

FDA APPROVED MEDICATIONS FOR THE TREATMENT OF BIPOLAR MOOD DISORDERS IN ADULTS+**

Antiepileptic Drugs:

Drug Generic Name	Brand Name(s)	Doses Per Day	Daily Dosage Range	Serum Drug Level Monitoring	Additional Monitoring Recommended±	Pregnancy Category++	Potential Side Effects^{1,§}
Lamotrigine	Lamictal® ²	1	25 mg/day initially, titrated up to 200mg/day Dosing in the elderly should start at the low end of the dose range and consider concomitant diseases and hepatic and renal function	No	None	C	<p><u>Possible Side Effects</u> Back pain, fatigue, abdominal pain, nausea, constipation, vomiting, insomnia, somnolence, rhinitis, dry mouth, exacerbation of cough, pharyngitis, rash (nonserious), headache, infection, xerostomia, blurred vision, dizziness, double vision, insomnia, rhinorrhea, sleepiness, sore throat, and uncoordinated movements.</p> <p><u>Common and Serious Side Effects</u> Rash, including Stevens-Johnson syndrome and toxic epidermal necrolysis</p>
Valproic Acid/ valproate/ divalproex	Depakote® Depakene® Depakote ER® ³	3 1	750-1500mg 25-60 mg/kg/day 20-60mg/kg/day	Yes	LFTs, bilirubin, CBC with platelets, coagulation test	D	<p><u>Possible Side Effects</u> Gastrointestinal distress (e.g., anorexia, nausea, dyspepsia, vomiting, diarrhea), benign hepatic transaminase elevations, osteoporosis, tremor, sedation, abnormal thinking, breathing difficulty, bronchitis, bruising, depression, dizziness, emotional changeability, fever, flu symptoms, hair loss, headache, incoordination, infection, insomnia, loss of appetite, memory loss, nasal inflammation, nervousness, ringing in the ears, sleepiness, sore throat, vision problems, weakness, and weight loss or gain.</p> <p><u>Other Side Effects Specific to Depakot ER</u> Somnolence, asthenia, abdominal pain, rash, increased appetite, back pain, alopecia, anorexia, constipation, diplopia, ambylopia/blurred, ataxia, nystagmus, emotional lability, amnesia, infection, rhinitis, ecchymosis, peripheral edema, pharyngitis, dyspnea, tinnitus</p> <p><u>Rare, But Serious Side Effects</u> Hepatic failure, hemorrhagic, pancreatitis, and agranulocytosis.</p> <p><u>Toxicity/Overdose:</u> may result in somnolence, heart block, and deep coma. Fatalities have been reported; however patients have recovered from valproate levels as high as 2120 mcg/mL</p>

Drug Generic Name	Brand Name(s)	Doses Per Day	Daily Dosage Range	Serum Drug Level Monitoring	Additional Monitoring Recommended±	Pregnancy Category++	Potential Side Effects ^{1, §}
Carbamazepine	Tegretol® Tegretol XR® ⁴ Equetro™ ⁵	2-4	800-1200mg, adjust in 200mg increments. Max: 1600mg/day	Yes	CBC with platelets, reticulocytes, iron, LFTs, urinalysis, BUN, TFTs, sodium, cholesterol, eye exams <u>NOTE:</u> May be sufficient to monitor only clinical symptoms in many patients, but monitoring these laboratory tests may be useful in patients who cannot reliably report symptoms	D	<u>Possible Side Effects</u> Neurological symptoms (e.g., diplopia, blurred vision, fatigue, nausea, ataxia), dizziness, rash, weight gain, drowsiness, unsteadiness, nausea and vomiting., pruritis, dry mouth, speech disorder <u>Rare, But Serious Side Effects</u> Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), Agranulocytosis, aplastic anemia, thrombocytopenia, hepatic failure, exfoliative dermatitis, and pancreatitis (patients of Asian ancestry should be genetically tested due to increased risk of developing TEN/SJS [†]). <u>Toxicity/Overdose</u> Yes, can be fatal in overdose
Gabapentin	Neurontin® ⁶				Not approved for use in Bipolar Mood Disorders		
Topiramate	Topamax® ⁷				Not approved for use in Bipolar Mood Disorders		

†The FDA recommends that patients, particularly of Asian ancestry, be genetically tested for a specific allele of human leukocyte antigen B (HLA-B*1502) prior to starting a carbamazepine treatment regimen. HLA-B*1502 is found primarily in Asian populations, including India and South Asia. Patients carrying the HLA-B*1502 allele have increased risk of developing SJS/TEN shortly after beginning treatment.

Lithium carbonate:

Drug Generic Name	Brand Name(s)	Doses Per Day	Daily Dosage Range	Serum Drug Level Monitoring	Additional Monitoring Recommended±	Pregnancy Category++	Potential Side Effects ^{1, §}
Lithium	Lithobid® ER ⁸ Eskalith® Eskalith-CR® ⁹	2-4	900-1800mg Elderly: start with a lower dose	Yes (q 2 mos)	BUN/creatinine, TFTs, calcium, EKG	D	<u>Possible Side Effects</u> Polyuria, polydipsia, weight gain, cognitive problems (e.g., dulling, impaired memory, poor concentration, confusion, mental slowness) tremor, sedation, impaired coordination, gastrointestinal distress (e.g., nausea, vomiting, dyspepsia, diarrhea), hair loss, benign leukocytosis, acne, edema, discomfort, and muscle weakness. <u>Toxicity/Overdose</u> Likely as serum level rises

Atypical Antipsychotics:

Drug Generic Name	Brand Name(s)	Doses/Day	Daily Dosage Range	Serum Drug Level Monitoring	Additional Monitoring Recommended [±]	Pregnancy Category ⁺⁺	Potential Side Effects ^{1, §}
Aripiprazole	Abilify® ¹⁰	1	15-30 mg once daily 30 mg Elderly: No dosage adjustment recommended	No	No	C	<u>Common Side Effects:</u> Nausea, constipation, akathisia, sedation, tremor, restlessness, and extrapyramidal disorder <u>Serious Side Effects:</u> Suicidal thinking and behavior, Neuroleptic Malignant Syndrome (NMS), Tardive Dyskinesia, Hyperglycemia and Diabetes Mellitus, Orthostatic Hypotension, Seizures/Convulsions, body temperature regulation, dysphagia
Olanzapine	Zyprexa® ¹¹	1	Initial monotherapy: 10-15 mg once daily Short-term anti-manic, 5-20 mg/d Maintenance monotherapy: 5-20 mg/d Elderly: lower starting dose	No	ALT (SGPT) in pts w/ severe hepatic impairment, weight	C	<u>Common Side Effects:</u> Asthenia, dry mouth, constipation, dyspepsia, increased appetite, somnolence, dizziness, tremor <u>Serious Side Effects:</u> Suicidal thinking and behavior, hyperglycemia, hyperlipidemia, weight gain, Neuroleptic Malignant Syndrome (NMS), Tardive Dyskinesia
Quetiapine	Seroquel® ^{12,13 **}	1 for depression; 2 for mania	Bipolar Depression: Initial: 50mg, increase to 300 mg at bedtime Max: 600 mg/d Bipolar Mania: Initial: 100 mg, increase to 400 mg/d Max: 800 mg/d Elderly: slower rate of dose titration and lower total dose , starting at 25 mg/d	No	CBC in pts w/ low WBC or neutropenia/leukopenia	C	<u>Common Side Effects:</u> Somnolence, dizziness, dry mouth, constipation, weight gain, dyspepsia, SGPT increased, asthenia, abdominal pain, postural hypotension, pharyngitis, lethargy, nasal congestion, sedation <u>Serious Side Effects:</u> Suicidal thinking and behavior, Neuroleptic Malignant Syndrome (NMS), Tardive Dyskinesia, Hyperglycemia and Diabetes Mellitus

Drug Generic Name	Brand Name(s)	Doses/Day	Daily Dosage Range	Serum Drug Level Monitoring	Additional Monitoring Recommended±	Pregnancy Category++	Potential Side Effects ^{L, §}
Risperidone	Risperdal® ¹⁴	1	Bipolar Mania: Initial: 2-3 mg once daily Short-term anti-manic: 1-6 mg/d Max: 6 mg/d Elderly: Lower initial dose (0.5 mg twice daily), followed by increases in dose in increments of no more than 0.5 mg twice daily. Increases to dosages above 1.5 mg twice daily should occur at intervals of at least 1 week	No	No	C	<i>Common Side Effects:</i> Somnolence, increased appetite, fatigue, rhinitis, upper respiratory tract infection, vomiting, coughing, urinary incontinence, saliva increased, constipation, fever, Parkinsonism, dystonia, abdominal pain, anxiety, nausea, dizziness, dry mouth, tremor, rash, akathisia, and dyspepsia <i>Serious Side Effects:</i> Suicidal thinking and behavior, Neuroleptic Malignant Syndrome, Tardive dyskinesia, Hyperglycemia and diabetes mellitus, Hyperprolactinemia, Orthostatic hypotension, Seizures, Dysphagia, Priapism, Disruption of body temperature regulation
Ziprasidone	Geodon® ¹⁵	2	Bipolar Mania: Initial:80-160 mg/d (BID) Maintenance: no data beyond three weeks Max: 160 mg/d (BID) Elderly: Lower starting dose, slower titration recommended	No	Potassium and magnesium in pts on diuretics	C	<i>Common Side Effects:</i> Somnolence, extrapyramidal symptoms, dizziness, akathisia, abnormal vision, asthenia, vomiting <i>Serious Side Effects:</i> Suicidal thinking and behavior, QT Prolongation and Risk of Sudden Death, Neuroleptic Malignant Syndrome, Tardive dyskinesia, Hyperglycemia and diabetes mellitus

* Please note that these charts include information regarding utilization of selected drugs in the treatment of bipolar disorder. There are additional effective pharmacological treatments and psychosocial interventions; however, they are outside the purview of this project. For information regarding additional treatment options, please refer to Hirshfeld, R.M.A et al. (2002). *Practice guideline for the treatment of patients with bipolar disorder, 2nd Edition*, American Psychiatric Association and Hirshfeld, R.M.A. (2005). *Guideline Watch: Practice guideline for the treatment of patients with bipolar disorder, 2nd Edition*, American Psychiatric Association. Both are available at: http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm

+ Drug-drug interactions are an important concern in all cases where patients are taking more than one medication. It is advisable to consult expert opinion in such cases.

± **BUN:** blood urea nitrogen; **CBC:** complete blood count; **ECG:** electrocardiography; **LFT:** liver function tests; **TFTs:** thyroid function tests

§ Common side effects reported are from each product's prescribing information and are those that were most frequently reported in clinical trials (at least 5% and twice that of placebo). This list is not all inclusive and one should refer to the prescribing information for the complete listing. Serious side effects are those listed in the Contraindications or Warnings sections of each product's prescribing information. Note: FDA black box warning - Conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis (http://www.fda.gov/CDER/drug/InfoSheets/HCP/antipsychotics_conventional.htm).

** Seroquel® XR formulation is not indicated for bipolar mood disorders

++ For more information about the use of these medications during lactation, please see American Academy of Pediatrics Committee on Drugs. The Transfer of Drugs and Other Chemicals into Human Milk. *Pediatrics*; 2001; 108(3), available from <http://www.aap.org/healthtopics/breastfeeding.cfm> and Hale, Thomas. *Medications and Mothers' Milk*, 12th Edition. Hale Publishing, 2006, <http://neonatal.ttuhscc.edu/lact/index.html>

¹ Hirshfeld, R.M.A et al. (2002). *Practice guideline for the treatment of patients with bipolar disorder, 2nd Edition*, American Psychiatric Association.

² Prescribing Information for Lamictal®, dated May 2007. Accessed April 10, 2008 at www.lamictal.com

³ Prescribing Information for Depakote ER®, dated March 2008. Accessed April 10, 2008 at www.fda.gov

⁴ Prescribing Information for Tegretol XR®, dated December 2007. Accessed April 10, 2008 at www.fda.gov

⁵ Prescribing Information for Equetro™, dated December 2007. Accessed April 10, 2008 at www.equetro.com

⁶ Prescribing Information for Neurontin®, dated January 2007. Accessed April 15, 2008 at www.pfizer.com

⁷ Prescribing Information for Topamax®, dated March 2007. Accessed April 15, 2008 at www.topamax.com

⁸ Prescribing Information for Lithobid® ER, dated January 2006. Accessed April 14, 2008 at www.lithobid.net

⁹ Prescribing Information for Eskalith® and Eskalith-CR®, dated September 2003. Accessed April 10, 2008 at www.fda.gov

¹⁰ Prescribing Information for Abilify®, dated February 2008. Accessed April 14, 2008 at www.abilify.com

¹¹ Prescribing Information for Zyprexa®, dated March 2008. Accessed April 14, 2008 at www.zyprexa.com

¹² Prescribing Information for Seroquel®, dated February 2008. Accessed April 14, 2008 at www.seroquel.com

¹³ Prescribing Information for Seroquel®, dated February 2008. Accessed April 14, 2008 at www.seroquel.com

¹⁴ Prescribing Information for Risperdal®, dated February 2008. Accessed April 14, 2008 at www.risperdal.com

¹⁵ Prescribing Information for Geodon®, dated March 2007. Accessed April 14, 2008 at www.geodon.com