; gabapentin
CANMAT	Lithium or divalproex; ECT for severe behavior disturbance; add neuroleptic ± benzodiazepine if psychotic; add benzodiazepine ± neuroleptic for marked behavior disturbance	2 mood stabilizers or switch to different mood stabilizer if partial or nonresponse	Add carbamazepine to lithium or divalproex if no response; reconsider ECT; add lamotrigine, gabapentin, risperidone, or calcium channel blocker; consider clozapine

[a]Abbreviations: APA = American Psychiatric Association Practice Guideline for the Treatment of Patients With Bipolar Disorder,[12] CANMAT = Canadian Network for Mood and Anxiety Treatments,[15,24] ECT = electroconvulsive therapy, TMAP = Texas Medication Algorithm Project,[6,7,11] VA = Department of Veterans Affairs.[5]

ation. For example, when a rapid response is crucial, some guidelines favor the use of divalproex[14] or electroconvulsive therapy (ECT).[12] VA practice guidelines[5] emphasize the elimination of antidepressants in the management of acute mania.

Despite the broadening use of polypharmacology regimens for both the acute and long-term treatment of bipolar disorder,[18] existing guidelines generally regard mood-stabilizer monotherapy as an optimal initial strategy, although they vary about whether to augment with a second mood stabilizer, if necessary, as a next step[4,12,14] or to switch to a different mood stabilizer altogether if no response occurs.[4,5] In the TMAP,[11] sequential approaches to nonresponse are described in which dual therapy with lithium plus an anticonvulsant mood stabilizer is recommended after nonresponse to monotherapy with either agent, followed by dual anticonvulsants, the introduction of atypical neuroleptics, then ECT, then more experimental agents (e.g., lamotrigine, gabapentin). At present, antipsychotic medications (either conventional or atypical) are not recommended as first-line monotherapies or adjunctive agents to treat euphoric mania, unless psychosis clearly is present[4] or management of behavioral agitation is needed.[24] However, a newly emerging database on the efficacy of atypical antipsychotics such as olanzapine as monotherapy for acute mania[19] may prompt the reassessment of their role in future guidelines. Similarly, the adjunctive use of benzodiazepines for agitation is usually described as appropriate augmentation if and when clinically necessary.

In several guidelines, mixed states or dysphoric manias have been accorded separate commentary from euphoric manias, largely in the context of a literature that describes a differential treatment response to anticonvulsant mood stabilizers such as divalproex[20,21] or carbamazepine[22] as compared with lithium, as well as a different course of illness and longer time to recovery in mixed versus pure mania.[23] As outlined in Table 3, some guidelines embrace this literature by recommending divalproex[4,14] and/or carbamazepine[11,24] as the initial treatment of choice for dysphoric mania, while others regard existing data as more provisional and recommend lithium as the first-line treatment for both pure and mixed manias.[5]

Evidence-based information about continuation therapy and long-term prophylaxis in bipolar disorder is not extensive. As described in Table 4, most guidelines advocate the long-term or indefinite use of a mood stabilizer for all bipolar I patients who have had 2 or more manias or 1 "severe" mania, especially those with a family history of bipolar disorder.[4,11,15,25]

Bipolar Depression

Controversy persists regarding the use of antidepressants in patients with bipolar disorder on the basis of literature which suggests that antidepressants may induce manias in at least one third of bipolar patients[26,27] and may hasten cycle accelerations via a kindling mechanism in approximately one quarter of bipolar patients who develop rapid cycling.[27] At the same time, some of the literature supports the safety and efficacy of standard antidepressants as monotherapies for depression in patients with bipolar II disorder, including fluoxetine[28] and venlafaxine.[29] Few empirical data substantiate recommendations about the relative merits of treating bipolar depression with mul-

Table 3. Treatments for Mixed/Dysphoric Mania Across Practice Guidelines[a]

Guideline	1st-Line Treatment	Next Interventions	Later Interventions
APA	Same as for pure mania; discontinue antidepressants	Same as for pure mania	
Expert Consensus[4]	Divalproex[b]	Same as for pure mania	
VA	Lithium; discontinue antidepressants	Same as for pure mania	
TMAP	Divalproex or carbamazepine	Carbamazepine + lithium or divalproex + lithium; divalproex + carbamazepine	Add atypical neuroleptic; consider ECT; lamotrigine; gabapentin
CANMAT	Divalproex or carbamazepine; + neuroleptic if mood-incongruent psychosis; ± benzodiazepine for behavior disturbance	2 mood stabilizers or switch to different mood stabilizer if partial or nonresponse	Add carbamazepine to lithium or divalproex if no response; consider ECT; add lamotrigine, gabapentin, risperidone, or calcium channel blocker; consider clozapine

[a]Abbreviations are explained in the first footnote to Table 2.
[b]Divalproex considered treatment of choice.

Table 4. Continuation and Maintenance Treatment Across Practice Guidelines[a]

Guideline	1st-Line Treatment	Next Interventions	Additional Comments
APA	Lithium	Divalproex or carbamazepine	Longevity of treatment based on "individual risks/benefits"
Expert Consensus[4]	Lithium and divalproex	Carbamazepine: 2nd line	Lifetime prophylaxis after 2 episodes of mania or 1 episode of severe mania; bipolar II after 3 episodes of hypomania or antidepressant-induced mania
VA	Preferred agents and duration of prophylaxis not specified		Taper neuroleptics or benzodiazepines; psychosocial rehabilitation emphasized
TMAP	No specific agent(s) preferred		Prophylaxis after 2 episodes of mania or 1 episode of mania with positive family history; use lowest doses to achieve therapeutic blood levels, taper adjunctive medications
CANMAT	Maintain mood stabilizer at optimal levels, taper off benzodiazepine ± neuroleptics once asymptomatic for 2–3 weeks; taper after 6–12 weeks of euthymia		Indefinite prophylaxis if history of recurrent episodes, especially if severe or with positive family history of bipolar disorder; after a single episode of low severity, may taper off pharmacotherapy after 6–12 months over a 1–3 month period, and monitor annually

[a]Abbreviations are explained in the first footnote to Table 2.

tiple mood stabilizers versus a single mood stabilizer plus an antidepressant, although a recent report[30] suggested a superior response to lithium or valproate plus paroxetine as compared with lithium plus valproate. Unlike the case for unipolar depression, sequential trials of antidepressants are shunned by some guidelines[31] after nonresponse to an initial antidepressant, in favor of other serial interventions (Table 5). Data also are scant regarding the optimal duration of antidepressant use after the remission of depressive symptoms, although some guidelines[4,25] advise tapering off antidepressants as soon as 6 to 12 weeks after remission.

Despite these limitations, most treatment guidelines advocate the use of a mood stabilizer at optimal doses as a first-line intervention for the treatment of pure depressed phases of bipolar disorder. Lithium is ranked as a first choice in some guidelines,[5,12,31] with combinations of mood stabilizers and/or the addition of antidepressants reserved for nonresponders after several weeks.[5,12] The simultaneous initiation of a mood stabilizer and an antidepressant is described as an appropriate first step in the TMAP.[11] The CANMAT guidelines[31] propose rapid consideration of ECT in the presence of either suicidality or psychosis.

Specific Antidepressants

The introduction of antidepressants is generally advised after nonresponse to one (or more[5]) mood stabilizers. Reflecting the small database of clinical trials using standard antidepressants for bipolar depression, guidelines that recommend particular antidepressants tend to favor bupropion or selective serotonin reuptake inhibitors (SSRIs; especially paroxetine, studied in one double-blind trial[32]) as first-line agents.[4,11] In the revised Expert Con-

Table 5. Treatment of Bipolar Depression Across Guidelines[a]

Guideline	1st-Line Treatment	Next Interventions
APA	Begin and optimize mood stabilizer (lithium preferred)	Add specific psychotherapy and/or antidepressant
Expert Consensus[4]	Begin and optimize mood stabilizer	
VA	Begin and optimize mood stabilizer (lithium 1st choice)	Add divalproex or carbamazepine to lithium if no response after 2–4 weeks; then, conservative use of antidepressants at "lowest doses for shortest possible times" (no specific agents preferred); ECT if no response
TMAP	Mood stabilizer plus antidepressant (SSRI or bupropion preferred)	Switch antidepressants (SSRI > bupropion or vice-versa; nefazodone; venlafaxine); then 2 antidepressants + mood stabilizer; then MAOI + mood stabilizer; then ECT; then experimental agents (eg, lamotrigine)
CANMAT	Begin and optimize mood stabilizer; ECT if marked suicidality or psychosis	CBT or IPT if mild severity; 2 mood stabilizers or mood stabilizer + antidepressant; neuroleptic if psychotic; if nonresponse: 3 mood stabilizers or clozapine, ECT, or novel treatments

[a]Abbreviations: CBT = cognitive-behavioral therapy, IPT = interpersonal psychotherapy, MAOI = monoamine oxidase inhibitor, SSRI = selective serotonin reuptake inhibitor. Additional abbreviations are explained in the first footnote to Table 2.

sensus Guideline,[4] first-line treatments for melancholic depressions included venlafaxine, bupropion, or paroxetine, followed by other SSRIs (sertraline, citalopram, and fluoxetine). In the presence of atypical depressive features, bupropion was ranked as a leading first-line treatment, followed by paroxetine, sertraline, venlafaxine, and citalopram. Bupropion was considered the antidepressant of first choice for moderate depression, followed by paroxetine, sertraline, citalopram, fluoxetine, and venlafaxine. Other guidelines list a range of appropriate antidepressant classes for bipolar depression, broadly including SSRIs, serotonergic-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and bupropion.[31] Many recommend avoiding tricyclic antidepressants (TCAs) because of the reported increased risk for inductions of mania and cycle acceleration.[26,27]

Rapid Cycling

Originally defined by Dunner and Fieve[33] as a robust predictor of the failure of lithium prophylaxis, rapid cycling has been associated with a potentially better relative response to divalproex and possibly other anticonvulsant mood stabilizers such as lamotrigine.[34] These observations are reflected by guidelines that recommend divalproex as a mood stabilizer of choice for rapid cycling in any given phase.[4,24] Nonetheless, some guidelines question the reputed differences in treatment outcome between lithium and anticonvulsant mood stabilizers on the basis of the limited data available and recommend either as an appropriate mood stabilizer in patients with rapid cycling.[5] Subsequent treatment recommendations for partial or nonresponses generally involve adding additional mood stabilizers or atypical antipsychotics,[4] followed by ECT or more experimental treatments if necessary (e.g., lamotrigine, gabapentin, calcium channel blockers, thyroid hormone).[24] Some guidelines also focus less on the specific choice of mood stabilizer(s) for rapid cycling than on other aspects of treatment, such as optimization of thyroid function[12] and/or the elimination of antidepressant medications whenever possible.[5]

Reflecting recent literature on bipolar depression and on rapid cycling,[34,35] revised Expert Consensus Guidelines[4] recommend lamotrigine as a first-line option for current depression in patients with rapid cycling. Atypical antipsychotics are described as a second-line alternative monotherapy.

SUMMARY

In summary, most currently published guidelines recommend using a single mood stabilizer as a first step for acute mania; combinations of mood stabilizers are described as appropriate second steps. In mixed states, several guidelines favor divalproex or carbamazepine as first-line mood stabilizers, although others advise using lithium no less often than anticonvulsants. Many urge discontinuing antidepressants in both pure manias and mixed states. Bipolar depression should initially be treated with an optimally dosed mood stabilizer, but guidelines vary in their subsequent recommendations: an antidepressant plus a mood stabilizer is often described as a desirable option. Atypical neuroleptics are widely favored over conventional neuroleptics, although their role currently remains uncertain beyond the treatment of psychosis during mania or depression, as second-line agents for rapid cycling, or in affective episodes unresponsive to standard mood stabilizers. During long-term maintenance treatment, most guidelines favor the simplification of drug regimens and lithium monotherapy as a first choice for lifetime prophylaxis.

Drug names: bupropion (Wellbutrin), carbamazepine (Tegretol and others), citalopram (Celexa), clozapine (Clozaril and others), divalproex sodium (Depakote), fluoxetine (Prozac), gabapentin (Neurontin), lamotrigine (Lamictal), nefazodone (Serzone), olanzapine (Zyprexa), paroxetine (Paxil), risperidone (Risperdal), sertraline (Zoloft), topiramate (Topamax), venlafaxine (Effexor).

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