When is lamotrigine a good choice?

Michael Casher, MD, Jolene Bostwick, PharmD, BCPS, BCPP, and Louis Feurino III, MD

Lamotrigine does not appear to increase risk of hypomania or mania in bipolar patients and is well tolerated

FDA-approved for maintenance treatment of bipolar I disorder, lamotrigine is more effective than lithium for preventing depressive relapses. Lamotrigine combined with lithium, carbamazepine, or valproate provides good protection against recurrences of mania and depression.

Unlike selective serotonin reuptake inhibitors and other antidepressants, lamotrigine does not appear to increase risk of hypomania or mania in bipolar patients.[1] Unlike valproate and lithium, it is weight-neutral and requires no serum level monitoring.[2] Although lamotrigine's slow titration and prolonged period until reaching therapeutic effect limits its efficacy as monotherapy in an inpatient setting, the drug can be initiated along with quicker acting agents in the hospital and then titrated after discharge. This strategy allows close monitoring during initial exposure.

Consider lamotrigine as an adjunct for treatment-resistant major depression.[3] It is useful for treating aggression and agitation in patients with traumatic brain injury[4] or dementia.[5] Borderline personality disorder patients treated with lamotrigine may show less affective lability, impulsivity, or aggression.[6,7] Lamotrigine can act synergistically with clozapine in some patients with refractory schizophrenia.[8]

Metabolism and drug interactions

Lamotrigine is metabolized via glucuronidation and eliminated renally. Other drugs metabolized by glucuronidation could interact with lamotrigine ***(Table)***.[9]

Table

Drug interactions associated with lamotrigine

Interacting drug	Effect on lamotrigine	Management
Carbamazepine Phenytoin Phenobarbital Primidone Rifampin	Increased clearance	Double dose of lamotrigine when used concomitantly
Oral contraceptives containing estrogen	Increased clearance	Lamotrigine dose may need to be increased. Efficacy of oral contraceptives may be decreased; dose modification of oral contraceptive also may be required
Valproic acid	Decreased clearance	Reduce dose by at least half, even if your patient is on a medication with the potential to increase clearance

Source: Reference 9

Adverse reactions

Lamotrigine is well tolerated chronically, with fewer adverse effects than other mood stabilizers. Serious rashes, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported in 0.08% to 0.13% of patients treated with

Dr. Casher is clinical assistant professor and director, adult inpatient psychiatry program, Dr. Bostwick is clinical assistant professor of pharmacy, and Dr. Feurino is psychiatry resident, University of Michigan, Ann Arbor, MI.

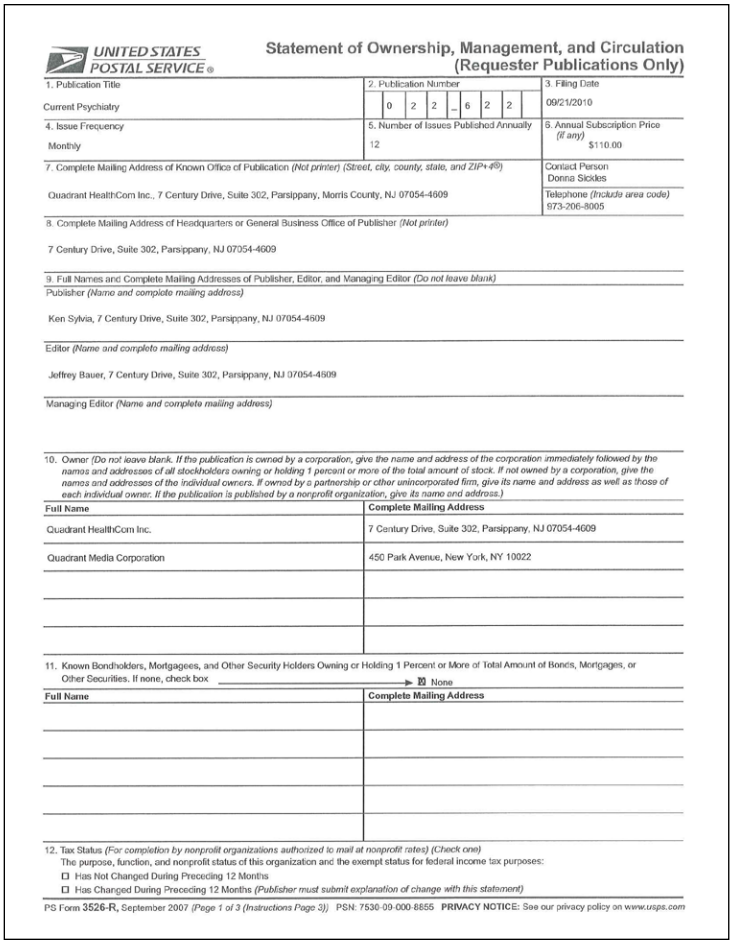
lamotrigine for bipolar disorder or other mood disorders.[9] The risk of developing a skin rash within 2 to 8 weeks of therapy necessitates starting with a low dose, usually 25 mg/d, and gradually titrating.[2,9]

The FDA added a warning about increased risk of suicidality to the labeling of all anticonvulsants, regardless of indication.[10] In a meta-analysis of 199 trials, for every 530 patients treated with anticonvulsants there was 1 additional case of suicidality—not completed suicide.[10] Inform patients and their families about the potential risk for increased suicidality and document this discussion of risk vs benefit. All patients should be monitored for worsening depression or suicidal thoughts or behavior throughout treatment.

Other potential side effects occurring in at least 5% of patients receiving lamotrigine include somnolence, headache, rash, and the dose-related side effects of nausea, vomiting, dizziness, ataxia, blurred vision, and diplopia.[9]

References

1. Bowden CL. Lamotrigine in the treatment of bipolar disorder. Expert Opin Pharmacother. 2002;3(10):1513-1519.
2. Goldsmith DR, Wagstaff AJ, Ibbotson T, et al. Lamotrigine: a review of its use in bipolar disorder. Drugs. 2003;63(19):2029-2050.
3. Gabriel A. Lamotrigine adjunctive treatment in resistant unipolar depression: an open descriptive study. Depress Anxiety. 2006;23:485-488.
4. Pachet A, Friesen S, Winkelaar D, et al. Beneficial behavioural effects of lamotrigine in traumatic brain injury. Brain Inj. 2003;17(8):715-722.
5. Sajatovic M, Ramsay E, Nanry K, et al. Lamotrigine therapy in elderly patients with epilepsy, bipolar disorder or dementia. Int J Geriatr Psychiatry. 2007;22:945-950.
6. Pinto OC, Akiskal HS. Lamotrigine as a promising approach to borderline personality: an open case series without concurrent DSM-IV major mood disorder. J Affect Disord. 1998;51:333-343.
7. Bellino S, Paradiso E, Bogetto F. Efficacy and tolerability of pharmacotherapies for borderline personality disorder. CNS Drugs. 2008;22(8):671-692.
8. Dursun SM, Deakin JF. Augmenting antipsychotic treatment with lamotrigine or topiramate in patients with treatment-resistant schizophrenia: a naturalistic case-series outcome study. J Psychopharmacol. 2001;15:297-301.
9. Lamictal [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2007.
10. Food and Drug Administration. Statistical review and evaluation: antiepileptic drugs and suicidality. Available at: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugsSafetyInformationforpatientsand%20providers/ucm192556.pdf. Accessed August 23, 2010.



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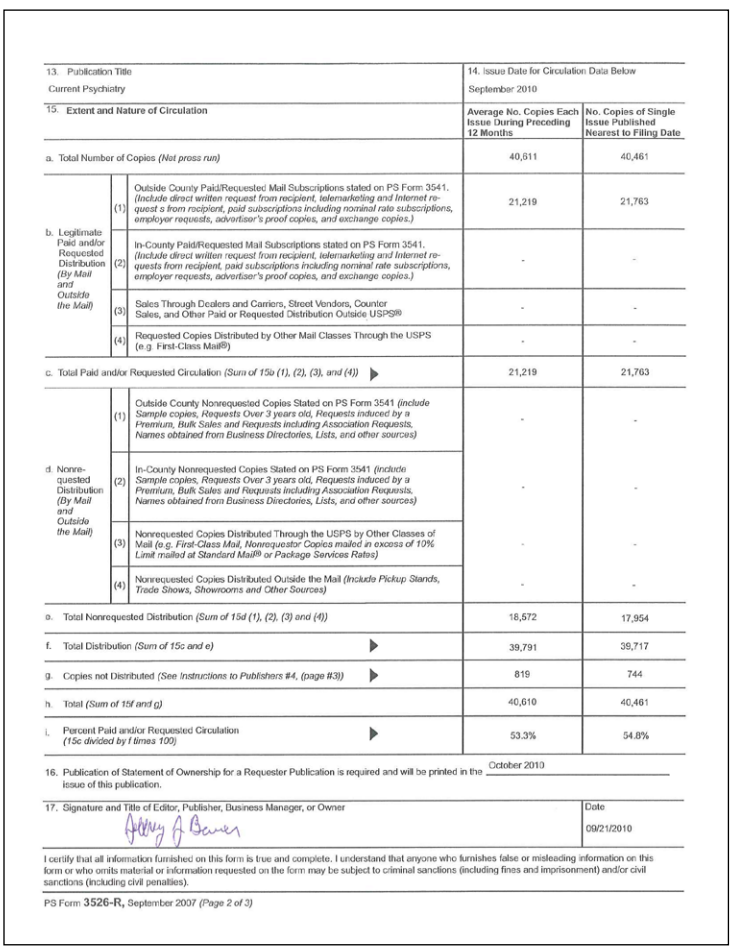

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