

**SCORE**<sup>SM</sup>  
SOUTH CAROLINA OFFERING  
PRESCRIBING EXCELLENCE

**SC**  
SOUTH CAROLINA  
COLLEGE OF  
PHARMACY

## Evidence-Based Best Practices for the Treatment of Bipolar Disorder in South Carolina Primary Care

The SCORxE bipolar disorder algorithms offer providers balanced, evidence-based clinical information about drug therapy and best practices to assist with clinical management decisions.

### **A**ccurate and timely diagnosis is critical to optimize clinical outcomes.

- Many patients are initially misdiagnosed with major depression; screening for a history of mania/hypomania in patients presenting with depressive symptoms is crucial.
- Rating scales, such as the Mood Disorder Questionnaire (MDQ) for manic/hypomanic symptoms and the Patient Health Questionnaire (PHQ-9) for depressive symptoms, should be used together to improve diagnostic accuracy.
- Family and friends can help confirm the diagnosis and identify relapse symptoms.

### **R**eturn to full psychosocial functioning is the goal of treatment.

- The goal is complete symptom remission and prevention of symptom exacerbation.
- Tailor management strategies to an individual's particular relapse symptoms (e.g., sleep disturbances).
- Brief symptom ratings (e.g., mood chart) reviewed at every visit can help guide treatment.
- Ongoing assessment of suicidality and use of suicide prevention strategies are essential.

### **M**edication is the mainstay of treatment for initial mood stabilization and maintenance.

- Bipolar patients should receive continuous treatment with a mood stabilizer(s).
- Avoid antidepressant monotherapy; if necessary, use with a concomitant mood stabilizer to minimize the risk of affective switches.
- Emphasize patient adherence through intensive education, lifestyle management training, and cognitive behavioral therapy.

### **S**creen for substance abuse to increase the chance of clinical improvement.

- Concomitant treatment of bipolar disorder and coexisting substance abuse is critical.

University of South Carolina | Medical University of South Carolina

843-792-5915 | [www.sccp.sc.edu/SCORxE](http://www.sccp.sc.edu/SCORxE) | [SCORxE@sccp.sc.edu](mailto:SCORxE@sccp.sc.edu)

The information contained in this summary is intended to supplement the knowledge of clinicians regarding best practices and drug therapy to treat bipolar disorder in primary care patients ≥ 18 years. This information is advisory only and is not intended to replace sound clinical judgment, nor should it be regarded as a substitute for individualized diagnosis and treatment. Special considerations are needed when treating some populations such as the elderly, pregnant or breast-feeding women, and patients with certain medical conditions (e.g., cardiac disease, liver and renal impairment).

## Mood Disorder Questionnaire (MDQ)

Patient Name _____ Date of Visit _____		
<b>Please answer each question to the best of your ability.</b>	<b>Yes</b>	<b>No</b>
1. Has there ever been a period of time when you were not your usual self and ...		
... you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?		
... you were so irritable that you shouted at people or started fights or arguments?		
... you felt much more self-confident than usual?		
... you got much less sleep than usual and found that you didn't really miss it?		
... you were more talkative or spoke much faster than usual?		
... thoughts raced through your head or you couldn't slow your mind down?		
... you were so easily distracted by things around you that you had trouble concentrating or staying on track?		
... you had more energy than usual?		
... you were much more active or did many more things than usual?		
... you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?		
... you were much more interested in sex than usual?		
... you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?		
... spending money got you or your family in trouble?		
2. If you checked YES to <u>more than one</u> of the above, have several of these ever happened during the same period of time?		
3. How much of a problem did any of these cause you—like being unable to work; having family, money, or legal troubles; getting into arguments or fights? <input type="checkbox"/> No problems <input type="checkbox"/> Minor problem <input type="checkbox"/> Moderate problem <input type="checkbox"/> Serious problem		
4. Have any of your blood relatives (i.e., children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?		
5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?		

This instrument is designed for screening purposes only and not to be used as a diagnostic tool.  
© 2000 Dr. Robert M.A. Hirschfeld; licensed by Compact Clinicals, a Jones and Bartlett Company, Sudbury, MA 01776

### Scoring the MDQ

In order to screen positive for possible bipolar disorder, ALL 3 parts of the following criteria must be met:

1. YES to seven or more of the 13 items in question #1, **AND**
2. YES to question #2, **AND**
3. MODERATE or SERIOUS to question #3

## Oral Medication Dosing Guidelines in the Management of Bipolar Disorder (BPD)

Medication (i) [Brand Examples (ii)]	Starting Daily Dose	Target Daily Dose <i>Serum Level (iii)</i>	Maximum Daily Dose <i>Maximum Serum Level (iii)</i>	Recommended Administration
<b>Lithium and Anticonvulsants</b>				
<b>Carbamazepine</b> [Tegretol, Equetro]	200–600 mg/ day	400–1600 mg/day <i>Serum level: 4–12 mcg/mL</i>	1600 mg/day (iv) <i>Serum level: 12 mcg/mL</i>	BID or TID
<b>Divalproex Sodium (v)</b> [Depakote] <b>Valproic Acid (v)</b> [Depakene, Stavzor]	500–1000 mg/ day	750–2000 mg/day <i>Serum level: 50–150 mcg/mL</i>	60 mg/kg/day (iv) <i>Serum level: 150 mcg/mL</i>	BID or HS
<b>Lamotrigine (vi)</b> [Lamictal]	25 mg/day	200 mg/day	400 mg/day	1–2 times daily
<b>Lithium</b> [Eskalith, Lithobid]	300–900 mg/ day	900–2400 mg/day <i>Serum level:</i> <i>Acute mania: 1.0–1.2 mEq/L</i> <i>Depression: ≥ 0.8 mEq/L</i> <i>Maintenance: 0.8–1.0 or</i> <i>lower (0.6) mEq/L</i>	3600 mg/day (iv) <i>Serum level:</i> <i>Acute mania: 1.2–1.5 mEq/L</i> <i>Depression &amp; maintenance:</i> <i>1.0–1.2 mEq/L</i>	1–2 times daily
<b>Oxcarbazepine</b> [Trileptal]	600 mg/day	600–2100 mg/day	2400 mg/day	BID or TID
<b>First Generation Antipsychotics (FGAs)</b>				
<b>Chlorpromazine</b> [Thorazine]	300 mg/day	400–1000 mg/day	2000 mg/day	TID
<b>Fluphenazine</b> [Prolixin]	2.5 mg/day	2.5–20 mg/day	40 mg/day	TID
<b>Haloperidol</b> [Haldol]	2 mg/day	2–20 mg/day	40 mg/day	1–3 times daily
<b>Perphenazine</b> [Trilafon]	6–8 mg/day	24 mg/day	64 mg/day	TID
<b>Second Generation Antipsychotics (SGAs)</b>				
<b>Aripiprazole</b> [Abilify]	15 mg/day	15–30 mg/day	30 mg/day	AM or HS
<b>Olanzapine</b> [Zyprexa]	5–10mg/day	5–20 mg/day	20 mg/day	HS
<b>Olanzapine/fluoxetine</b> [Symbyax]	3/25–6/25 mg/ day	6/25–12/50 mg/day	12/50 mg/day	HS
<b>Paliperidone</b> [Invega]	3 mg/day	6–12 mg/day	12 mg/day	HS or AM
<b>Quetiapine</b> [Seroquel]	100 mg/day	300–800 mg/day (depression) 550–800 mg/day (mania)	800 mg/day	BID or HS
<b>Risperidone</b> [Risperdal]	1–2 mg/day	4–6 mg/day	8 mg/day (vii)	HS or AM
<b>Ziprasidone</b> [Geodon]	80 mg/day	80–160 mg/day	160 mg/day	AM or BID with food (viii)

(i) All agents are FDA approved for the treatment of mania except: lamotrigine, oxcarbazepine, fluphenazine, haloperidol, perphenazine, olanzapine/fluoxetine combination, and paliperidone. FDA approved agents for the treatment of mixed episodes are: carbamazepine, valproate, aripiprazole, olanzapine, risperidone, and ziprasidone. FDA approved agents for the treatment of bipolar depression are: olanzapine/fluoxetine combination and quetiapine. FDA approved agents for the maintenance treatment of BPD are: lamotrigine, lithium, aripiprazole, olanzapine, and quetiapine (as adjunctive therapy).

(ii) Not all brand name examples provided are FDA approved for the treatment of BPD. Many medications are available generically.

(iii) Therapeutic serum level monitoring should be drawn 12 hours after the last dose, except for Depakote ER which should be drawn 18 hours after the last dose or at trough prior to the next dose.

(iv) Maximum daily dosage should be based upon the serum level in the individual patient in the context of clinical response and tolerability.

(v) Commonly referred to as valproate.

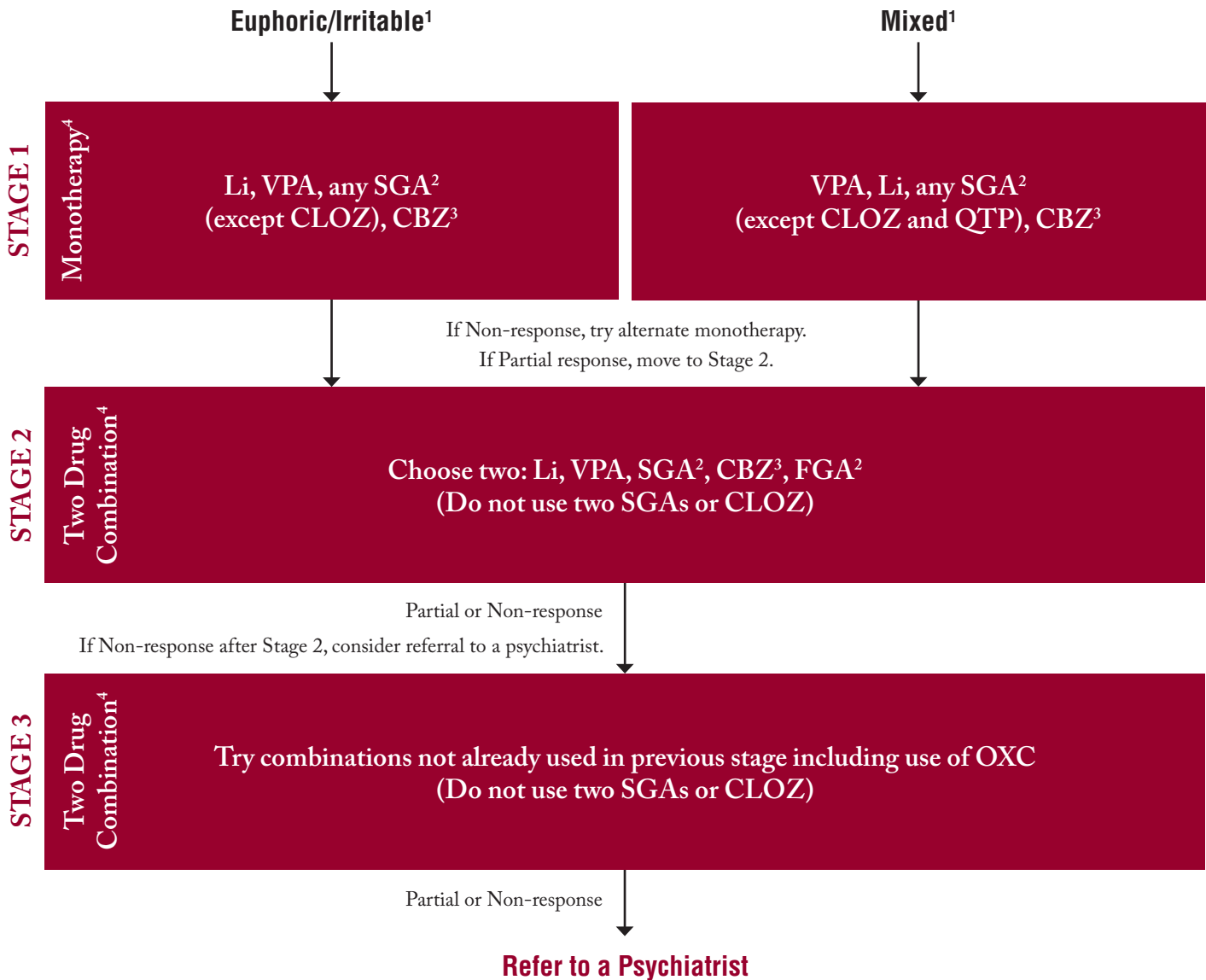
(vi) Lower starting dose, slower titration schedule, and lower maximum daily dose recommended for patients on concomitant valproate.

(vii) The risk of extrapyramidal side effects is significantly increased by using doses > 6 mg daily.

(viii) Presence of food can increase absorption twofold.

# Algorithm for the Acute Treatment of Bipolar Disorder Currently Hypomanic/Manic

Psychoeducation and cognitive therapy have been shown to benefit patients with bipolar disorder and should be a treatment option at all stages in combination with medications.



<sup>1</sup> It is appropriate to try more than one monotherapy in Stage 1 or combination therapy at any other given stage.

<sup>2</sup> Routine metabolic monitoring should occur for patients receiving SGAs or FGAs.

<sup>3</sup> CBZ has numerous significant drug interactions. Clinicians should closely monitor.

<sup>4</sup> Use targeted adjunctive treatment as necessary before moving to next stage.

## Abbreviation Key

**CBZ:** carbamazepine

**CLOZ:** clozapine

**FGA:** 1st generation antipsychotic

**Li:** lithium

**OXC:** oxcarbazepine

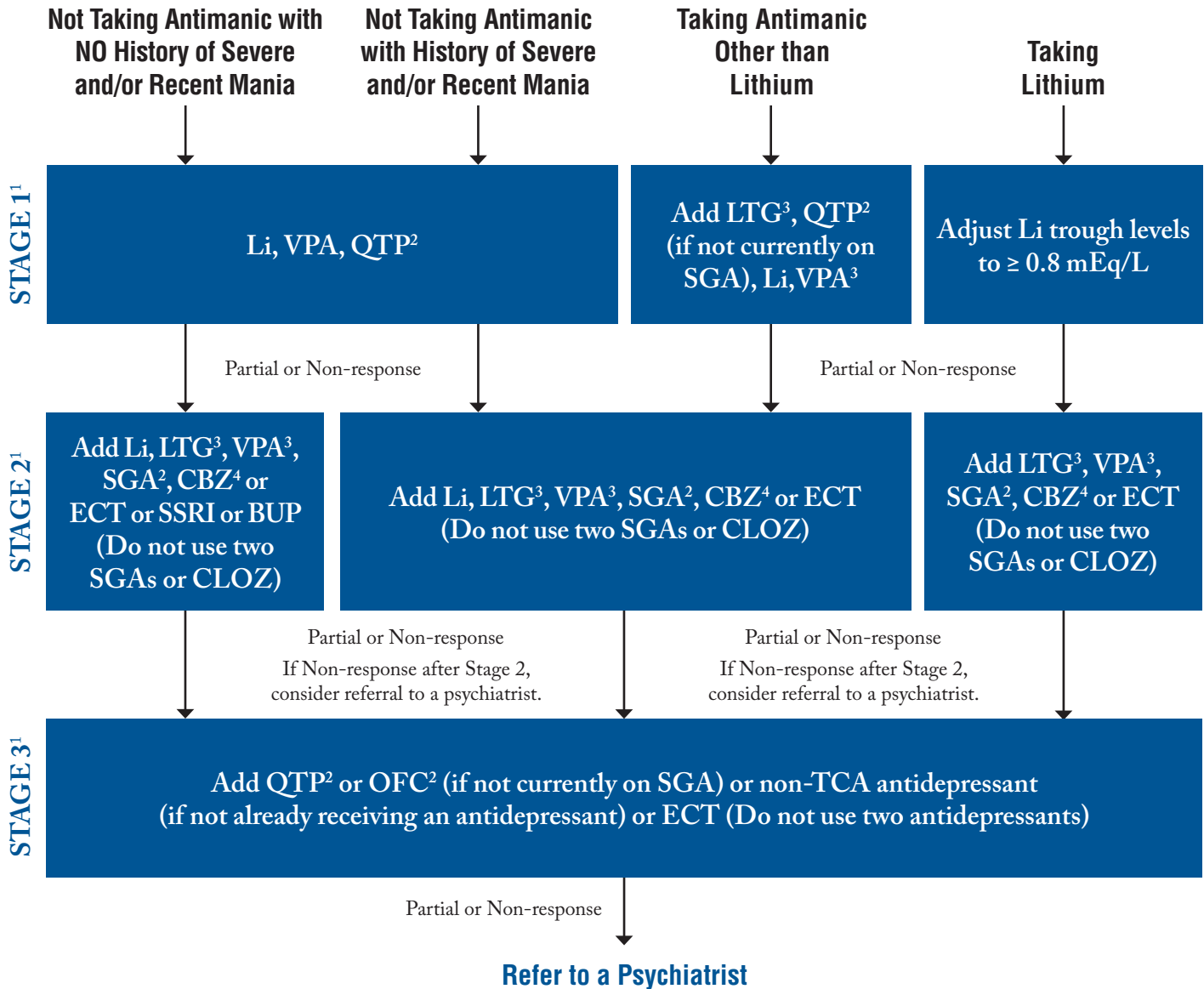
**QTP:** quetiapine

**SGA:** 2nd generation antipsychotic

**VPA:** valproate

# Algorithm for the Acute Treatment of Bipolar Disorder Currently Depressed

Psychoeducation and cognitive therapy have been shown to benefit patients with bipolar disorder and should be a treatment option at all stages in combination with medications.



- <sup>1</sup> Use targeted adjunctive treatment as necessary before moving to next stage.
- <sup>2</sup> Routine metabolic monitoring should occur for patients receiving SGAs.
- <sup>3</sup> Caution: The combination of LTG and VPA results in a significant drug interaction.
- <sup>4</sup> CBZ has numerous significant drug interactions. Clinicians should closely monitor.

Adapted from Texas Implementation of Medication Algorithm (TIMA);  
Copyright © 2005, Texas Department of State Health Services

## Abbreviation Key

<b>BUP:</b> bupropion	<b>QTP:</b> quetiapine
<b>CBZ:</b> carbamazepine	<b>SGA:</b> 2nd generation antipsychotic
<b>CLOZ:</b> clozapine	<b>SSRI:</b> selective serotonin reuptake inhibitor
<b>ECT:</b> electroconvulsive therapy	<b>TCA:</b> tricyclic antidepressant
<b>Li:</b> lithium	<b>VPA:</b> valproate
<b>LTG:</b> lamotrigine	
<b>OFC:</b> olanzapine/fluoxetine combination	

## Common Side Effects of Lithium and Anticonvulsants

U = unknown, 0 = absent to 4+ = common

Affected Organ System	Reaction	CBZ	Li	LTG	OXC	VPA
Blood Dyscrasias	Leukocytosis	1+	3+	0	1+	1+
	Leukopenia	3+	1+	1+	1+	1+
	Thrombocytopenia	2+	0	1+	0	4+ (i)
Central Nervous System	Asthenia	3+	4+ (ii)	2+	3+	3+
	Cognitive blunting	2+	3+	2+	2+	2+
	Drowsiness	3+	1+ (ii)	3+	3+	3+
	Headache	2+	2+	3+	4+	3+
Cardiovascular (iii)	ECG Changes	2+	3+	1+	1+	2+
Dermatological	Rash	3+ (iv) (v)	3+	3+ (iv)	2+ (iv)	2+ (iv)
Endocrine	Hair loss/thinning	2+	3+	0	1+	3+
	Hypothyroidism	1+	4+	1+	U	1+
	Menstrual disturbances	4+	3+	2+	1+	4+
	PCOS	3+	0	0	U	4+
	Polyuria/polydipsia	2+	4+	0	1+	0
Gastrointestinal	Diarrhea	2+	3+ (ii)	2+	2+	3+
	Nausea/vomiting	3+	4+	3+	3+	3+
	Weight gain	2+	4+	1+	2+	4+
Hepatic	Enzyme elevation	3+	0	1+	1+	4+ (i)
Neurological	Ataxia	3+	1+ (ii)	3+	2+	2+
	Diplopia	3+	0	3+	3+	3+
	Dizziness	3+	0	4+	2+	3+
	Incoordination	3+	1+ (ii)	2+	2+	2+
	Tremor	4+	4+ (ii)	2+	3+	3+

CBZ: carbamazepine ECG: electrocardiogram Li: lithium LTG: lamotrigine OXC: oxcarbazepine PCOS: Polycystic ovary syndrome VPA: valproate

(i) Greater with higher doses; (ii) Higher incidence and severity with higher serum lithium levels; may be early sign of toxicity; (iii) ECG abnormalities usually without cardiac injury; including: ST segment depression, flattened T waves, increased U wave amplitude; (iv) Severe dermatological reactions reported; (v) Risk of dangerous and/or fatal skin reactions higher in patients with HLA-B\*1502 allele.

References: *Clinical Handbook of Psychotropic Drugs*. Bezchlibnyk-Butler KZ, Jeffries JJ, editors. Toronto, ON, Hogrefe & Huber, 2006; *Drug Information Handbook for Psychiatry*. Fuller M.A., Sajatovic M., editors. Hudson, OH, Lexi-Comp, 2007.

## Common Side Effects of Antipsychotics

(-) = none reported, (+/-) = absent or rare to (+++++) = common

Antipsychotic	Extra-Pyramidal Side Effects	Tardive Dyskinesia	Orthostatic Hypotension	Increased Prolactin	Sedation	Weight Gain	Anti-Cholinergic Effects	Dyslipidemia	Glucose Dysregulation
<b>First Generation Antipsychotics (FGAs)</b>									
Chlorpromazine	++	+++	++++	++	++++	++	+++	+++	+++
Fluphenazine*	++++	++++	+	+++	+	++	+	-	+/-
Haloperidol	++++	++++	+	+++	+	+	+	-	-
Perphenazine*	+++	+++	++	++	++	+	++	-	+/-
<b>Second Generation Antipsychotics (SGAs)</b>									
Aripiprazole	+/-	+/-	-	-	+	+/-	+	+/-	+
Olanzapine	+	+	+	+/-	+++	+++	++	++++	+++
Paliperidone	+ / ++	+	+	+++	+	++	+	+	+
Quetiapine	+/-	+/-	++	+/-	++++ (i)	++	+	+	+
Risperidone	+ / ++ (ii)	+	+	+++	+	++	+	+	+
Ziprasidone	+	+	+	+	+	+/-	+	+/-	-

(i) During dose titration phase; (ii) ++ at doses > 6 mg/day

\*Reference: *Clinical Handbook of Psychotropic Drugs*. Bezchlibnyk-Butler KZ, Jeffries JJ, editors. Toronto, ON, Hogrefe & Huber, 2006.

Scales on the two side effects tables are not directly comparable.

## Monitoring Parameters for Lithium and Anticonvulsants

Medications	Monitoring Parameters	Frequency					Comments
		Baseline	Week 1	6 Months	Annually	As Clinically Indicated	
Carbamazepine	CBC, platelets	✓	✓ (i)			✓	(i) After initiation and each dose increase
	Electrolytes	✓				✓	To monitor for hyponatremia
	HLA-B*1502	✓					In genetically at-risk patients (ancestry across broad areas of Asia). If positive, avoid using CBZ unless benefit clearly outweighs risk.
	LFTs	✓				✓	
	Pregnancy test					✓	
	Serum level		✓ (i)	✓ (ii)		✓	(i) After initiation and dose adjustment and until stable (ii) every 3–6 months
Lithium	BUN/creatinine	✓				✓	
	CBC	✓			✓	✓	
	ECG	✓			✓	✓	
	Electrolytes	✓				✓	
	Pregnancy test					✓	
	Serum level		✓ (i)			✓	(i) After initiation and dose adjustment
	Thyroid	✓		✓ (i)		✓ (i)	(i) TSH
	UA	✓				✓	
Lamotrigine	Pregnancy test					✓	
Oxcarbazepine	Electrolytes	✓				✓	To monitor for hyponatremia
	Pregnancy test					✓	
Valproate	CBC, platelets	✓	✓ (i)			✓	(i) After initiation and each dose increase
	LFTs	✓				✓	
	Pregnancy test					✓	
	Serum level		✓ (i)			✓	(i) After initiation and dose adjustment

**BUN:** blood urea nitrogen    **CBC:** complete blood count    **ECG:** electrocardiogram    **HLA-B\*1502:** human leukocyte antigen allele B\*1502    **LFTs:** liver function tests    **UA:** urine analysis

## Monitoring Parameters for Patients on SGAs

Monitoring Parameters	Frequency					
	Baseline	Week 4	Week 8	Week 12	Quarterly	Annually
Personal/Family History	✓					✓
Weight (BMI)	✓	✓	✓	✓	✓	
Waist Circumference	✓					✓
Blood Pressure	✓			✓		✓
Fasting Plasma Glucose	✓	✓*		✓	✓*	
Fasting Lipid Profile	✓	✓*		✓		✓*

\*The SCORxE mental health panel suggests additional monitoring of fasting plasma glucose at 4 weeks and quarterly and fasting lipid profile at 4 weeks and annually.

Adapted from the Consensus Statement endorsed by the American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association For The Study of Obesity. Copyright © 2004 American Diabetes Association, From Diabetes Care®, Vol. 27, 2004; 596-601. Modified with permission from The American Diabetes Association.

# SCORE<sup>SM</sup>

SOUTH CAROLINA OFFERING  
PRESCRIBING EXCELLENCE X



University of South Carolina | Medical University of South Carolina

---

843-792-5915 | [www.sccp.sc.edu/SCORxE](http://www.sccp.sc.edu/SCORxE) | [SCORxE@sccp.sc.edu](mailto:SCORxE@sccp.sc.edu)