

# **TEXAS IMPLEMENTATION OF MEDICATION ALGORITHMS (TIMA)**

## **Guidelines for Treating Major Depressive Disorder**

### **TIMA PHYSICIAN PROCEDURAL MANUAL**

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These guidelines reflect the state of knowledge, current at the time of publication, on effective and appropriate care, as well as clinical consensus judgements when knowledge is lacking. The inevitable changes in the state of scientific information and technology, mandate that periodic review, updating, and revisions will be needed. These guidelines (algorithms) do not apply to all patients, and each must be adapted and tailored to each individual patient. Proper use, adaptation modifications or decisions to disregard these or other guidelines, in whole or in part, are entirely the responsibility of the clinician who uses the guidelines.

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## Overview of TIMA

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Algorithms facilitate clinical decision making by providing physicians with large amounts of current information on the newest psychotropic medications and research data, as well as specific treatment sequences with tactical recommendations. Patients receive the benefit of patient education, which should enhance adherence to the treatment program. Algorithms are designed with the objectives of long-term safety, tolerability, and full symptom remission — not just response. The employment of such treatment guidelines to aggressively treat the severely and persistently mentally ill (SPMI) population may bring about a decrease in the use of crisis/hospital services and the number of clinical visits — while presenting an accountability for scarce resources — thereby increasing the overall efficiency of patient care.

Beginning in 1995, The Texas Medication Algorithm Project (TMAP) was developed by the Texas Department of Mental Health and Mental Retardation (TDMHMR) in collaboration with Texas universities to assess the value of algorithms — along with clinical support and a patient/family educational package — in the pharmacological management of mentally ill patients. The result has been a set of algorithms for the treatment of the three major disorders most commonly encountered in the Texas public mental health system: schizophrenia (SCZ), bipolar disorder (BPD), and major depressive disorder (MDD). TDMHMR has defined a best practice treatment as a series of treatment steps which guides physicians in determining medication treatment plans, thereby generating the best outcome for each individual consumer. Practitioners, patients, families, and administrators all contributed to the formulation and implementation of TMAP, ensuring an optimum level of efficacy and practicality. Phase 1 of TMAP dealt with the development of these algorithms using expert consensus. In Phase 2, the feasibility of algorithm implementation in the TDMHMR system was evaluated. The goal of Phase 3 was to evaluate the clinical and economic impact of medication treatment algorithms for MDD, SCZ, and BPD in comparison with treatment as usual (TAU).

Up until now, the effectiveness of these medication algorithms has only been put to use with a limited sample of patients. Implementation of the algorithms on a systemwide basis is the next step in offering a higher quality of care to the SPMI patient population in the public mental health sector. Texas Implementation of Medication Algorithms (TIMA) is Phase 4 of TMAP: the "roll-out" of these depression algorithms to TDMHMR clinics throughout the state. The roll-out of TIMA has begun with the training of physicians and support personnel in algorithm implementation. Revisions may be required in the structure and function of clinical staff to increase patient education and adherence, to improve follow up, and to develop psychosocial supports to improve symptom recognition, symptom control, and functional restoration. Continuous education, consultation, and collaboration are necessary for both clinicians and administrators in making timely revisions in clinical procedures and budgetary allocations. From a clinical and administrative perspective, medication algorithms should demonstrate validity with far-reaching and long-term applications.

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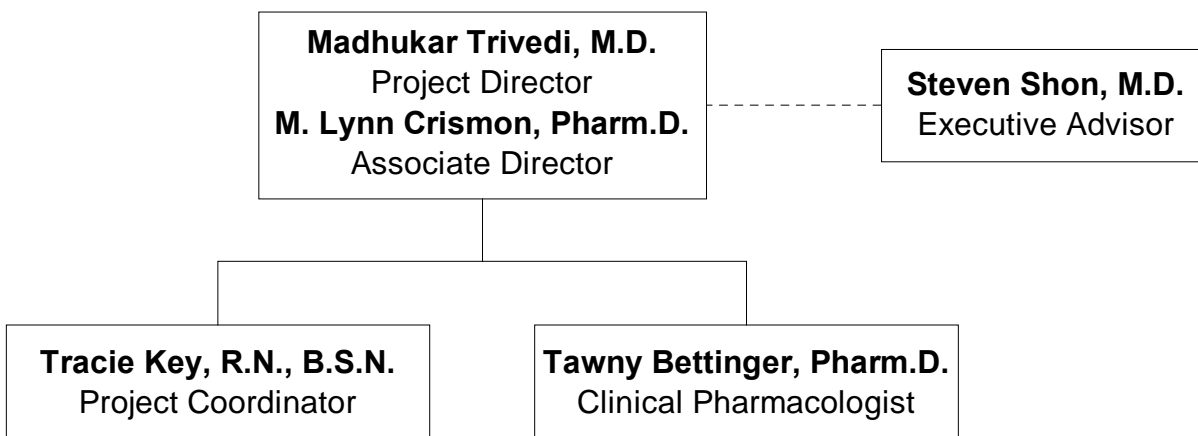
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## ***Administrative Structure***

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### ***Project Management Team***

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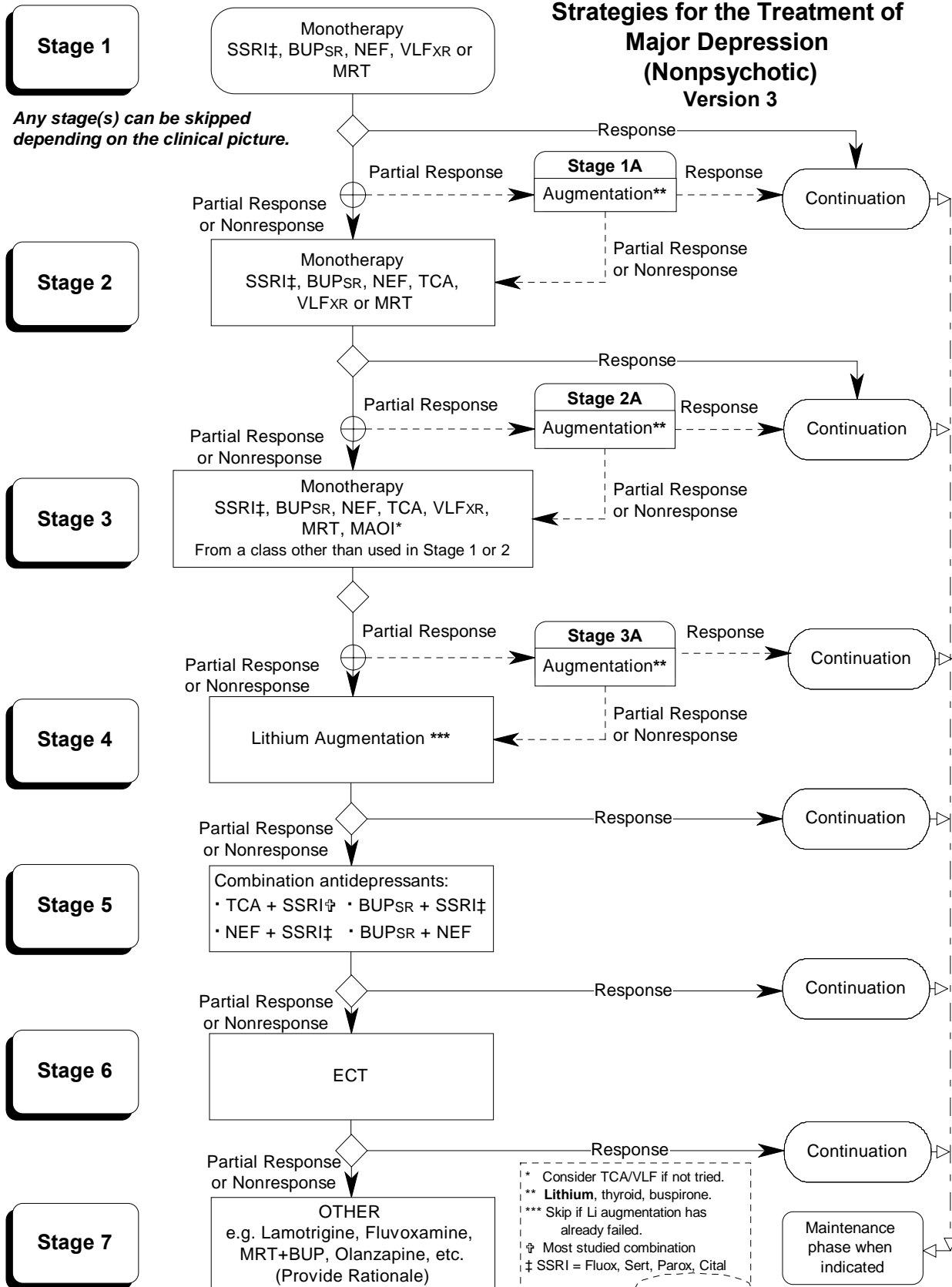
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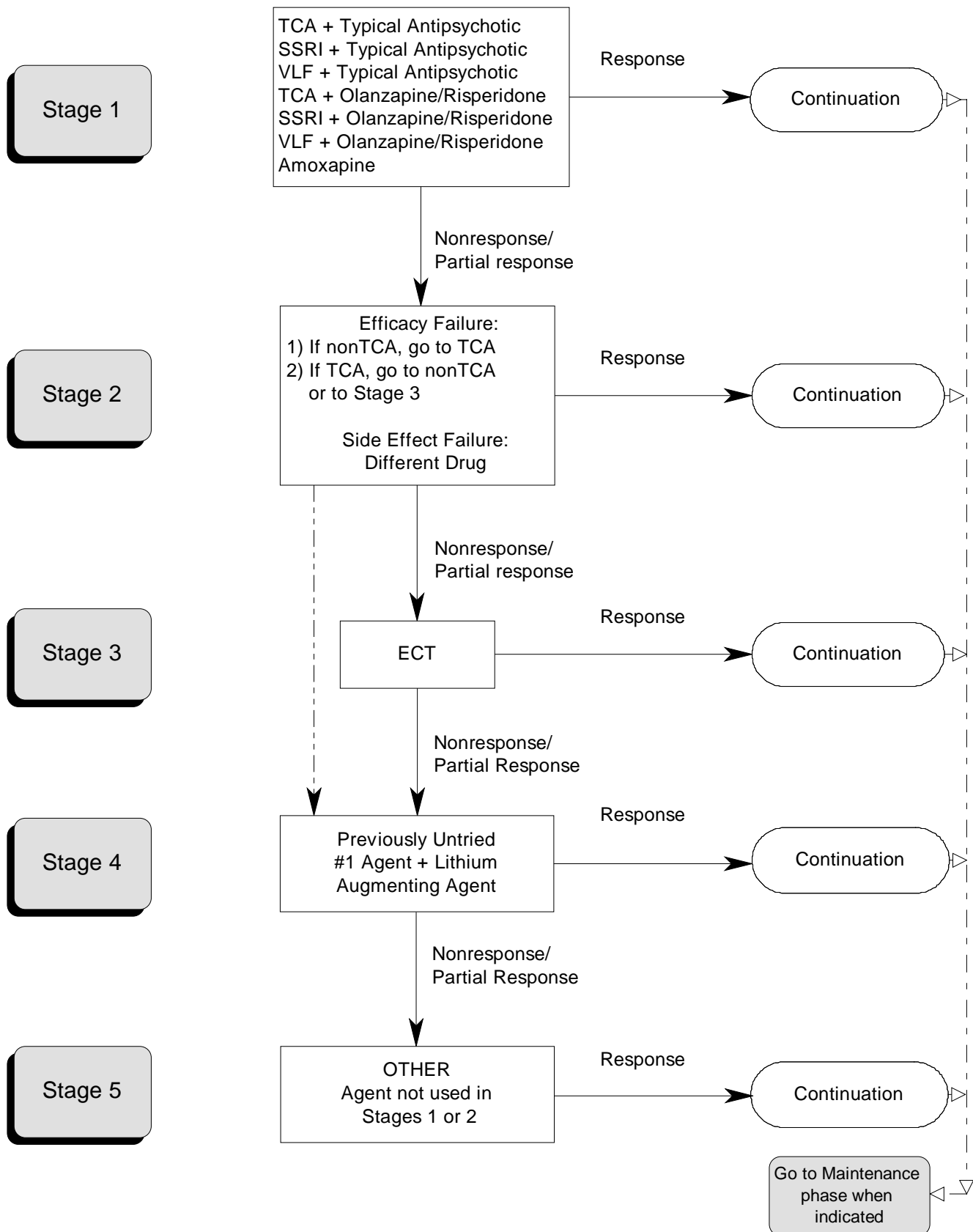
# Depression Algorithms

## Strategies for the Treatment of Major Depression (Nonsychotic) Version 3



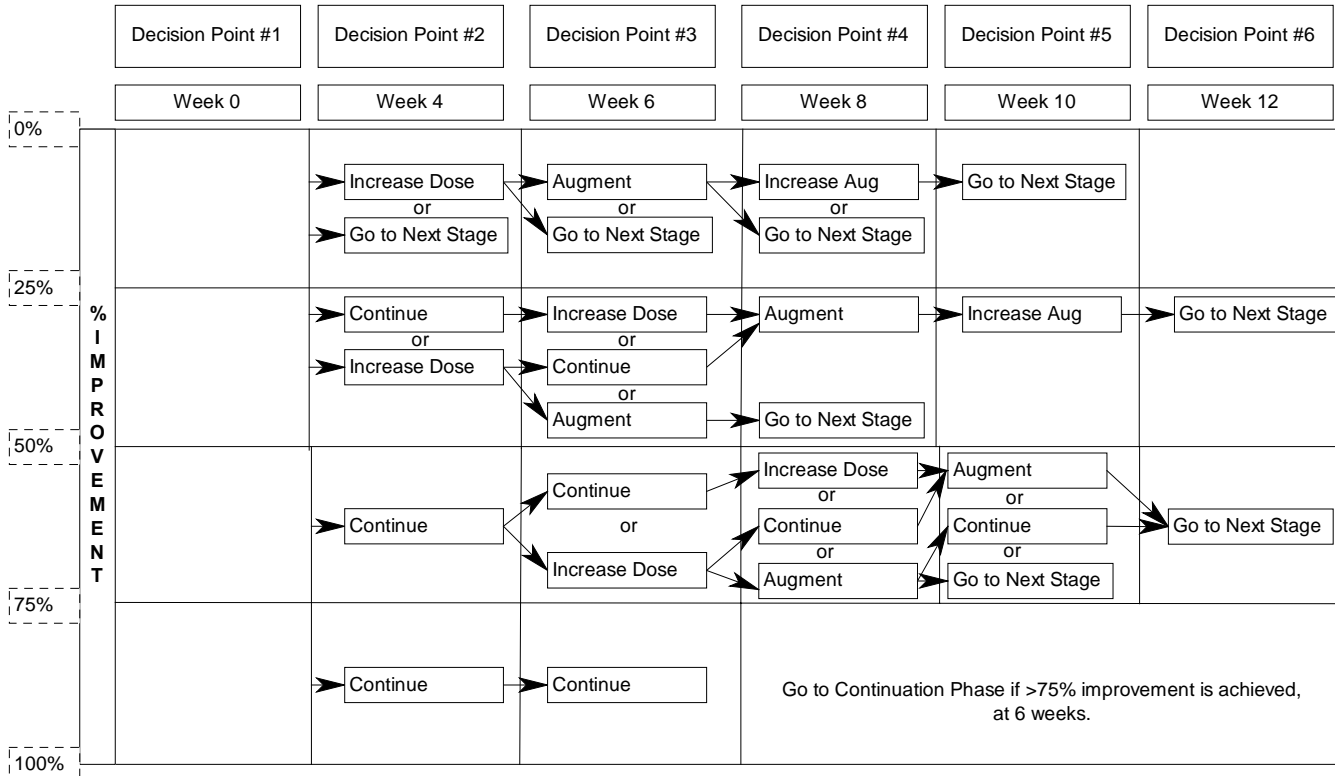
\* Consider TCA/VLF if not tried.  
 \*\* Lithium, thyroid, buspirone.  
 \*\*\* Skip if Li augmentation has already failed.  
 ‡ Most studied combination  
 † SSRI = Fluox, Sert, Parox, Cital

# Strategies for the Treatment of Major Depression (Psychotic)



# **Critical Decision Points (CDPs) for Major Depressive Disorder**

## **Tactics for the Treatment of Major Depression (Nonpsychotic)**



### At-a-Glance Depression Medication Algorithms

**Visit Frequency:** Weekly contact (office visit or by phone) for the first 4 weeks of each stage; then every 2 weeks until 50% improvement in symptoms is maintained for at least one month; then every 4 weeks until 75% improvement is maintained for at least one month; then every 3 months. Support personnel may contact patients by phone if the physician is unable to see them.

**Assessment Frequency:** Inventory of Depressive Symptomatology - Self-Report (IDS-SR) and Clinical Report Form (CRF) at each clinic visit. If the patient is contacted by phone, an Interim Contact Form (ICF) must be completed.

**Duration of Acute Treatment:** Until 75% symptom improvement is achieved for 4 weeks, then move to continuation phase. (See Critical Decision Points (CDP) Table 2, page 10.)

<b><u>Response:</u></b>	Nonresponse	(<25% improvement)
	Minimal response	(25–50% improvement)
	Partial response	(50–75% improvement)
	Full response/remission	(75–100% improvement)

**Criteria for Medication Change:** Anything less than 75% improvement or full response **may** require a medication change.

**Evaluations:** At each visit a physician assessment of core symptom severity, overall functional impairment, and side effect severity. Algorithm Coordinator (AC) assessments, using IDS-SR and patient global self-rating of symptom severity and side effects, should be done prior to patient contact with the physician.

**Medication Switching:** Discontinue or taper according to Table 11 on page 16 or the Guidelines for Switching Between Antidepressant Medications in the Appendix.

**Medication Doses:** See Tables 3, 5, and 7 on pages 11, 13, and 14 and the Guidelines in the Appendix for information on medications. ***Doses outside of the ranges should have a chart note indicating “change from algorithm recommended” and documentation of rationale for change.***

**Augmentation and Combination:** If a partial response is achieved, physicians may augment with lithium, thyroid medication (Cytomel), or buspirone to potentiate a greater response. A combination of 2 antidepressants, both at full doses, is suggested at Stage 5 of the algorithm.

**Table 1: Strategies for Acute Phase Treatment of Major Depressive Episodes**

Stage	Nonpsychotic Depression	Psychotic Depression
<b>Stage 1</b>	<p><b>Monotherapy<sup>1</sup></b></p> <ul style="list-style-type: none"> <li>◆ SSRI,<sup>2</sup> Bupropion (BUP), Nefazodone (NEF), Venlafaxine (VLF), Mirtazapine (MRT) (A evidence<sup>4</sup>)</li> </ul>	<p><b>Antidepressant + Antipsychotic</b></p> <ul style="list-style-type: none"> <li>◆ TCA + Antipsychotic (A-B evidence)<sup>4</sup></li> <li>◆ SSRI + Antipsychotic (B-C evidence)</li> <li>◆ Amoxapine (B evidence)</li> <li>◆ VLF + Antipsychotic (evidence)</li> </ul>
<b>Stage 2</b>	<p><b>Monotherapy</b></p> <ul style="list-style-type: none"> <li>◆ SSRI, BUP, NEF, VLF, Mirtazapine (MRT) <b>OR</b> a TCA</li> <li>◆ <b>EFFICACY FAILURE:</b> Switch to another antidepressant.</li> <li>◆ <b>SIDE EFFECT FAILURE:</b> Switch classes, or consider staying within the class if a contrasting SE profile is available or expected.</li> </ul>	<p><b>Antidepressant + Antipsychotic</b></p> <ul style="list-style-type: none"> <li>◆ <b>EFFICACY FAILURE:</b> If nonTCA used in Stage 1, switch to TCA. If TCA used, try an antidepressant from a different class.</li> <li>◆ <b>SIDE EFFECT FAILURE:</b> Switch to an agent from a different class.</li> </ul>
<b>Stage 3</b>	<p><b>Monotherapy</b></p> <ul style="list-style-type: none"> <li>◆ SSRI, BUP, NEF, VLF, MRT, TCA or MAOI</li> <li>◆ <b>Choose a medication from a different class than used in Stage 1 or 2.</b></li> </ul>	<p><b>ECT</b></p> <ul style="list-style-type: none"> <li>◆ If the patient refuses ECT or does not respond, go to the next stage or repeat an earlier stage with a different agent.</li> </ul>
<b>Stage 4</b>	<p><b>Augmentation</b></p> <ul style="list-style-type: none"> <li>◆ Previously untried antidepressant + lithium, thyroid,<sup>5</sup> or buspirone</li> <li>◆ Begin medications simultaneously.</li> </ul>	<p><b>Augmentation</b></p> <ul style="list-style-type: none"> <li>◆ Previously untried treatment + lithium, thyroid,<sup>5</sup> or buspirone</li> <li>◆ Begin medications simultaneously.</li> </ul>
<b>Stage 5</b>	<p><b>Combination Therapy</b></p> <ul style="list-style-type: none"> <li>◆ TCA + SSRI, SSRI + BUP, SSRI + NEF, BUP<sub>SR</sub> + NEF</li> </ul>	<p><b>Other</b></p> <ul style="list-style-type: none"> <li>◆ Any antidepressant + antipsychotic not tried in Stage 1 or 2</li> </ul>
<b>Stage 6</b>	<p><b>ECT</b></p> <ul style="list-style-type: none"> <li>◆ If patient refuses ECT or does not respond, go to next stage or repeat an earlier stage with a different agent.</li> </ul>	<p><b>Other</b></p> <ul style="list-style-type: none"> <li>◆ Any antidepressant + antipsychotic not tried previously</li> </ul>
<b>Stage 7</b>	<p><b>Other</b></p> <ul style="list-style-type: none"> <li>◆ Any antidepressant or combination not previously tried</li> </ul>	<p><b>Other</b></p> <ul style="list-style-type: none"> <li>◆ Any antidepressant + antipsychotic not tried previously</li> </ul>

<sup>1</sup> Acceptable antidepressants for Stage 1: Discuss treatment options with the patient and depending on prior treatment history, patient's clinical presentation, life style, and personal preferences, etc., assess the relative advantages of Stage 1 medications and make an initial treatment selection.

<sup>2</sup> FDA-approved SSRIs for depression include: fluoxetine (FLU), paroxetine (PRX), sertraline (SERT), and citalopram (CIT).

<sup>3</sup> Acceptable TCAs for psychotic depression include: desipramine (DMI), nortriptyline (NT), amitriptyline (AMI), clomipramine (CMI), or imipramine (IMI).

<sup>4</sup> Evidence level: A = controlled clinical trials; B = open trials and retrospective data analyses; C = clinical consensus and/or case reports.

<sup>5</sup> T<sub>3</sub> thyroid medication Cytomel (triiodothyronine) is suggested before T<sub>4</sub> Synthroid.

**Table 2: Critical Decision Points (CDPs) and Tactics for Acute Phase Treatment of Major Depression:**

Within each strategy stage, approaches to conducting a therapeutic trial with an antidepressant

<b>Critical Decision Point</b>	<b>Clinical Status</b>	<b>Plan<sup>1</sup></b>
Week 0 (CDP # 1)	Symptomatic	◆ Initiate medication; adjust dose to lower end of therapeutic dose range or serum level.
Week 4 (CDP # 2)	Full Response	◆ Continue current dose.
	Partial Response <sup>2</sup>	◆ Continue current dose. ◆ Consider increasing dose.
	Minimal or Nonresponse	◆ Increase dose. <sup>3</sup> ◆ Go to the next stage.
Week 6 (CDP # 3)	Full Response	◆ Go to continuation phase if full response sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	◆ Maximize dose. ◆ Augment with lithium, thyroid, or buspirone.
	Nonresponse or minimal response	◆ Augment with lithium or alternative augmenting agent. ◆ Go to the next stage.
Week 8 (CDP # 4)	Full Response	◆ Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	◆ Augment with lithium or alternative augmenting agent. ◆ Go to the next stage.
	Nonresponse or minimal response to lithium or alternative augmentation for 2–3 weeks	◆ Discontinue and go to the next stage.
Week 10 (CDP # 5)	Full Response	◆ Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	◆ Adjust dose (antidepressant and/or augmentation dose). ◆ Go to the next stage.
	Nonresponse or minimal response	◆ Go to the next stage.
Week 12 (CDP # 6)	Full Response	◆ Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	◆ Go to the next stage.

<sup>1</sup> For patients showing minimal or no response, total trial should not exceed 4–8 weeks. For patients with a partial response the trial may last up to 12 weeks to increase dose and implement augmentation strategy. Patients with only a partial response at any stage beyond 12 weeks should be considered for a medication change or a move to a subsequent treatment stage. In cases of treatment resistant depression (TRD), longer trials may be necessary in later stages.

<sup>2</sup> With partial response, the clinician and patient assess both the absolute degree of improvement and the rate of improvement. Nonresponse is <25% improvement in overall symptoms, minimal response is 25–50% improvement in overall symptoms, partial response is 50–75% improvement in overall symptoms, full response is >75% improvement in overall symptoms.

<sup>3</sup> In patients with psychotic depression, dose increases may include the antidepressant, the antipsychotic, and/or the augmenting agent.

**Table 3: Antidepressant Dosing Used for Acute Phase Treatment of Depression**

Type/ Class	Medication	Initial Target Dose (Level)	Maximum Dose (Level)	Recommended Administration Schedule
SSRI	Fluoxetine (Prozac)	20 mg	40–80 mg	QAM
	Paroxetine (Paxil)	20–30 mg	40–60 mg	QAM
	Sertraline (Zoloft)	50–100 mg	150–200 mg	QAM
	Citalopram (Celexa)	20 mg	60 mg	QAM
TCA	Amitriptyline	150–200 mg	300 mg	QHS
	Clomipramine	100–150 mg	250 mg	QHS
	Desipramine	150 mg (>125ng/ml)	300 mg	QHS
	Imipramine	150 mg (IMI+DMI>200 ng/ml)	300 mg (200–400ng/ml)	QHS
	Nortriptyline	75–100 mg (50–150 ng/ml)	150 mg (50–150 ng/ml)	QHS
Others	Amoxapine	200–300 mg	400 mg	QHS
	Bupropion SR (Wellbutrin SR)	200–300 mg	400 mg	bid <sub>≤</sub> 200 mg/dose
	Bupropion (Wellbutrin)	225–300 mg	450 mg	tid <sub>≤</sub> 150mg/dose
	Mirtazapine (Remeron)	30 mg	60 mg	QHS
	Nefazodone (Serzone)	200–400 mg	600 mg	bid
	Venlafaxine (Effexor)	150–225 mg	375 mg	bid
	Venlafaxine XR (Effexor XR)	75–225 mg	225 mg	QD
MAOIs	Phenelzine	45–60 mg	90–120 mg	QD–tid
	Tranylcypromine	30–40 mg	60–80 mg	QD–tid

Also refer to the Antidepressant Monographs section in the Appendix.

### **Treatment of Depression with Antidepressants**

- 50% of patients either do not receive adequate levels of antidepressants or are not treated for an adequate period of time.
- 10–20% of patients are intolerant to an initial trial of antidepressant medication.
- 25–30% of patients who complete an adequate trial do not show an acceptable response.
- The strategies for achieving remission include maximizing the dose as tolerated, switching to a different class if indicated, augmenting a partial response, or combining antidepressants when needed.

**Table 4. Common Side Effects (SEs) for Antidepressant Medications**

<b>MEDICATION</b>	<b>COMMON SIDE EFFECTS*</b>
<b>SSRIs</b> Citalopram Fluoxetine Paroxetine Sertraline Fluvoxamine	Dizziness, dry mouth, insomnia, agitation, nausea, sexual dysfunction, headache
<b>Bupropion SR</b> <b>Bupropion (immediate release)</b>	Headache, agitation, weight loss, insomnia, nausea
<b>Nefazodone</b>	Dizziness, headache, nausea, somnolence, insomnia
<b>Venlafaxine XR</b> <b>Venlafaxine</b>	Dizziness, somnolence, insomnia, decreased appetite, anxiety, headache, nausea, sexual dysfunction
<b>TCAs</b> Amitriptyline Clomipramine Desipramine Imipramine Nortriptyline	Sedation, dizziness, dry mouth, nausea, insomnia, anxiety, anticholinergic effects, tremor, constipation, blurred vision, arrhythmias
<b>Amoxapine</b>	Sedation, dizziness, dry mouth, nausea, anticholinergic effects, anxiety, insomnia, extrapyramidal reactions, seizures
<b>Mirtazapine</b>	Dizziness, diarrhea, increased appetite, drowsiness, dry mouth
<b>MAOIs</b> Phenelzine Tranylcypromine	Restlessness, dizziness, blurred vision, diarrhea, insomnia, weakness, arrhythmias, headache, sexual dysfunction

\* For complete side effects information, consult with the official product labeling or contact your MDD project consultants.



**Table 5: Antipsychotic Dosing for Treatment of Psychotic Depression**

Type/Class	Medication	Target Dose (Level)	Maximum Dose (Level)	Recommended Administration Schedule
Atypicals	Olanzapine (Zyprexa)	10–15 mg	20 mg	qHS
	Risperidone (Risperdal)	2–4 mg	6 mg	bid or qHS
	Quetiapine (Seroquel)	100–800 mg	800 mg	
High potency	Haloperidol (Haldol)	2–5 mg	5–15 mg	QHS
Medium potency	Perphenazine (Trilafon)	8–16 mg	64 mg	QHS

Also refer to the Antipsychotic Monographs section in the Appendix.

**Table 6: Common Side Effects (SEs) of Antipsychotic Medications**

Antipsychotic	EPS	Sedation	Tardive Dyskinesia	Anticholinergic Effects	Blood Pressure	Sexual Dysfunction	Weight Gain
Clozapine (Clozaril)	+/-	++++	-	++++	+++	+	++++
Haloperidol (Haldol)	++++	+	++++	+	+	+	+
Olanzapine (Zyprexa)	+	++	+	++	+	-	+++
Risperidone (Risperdal)	++	+	+	+	+	+	++
Quetiapine (Seroquel)	+/-	++	?	+/-	++	-	++

- = none + = mild +/- = mild to none ++ = moderate +++ = moderately severe ++++ = severe

### **Treatment of Psychotic Depression**

- Combination treatment with an antidepressant and antipsychotic agent has been shown to be significantly more effective than either given alone.
- Currently the majority of data in the treatment of psychotic depression has been demonstrated with tricyclic antidepressants and conventional antipsychotics, but data evaluating combinations of newer antidepressants and atypical antipsychotics is accumulating.
- The advent of atypical antipsychotics has greatly increased treatment options.
- Advantages of atypical antipsychotics include a) lower incidence of extrapyramidal symptoms (EPS), b) broader efficacy profile, and c) minimal impact on prolactin concentrations with olanzapine and quetiapine.

**Table 7: Augmentation Dosing for Inadequate Response**

Type/Class	Medication	Target Dose (Blood Level)	Maximum Dose (Blood Level)	Recommended Administration Schedule
<b>Recommended Augmentation Agents</b>	Lithium	600–1200 mg (0.4–0.6 mEq/L)	1200–1800 mg (0.8–1.0 mEq/L)	BID
	T <sub>3</sub> - Cytomel	25–50 micrograms	50 micrograms	QAM
	Buspirone	25–50 mg	45–60 mg	BID-TID
<b>Other Augmenting Agents</b>	Dextroamphetamine	5–30 mg	60 mg	QAM
	Methylphenidate	5–30 mg	40–60 mg	BID

Also refer to the Monographs for Augmentation Agents section in the Appendix.

**Table 8: Common Side Effects of Augmentation Agents**

Medication	Side Effects at Therapeutic Blood Level	
Lithium	Cognitive impairment	Tremor
	Drowsiness	Muscle weakness
	Nausea/vomiting	Thirst
	Polyuria	
Buspirone	Dizziness	Nausea/vomiting
	Insomnia	Dry mouth
	Nervousness	
Cytomel	Insomnia	Diarrhea
	Tremor	Increased/decreased appetite
	Headache	Heat intolerance
	Nausea	

### **Treatment of Depression using Augmentation Therapy**

- In randomized controlled trials, at least 30% of depressed patients fail to respond to first-line antidepressant treatment, despite adequate dose, duration, and compliance.
- Up to 21% of patients with major depression who seek treatment have not recovered after two years.
- Augmentation of treatment can result in a more rapid response to antidepressant medication. Studies have shown that, among partial responders to serotonin reuptake inhibitors, patients demonstrate a higher recovery rate with augmented antidepressant therapy in comparison to antidepressant treatment alone, as assessed by scores on standardized depression rating scales.
- When an antidepressant medication elicits only partial response (25–75%), augmentation agents can potentiate an improved response, thus preventing the necessity of discontinuing the initial antidepressant.

**Table 9: Dosing of Medications for Treatment of Associated Symptoms of Depression**

Associated Symptom	Medication	Usual Dose range, mg/day	Schedule
<b>Insomnia</b>	Lorazepam	0.5–2.0 mg	QHS; taper after 7-10 days or as soon as possible
	Clonazepam	0.5–2.0 mg	
	Zolpidem	5–10 mg	
	Trazodone	25–100 mg	
<b>Anxiety</b>	Lorazepam <sup>1</sup>	0.5–4.0 mg	Q4–6h prn throughout the day
	Alprazolam	0.75–4.0 mg	
	Clonazepam	1.5–3.0 mg	
<b>Anxiety</b> (if history of substance abuse or if benzodiazepines are contraindicated)	Buspirone	15–60 mg	BID-TID
<b>Severe Agitation</b>	Lorazepam	0.5–2.0 mg	QD
	Clonazepam	0.5–2.0 mg	
	Alprazolam	0.75–4.0 mg	
	Propranolol	10–30 mg	

**Table 10: Dosing of Medications for Treatment Emergent Side Effects**

Treatment Emergent Side Effect	Medication	Usual Dose Range (mg/day)	Schedule
<b>Insomnia Due to Medication (especially SSRI, BUP, or VLF)</b>	Lorazepam <sup>1</sup>	0.5–2.0 mg	QHS; taper as soon as possible
	Clonazepam	0.5–2.0 mg	
	Zolpidem	5–10 mg	
	Trazodone	25–100 mg	
<b>EPS from Antipsychotic</b>	Benzotropine	2–4 mg	QHS or BID
<b>Sexual Dysfunction</b>	Bupropion	75 mg	QD
	Amantadine	100–200 mg	
	Methylphenidate	10–15 mg	
	OR Consider switch to agent with low sexual side effects	→ bupropion, nefazodone, or mirtazapine	

<sup>1</sup> In general, treatment emergent side effects should be addressed first by dose reduction or medication switching, as pharmacological intervention may increase the risk of drug interaction and additional adverse effects, thus decreasing patient compliance.

<sup>2</sup> Benzodiazepines are best avoided in patients with prior history of substance abuse/dependence or who are at risk for substance abuse. Nonaddicting agents such as zolpidem or buspirone may be preferred.

**Table 11: Guidelines for Switching Between Antidepressant Medications**

FROM	TO	PLAN
SSRI	SSRI	<ul style="list-style-type: none"> <li>◆ Discontinue SSRI #1 and begin SSRI #2, or</li> <li>◆ Taper SSRI #1 and initiate SSRI #2.</li> </ul>
SSRI	TCA Bupropion	<ul style="list-style-type: none"> <li>◆ Discontinue SSRI and begin TCA or bupropion, or</li> <li>◆ Taper SSRI and initiate TCA or bupropion gradually as tolerated to therapeutic dose range.</li> </ul>
SSRI	Nefazodone Venlafaxine	<ul style="list-style-type: none"> <li>◆ Discontinue SSRI and begin nefazodone or venlafaxine, or</li> <li>◆ Taper SSRI and initiate nefazodone or venlafaxine gradually as tolerated to therapeutic dose range.</li> </ul>
SSRI	MAOI	<ul style="list-style-type: none"> <li>◆ Discontinue SSRI. After a 5-week washout period for fluoxetine or a 2-week washout period for sertraline, paroxetine or citalopram, MAOI therapy can safely be initiated.</li> </ul>
TCA Venlafaxine Nefazodone Bupropion	TCA	<ul style="list-style-type: none"> <li>◆ Discontinue TCA #1 (or venlafaxine, nefazodone, bupropion) by taper and then initiate TCA #2, or</li> <li>◆ Taper TCA #1 (or venlafaxine, nefazodone, bupropion) while initiating TCA #2 gradually as tolerated to therapeutic dose range.</li> </ul>
TCA Venlafaxine Nefazodone Bupropion	SSRI	<ul style="list-style-type: none"> <li>◆ Taper and discontinue TCA (or venlafaxine, nefazodone, bupropion) and then initiate SSRI, or</li> <li>◆ Taper TCA (or venlafaxine, nefazodone, bupropion) while initiating SSRI at a low dose.</li> </ul>
TCA Venlafaxine Nefazodone Bupropion	Nefazodone Venlafaxine Bupropion	<ul style="list-style-type: none"> <li>◆ Discontinue TCA (or venlafaxine, nefazodone, bupropion) and initiate nefazodone, venlafaxine, or bupropion, or</li> <li>◆ Taper and discontinue TCA (or venlafaxine, nefazodone, bupropion) to initiate nefazodone, venlafaxine, or bupropion gradually as tolerated to therapeutic dose range.</li> </ul>
TCA	MAOI	<ul style="list-style-type: none"> <li>◆ Discontinue TCA. After a 2-week washout, MAOI therapy can be safely initiated.</li> </ul>
MAOI	MAOI Nefazodone Venlafaxine Bupropion	<ul style="list-style-type: none"> <li>◆ Discontinue MAOI #1. After a 2-week washout, therapy with MAOI #2 (or TCA, venlafaxine, nefazodone, or bupropion) can be safely initiated.</li> </ul>

Also refer to the Guidelines for Switching Between Antidepressant Medications in the Appendix for case examples.

These principles apply to the tactics of switching antidepressant medications, depending on the reasons for switching and on the duration of exposure to the first agent.

- If the first antidepressant is being discontinued due to intolerance following a brief exposure (< 7 days), it can be stopped and the second drug started.
- If the first drug is being discontinued after a longer exposure (≥ 7 days), due to symptomatic breakthrough, or inadequate response, then it should be tapered and the second drug started gradually (notable exception being a switch from an MAOI).

- **Serotonin discontinuation syndrome** can occur following abrupt cessation of antidepressant therapy, particularly for those antidepressants with shorter half-lives (sertraline, paroxetine, fluvoxamine, citalopram) or no active metabolites. The syndrome is characterized by dizziness, insomnia, nervousness, nausea, and agitation. Initiating a medication taper does not always prevent its occurrence but may minimize severity.

**Table 12: Guidelines for Combining Antidepressant Medications**

Combination			Plan
SSRI	with	TCA	◆ Because SSRIs markedly increase blood levels of TCAs up to values exceeding therapeutically recommended ranges, serum levels of TCA should be monitored throughout treatment and adjusted accordingly.
SSRI	with	Bupropion SR	◆ Monitor for agitation.
SSRI	with	Nefazodone	◆ Initiate low dose of nefazodone as an addition to SSRI treatment, then gradually increase to therapeutic dose range. Monitor for increased side effects.

**Other Combinations<sup>1</sup>**

**Bupropion SR with Nefazodone** ◆ Monitor side effects.  
**Venlafaxine with Mirtazapine**

<sup>1</sup> No systematic studies available as yet.

**Combining Antidepressants for Treatment of Depression**

- Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in an adequate dose for a sufficient length of time.
- It is estimated that about 20% of depressed patients are resistant to monotherapy. Several studies have reported the efficacy of combining two antidepressants to treat patients with TRD.
- In general, because of the potential for drug interactions, antidepressant combination treatment should be used carefully, and patients monitored closely. The goal of combination antidepressant regimens is to combine medications to theoretically enhance clinical response.
- Stage 5 of the algorithm recommends combining two antidepressants. The medications should be initiated simultaneously at a low dose, then titrated upwards gradually to a therapeutically recommended dose.
- If a TCA is being used in combination treatment, plasma levels should be monitored.
- Because there is a risk of developing Serotonin Syndrome with combination antidepressant therapy, patients should be monitored for signs of confusion, disorientation, agitation, restlessness, diaphoresis, diarrhea, ataxia, and hyperreflexia.

## ***Algorithm Implementation***

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The purpose of treatment algorithms is to integrate available research information and clinical experience into the development of user-friendly, step-by-step "preferred practices," medication guidelines, or medication algorithms. **Algorithms do not decrease the need for clinicians having adequate education and clinical training, nor are they intended to restrict treatment options.** Rather, they are designed to facilitate a systematic approach to recommended treatment interventions.

It is assumed that a comprehensive psychiatric evaluation, a complete general medical history, and relevant diagnostic tests are completed prior to entry into any treatment algorithm. Some patients may not be appropriate for entry into the algorithms. In addition, patients may enter the algorithms at different stages depending upon their specific clinical features and previous treatment histories. For example, patients may enter Stage 2 or 3 if they have already failed to respond to an adequate trial of another antidepressant monotherapy.

**Treatment algorithms are not a substitute for clinical assessment or clinical judgment. They are tools to assist clinicians in making clinical decisions to optimize therapeutic outcomes. The purpose of this document is to amplify the steps in implementing a medication algorithm in order to maximize effectiveness. We describe issues related to the strategic choices for pharmacological interventions based on the TMAP Depression Algorithm. Additionally, preferred tactical steps and critical decision points are described to enable users to best apply the strategy selected for implementation.**

These algorithms focus on the pharmacotherapy and patient/family education for major depressive disorder. This does not imply that other nonpharmacological treatments including psychotherapy and rehabilitation are not indicated for the treatment of major depressive disorder (MDD). *Instead, this algorithm is restricted to a single focus: a multi-step medication approach in the treatment of patients with MDD in the public sector.* Other modalities used in the treatment of mental disorders are sufficiently complex that it is felt that patient care in TDMHMR can be best enhanced, initially, by utilizing algorithms that focus on one major aspect of treatment — in this case the use of pharmacological interventions. Additionally, patient and family education packages (ED packages) are also included in the overall protocol, since it is felt that proper implementation of the medication algorithm is enhanced through active participation of patients and families. Subsequent iterations may include psychological and rehabilitative services in the treatment package(s).

### **General Medical Principles Guiding Algorithm Implementation:**

#### Treatment Goals

1. The ultimate goal in the acute phase of treatment (0–12 weeks) is achieving symptomatic remission and full return of psychosocial functioning. The prevention of relapse and recurrence is the essential goal of the continuation and maintenance phases of treatment.

#### Medication Phasing

2. The treatment options recommended at various points in the algorithms are based upon available data from: (a) controlled clinical trials [level A evidence]; (b) open trials and retrospective data analyses [level B evidence]; and (c) case reports and clinical consensus [level C evidence]. The later stages in the algorithm involve more complicated single or combined regimens, while the earlier stages involve simpler, more routine medications in terms of safety, ease of use, side effect profiles, etc.

### Previous History

3. A patient's previous response to antidepressant treatments should always be considered when selecting the point of entry into an algorithm. If a patient responded well to a specific pharmacotherapy or other treatment intervention during a previous episode of depression, the same treatment should be used again. Similarly, if a patient failed to respond, or was unable to tolerate an adequate trial of a specific medication during a previous episode of depression, that medication is not recommended for the current or future depressive episodes.

### Physician-Patient Team

4. An adequate discussion between the clinician and the patient regarding available treatment options and information concerning specific medications (including expected results, routine dosing strategies, possible side effects, drug interactions, as well as potential toxicity in overdose) is essential. Medication selection should be dependent on these factors. When these considerations suggest that several medications are equivalent, patient preference becomes paramount and should define the particular option selected. It has been well documented that patient participation during this process is likely to enhance compliance to the chosen treatment option.

### Entering the Algorithm

5. Eligibility and point of entry into the algorithm for an individual patient should be determined by the physician based upon a review of relevant psychiatric factors (e.g., symptom severity, suicidality, comorbidity, etc.), medical status (e.g., concomitant medications or illnesses, age, etc.), and prior treatment history. **A rationale should be provided when a patient enters the algorithm at a later point/stage or when stages in the algorithm are skipped.**

### Visit Frequency

6. At the beginning of each stage, weekly contact is recommended (office visit or by phone) for the first 4 weeks; then every other week until 50% improvement in symptoms is attained for at least 4 weeks; then once per month until 75% improvement has been attained for at least 4 weeks. After 75% improvement has been reached, visits may be scheduled monthly and then every 3 months as the patient moves into the maintenance phase of treatment. Increased visit frequency is recommended in an attempt to optimize treatment outcomes by: a) encouraging patient adherence with treatment and b) rapidly identifying and correcting potential problems or adverse events associated with treatment (e.g., worsening of depression, potential suicidal ideology, etc.). Support personnel may contact patients by phone if the physician is unable to see them.

### Treatment Duration

7. Response to a medication is enhanced by ensuring an adequate treatment trial of at least 4–8 weeks of administration at the recommended dose range. However, if a patient fails to respond to an adequate dose of a specific medication for 4–6 weeks or has an unsatisfactory or partial response by weeks 6–8, an alternative treatment plan is recommended. The duration of a treatment trial may be extended to 8–12 weeks if an augmentation strategy has been instituted in patients with a partial response.

### Continuation Phase

8. Continuation phase treatment is recommended to prevent relapse for all patients with major depressive disorder who achieve a satisfactory clinical response, preferably symptom remission. After a full response, the medication(s) should be continued for 6–9 months at the dose effective during the acute phase. Patients should be evaluated at least once every 3 months during continuation treatment



(preferably every 1–2 months). Interim phone calls are also recommended one week before medication refills to enhance adherence.

### Maintenance Phase

9. Maintenance phase treatment is recommended for patients with major depressive disorder who: a) have had at least three episodes of major depression, or b) have experienced two episodes of major depression and have additional factors that contribute to an increased risk of recurrence (e.g., comorbid anxiety disorder or substantial residual functional impairment). Maintenance medication should be continued at full therapeutic doses and, as in the continuation phase, the regimen associated with symptom remission is recommended. The optimal duration of maintenance treatment has not been established, but depending on risk factors, is generally between one year past continuation phase and lifetime administration. Patients should be evaluated every 3–6 months during maintenance treatment.

### Lack of Significant Improvement Despite Treatment

10. A Structured Clinical Interview for DSM-IV (SCID) or further evaluation of symptoms should be considered:
- a) to confirm a diagnosis.
  - b) to reconfirm the diagnosis if there has been no response after 3 months.
  - c) if comorbid psychiatric conditions are present.
  - d) if patient has failed on 2 different classes or stages of medications.

### Documentation

11. Adequate documentation should be completed for each algorithm stage and treatment choice or critical decision point. If algorithm stages are skipped or if treatment deviates from the algorithm recommendations, the rationale behind the decision should be adequately documented.

### Psychotherapy

12. At baseline and throughout treatment, possible psychosocial interventions, including psychotherapy, should be considered to optimize treatment. The protocol allows for the addition of psychotherapy if clinically indicated based on individual patient situations.

### Treatment of Associated Symptoms and Side Effects

13. Adjunctive medications prescribed for the treatment of associated symptoms such as anxiety or treatment emergent side effects should be discontinued once these symptoms resolve. It should always be remembered that the prescription of additional medication also carries the risk of increased side effects. The rationale for their use should be carefully documented. The continued indication for these medications should be re-assessed on a regular basis.

## ***Critical Decision Points for the Nonpsychotic Depression Algorithm***

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Critical Decision Points (CDPs) are designed to prompt an assessment of symptoms and a determination of a need for a change in strategy or tactics. At each CDP, the physician should assess the patient for improvement and make a decision to either continue or change treatment based on improvement in symptoms or lack thereof. Note: Patients begin at CDP # 1 at the beginning of each stage.

### **STAGES 1,2,3**

Patients entered into one of these stages will be placed on a monotherapy treatment regimen. These medications are staged in the algorithm according to efficacy, side effect profile, and ease of use. Placement in the algorithm should be determined by the patient and physician based on prior history of antidepressant use, clinical presentation, and personal preferences.

***Patients should return to the clinic or be contacted by clinic personnel weekly (office visit or by phone) for the first 4 weeks of each treatment stage and then every 2 weeks until 50% improvement in symptoms is maintained for at least one month. Patients will then be evaluated monthly until 75% improvement is maintained for at least one month. Support personnel may contact patients by phone if the physician is unable to see them.***

### **CDP # 1, Week 0**

#### **Inclusion Criteria:**

Patients entering Stages 1, 2, or 3 of the nonpsychotic algorithm should have a diagnosis of major depressive disorder of sufficient severity to merit medication treatment and they a) have not been on any antidepressant medication for the current episode of MDD or b) need a medication change to another monotherapy antidepressant.

#### **Treatment Options:**

##### **Stage 1:**

- Selective Serotonin Reuptake Inhibitors (SSRIs) - citalopram, fluoxetine, paroxetine, sertraline
- Venlafaxine XR
- Bupropion SR
- Nefazodone
- Mirtazapine

##### **Stage 2:**

- Selective Serotonin Reuptake Inhibitors (SSRIs) - citalopram, fluoxetine, paroxetine, sertraline
- Venlafaxine XR
- Bupropion SR
- Nefazodone
- Mirtazapine
- Tricyclic Antidepressants – desipramine, nortriptyline, etc. ***Note: In general, secondary amines should be tried before tertiary amines.***

**Stage 3:**

- Selective Serotonin Reuptake Inhibitors (SSRIs) - citalopram, fluoxetine, paroxetine, sertraline
- Venlafaxine XR
- Bupropion SR
- Nefazodone
- Mirtazapine
- Tricyclic Antidepressants – desipramine, nortriptyline, etc. **Note: In general, secondary amines should be tried before tertiary amines.**
- MAOIs

<b>CDP # 2, Week 4</b>		<b>Stages 1, 2, and 3 Nonpsychotic MDD</b>
<b>Symptom Improvement (SEs tolerable)</b>		
0-50%		Gradually increase dose as tolerated for an additional 2 weeks.
50-75%		Continue current dose, <i>or</i> Gradually increase dose as tolerated for an additional 2 weeks.
75-100%		Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>		Continue current dose and address SEs, <i>or</i> Decrease dose and continue for 2 additional weeks, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>		Go to the next stage.
Return to clinic:		Return in 2 weeks.

<b>CDP # 3, Week 6</b>		<b>Stages 1, 2, and 3 Nonpsychotic MDD</b>
<b>Symptom Improvement (SEs tolerable):</b>		
0-25%		Strongly consider augmenting (refer to the Guidelines for Augmentation Therapy in the Appendix), <i>or</i> Go to the next stage.
25-50%		If dose was not increased at Week 4, increase dose, <i>or</i> If dose was increased at Week 4, augment or continue with current treatment.
50-75%		Increase dose, <i>or</i> Consider augmentation.
75-100%		Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>		Continue current dose and address SEs, <i>or</i> Decrease dose and continue for 2 additional weeks, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>		Go to the next stage.
Return to clinic:		If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stages 1, 2, and 3 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Increase augmentation, <i>or</i> Go to the next stage.
25-50%	Augment, if not done previously, <i>or</i> Go to the next stage.
50-75%	Maximize dose, if not done previously, <i>or</i> Consider augmentation.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 5, Week 10****Stages 1, 2, and 3 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Go to the next stage.
25-50%	Increase augmentation.
50-75%	Increase augmentation, <i>or</i> Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 6, Week 12****Stages 1, 2, and 3 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-75%	Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

## **Stage 4**

Clinical trials suggest that at least 30% of depressed patients fail to respond to first-line antidepressant treatment, despite adequate dose, duration, and compliance. In addition, up to 21% of patients with major depression who seek treatment have not recovered after two years. Clinicians have developed various pharmacological strategies to treat such refractory depression, including augmentation of therapy with thyroid (T<sub>3</sub> - Cytomel) medication, lithium, or buspirone. Studies have shown that, among nonresponders to serotonin reuptake inhibitors, patients demonstrate a higher recovery rate with augmented antidepressant therapy in comparison to antidepressant treatment alone, as assessed by scores on standardized depression rating scales. These augmentation strategies have clearly illustrated an efficacy and clinical utility, possibly resulting in complete or near-complete recovery in up to 60% of cases.

### **CDP # 1, Week 0**

#### **Inclusion Criteria:**

Stage 4 includes patients from Stages 1–3 who a) did not have a full response or b) were unable to tolerate side effects. Patients may enter at or skip to Stage 4 if their previous history or current condition suggests that Stage 4 is most clinically appropriate.

#### **Treatment Option:**

An antidepressant, preferably from a different class not tried in Stages 1–3, augmented by either lithium, buspirone, or a thyroid agent. Both medications should be started at the same time, following critical decision points on the CDP Table (Table 2, page 10) and the CDP Flowchart, page 7. If lithium augmentation was not used in a previous stage, consider using it here due to Level A evidence of lithium augmentation.

<b>CDP # 2, Week 4</b>	<b>Stage 4 Nonpsychotic MDD</b>
<b>Symptom Improvement (SEs tolerable):</b>	
0-50%	Gradually increase antidepressant dose as tolerated and continue for an additional 2 weeks and/or increase the dose of the augmenting agent. See Table 3 on page 11 and Table 7 on page 14 for dosing. <b>Note:</b> A gradual dose increase is critical for the Stage 4 antidepressants since response is enhanced by titration within a therapeutic dose range.
50-75%	Continue current dose(s), <i>or</i> Gradually increase the dose(s) as tolerated.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	Return in 2 weeks.

**CDP # 3, Week 6****Stage 4 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Maximize the antidepressant dose and/or augmentation dose.
25-50%	Maximize the antidepressant dose and attain lithium serum levels of 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy.
50-75%	Continue with current dose(s), <i>or</i> Gradually increase the antidepressant dose, <i>or</i> If already at maximum dose of the antidepressant, increase the dose of augmentation dose (if not at maximum).
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable:</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stage 4 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Increase augmentation dose, if not at maximum.
50-75%	If patient is at maximal tolerable therapeutic dose, consider an alternative augmenting agent, <i>or</i> Continue with current dose(s).
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 5, Week 10****Stage 4 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Go to the next stage.
25-50%	Increase augmentation dose.
50-75%	Maximize the antidepressant dose and increase augmentation dose to achieve a lithium steady-state serum concentration of 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy, <i>or</i> If the patient is receiving the maximal therapeutic lithium or alternative augmentation agent dose, go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 6, Week 12****Stage 4 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Go to the next stage.
50-75%	Maximize the antidepressant dose and maximize augmentation dose to achieve a lithium steady-state serum concentration of 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy, <i>or</i> If the patient is receiving the maximal therapeutic lithium or alternative augmentation agent dose, go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

## **Stage 5**

Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in adequate doses for sufficient lengths of time. It is estimated that about 20% of depressed patients are resistant to monotherapy. Several studies have reported the efficacy of combining two antidepressants to treat patients with TRD.

### **CDP #1, Week 0**

#### **Inclusion Criteria:**

Stage 5 includes patients who did not have a full response during Stage 4 or who had intolerable side effects.

#### **Treatment Options:**

Antidepressant combination therapy may be considered if patients have failed to respond in previous stages. If a TCA or SSRI is being used as monotherapy, consider a TCA/SSRI combination [level B evidence]. Both antidepressants should be initiated simultaneously. Since the SSRIs — particularly fluoxetine and paroxetine — may inhibit the metabolism of TCAs, close monitoring of TCA serum concentrations should occur during TCA/SSRI combination treatment [level A evidence]. Because of norfluoxetine's long elimination half-life, maximum effects of fluoxetine on elevation of the TCA serum concentrations may not be observed for 4–6 weeks. If a TCA is added to an SSRI, it will not take this long, as maximal enzyme inhibition will have already occurred and time to steady state is dependent on the particular TCA used. The goal is to obtain two serial TCA levels — at least one week apart — that are essentially the same. Since evidence for the efficacy of other antidepressant combinations are derived entirely from case series, they are recommended only as additional options at this stage.

<p>In general, because of the potential for drug interactions, antidepressant combination treatment should be used carefully, and patients monitored closely. The goal of combination antidepressant regimens is to combine medications to theoretically enhance clinical response.</p>
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Considerable care is required to obviate potential drug interactions associated with combined regimens. Table 12 on page 18 is provided as a guideline for the tactic of antidepressant combinations. Other treatment tactics included in Stage 5 are identical to those outlined in Stage 4.



**CDP # 2, Week 4****Stage 5 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Gradually increase dose(s) as tolerated for an additional 2 weeks.
50-75%	Continue current dose(s), <i>or</i> Gradually increase dose(s) as tolerated for an additional 2 weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	Return in 2 weeks.

**CDP # 3, Week 6****Stage 5 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Go to the next stage.
50-75%	Continue current dose(s), <i>or</i> Gradually increase dose(s) as tolerated for an additional 2 weeks, <i>or</i> Increase to maximum therapeutic dose(s) and continue to monitor for an additional 2 weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stage 5 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-75%	Consult with the Project Director, <i>or</i> Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 5, Week 10****Stage 5 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-75%	Consult with the Project Director, <i>or</i> Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 6, Week 12****Symptom Improvement (SEs tolerable):**

0-75%	Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

## **Stage 6**

Electroconvulsive therapy (ECT) has been shown to be an effective treatment option for mentally ill patients who are nonresponders to antidepressant medications or intolerant of the side effects. Patient groups expected to be favorable responders to ECT are manic-depressive and psychotic depressive patients. The antidepressive effects of ECT are immediate and comprehensive, and can elicit an improved response from medication when used in combination. Schizophrenia patients have also derived benefits from ECT therapy, when administered concurrently with antipsychotic medication.

### **CDP #1, Week 0**

#### **Inclusion Criteria:**

Stage 6 includes patients who did not have a full response during Stage 4 or 5 or who were unable to tolerate side effects. Depending on a patient's current condition or past treatment history, a patient may initially enter the algorithm at Stage 6. For example, a severely depressed patient with significant risk of suicide should be considered for initial entry at Stage 6 — treatment with ECT.

#### **Treatment Options:**

Stage 6 treatment is ECT. If the patient refuses ECT, or if ECT is unavailable or contraindicated, go to Stage 7.

As cognitive side effects are generally less severe compared with bilateral ECT, treatment may begin with right unilateral ECT. However, before declaring a patient resistant to ECT, a course of bilateral ECT should be considered. The electrical dose of right unilateral ECT should be at least 2.5 times the initial seizure threshold, while bilateral ECT should be dosed no more than 1.5 times the initial threshold. ECT should be terminated when patients are in full remission or fail to sustain additional improvement over 1–2 treatments. With either ECT modality, at least 6–10 ECT treatments should be attempted before declaring a patient resistant to treatment. (Note: Avoid ECT when the patient is taking lithium because CNS lithium toxicity may ensue.)

## Stage 7

Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in adequate doses for sufficient lengths of time. It is estimated that about 20% of depressed patients are resistant to monotherapy. If a patient has not attained complete remission of symptoms after adequate trials of medication treatment, then it may be necessary to accept partial response (25–75%) as a satisfactory outcome. The duration of critical decision points (CDPs) may need to be extended in order to allow slow responders a longer period of time on their medication.

### **CDP # 1, Week 0**

#### **Inclusion Criteria:**

Stage 7 includes patients who fail to fully respond during Stages 1–6 (including patients who refuse consent to ECT) or who are unable to tolerate side effects.

#### **Treatment Options:**

Stage 7 includes the alternatives not used previously during earlier stages (e.g., olanzapine, lamotrigine or one of the newer antidepressants). It also includes other antidepressant combinations (not included in Stage 5) that are more speculative than those previously discussed in earlier stages. Alternative augmenting agents such as T<sub>3</sub>, buspirone, and methylphenidate are also included in Stage 7. At Stage 7, combinations of antidepressants or antidepressants plus an alternative augmenting agent are preferable to a monotherapy not previously tried. Even though stage(s) can be skipped in the algorithm, Stage 7 is most likely to be indicated for those patients who have already failed to respond to multiple earlier stages in the algorithm.

#### **Antidepressant Switching Tactics:**

Because of the possibility of drug interactions, care should be taken when switching from one antidepressant to another. Please refer to page 16 for guidelines concerning switching from one antidepressant to another.

<b>CDP # 2, Week 4</b>		<b>Stage 7 Nonpsychotic MDD</b>
<b>Symptom Improvement (SEs tolerable):</b>		
0-50%		Gradually increase dose(s) as tolerated for an additional 2 weeks.
50-75%		Continue current dose(s), <i>or</i> Gradually increase dose(s) as tolerated for an additional 2 weeks.
75-100%		Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>		Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP # 1; <i>or</i> Consult with the Project Director.
<b>Not improved and SEs are intolerable</b>		Consult with the Project Director.
Return to clinic:		Return in 2 weeks.

**CDP # 3, Week 6****Stage 7 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Consider switching to an alternative medication. If beginning a trial of an antidepressant, return to CDP # 1; <i>or</i> Consult with the Project Director.
50-75%	Continue current dose(s), <i>or</i> Gradually increase dose as tolerated for an additional 2 weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP # 1; <i>or</i> Consult with the Project Director.
<b>Not improved and SEs are intolerable</b>	Consult with the Project Director.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stage 7 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Consult with the Project Director.
50-75%	If patient is at maximum tolerable therapeutic dose(s), consult the Project Director.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP # 1; <i>or</i> Consult with the Project Director.
<b>Not improved and SEs are intolerable</b>	Consult with the Project Director.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 5, Week 10****Stage 7 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Consult with the Project Director.
50-75%	If patient is at maximum tolerable therapeutic dose(s), consult the Project Director.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue, <i>or</i> Consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP # 1; <i>or</i> Consult with the Project Director.
<b>Not improved and SEs are intolerable</b>	Consult with the Project Director.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 6, Week 12****Stage 7 Nonpsychotic MDD****Symptom Improvement (SEs tolerable):**

0-75%	Consult the Project Director.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Consult with the Project Director.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

## ***Critical Decision Points for the Psychotic Depression Algorithm***

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Critical Decision Points are designed to prompt an assessment of symptoms and a determination of a need for a change in strategy or tactics. At each critical decision point or CDP, the physician should assess the patient for improvement and make a decision to either continue or change treatment based on improvement in symptoms or lack thereof. **Note: Patients begin at CDP # 1 at the beginning of each stage.**

### **Stage 1**

The advent of a new generation of antipsychotic medications has opened up more treatment options for psychiatrists in treating disorders with psychotic symptoms. The newer medications, signified as "atypical" antipsychotics, have several advantages to their predecessors and are more desirable candidates for this patient population. These include: olanzapine (Zyprexa), risperidone (Risperdal), and quetiapine (Seroquel). Notable benefits include a lower incidence of extrapyramidal symptoms, a broader efficacy profile — particularly with negative symptoms — and minimal impact on prolactin concentrations (olanzapine and quetiapine). Older antipsychotic agents have demonstrated a higher incidence of problematic side effects that hinder their use. Combination treatment with an antidepressant and an antipsychotic agent has shown to be significantly more effective than either given alone. Initial findings have demonstrated this with tricyclics and conventional antipsychotics, and data evaluating combinations of newer antidepressants and atypical antipsychotics are now accumulating.

***Patients should return to the clinic or be contacted by clinic personnel weekly for the first 4 weeks of each treatment stage; then every other week until 50% improvement is maintained for at least one month; then every 4 weeks until 75% improvement is maintained for at least one month.***

### **CDP #1, Week 0**

#### **Inclusion Criteria:**

The patient entered into the algorithm at Stage 1 is most likely either experiencing his/her first episode of major depression complicated by psychotic features or has previously responded to a Stage 1 regimen during a past episode.

#### **Treatment Options:**

- A tricyclic antidepressant (TCA) [amitriptyline, clomipramine, desipramine, imipramine, or nortriptyline] plus an antipsychotic [level A evidence], or
- A Serotonin Selective Reuptake Inhibitor (SSRI) plus an antipsychotic or venlafaxine XR plus an antipsychotic, [level B evidence], or
- Amoxapine [level A evidence].

**CDP # 2, Week 4****Stage 1 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Gradually increase dose(s) as tolerated for an additional 2 weeks.
50-75%	Continue current dose(s), <i>or</i> Gradually increase dose(s) as tolerated for an additional 2 weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose of drug thought to be causing side effect (i.e., antidepressant or antipsychotic) and continue for 2 additional weeks, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	Return in 2 weeks.

**CDP # 3, Week 6****Stage 1 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Strongly consider augmenting (refer to the Guidelines for Augmentation Therapy in the Appendix), <i>or</i> Go to the next stage.
25-50%	If dose(s) were not increased at Week 4, increase dose(s). If dose(s) were increased at Week 4, augment or continue with current treatment.
50-75%	Increase dose(s), <i>or</i> Consider augmentation.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue for 2 additional weeks, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stage 1 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Increase augmentation, <i>or</i> Go to the next stage.
25-50%	Augment if not done previously, <i>or</i> Go to the next stage.
50-75%	Increase dose(s), <i>or</i> Consider augmentation.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.



**CDP # 5, Week 10****Stage 1 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Go to the next stage.
25-50%	Increase augmentation.
50-75%	Increase augmentation, <i>or</i> Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 6, Week 12****Stage 1 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-25%	Go to the next stage.
25-50%	Increase augmentation.
50-75%	Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**Stage 2****CDP #1, Week 0****Inclusion Criteria:**

Stage 2 includes patients who did not have a full response at Stage 1 or who were unable to tolerate side effects. Patients may enter the algorithm at Stage 2 if their history of response during previous depressive episodes suggests that Stage 1 is not appropriate. If the patient's clinical presentation dictates a need for more immediate clinical response (e.g., emergent suicidality) or if the patient has a history of previous response to ECT, entry at Stage 3 should be considered.

**Treatment Options:**

1. Patient did not have full response at Stage 1.
  - a) If the patient received a TCA during Stage 1 and did not respond, consider venlafaxine XR (increase the dose to > 225 mg/d) with an antipsychotic or proceed to Stage 3 (ECT).
  - b) If an SSRI was the antidepressant used in Stage 1, consider a TCA with an antipsychotic.
  - c) If amoxapine was the antidepressant used in Stage 1, consider a TCA with an antipsychotic.

- If the patient did not respond during Stage 1 due to intolerable side effects, select an antidepressant from a different class than the previous choice and with a contrasting side effect profile (e.g., from a TCA to an SSRI). If a patient is unable to tolerate 2 different antidepressant monotherapies from distinct chemical classes, consider proceeding to Stage 3.
- The tactics for drug treatment in Stage 2 are essentially the same as those outlined in Stage 1. Patients should be initiated with doses of antidepressants at the lower end of the therapeutic range and the dose gradually increased as tolerated if response is not attained. Patients should be seen and monitored frequently during the initial month. At week 4, if full response is absent, response and medication tolerability should be assessed. Further assessments at subsequent critical time points on a 2-week basis should be completed to assess for dose increase as outlined in treatment tactics (see Table 2).

<b>CDP # 2, Week 4</b>		<b>Stage 2 Psychotic MDD</b>
<b>Symptom Improvement (SEs tolerable):</b>		
0-50%		Increase antidepressant dose to a maximal therapeutic level and continue for two additional weeks.
50-75%		Continue current antidepressant dose, <i>or</i> Gradually increase antidepressant dose as tolerated to a maximal therapeutic range.
75-100%		Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current antidepressant dose.
<b>Improved, but SEs are intolerable</b>		Continue current antidepressant dose and address side effects, <i>or</i> Decrease antidepressant dose and continue for 2 additional weeks, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>		Go to the next stage.
Return to clinic:		Return in 2 weeks.

<b>CDP # 3, Week 6</b>		<b>Stage 2 Psychotic MDD</b>
<b>Symptom Improvement (SEs tolerable):</b>		
0-50%		If the antidepressant dose was maximized at week 4, go to the next stage; <i>or</i> If the antidepressant dose was not maximized at week 4, increase the dose to the maximum therapeutic level (monitor serum concentration for TCAs).
50-75%		Continue current antidepressant dose, <i>or</i> Gradually increase antidepressant dose as tolerated to a maximal therapeutic range.
75-100%		Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>		Continue current antidepressant dose and address side effects, <i>or</i> Decrease antidepressant dose and continue for 2 additional weeks, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>		Go to the next stage.
Return to clinic:		If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stage 2 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Go to the next stage.
50-75%	Continue at maximal doses for 2 additional weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 5, Week 10****Stage 2 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-75%	Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

### **Stage 3**

ECT has been shown to be an effective treatment option for mentally ill patients who are nonresponders to antidepressant medications or intolerant of the side effects. Patient groups expected to be favorable responders to ECT are manic-depressive and psychotic depressive patients. The antidepressive effects of ECT are immediate and comprehensive, and can elicit an improved response from medication when used in combination. Schizophrenia patients have also derived benefits from ECT therapy, when administered concurrently with antipsychotic medication.

#### **Inclusion Criteria:**

Stage 3 includes patients who did not have a full response at Stage 2 or who were unable to tolerate side effects. Patients may enter the algorithm at Stage 3 if their current condition, associated features, or history of response during a previous depressive episode suggest that Stage 1 or 2 is not appropriate or is contraindicated. If the patient's clinical presentation warrants a more immediate clinical response (e.g., emergent suicidality) or history of previous response to ECT, entry at Stage 3 should be considered.

#### **Treatment Options:**

- Stage 3 treatment is ECT.

As cognitive side effects are generally less severe compared with bilateral ECT, treatment may begin with right unilateral ECT. However, before declaring a patient resistant to ECT, a course of bilateral ECT should be considered. The electrical dose of right unilateral ECT should be at least 2.5 times the initial seizure threshold, while bilateral ECT should be dosed no more than 1.5 times the initial threshold. ECT should be terminated when patients are in full remission or fail to sustain additional improvement over 1–2 treatments. With either ECT modality, at least 6–10 ECT treatments should be attempted before declaring a patient resistant to treatment. **(Note: Avoid ECT when the patient is taking lithium because CNS lithium toxicity may ensue.)**

- In general, any antidepressant or antipsychotic medication should be discontinued before initiating ECT.
- If a patient does not give informed consent for ECT, fails to respond to ECT, or ECT is not available, proceed to Stage 4.

## Stage 4

Clinical trials suggest that at least 30% of depressed patients fail to respond to first-line antidepressant treatment, despite adequate dose, duration, and compliance. In addition, up to 21% of patients with major depression who seek treatment have not recovered after two years. Clinicians have developed various pharmacological strategies to treat such refractory depression, including augmentation of therapy with thyroid (T<sub>3</sub> - Cytomel) medication, lithium, and buspirone. Studies have shown that, among partial-responders to serotonin reuptake inhibitors, patients demonstrate a higher recovery rate with augmented antidepressant therapy in comparison to antidepressant treatment alone, as assessed by scores on standardized depression rating scales. These augmentation strategies have clearly illustrated an efficacy and clinical utility, possibly resulting in complete or near-complete recovery in up to 60% of cases.

### CDP #1, Week 0

#### **Inclusion Criteria:**

Stage 4 includes patients from Stage 3 who a) did not have a full response or b) were unable to tolerate side effects. Patients may enter or skip to Stage 4 if their previous history or current condition suggests that Stage 4 is most clinically appropriate.

If the patient did not have a full response to any of the combinations in Stages 1 or 2, Stage 4 should be completed prior to beginning Stage 5.

#### **Treatment Options:**

At least one attempt at lithium augmentation should be initiated (unless contraindicated) before proceeding to Stage 5. Both the antidepressant and the augmenting agent should be started simultaneously.

If the patient fails an adequate trial of lithium augmentation (or is unable to tolerate lithium), alternative augmenting agents such as T<sub>3</sub> or buspirone should be strongly considered.

CDP # 2, Week 4		Stage 4 Psychotic MDD
<b>Symptom Improvement (SEs tolerable):</b>		
0-50%		Increase antidepressant dose to a maximal therapeutic level and continue for two additional weeks.
50-75%		Continue current dose(s), <i>or</i> Gradually increase dose(s) as tolerated to a range of 0.4–0.8 mEq/L for lithium or the maximal therapeutic dose for the selected augmentation strategy and to the therapeutic range appropriate for the antidepressant.
75-100%		Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>		Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue for 2 additional weeks, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>		Go to the next stage.
Return to clinic:		Return in 2 weeks.

**CDP # 3, Week 6****Stage 4 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	If the antidepressant dose was already maximized at week 4, increase the lithium dose so that serum levels between 0.8–1.2 mEq/L are attained or the maximal therapeutic dose for the selected augmentation strategy; <i>or</i> If the antidepressant dose was not maximized at week 4 and the patient is currently tolerating the antidepressant, the dose should be increased to the usual maximum dose (monitor serum concentration for TCAs).
50-75%	If the antidepressant dose was maximized at week 4, continue current dose(s) for an additional 2 weeks; <i>or</i> Maximize the antidepressant dose within the therapeutic range and the lithium dose should be increased to 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy for an additional 2 weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose(s).
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue for 2 additional weeks, <i>or</i> Consider switching medications if side effects are attributable to a particular medication, <i>or</i> Go to the next stage.
<b>Not improved and SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stage 4 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Go to the next stage.
50-75%	Continue at maximal doses for 2 additional weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current doses.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 5, Week 10****Stage 4 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-75%	Go to the next stage.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Go to the next stage.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

## **Stage 5**

Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in an adequate dose for a sufficient length of time. It is estimated that about 20% of depressed patients are resistant to monotherapy. If a patient has not attained complete remission of symptoms after adequate trials of medication treatment, then it may be necessary to accept partial response (25–75%) as a satisfactory outcome. The duration of critical decision points (CDPs) may need to be extended in order to allow slow responders a longer period of time on their medication.

### **CDP #1, Week 0**

#### **Inclusion Criteria:**

Stage 5 includes patients who fail to fully respond during Stages 1–4 or who are unable to tolerate side effects.

#### **Treatment Options:**

Stage 5 includes the alternatives not used previously during earlier stages (e.g., lamotrigine or one of the newer antidepressants). It also includes antidepressant combinations. Alternative augmenting agents such as T<sub>3</sub> or buspirone should be strongly considered, and methylphenidate is also included in Stage 5. **Even though stage(s) can be skipped in the algorithm, Stage 5 is most likely to be indicated for those patients who have already failed to respond to multiple earlier stages in the algorithm.**

<b>CDP # 2, Week 4</b>	<b>Stage 5 Psychotic MDD</b>
<b>Symptom Improvement (SEs tolerable):</b>	
0-50%	Increase antidepressant dose to a maximal therapeutic level and continue for 2 additional weeks.
50-75%	Continue current dose(s), <i>or</i> Gradually increase dose(s) as tolerated to a maximal therapeutic range.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue for 2 additional weeks, <i>or</i> Consult Project Director.
<b>Not improved and SEs are intolerable</b>	Consult Project Director.
Return to clinic:	Return in 2 weeks.

**CDP # 3, Week 6****Stage 5 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	If the antidepressant dose was maximized at week 4, consult the Project Director; <i>or</i> If the antidepressant dose was not maximized at week 4, increase the dose to the usual maximum dose (monitor serum concentration for TCAs).
50-75%	If the antidepressant dose was maximized at week 4, continue current dose(s) for an additional 2 weeks; <i>or</i> Maximize the antidepressant dose within the therapeutic range and continue for an additional 2 weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose(s).
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue for 2 additional weeks, <i>or</i> Consider switching medications if side effects are attributable to a particular medication, <i>or</i> Consult the Project Director.
<b>Not improved and SEs are intolerable</b>	Consult the Project Director.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 4, Week 8****Stage 5 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-50%	Consult the Project Director.
50-75%	Continue at maximal doses for 2 additional weeks.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>Improved, but SEs are intolerable</b>	Continue current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue for 2 additional weeks, <i>or</i> Consider switching medications if side effects are attributable to a particular medication, <i>or</i> Consult the Project Director.
<b>Not improved and SEs are intolerable</b>	Consult the Project Director.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**CDP # 5, Week 10****Stage 5 Psychotic MDD****Symptom Improvement (SEs tolerable):**

0-75%	Consult the Project Director.
75-100%	Go to <b>Continuation</b> if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
<b>SEs are intolerable</b>	Consult the Project Director.
Return to clinic:	If > 50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

**Continuation and Maintenance Phase Treatment**



## **Continuation Phase Treatment**

### **1. Patient received pharmacotherapy during acute phase:**

At baseline and throughout treatment, other psychosocial or nonmedication treatment modalities such as concomitant psychotherapy should be considered. After full response, the medication(s) should be continued for 6–9 months at the dose effective during the acute phase. Patients should be evaluated at least once every 3 months during continuation treatment (preferably every 1–2 months). For initial episodes of major depression, medication tapering and discontinuation should be considered after the continuation period is completed. If previous depressive episodes have occurred, maintenance treatment should be considered. When discontinuing the antidepressant, the dose should be tapered no more rapidly than 25% per week and not before 6–8 months of full remission has occurred. Tapering and discontinuation usually can be completed over a 2–3 month period. Patients should be educated concerning the signs and symptoms of recurrence of depressive symptoms. A new depressive episode is most likely to occur within the first 8 months of medication discontinuation; therefore, patients should be evaluated every 2–4 months during that period. If depression recurs, prompt treatment with the medication previously effective should be initiated (i.e., initiate algorithm stage and tactic that previously resulted in remission of depressive symptoms).

No systematic studies regarding the optimal duration of antipsychotic treatment during the continuation phase have been reported. It is recommended that the acute phase antipsychotic at the same dose be maintained at least for 1–2 months and then slowly tapered over the continuation phase. The duration of antipsychotic treatment should be limited to the minimum duration indicated in order to reduce the risk of tardive dyskinesia. If a patient is receiving a TCA, the serum concentration should be monitored, and the dose adjusted as necessary to maintain the level with the recommended therapeutic window (with and without the neuroleptic co-administered).

### **2. Patient received ECT during acute phase:**

Continuation treatment with an antidepressant is recommended. It is preferable to select an antidepressant that the patient has not received or one that the patient has responded to during a previous episode of depression. However, if necessary, a previously ineffective antidepressant may be used in combination with lithium. Dosing, duration of treatment, monitoring, and medication tapering are as above.

If a patient relapses during continuation treatment with an antidepressant, continuation ECT should be considered.

## **Maintenance Phase Treatment**

Patients experiencing an initial episode of major depression have at least a 50% chance of having a second episode, and by the third episode of major depression, there is a 90% chance of recurrence. Therefore, all patients having a third depressive episode and some patients experiencing a second episode should be evaluated for maintenance antidepressant treatment.

### **Indications for Maintenance Medication**

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<b><u>Feature</u></b>	<b><u>Strength of Indication</u></b>
1. Three or more episodes of major depression	Very strongly recommended
2. Two episodes of major depressive disorder, and one or more of the following:	
a) Family history of bipolar disorder	Strongly recommended
b) History of recurrence within one year after previously effective medication was discontinued	Strongly recommended
c) A family history of recurrent major depression	Strongly recommended
d) Early onset (before age 20) of the first depressive episode	Strongly recommended
e) Depressive episodes were severe, sudden, or life-threatening within the past 3 years	Strongly recommended

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(Source: AHCPR Guidelines (1993), Vol. 2, page 111.)

Maintenance medication should be continued at full therapeutic doses and, as in the continuation phase, the regimen associated with symptom remission is recommended. The optimal duration of maintenance treatment has not been established, but depending on risk factors, is generally between one year past continuation phase and lifetime administration.

Active discussions regarding the initiation and duration of maintenance treatment are an important element in the clinician-patient collaboration for this as well as other phases of pharmacological management of major depressive disorder. The patient's personal preference, as well as the risk factors for recurrence, should be considered in the decision process.

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## **DSM-IV Criteria for Major Depressive Disorder**

### **Criteria for Major Depressive Episode**

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

**Note:** Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

(1) depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood.

(2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)

(3) significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gains.

(4) insomnia or hypersomnia nearly every day

(5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)

(6) fatigue or loss of energy nearly every day

(7) feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)

(8) diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)

(9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

- B. Symptoms do not meet criteria for a Mixed Episode.

- C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

- D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

- E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

## Diagnostic criteria for 296.2x Major Depressive Disorder, Single Episode

- A. Presence of a single Major Depressive Episode.
- B. The Major Depressive Episode is not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- C. There has never been a Manic Episode, A Mixed Episode, or a Hypomanic Episode. **Note:** This exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

*Specify* (for current or most recent episode):

**Severity/Psychotic/Remission Specifiers**

**Chronic**

**With Catatonic Features**

**With Melancholic Features**

**With Atypical Features**

**With Postpartum Onset**

## Diagnostic criteria for 296.3x Major Depressive Disorder, Recurrent

- A. Presence of two or more Major Depressive Episodes.  
  
**Note:** To be considered separate episodes, there must be an interval of at least 2 consecutive months in which criteria are not met for a Major Depressive Episode.
- B. The Major Depressive Episodes are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- C. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode. **Note:** This exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

*Specify* (for current or most recent episode)

**Severity/Psychotic/Remission Specifiers**

**Chronic**

**With Catatonic Features**

**With Melancholic Features**

**With Atypical Features**

**With Postpartum Onset**

*Specify:*

**Longitudinal Course Specifiers (With and Without Interepisode Recovery)**

**With Seasonal Pattern**

## ***Antidepressant Monographs***

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**Amitriptyline:** Tricyclic antidepressant which blocks reuptake of norepinephrine and serotonin, into nerve endings. Peak plasma concentrations are reached within 2–12 hours. It is 90-97% protein bound and thus may cause drug interactions by displacing other agents from protein-binding sites. Amitriptyline and its metabolites are metabolized via multiple pathways, however amitriptyline is metabolized by the liver via cyt P450 2C9/19, with a half-life 10–50 hours. It does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, seizure disorders and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs; a 2-week washout is recommended before switching between TCA's and MAOI's.

**Amoxapine:** Tetracyclic antidepressant which blocks the reuptake of norepinephrine primarily, and serotonin weakly, into nerve endings. Its 7-hydroxy metabolite blocks dopamine receptors with potency comparable to that of haloperidol. Peak plasma concentrations are reached within 1-2 hours. It is 90% protein bound. It is metabolized by the liver, with a half-life of 8-30 hours, and does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs; a 2-week washout is recommended before switching between TCA's and MAOI's.

**Bupropion (immediate release)/bupropion SR:** an antidepressant which inhibits the reuptake of dopamine and norepinephrine, with little effect on serotonin. Uses include major depression and smoking cessation. Peak plasma concentrations are reached within 3 hours, its half-life is 10-21 hours, and steady state is achieved in 1 week. It is not highly protein bound. Bupropion is metabolized through the liver via multiple isoenzymes and may be a weak inhibitor of cyt P450 2D6 activity. It is contraindicated in patients with seizure disorders or eating disorders. Use cautiously in patients with renal and hepatic disease, recent MI or cranial trauma, or any patient with factors that may increase the risk of seizures.

**Citalopram:** an SSRI which is an effective inhibitor of neuronal serotonin reuptake. Absorption is fast, almost complete, and unaffected by food. Bioavailability is 80%, time to peak is 2-4 hours, with a half-life of 33 hours. Citalopram is 80 % protein bound with a low potential for displacement interactions. It is hepatically metabolized via cyt P450 2C9/19 isoenzymes and possesses very weak inhibitory effects on 1A2, 2C9, and 2D6. Should not be used with MAOIs because the combination may lead to serotonin syndrome (altered mental status, restlessness, hyperreflexia, diaphoresis, tremor).

**Clomipramine:** Tricyclic antidepressant which potently inhibits serotonin reuptake and increases dopamine metabolism. Uses include major depression, dysphoria, phobias, anxiety, agoraphobia and obsessive-compulsive disorder. Extensively bound to tissue and plasma proteins and thus may displace other agents from protein-binding sites. Peak plasma concentrations are reached within 2-6 hours and the half-life is 21 hours for the parent compound and 36 hours for metabolites. It is hepatically metabolized via cyt P450 2C9/19 isoenzymes but does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs.

**Desipramine**: Tricyclic antidepressant which blocks the reuptake of norepinephrine into nerve ending. Peak plasma concentration is reached within 3-6 hours and protein binding ranges from 73-92%. It is hepatically metabolized via cyt P450 2D6, with a half-life of 11-46 hours. It does not alter hepatic metabolism, however. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders and prostatic hypertrophy. Increases vasopressor effects of epinephrine, and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs.

**Fluoxetine**: an SSRI which is an effective inhibitor of neuronal serotonin reuptake. Uses include major depression, obsessive-compulsive disorder and bulimia nervosa. Peak plasma concentrations are reached within 4-8 hours. It is >90% protein bound and thus may displace other agents from protein-binding sites. It is hepatically metabolized by cyt P450 2C9/19, with a half-life of 4-6 days and 4-16 days for its active metabolite, norfluoxetine. Fluoxetine is a potent cyt P450 2D6 inhibitor, and norfluoxetine is a cyt P450 3A4 inhibitor. Fluoxetine may increase the half-life of diazepam, tricyclic antidepressants, nefazodone, and some antipsychotics. TCA plasma concentration monitoring is recommended when this combination is used. Should not be used with MAOIs.

**Fluvoxamine**: an SSRI which is an effective inhibitor of neuronal serotonin reuptake. Time to peak ranges between 2 and 8 hours and is not highly protein bound. It is eliminated via cyt P450 1A2, with an elimination half-life of 15-26 hours. Fluvoxamine is a potent inhibitor of cyt P450 1A2 and 2C19. An increase in the half-life of TCA's may occur, therefore, TCA plasma concentration monitoring is recommended. Like other SSRI's, fluvoxamine should not be combined with MAOIs. The current FDA indication is for the treatment of Obsessive/Compulsive Disorder. However, since it is an SSRI, it is used investigationally for the treatment of depression.

**Imipramine**: Tricyclic antidepressant which blocks the reuptake of norepinephrine and serotonin into nerve endings. It reaches peak plasma concentrations in 1.5-3 hours and is highly protein bound. It is metabolized via cyt P450 1A2, with a half-life of 6-34 hours. Imipramine does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs. Do not break, crush or chew imipramine film-coated tablets.

**Mirtazapine**: An antidepressant which blocks presynaptic alpha 2 inhibitory receptors and postsynaptic serotonin receptors, thereby enhancing noradrenergic and serotonergic activity. Peak plasma levels are reached within 2 hours, and plasma protein binding is low. Mirtazapine is likely metabolized by cyt P450 2D6, 1A2 and 3A4 but does not alter hepatic metabolism itself. The presence of food in the stomach has a minimal effect on both the rate and extent of absorption.

**Nefazodone**: An antidepressant which selectively inhibits serotonin reuptake in the brain. Peak concentrations are reached in 1-2 hours and is not highly protein bound. Metabolized in the liver via cyt P450 3A4 with an elimination half-life of 2-4 hours. It is a potent inhibitor of cyt P450 3A4, and thus increases plasma concentrations of some benzodiazepines, quetiapine, carbamazepine, and cisapride. Increases the effect of CNS depressants. Possible hypertensive crisis when combined with MAOIs. Drug use and smoking can increase metabolism and decrease effects. Use cautiously in patients with cardiovascular disease or seizure disorder.

**Nortriptyline**: Tricyclic antidepressant which blocks the reuptake of norepinephrine and serotonin into nerve endings. Peak plasma concentration is reached in 3-12 hours, and it is highly protein bound. It is hepatically metabolized by primarily cyt P450 2D6, with a half-life of 16-88 hours. It does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of

alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs.

**Paroxetine**: an SSRI which is an effective inhibitor of neuronal serotonin reuptake. Uses include major depression, obsessive-compulsive disorder, panic disorder and social phobia. Peak plasma concentrations are achieved in 5-7 hours. Protein binding is 95%. Paroxetine is metabolized through the liver via cyt P450 2D6, with a half-life of 21 hours. It is a potent inhibitor of cyt P450 2D6 metabolism, thus it may increase plasma levels of TCAs and some antipsychotics. Like other SSRI's, it should not be used with MAOIs.

**Phenelzine**: MAOI antidepressant which increases concentrations of endogenous epinephrine, norepinephrine, serotonin, and dopamine in storage sites in the central nervous system by inhibiting MAO. Contraindicated in hypertension, elderly, CHF, severe hepatic disease, pheochromocytoma, severe renal disease and severe cardiac disease.

**Sertraline**: an SSRI which is an effective inhibitor of neuronal serotonin reuptake. Uses include major depression, obsessive-compulsive disorder, panic disorder and posttraumatic stress disorder. Sertraline plasma concentrations peak in 5–9 hours reaching steady state in 1 week. Taking with food decreases the time required to reach peak plasma levels but does not affect total concentration of drug absorbed. It is 99% plasma protein binding with a half-life of 27 hours. It is hepatically metabolized via cyt P450 2C9/19 and also has the ability to inhibit 2C9/19 and 2D6 activity, particularly at higher doses. May cause fatal reactions when used in combination with MAOIs.

**Tranylcypromine**: MAOI antidepressant which increases concentrations of endogenous epinephrine, norepinephrine, serotonin, and dopamine in storage sites in the central nervous system by inhibiting MAO. Contraindicated in hypertension, elderly, CHF, severe hepatic disease, pheochromocytoma, severe renal disease and severe cardiac disease.

**Venlafaxine/venlafaxine XR**: Potent inhibitor of neuronal serotonin and norepinephrine reuptake and a weak inhibitor of dopamine reuptake. Peak plasma concentration is reached within 2 hours and protein binding is minimal. Extensively hepatically metabolized primarily via cyt P450 2D6 to an active metabolite with 87% of drug recovered in the urine. The half-life for regular release and extended release are 5 hours and 48 hours, respectively. May cause hyperthermia, rigidity, rapid fluctuations of vital signs and mental status changes when used with MAOIs. Use cautiously in patients with mania, hypertension or seizure disorder.



**Note: When using any antidepressant agent in a patient with a history of manic symptoms, caution should be taken to monitor for precipitation of a manic episode.**

**Table 1. Characteristics of Antidepressant-Induced Sexual Dysfunction**

<b>Antidepressant</b>	<b>Type of Sexual Dysfunction♦</b>	<b>Incidence♦</b>
Venlafaxine	Impaired ejaculation, delayed/absent orgasm	12%
Paroxetine	Impaired ejaculation, delayed/absent orgasm	13-28% 2-10%
Fluvoxamine	Impaired ejaculation, delayed/absent orgasm	2-8%
Sertraline	Impaired ejaculation, delayed/absent orgasm	14%
Citalopram	Impaired ejaculation, delayed/absent orgasm, decreased libido	1-3%*
Fluoxetine	Impaired ejaculation, delayed/absent orgasm, decreased libido, and erectile impairment	2-11%
Mirtazapine	Decreased libido	2-6%*
Nefazodone	Decreased libido	1%*
Bupropion	Decreased libido	1-3%*
MAOI's	Impaired ejaculation, delayed/absent orgasm, erectile impairment, decreased libido	NA <sup>⊖</sup>
TCA's	Impaired ejaculation, delayed/absent orgasm, erectile impairment, decreased libido	NA <sup>⊖</sup>

- ♦ **Based on AHFS Drug Information and** Hirschfeld RM, *J Clin Psychiatry* 1999;60(suppl 14):27-30  
Rothschild AJ, *J Clin Psychiatry* 2000;61(suppl 11):28-36.  
Montego-Gonzalez AL, et al. *Journal of Sex & Marital Therapy* 1997;23(3):176-94.

\* No different than placebo

⊖ Case reports available

Note: Higher incidences of sexual dysfunction have been reported in settings where patients are specifically queried about sexual problems.

## ***Monographs for Augmentation Agents***

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**Lithium**: Antimanic which may alter sodium, potassium ion transport across cell membrane in nerve cells and may balance noradrenergic and serotonergic activity in the CNS by acting on postsynaptic second messengers. Peak plasma concentration is reached in 1-12 hours with no protein binding. It does not undergo hepatic metabolism but rather is eliminated renally. Half-life is 14-30 hours. Therapeutic range is 0.5-1.2 mEq/L. When adjusting dose, 300 mg of lithium will generally increase lithium serum levels by 0.2-0.4 mEq/L. Sodium restriction, renal impairment, dehydration, vomiting/diarrhea, or other factors that may alter sodium levels or renal function may cause lithium toxicity. Contraindicated in hepatic disease, renal disease, brain trauma, and severe cardiac disease.

**Buspirone**: Antianxiety agent which acts by regulating the action of serotonin. May be used as augmentation therapy due to increased effects when used with psychotropic drugs. Peak plasma concentration is reached within 1 hour. It is 95% protein bound, with a half-life of 2-3 hours. It is hepatically metabolized via cyt P450 3A4. Use cautiously in elderly patients and patients with impaired hepatic/renal functioning. Increased ALT when combined with trazodone. Do not use with MAOIs.

**Liothyronine (T<sub>3</sub>)**: Increases metabolic rates, cardiac output, oxygen consumption, body temperature, blood volume, growth, and development at the cellular level. Peak plasma concentration is reached within 2 hours, with a half-life of 1.5 days. Use cautiously in elderly patients and patients with angina pectoris, hypertension, ischemia, cardiac disease, pregnancy, and lactation. Increases the effects of TCAs, as well as anticoagulants and sympathomimetics. Decreases the effects of digitalis drugs, insulin, hypoglycemics, liothyronine, and estrogens.

## ***Antipsychotic Monographs***

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**Haloperidol**: A high potency traditional antipsychotic which blocks dopamine (D<sub>2</sub>) receptors at the mesolimbic and mesocortical areas of the brain, thus treating psychotic symptoms. Peak plasma concentration is achieved within 3 hours and protein binding is low. Haloperidol is hepatically metabolized via cyt P450 1A2 and 3A4, with a half-life of 15-30 hours. Contraindicated in alcohol and barbiturate withdrawal states, Parkinson's disease, angina, epilepsy, and urinary retention. Possible toxicity when combined with epinephrine.

**Olanzapine**: An atypical antipsychotic which may mediate antipsychotic activity by both dopamine and serotonin type 2 antagonism. Peak plasma levels are reached within 5 hours. It is hepatically metabolized via cyt P450 1A2 and 2D6, with a half-life of 27 hours. Use cautiously in patients with hypertension, hepatic disease, cardiac disease and in elderly patients. Patients on olanzapine should be monitored for weight gain, glucose intolerance and hyperlipidemia.

**Perphenazine**: A medium potency traditional antipsychotic which blocks dopamine (D<sub>2</sub>) receptors at the mesolimbic and mesocortical areas of the brain, thus treating psychotic symptoms. Peak plasma level is achieved in 3-5 hours and protein binding is low. It is hepatically metabolized, with a half-life of 10-20 hours.

**Quetiapine**: Neuroleptic antipsychotic which functions as an antagonist at dopaminergic and serotonergic receptors in the brain. It has a higher affinity for serotonergic receptors than dopamine receptors. Peak plasma level is achieved in 1-2 hours, and protein binding is considered low (83%). Quetiapine is

hepatically metabolized by cyt P450 3A4 and possibly 2D6, with a half-life of 6 hours. It should be used with caution in patients taking antihypertensives and CNS depressants, and baseline liver function tests and thyroid panel should be obtained.

**Risperidone:** Neuroleptic antipsychotic which may mediate antipsychotic activity through both dopamine type 2 and serotonin type 2 antagonism. Peak plasma concentration is reached in 1-2 hours, and protein binding is 90%. Risperidone is metabolized by cyt P450 2D6 to an active metabolite, 9-hydroxy-risperidone. The active metabolite is then eliminated renally. Half-lives for the parent compound and active metabolite are 3 and 24 hours, respectively. Contraindicated in seizure disorders.

**Note for all antipsychotic medications: Once psychotic symptoms have remitted, maintain the patient on the lowest necessary dose to maintain remission for a period of 3 months. After 3 months of no psychotic symptoms, gradually taper the patient off the antipsychotic medication over a period of 2 weeks.**

**Table 2. Antidepressant/Antipsychotic Interactions**

INHIBITOR (Inhibits substrate)	SUBSTRATE (Drug metabolized by pathway)		
	1A2	2D6	3A3/4
Bupropion (Wellbutrin)		<i>Phenothiazines (some)</i> Clozapine* Olanzapine*	
Citalopram (Celexa)		Phenothiazines Clozapine* Olanzapine*	
Fluoxetine (Prozac)		<b>PHENOTHIAZINES</b> Clozapine* Olanzapine*	<b>Clozapine</b> <b>Quetiapine</b>
Fluvoxamine (Luvox)	<b>CLOZAPINE</b> <b>HALOPERIDOL</b> <b>OLANZAPINE</b>		<b>Clozapine</b> <b>Quetiapine</b>
Nefazodone (Serzone)			<b>CLOZAPINE</b> <b>QUETIAPINE</b>
Paroxetine (Paxil)		<b>PHENOTHIAZINES</b> Clozapine* Olanzapine*	
Sertraline (Zoloft)		Phenothiazines Clozapine* Olanzapine*	Clozapine Quetiapine

Venlafaxine (Effexor) increases haloperidol levels, but not by Cytochrome P450 interaction.  
 Regular type = small changes in levels (low probability of clinically significant interaction)  
**Bold type** = moderate changes in levels (moderate probability of clinically significant interaction)  
**BOLD CAPS** = very large changes in levels (high probability of clinically significant interaction)  
 \* = minor pathway

## ***Monographs for other agents used to manage associated symptoms or treatment emergent side effects***

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**Amantadine:** a antiparkinsonian agent that exerts its therapeutic effect by enhancing dopaminergic activity, primarily through dopamine reuptake blockade. Peak plasma concentration is achieved in 1-4 hours, and protein binding is low. The elimination half-life ranges between 10 and 31 hours, and it is primarily excreted unchanged by the kidneys. Therefore, lower doses are recommended in patients with compromised renal function. Because amantadine causes increases in dopamine levels initially, patients may experience visual hallucinations or symptoms of delirium. Symptoms will usually subside with continued treatment, however the lowest effective dose should always be used. In addition, to minimize this effect, amantadine should not be combined with anticholinergic agents.

**Alprazolam:** a short-acting benzodiazepine that is FDA approved for the treatment of GAD. It exerts its anxiolytic effect by enhancing GABA inhibition. Peak plasma level is reached in 1 hour, and protein binding is considered low (<90%). It is hepatically metabolized via cyt P450 3A4, and its half-life is 12-15 hours. It has no active metabolites, and thus drug accumulation with chronic use is minimal. As with any benzodiazepine, CNS depressant effects may be increased if combined with agents that have CNS depressant properties (alcohol, barbiturates, narcotic analgesics, etc.). Tapering (25% reduction weekly) rather than abrupt discontinuation is recommended if a patient has been receiving benzodiazepine therapy for at least 6 weeks. Withdrawal symptoms to monitor for include increased anxiety, insomnia, restlessness, and agitation/irritability.

**Benzotropine:** an antimuscarinic, antiparkinsonian agent that acts to block acetylcholine and possibly enhance dopaminergic activity, thus correcting the proposed dopamine deficiency-cholinergic excess theory of pseudoparkinsonism. Peak plasma level is reached in and its half-life is > 24 hours. To minimize sedation from its antihistaminic activity, bedtime administration is suggested.

**Clonazepam:** a benzodiazepine that is FDA approved for the treatment of seizures and panic disorder, but has clinical utility in the management of anxiety, drug-induced akathisia, catatonia and depression. It acts by enhancing GABA activity. Peak plasma level is reached within 1-4 hours and protein binding is 85%. Clonazepam is metabolized via cyt P450 3A4, with no active metabolites, and has an elimination half-life of 30-40 hours. Its CNS depressant effects may be increased if combined with other agents that have CNS depressant properties. If discontinuation is necessary, tapering (25% reduction weekly) is recommended for patients taking clonazepam chronically for at least 6 weeks. Withdrawal symptoms to monitor for include increased anxiety, insomnia, restlessness, and agitation/irritability. Clonazepam is contraindicated in acute narrow angle glaucoma and significant liver disease.

**Dextroamphetamine:** a stimulant that is FDA approved for the treatment of ADHD and narcolepsy, but has been tried clinically for the management of depression and obesity. Peak plasma levels are reached within 1-2.5 hours, with a half-life of 10-12 hours. Adverse effects include nervousness, insomnia, anorexia, tachycardia, and changes in blood pressure. Most adverse effects can be resolved by lowering the dose. As with other stimulants, it is contraindicated in arteriosclerosis, moderate/severe hypertension, hyperthyroidism, glaucoma, diabetes mellitus, agitated states, patients with a history of drug abuse/dependence and those on a monoamine oxidase inhibitor.

**Lorazepam:** a short-acting benzodiazepine that is FDA approved for the treatment of GAD. It exerts its anxiolytic effect by enhancing GABA inhibition. Peak plasma level is reached within 2-4 hours. Protein

binding is considered low (< 90%). Lorazepam undergoes conjugation only and thus is not at risk for hepatic cytochrome P450 drug interactions. Lorazepam has no active metabolites and therefore drug accumulation with repeated use is minimal. As with any benzodiazepine, CNS depressant effects may be increased if combined with agents that have CNS depressant properties (alcohol, barbiturates, narcotic analgesics, etc.). Tapering (25% reduction weekly) rather than abrupt discontinuation is recommended if a patient has been receiving benzodiazepine therapy for at least 6 weeks. Withdrawal symptoms to monitor for include increased anxiety, insomnia, restlessness, and agitation/irritability.

**Methylphenidate:** a stimulant that is FDA approved for the treatment of ADHD and narcolepsy, but has been tried clinically for alleviation of antidepressant-induced sexual dysfunction, in doses of 5-25 mg taken either daily or 1 hour before intercourse, and as augmentation therapy in depression, in doses of 5-30 mg daily. It is proposed that dopamine agonist activity may be responsible for its clinical benefits in sexual dysfunction. Adverse effects include nervousness, insomnia, anorexia, tachycardia, and changes in blood pressure. Most adverse effects can be resolved by lowering the dose. Should be used with caution in patients with hypertension, seizures or EEG abnormalities. It is contraindicated in glaucoma, Tourette's Disorder, severe hypertension, hyperthyroidism, arteriosclerosis, patients with a history of drug abuse/dependence, persons with severe anxiety or agitation, and those on a monoamine oxidase inhibitor.

**Propranolol:** a beta-adrenergic receptor blocker that is FDA approved as an antihypertensive agent, but is clinically used for the management of moderate anxiety and agitation in doses of 10-30 mg daily. Peak plasma level is reached within 1-1.5 hours and protein binding is high. Propranolol is hepatically metabolized via cytochrome P450 1A2, 2D6, 2C19 and has a half-life of 3-5 hours. Primary adverse effects include bradycardia, dizziness, nausea/vomiting, fatigue and constipation. Should be used with caution in patients with CHF, coronary artery disease, sinus node dysfunction, chronic bronchitis or emphysema. It is contraindicated in patients with Raynaud's syndrome, asthma, and 2<sup>nd</sup> or 3<sup>rd</sup> degree heart block.

**Trazodone:** an antidepressant that is chemically unrelated to TCA's and SSRI antidepressants. It inhibits serotonin reuptake and decreases adrenergic sensitivity. Trazodone is also highly sedating (antihistaminic effects) and therefore is clinically used to alleviate insomnia, in doses of 25-100 mg, 30-60 minutes before bedtime. Peak plasma level is reached within 2 hours and protein binding ranges from 85-95%. It is hepatically metabolized by cytochrome P450 2D6 and has a half-life of 7-8 hours. Primary adverse effects are sedation, orthostatic hypotension, tachycardia, dry mouth, constipation, and blurred vision.

**Zolpidem:** a nonbenzodiazepine sedative-hypnotic that acts to enhance GABA inhibitory activity. Peak plasma level is reached within 0.5 hours and protein binding is high (92%). It is hepatically metabolized by cytochrome P450 3A4 and has a half-life of 2 hours. Unlike benzodiazepines, zolpidem has minimal effect on sleep architecture, and the development of tolerance/physical dependence is rare. In doses of 5-10 mg nightly, no significant amnesic effect is observed.

**Table 3. Fetal Effects of Psychotropic Agents**

Medication	1 <sup>st</sup> Trimester	2 <sup>nd</sup> Trimester	3 <sup>rd</sup> Trimester	Category*	Summary
Tricyclic antidepressants	±	+	+	D	Possible association between 1 <sup>st</sup> trimester and limb malformation by some case reports but further studies showed no association. Perinatal syndromes: antidepressant withdrawal with jitteriness and irritability
Serotonin Selective Agents	±	+	+	C	Fluoxetine has been the most studied. No higher rates of major congenital malformation those who took fluoxetine in the 1 <sup>st</sup> trimester than the general population.
Other Antidepressants	±	+	+	C	
Lithium	∅	+	±	D	Associated with cardiac anomalies when used in 1 <sup>st</sup> trimester. Prematurity associated with use in 2 <sup>nd</sup> & 3 <sup>rd</sup> trimester. Watch for maternal lithium toxicity after deliver due to volume change-need to decrease dose by half before delivery. Lithium levels may be increased in neonates-risk of "floppy baby" & hypothyroidism
Valproic acid	∅	∅	∅	D	Associated with neural tube defects/1-5% risk of spina bifida
Carbamazepine	±	±	±	C	0.5-1% risk of spina bifida
Typical antipsychotics Haloperidol Chlorpromazine Fluphenazine Loxapine Mesoridazine Thioridazine Thiothixene	±	±	±	C	Most common malformations reported include cardiac, genital, skeletal (3.5%). Use of high potency agents is recommended. Avoid low potency agents due to decrease BP & uteroplacental blood flow. Use in 3 <sup>rd</sup> trimester associated with neonatal associated extrapyramidal effects such as agitation, tremor, poor sucking, swallowing, primitive reflexes, and hypertonicity/DC drugs 5-10 days prior to delivery to allow fetal drug level to decrease.
Atypical antipsychotics Clozapine	±	±	±	C B	Little information on atypical antipsychotics.
Anticholinergics Bentropine Trihexiphenidyl Diphenhydramine	±	± ± +	± ± +	C C B	Main association is suggested cardiovascular effects. Possible association with minor malformations Benadryl is the preferred agent
Propranolol	±	+	±	C	It has been used to treat pregnancy induced hypertension and does not appear to be associated with malformations. Neonatal adverse effects have included hyperbilirubinemia, bradycardia, respiratory depression, and low birth weights.
Benzodiazepines	∅	±	±	D	Increase risk of cleft palate in 1 <sup>st</sup> trimester, especially diazepam & alprazolam. 3 <sup>rd</sup> trimester exposure leads to tremors, hypertonicity, failure to feed, cyanosis and apnea. Best avoided but if needed use lorazepam (prn only).
Buspirone	±	±	±	B	Little information is available

\* Based on Drugs in Pregnancy and Lactation, 5<sup>th</sup> edition ∅ Use is not recommended

+ May be used -least risk

± May be used if no other alternative available

# **Guidelines for Switching Between Antidepressant Medications**

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## **Switching From an SSRI**

### **1. SSRI/#1 to SSRI/#2:**

- discontinue SSRI/#1 and then start SSRI/#2
- or-
- decrease SSRI/#1 to initiate SSRI/#2 to taper and discontinue SSRI/#1

Case Example: If patient is on 40 mg po qam of fluoxetine: a) stop the fluoxetine and start paroxetine (or sertraline) the next day; or b) decrease the fluoxetine to 20 mg per day and add in paroxetine 20 mg (or sertraline 50 mg) per day for 1–3 days and discontinue the fluoxetine.

### **2. SSRI to TCA or bupropion:**

- discontinue SSRI and then start TCA or bupropion
- or-
- decrease SSRI to initiate TCA or bupropion at low dose to taper and discontinue SSRI, while gradually increasing TCA or bupropion as tolerated to therapeutic dose range.\*

\* Both the TCAs and bupropion are associated with significant toxicity at elevated plasma concentrations. Since SSRIs increase the plasma concentrations of TCAs and bupropion (paroxetine > fluoxetine > sertraline > citalopram), caution is indicated when co-administering these agents or when therapy with bupropion or a TCA is undertaken in close proximity to cessation of an SSRI.

Case Example: If pt. is on 40 mg po qam of fluoxetine: a) stop the fluoxetine and start nortriptyline (or other TCA) or bupropion the next day; or b) decrease the fluoxetine to 20 mg po qam and add in nortriptyline (25 mg po qhs or another TCA) or bupropion (50–75 mg po qd) for 1–3 days to discontinue fluoxetine and increase nortriptyline or bupropion as tolerated to therapeutic dose range.

### **3. SSRI to nefazodone or venlafaxine:**

- discontinue SSRI and then start nefazodone or venlafaxine
- or-
- decrease SSRI to initiate nefazodone (50–100 mg po qhs) or venlafaxine (37.5–75 mg po qd) to taper and discontinue SSRI, while gradually increasing nefazodone or venlafaxine as tolerated to therapeutic dose range.

Case Example: If patient is on 40 mg po qam of fluoxetine: a) stop the fluoxetine and start nefazodone (50–100 mg po qhs) or venlafaxine (37.5–75 mg po qd) the next day; or b) decrease the fluoxetine to 20 mg po qam and add in nefazodone (50–100 mg po qhs) or venlafaxine (37.5–75 mg po qd) for 1–3 days to discontinue fluoxetine and increase nefazodone and venlafaxine as tolerated to therapeutic dose range.

### **4. SSRI to MAOI:**

- discontinue SSRI and then after a 5 week washout period for fluoxetine or after a 2 week washout period (sertraline or paroxetine), MAOI therapy can be safely initiated.

## **Switching from TCA, Venlafaxine, Nefazodone, or Bupropion**

### 1. TCA/#1 (or venlafaxine, nefazodone, or bupropion) to TCA/#2:

- discontinue TCA/#1 (or venlafaxine, nefazodone, or bupropion) by taper and then start TCA/#2
- or-
- decrease TCA/#1 (or venlafaxine, nefazodone, or bupropion) to initiate TCA/#2 to taper and discontinue TCA/#1 (or venlafaxine, nefazodone, or bupropion), while gradually increasing TCA/#2 as tolerated.

Case Example: If patient is on 100 mg po qhs of nortriptyline (or venlafaxine, nefazodone, or bupropion): a) taper and then discontinue the nortriptyline (or venlafaxine, nefazodone, or bupropion) and start the other TCA the next day; or b) decrease the nortriptyline (or venlafaxine, nefazodone, or bupropion) and add in doxepin (50–100 mg po qhs or other TCA) for 1–3 days and then taper and discontinue the nortriptyline (or venlafaxine, nefazodone, or bupropion).

### 2. TCA (or venlafaxine, nefazodone, or bupropion) to SSRI:

- taper and discontinue TCA (or venlafaxine, nefazodone, or bupropion) and then start SSRI
- or-
- decrease TCA (or venlafaxine, nefazodone, or bupropion) to initiate SSRI at low dose to taper and discontinue TCA (or venlafaxine, nefazodone, or bupropion).

Case Example: If patient is on nortriptyline (or venlafaxine, nefazodone, or bupropion): a) taper and discontinue the nortriptyline (or venlafaxine, nefazodone, or bupropion) and start fluoxetine (or other SSRI) the next day; or b) decrease the nortriptyline (or venlafaxine, nefazodone, or bupropion) and add in fluoxetine (20 mg po qam or another SSRI) for 1–3 days to taper and discontinue nortriptyline (or venlafaxine, nefazodone, or bupropion).

### 3. TCA (or venlafaxine, nefazodone, or bupropion) to nefazodone, venlafaxine, or bupropion:

- discontinue TCA (or venlafaxine, nefazodone, or bupropion) and then start nefazodone, venlafaxine, or bupropion
- or-
- decrease TCA (venlafaxine, nefazodone, or bupropion) to initiate nefazodone (50–100 mg po qhs), venlafaxine (37.5–75 mg po qd), or bupropion (37.5–50 mg po qd) to taper and discontinue TCA (venlafaxine, nefazodone, or bupropion), while gradually increasing nefazodone, venlafaxine, or bupropion as tolerated to therapeutic dose range.

Case Example: If patient is on nortriptyline (or venlafaxine, nefazodone, or bupropion): a) stop the nortriptyline (or venlafaxine, nefazodone, or bupropion) and start nefazodone (50–100 mg po qhs), venlafaxine (37.5–75 mg po qd), or bupropion (37.5–50 mg po qd) the next day; or b) decrease the nortriptyline (or venlafaxine, nefazodone, or bupropion) and add in nefazodone (50–100 mg po qhs), venlafaxine (37.5–75 mg po qd), or bupropion (37.5–50 mg po qd) for 1–3 days to discontinue nortriptyline (or venlafaxine, nefazodone, or bupropion) and increase nefazodone, venlafaxine, or bupropion as tolerated to therapeutic dose range.

### 4. TCA to MAOI:

- discontinue TCA and then after a 2 week washout period, MAOI therapy can be safely initiated.



## **Switching from an MAOI**

1. MAOI/#1 to MAOI/#2, SSRI, TCA, venlafaxine, bupropion, nefazodone:
  - discontinue MAOI/#1 and then after a 2 week washout period, therapy with MAOI/#2 (or SSRI, TCA, venlafaxine, or nefazodone) can be safely initiated.

## ***Process Measures***

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### ***Quick Inventory of Depressive Symptomatology (Self-Report) (QIDS-SR)***

#### ***Scoring Criteria for QIDS-SR***

#### ***Scoring Criteria for Physician- and Patient-Rated Overall Symptom and Side Effect Ratings***

The QIDS-SR consists of 16 individual items that the patient is asked to read and rate based upon his/her individual perception of the presence and severity of common depression-related symptoms. If the patient has difficulty reading or interpreting an item, it is appropriate for a staff member to read the question to the patient, but staff should not lead or influence the patient's answer. Although some patients may have difficulty using the form for the first time, most individuals should be able to easily complete it after the second or third time. Most patients also appreciate the opportunity to be able to tell the physician and other staff about the symptoms that are bothering them. The QID-SR is constructed in order to capture a range of DSM-IV related depressive symptoms in an individual patient, while at the same time minimizing the tendency to over rate selected symptoms (e.g., sleep disturbance). For this reason, the patient does not answer all of the questions. For example, on questions 6 and 7, addressing appetite disturbance, the patient only answers one of the questions (addressing either decreased or increased appetite). If the patient has no appetite disturbance, they can answer either question. The same principles apply to questions 8 and 9. The QIDS-SR is also available in Spanish, and this version should be used for individuals who primarily read Spanish.

In scoring the QIDS-SR, the clinician does NOT sum all of the items to get the rating score. The scoring instructions are listed on page two of the form. If the form is scored correctly, only 12 of the questions will be summed to obtain the patient's depression rating score, with a maximum possible score of 27. The scoring criteria for the severity of depressive symptoms are listed below. Please note that these scoring criteria are a guideline, and they should never be used as a substitute for the clinician's judgement regarding the clinical status of the patient. Rather they are intended as a tool for the clinician to use in quantifying the severity of depressive symptoms and the response to treatment.

## QIDS-SR Scoring Criteria

<b>Normal</b>	<b><math>\leq 7</math></b>
<b>Mild</b>	<b>8 - 12</b>
<b>Moderate</b>	<b>13 - 16</b>
<b>Moderate to Severe</b>	<b>17 - 20</b>
<b>Severe</b>	<b>21 +</b>

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# Scoring Criteria for Physician and Patient Overall Symptom and Side Effect Ratings

- 0 = No Symptoms**
- 1 = Borderline**
- 2 = Mild**
- 3 = Mild – Moderate**
- 4 = Moderate**
- 5 = Moderate – Marked**
- 6 = Marked**
- 7 = Marked – Severe**
- 8 = Severe**
- 9 = Severe – Extreme**
- 10 = Extreme**

# Documentation

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## Instructions for Outpatient Data Collection

### Outpatient Intake Form

The clinician documents the following identifying information on the intake form:

- **Local Case #**
- **MHMR Physician Code**  
(or first 4 digits of the physician's Social Security number)
- **Component/Clinic #**
- **Date of Visit** (i.e., date intake procedures initiated)  
Note: Write in the month, day, year (e.g., 3/1/98)
- **Age**
- **Gender**
- **Ethnic or Racial Group** (check one only)
- **Principal Diagnosis** (i.e., DSM-IV Axis Code).  
(This diagnosis should coincide with the disease-specific module under consideration (i.e., major depressive disorder, schizophrenia, or bipolar disorder).)
- **Age of Onset** (pertains to principal diagnosis).
- **Other Current Diagnoses**  
Not including principal diagnosis (i.e., other comorbid Axis I conditions using the DSM-IV Axis I code).
- **Alcohol/Substance Problem**  
(Clinician rating within last six (6) months).
- **Axis III**  
(Record general medical conditions that the patient is currently receiving treatment for. Check all that apply.)
- Note there is no need to document Axis IV.
- **Family History of Mental Illness**  
Check all that apply for each family member, indicating effective treatment in the last column.
- **Number of Psychiatric Hospitalizations**
- **Psychoactive Medications** Record past and current psychoactive medications taken in the last two years. Indicate the highest (daily) dose given for each.

## **Outpatient Clinic Visit Clinical Record Form**

The following information is entered into the CRF by the clinician:

- **Local Case #**
- **MHMR Physician Code**  
(or first 4 digits of the physician's Social Security number)
- **Service Activity Code** (Service activity or billing code for this visit.)
- **Date of Visit** (i.e., date intake procedures initiated)  
Note: Write in the month, day, year (e.g., 3/1/98)
- **Duration:**  
The difference between stop time and start time in minutes.
- **Primary Current Dx:**  
Please check the patient's primary Axis I diagnosis for which the algorithm is being used.
- **Stage in the Algorithm**  
Record how many weeks the patient has been in this stage.
- **Vital Signs**
- **Most Recent Drug Levels**
- **Prescription Medications**  
Check whether medications were or were not taken as prescribed.
- **Other Medications Taken During Past Week**  
(Not including medications prescribed by the physician.)
- **Patient Global Self Report**  
Record patient's self-reported symptom and side effect severity on a scale of 0–10, "0" being none and "10" being extreme.
- **Clinical Rating Scales**  
Record positive symptoms, negative symptoms, IDS-SR score, Altman score, and any others.
- **Physician Ratings**  
Each of the symptom clusters is rated on a 10-point scale (from "no symptoms" to "extremely severe"). The rating is based on your impression of the patient at this visit, as well as information you have about the patient's clinical status during the week prior to the visit.
  - **Core Symptoms:**  
Based upon all available information, clinician impression of the level of the presence of each of the symptoms in this patient.
  - **Other Symptoms:**  
Clinician rating of other symptoms associated with the patient's disorder, but not core symptoms of the patient's illness. Rate your impression for each of the specific "other symptoms" listed (irritability, mood lability, insomnia, agitation, anxiety, level of interest, appetite, energy level). Under "other," specify and rate any other symptom that you feel is significant.
  - **Overall Side Effect Severity:**  
Overall rating of side effects from all medications being taken by the patient.

- **Overall Functioning:**  
Overall impression of this patient's ability to function on a daily basis. "10" is the highest possible functioning, and "1" is the lowest possible functioning.

- **Prescription Information**

- **Medication Name:**  
List the names of all psychotropic medications (for the core syndrome, other symptoms, or side effects) the patient is receiving — both **new** medications prescribed at this visit and **continuing** medications. Check the appropriate box. If a medication is being **discontinued**, list the medication name and check the **D/C** box.

List the complete SIG (dose and frequency) for each medication the patient is receiving. If a medication is being titrated or tapered, please outline the schedule. Indicate stop dates, if applicable. Please check whether the medication is for core syndrome (**S**), other symptoms (**OS**), or side effects (**SE**).

- **Medication Response**  
Indicate whether response to medication was full, partial, minimal, none, or the symptoms are worsening.
- **Reason for Medication Change**  
Note that this includes changing the dose for a current medication. Check all reasons that apply.
- **Reasons for Medication Choice**  
Check reasoning for antidepressant, antipsychotic, mood stabilizer, and/or augmentation choice.
- **Patient/Family Education**  
Indicate whether patient education was done at this visit and between last and current visit.
- **Progress Note**
  - **Subjective**  
Patient report of sleep, appetite, side effects, medication efficacy, etc.
  - **Objective**  
Physician impression of patient's orientation, appearance, rapport, speech patterns, suicidal or homicidal ideations, psychosis, thought content and process, mood, affect, insight, judgement, cognition, etc.
  - **Assessments**  
Record diagnosis, clinical progress, formulations, problems, prognosis, and other appraisals.
  - **Plan**  
Current direction for biopsychosocial treatment, discharge planning, placements, and other needs.
- **Next visit**  
Indicate how many weeks until patient should return to clinic, and what date the next appointment has been set for.
- **Physician Signature/Title**

### **Outpatient Interim Contact Form**

In the event that the patient does not come into the clinic or there is not time for a complete visit, the ICF is documented by support personnel or the physician.

- **Case Number**
- **Date of Patient Contact**
- **Primary Diagnosis**
- **Type of Contact**  
Indicate whether telephone or office visit.
- **Prescription Medication in Last Week**  
Record medication name, dosing and frequency information, and indicate whether medication was taken as prescribed.
- **Adherence to Medication Treatment**  
Indicate yes or no. If no, document in progress note.
- **Significant Side Effects Reported**  
Indicate yes or no. If yes, describe side effects.
- **Overall Patient Global Report**  
Record symptom and side effect severity on a scale of 0–10.
- **Suicidal/Homicidal**  
Indicate yes or no.
- **Progress Note**  
Record any pertinent information regarding the patient's clinical status (e.g., most prominent symptoms, specific side effects, serum level results, psychosocial stressors, compliance, crisis interventions, ER visits, information given to patient, etc.)
- **Stage in the Algorithm**  
Indicate what stage, how many weeks in this stage, and whether a change to the current treatment is recommended. If a treatment change is recommended, schedule a physician visit.
- **Next Appointment Date**
- **Signature/Title**



## **Forms for Outpatient Data Collection**

***Outpatient Intake Form***

***Outpatient Clinic Visit Clinical Record Form***

***Outpatient Interim Contact Form***

# TIMA Texas Implementation of Medication Algorithms

## Outpatient Intake Form

Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_ MHRM Physician Code: \_\_\_\_\_  
mm dd yy



Age: \_\_\_\_ Gender:  Female  Male Ethnic or Racial Group (please check only one response):  White  Hispanic  African-American  Asian or Pacific Islander  American Indian or Alaskan Native  Other

Principal Diagnosis (DSM-IV Axis I code): \_\_\_\_\_

Age at Onset: \_\_\_\_ # of Episodes: \_\_\_\_ Onset of Current Episode: \_\_\_\_\_

Other current diagnoses not including principal diagnosis:

Axis I: \_\_\_\_\_ Axis II: \_\_\_\_\_

Alcohol/Substance Abuse:  No  Yes If yes,  Current  Past

Axis III (Current General medical conditions, check all that apply):

- Hypertension  Hypothyroidism  Head Injury  HIV
- CHF  Diabetes  Seizure Disorder  Cancer
- Heart Disease  Endocrine (Other)  Stroke  Chronic Lung Disorder
- Cardiac (Other)  Asthma  Neurological (Other)
- Allergies (If yes, explain below)  Other Significant Systemic Illness (specify): \_\_\_\_\_

Additional Information:

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Any family members with a history of any of the following (please check all that apply):

	Depression	Schizophrenia	Bipolar	Substance Abuse	Suicide	Other	Effective Treatments
Parent							
Sibling							
Children							
Aunt/Uncle							
Grandparent							

Number of Psychiatric Hospitalizations (best estimate): Past Year: \_\_\_\_ Past 5 Years: \_\_\_\_ Lifetime: \_\_\_\_

Past and Current Psychoactive Medications (Patient Self-Report/Records):

Medication <small>Please provide medications for the past two years, record the highest dose given</small>	Taken for this episode?	Dose	Freq.	Start/Stop (Mo/Yr)	Response	Well Tolerated
1.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
2.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
3.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
4.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
5.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
6.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
7.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
8.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No

Signature/ title \_\_\_\_\_ Date \_\_\_\_\_

**TIMA** Texas Implementation of Medication Algorithms  
**OutPatient Clinic Visit**  
**Clinical Record Form**



Date: \_\_\_/\_\_\_/\_\_\_ Service Activity Code: \_\_\_\_\_

Physician Code: \_\_\_\_\_ Start Time: \_\_\_\_\_ Stop Time: \_\_\_\_\_

Primary Current Dx:  MDD-NP  BPD-M  BPD-D  SCZ  
 (check one)  MDD-P  BPD-MX  SCZ-A (BP)  SCZ-A  Other (specify): \_\_\_\_\_

Stage: \_\_\_\_\_ Weeks in this stage: \_\_\_\_\_

Vital Signs: BP \_\_\_/\_\_\_ Pulse \_\_\_ Temp \_\_\_ Weight \_\_\_ Height \_\_\_ (if needed)

**Most Recent Drug Levels:**

Medication Name	Date Drawn	Serum Level	WNL

Medications taken as Prescribed?  Yes/Mostly  No/Inadequate

Any other medications taken during the past week?  No  Yes (if yes, specify below) \_\_\_\_\_

\_\_\_\_\_

**Patient Global Self Report (0-10) 0 = No symptoms 5 = moderate 10 = extreme**  
 Symptom Severity: \_\_\_\_\_ Side Effects: \_\_\_\_\_

**Clinical Rating Scales**  
 POS SX: \_\_\_\_\_ NEG SX: \_\_\_\_\_ IDS-SR: \_\_\_\_\_ Altman: \_\_\_\_\_ OTHER \_\_\_\_\_

**Use for all physician's ratings below: (0-10) 0 = No symptoms 5 = moderate 10 = extreme**  
**Core Symptoms:** \_\_\_ Mania \_\_\_ Depression \_\_\_ Positive Sx or Psychoses \_\_\_ Negative Sx  
**Other Symptoms:** \_\_\_ Irritability \_\_\_ Mood Lability \_\_\_ Insomnia \_\_\_ Agitation \_\_\_ Anxiety  
 \_\_\_ Level of Interest \_\_\_ Appetite \_\_\_ Energy Level  
 \_\_\_ Other (specify): \_\_\_\_\_ **Overall Side Effect Severity: \_\_\_\_\_ (0-10)**  
 Is patient presently suicidal?  Yes  No homicidal?  Yes  No **Overall Functioning: \_\_\_\_\_ (0-10)**  
 If yes, comment in progress note. 0=Low 10=High

**Prescription Information**

Medication Name Change from previous visit? <input type="checkbox"/> No <input type="checkbox"/> Yes	New/ Continuing/ Discontinue	Please provide information on titration, dose, dose frequency, duration the medication is to be taken, start and stop date (if applicable), and any other pertinent information describing this medication.	Indication (check all that apply) <sup>1</sup>
	<input type="checkbox"/> New <input type="checkbox"/> Cont. <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
	<input type="checkbox"/> New <input type="checkbox"/> Cont. <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
	<input type="checkbox"/> New <input type="checkbox"/> Cont. <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
	<input type="checkbox"/> New <input type="checkbox"/> Cont. <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE

<sup>1</sup>S=Meds Targeted at core syndrome. OS=Meds targeted at other symptoms. SE=Meds for side effects of S or OS

Are serum levels needed?  Yes  No (if yes, specify in progress note)

# TIMA Texas Implementation of Medication Algorithms

Medication Response:  Full  Partial  Minimal  None  Symptoms Worsening

Reason for Medication Change (Include Dose Changes):

Critical Decision Point Indicates Change Necessary  Insufficient Improvement  Patient Preference

Side Effects Intolerable  Symptoms Worsening  Diagnosis Change  Other: \_\_\_\_\_

Reason for Antidepressant Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

Reason for Antipsychotic Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

Reason for Mood Stabilizer Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

Reason for Augmentation Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

Patient/Family Education:

Done at this visit?  Yes  No

Between last visit and this visit?  Yes  No

Progress Note: ( Check here if note was dictated. Date of dictation \_\_\_\_/\_\_\_\_/\_\_\_\_)

Subjective (Sleep, appetite, side effects, medication efficacy, other patient reports.)

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Objective (Orientation, appearance, rapport, speech patterns, suicidal or homicidal ideations, psychosis thought content & process, mood, affect, insight, judgement, cognition, other observations)

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Assessments (Diagnosis, clinical progress, formulations, problems, prognosis, other appraisals.)

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Plan (Current direction for biopsychosocial treatment, discharge planning, placements, other needs.)

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Return to clinic: \_\_\_\_\_ weeks

Next appointment date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Signature/Title: \_\_\_\_\_



## Instructions for Inpatient Data Collection

### Inpatient Intake Form/Annual Update

The clinician documents the following identifying information on the intake form:

- **Initial Visit or 90-Day Review** (Check which applies.)
- **Date of Visit**  
Note: Write in the month, day, year (e.g., 3/1/98)
- **Local Case #**
- **MHMR Physician Code**  
(or first 4 digits of the physician's Social Security number)
- **Age**
- **Gender**
- **Ethnic or Racial Group** (check one only)
- **Principal Diagnosis** (i.e., DSM-IV Axis Code).  
(This diagnosis should coincide with the disease-specific module under consideration (i.e., major depressive disorder, schizophrenia, or bipolar disorder).)
- **Age of Onset** (pertains to principal diagnosis).
- **Number of Episodes**
- **Onset of Current Episode**
- **Other Current Diagnoses**  
Not including principal diagnosis (i.e., other comorbid Axis I conditions using the DSM-IV Axis I code).
- **Alcohol/Substance Problem**  
(Clinician rating within last six (6) months).
- **Axis III**  
(Record general medical conditions that the patient is currently receiving treatment for. Check all that apply.)  
Note there is no need to document Axis IV.
- **Family History of Mental Illness**  
Check all that apply for each family member, indicating effective treatment in the last column.
- **Number of Psychiatric Hospitalizations**  
Best estimate for the past year, past five years, and complete lifetime.
- **Psychoactive Medications**  
Record past and current psychoactive medications taken in the last two years. Note which (if any) medications were taken for this episode. Indicate the highest (daily) dose given for each, frequency, start/stop dates, response, and whether medication was tolerable.

## **Inpatient Clinical Record Form**

The following information is entered into the CRF by the clinician:

- **Local Case #**
- **Date of Visit** (i.e., date intake procedures initiated)  
Note: Write in the month, day, year (e.g., 3/1/98)
- **Time of Day**
- **TIMA Stage**  
Note what stage patient is in and the number of weeks in this stage.
- **Physician Code**
- **Type of Review**  
Indicate whether daily, weekly, monthly, quarterly, or other.
- **Patient Seen and Chart Reviewed**  
Indicate yes or no.
- **Level of Service**  
Indicate low, medium, or high.
- **Primary Current Dx:**  
Please check the patient's primary Axis I diagnosis for which the algorithm is being used.
- **Physician Ratings**  
Each of the symptom clusters is rated on a 10-point scale (from "no symptoms" to "extremely severe"). The rating is based on your impression of the patient at this visit, as well as information you have about the patient's clinical status during the week prior to the visit.
  - **Core Symptoms:**  
Based upon all available information, clinician impression of the level of the presence of each of the symptoms in this patient.
  - **Other Symptoms:**  
Clinician rating of other symptoms associated with the patient's disorder, but not core symptoms of the patient's illness. Rate your impression for each of the specific "other symptoms" listed (irritability, mood lability, insomnia, agitation, anxiety, level of interest, appetite, energy level). Under "other," specify and rate any other symptom that you feel is significant.
- **Psychotropic Medication Information**
  - **Medication Name:**  
List the names of all psychotropic medications (for the core syndrome, other symptoms, or side effects) the patient is receiving — both **new** medications prescribed at this visit and **continuing** medications. Check the appropriate box. If a medication is being **discontinued**, list the medication name and check the **D/C** box.  
  
List the complete SIG (dose and frequency) for each medication the patient is receiving. If a medication is being titrated or tapered, please outline the schedule. Indicate stop

dates, if applicable. Please check whether the medication is for core syndrome (**S**), other symptoms (**OS**), or side effects (**SE**).

- **Change from Medication Algorithm**

Indicate yes or no. If yes, check all reasons for changing the medication that apply.

- **Reasons for Medication Choice**

Check reasoning for antidepressant, antipsychotic, mood stabilizer, and/or augmentation choice.

- **Patient Global Self Report**

Record patient's self-reported symptom and side effect severity on a scale of 0–10, "0" being none and "10" being extreme.

- **Clinical Rating Scales**

Record MMSE score, AIMS score, positive symptoms, negative symptoms, IDS-SR score, Altman score, and any others.

- **Serum Levels Needed**

Indicate yes or no. Record medication name, the date that serum level was drawn, and the serum level.

- **Labs WNL**

Indicate yes or no. If no, describe pertinent lab data.

- **Patient/Family Education**

Indicate whether patient education was done at this visit and between last and current visit.

- **Progress Note**

- **Subjective**

Patient report of sleep, appetite, side effects, medication efficacy. Check all that apply, and note any pertinent comments.

- **Objective**

Physician impression of patient's orientation, appearance, rapport, speech patterns, thought content and process, mood, affect, insight, judgement, cognition, psychomotor activity, and memory. Check all that apply, and note any pertinent comments.

- **Assessments**

Note whether psychiatric condition is generally improving, unchanged, or deteriorating. Record diagnosis, clinical progress, formulations, problems, prognosis, and other appraisals.

- **Plan**

Current direction for biopsychosocial treatment, discharge planning, placements, and other needs.

- **Continuation of Psychiatric Hospital Services**

Indicate whether this is necessary because treatment can reasonably be expected to improve the patient's condition and/or for the purposes of Diagnostic Study.

- **Physician Signature**



# TIMA Texas Implementation of Medication Algorithms

## Inpatient Intake Form/Annual Update

Initial Visit  90-day review Date: \_\_\_\_/\_\_\_\_/\_\_\_\_



MHMR Physician Code: \_\_\_\_\_ Length of Contact: \_\_\_\_\_

Age: \_\_\_\_ Gender:  Female  Male Ethnic or Racial Group (please check only one response):  White  Hispanic  African-American  Asian or Pacific Islander  American Indian or Alaskan Native  Other

Principal Diagnosis (DSM-IV Axis I code): \_\_\_\_\_

Age at Onset: \_\_\_\_\_ # of Episodes: \_\_\_\_\_ Onset of Current Episode: \_\_\_\_\_

Other current diagnoses not including principal diagnosis:

Axis I: \_\_\_\_\_ Axis II: \_\_\_\_\_

Alcohol/Substance Problem (within last 6 months):  Yes  No (If yes, specify substance): \_\_\_\_\_

Axis III (Current General medical conditions, check all that apply):

- Hypertension  Hypothyroidism  Head Injury  HIV
- CHF  Diabetes  Seizure Disorder  Cancer
- Heart Disease  Endocrine (Other)  Stroke  Chronic Lung Disorder
- Cardiac (Other)  Asthma  Neurological (Other)
- Allergies (If yes, explain below)  Other Significant Systemic Illness (specify): \_\_\_\_\_

Additional Information:

Any family members with a history of any of the following (please check all that apply):

	Depression	Schizophrenia	Bipolar	Substance Abuse	Suicide	Other	Effective Treatments
Parent							
Sibling							
Children							
Aunt/Uncle							
Grandparent							

Number of Psychiatric Hospitalizations (best estimate): Past Year: \_\_\_\_\_ Past 5 Years: \_\_\_\_\_ Lifetime: \_\_\_\_\_

**Past and Current Psychoactive Medications (Patient Self-Report/Records):** Please provide medications for the past two years, record the highest dose given.

Medication	Taken for this episode?	Dose	Freq.	Start/Stop (Mo/Yr)	Response	Well Tolerated
1.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
2.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
3.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
4.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
5.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
6.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
7.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No
8.	<input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Minimal <input type="checkbox"/> None	<input type="checkbox"/> Yes <input type="checkbox"/> No

Signature/ title

Date



**Clinical Inpatient Record Form**

Date: \_\_\_/\_\_\_/\_\_\_ Time: \_\_\_\_\_

TIMA Stage: \_\_\_\_\_ Weeks in this stage: \_\_\_\_\_ Physician Code: \_\_\_\_\_

Type of Review :  Daily  Weekly  Monthly  Quarterly  Other

Patient seen and chart reviewed?  Yes  No Level of Service  Low  Medium  High

Primary Current Dx :  MDD-NP  BPD-M  BPD-D  SCZ  Other (specify): \_\_\_\_\_  
 (check one)  MDD-P  BPD-MX  SCZ-A (BP)  SCZ-A \_\_\_\_\_

**Use for all physician's ratings below: (0-10) 0 = No symptoms 5 = moderate 10 = extreme**

Core Symptoms: \_\_\_ Mania \_\_\_ Depression \_\_\_ Positive Sx of Psychosis \_\_\_ Negative Sx of Psychosis  
 Other Symptoms: \_\_\_ Irritability \_\_\_ Mood Lability \_\_\_ Insomnia \_\_\_ Agitation \_\_\_ Anxiety  
 \_\_\_ Appetite \_\_\_ Level of Interest \_\_\_ Energy Level Other: \_\_\_\_\_

**Psychotropic Medication Information**

<u>Medication Name</u> Document any new or discontinued medications, or dosage changes of established medications.	<u>Dosing Information</u> Please provide information on titration, dose, dose frequency, duration the medication is to be taken, start and stop date (if applicable) and any other pertinent information describing this medication.	<u>Indication</u> (Check all that apply.) <sup>1</sup>
<input type="checkbox"/> New <input type="checkbox"/> Change <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
<input type="checkbox"/> New <input type="checkbox"/> Change <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
<input type="checkbox"/> New <input type="checkbox"/> Change <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
<input type="checkbox"/> New <input type="checkbox"/> Change <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
<input type="checkbox"/> New <input type="checkbox"/> Change <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE
<input type="checkbox"/> New <input type="checkbox"/> Change <input type="checkbox"/> D/C		<input type="checkbox"/> S <input type="checkbox"/> OS <input type="checkbox"/> SE

S=Meds Targeted at core syndrome. OS=Meds targeted at other symptoms. SE=Meds for side effects of S or OS<sup>1</sup>

**Change from medication algorithm recommended?**  YES  NO (If yes, check all that apply)

Patient previously failed next step.  Next step not acceptable to patient.  Next step not available at this site.  
 Next step not medically safe for this patient.  No options left.  Other \_\_\_\_\_

Reason for Antidepressant Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

Reason for Antipsychotic Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

Reason for Mood Stabilizer Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

Reason for Augmentation Choice:  SE Profile  Pattern of Associated Sx  Past Response  Other: \_\_\_\_\_

**Patient Global Self Report (0-10) 0 = No symptoms 5 = moderate 10 = extreme**

Symptom Severity: \_\_\_\_\_ Side Effects: \_\_\_\_\_

**Clinical Rating Scales**

MMSE \_\_\_ AIMS \_\_\_ POS SX: \_\_\_ NEG SX: \_\_\_ IDS-SR: \_\_\_ Altman: \_\_\_ OTHER: \_\_\_\_\_

# TIMA Texas Implementation of Medication Algorithms

Are serum levels needed?  Yes  No

Labs WNL?  Yes  No If no, describe below.

<u>Medication Name</u>	<u>Date Drawn</u>	<u>Serum Level</u>

Pertinent Lab Data :

Patient Education Completed?  Yes  No

**Progress Note** ( Check here if note was dictated. Date of dictation \_\_\_\_/\_\_\_\_/\_\_\_\_)

**Subjective** (Sleep, appetite, side effects, medication efficacy, other patient reports.)

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**Objective** (Orientation, appearance, rapport, speech patterns, suicidal or homicidal ideations, psychosis thought content & process, mood, affect, insight, judgement, cognition, other observations)

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**Assessments** (Diagnosis, clinical progress, formulations, problems, prognosis, other appraisals.)

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**Plan** (Current direction for biopsychosocial treatment, discharge planning, placements, other needs.)

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**Inpatient Psychiatric Hospital Services continues to be medically necessary for :**

Treatment which can reasonably be expected to improve the patient's condition and/or  Diagnostic Study

**Physician Signature :** \_\_\_\_\_

**Important Phone Numbers**

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Dallas, TX 75235-9101

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M. Lynn Crismon, Pharm. D.  
Clinical Pharmacy Division  
UT College of Pharmacy  
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Office number (512) 232-2630  
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Pager number (512) 397-7102  
TDMHMR number (512) 206-5068  
TDMHMR fax (512) 206-4744  
E-mail address: crismonl@mail.utexas.edu

**Conference Call Schedule**

Teleconferences are designed to be a forum for discussion of the implementation of the algorithm. General and specific questions related to the algorithm may be asked during these time periods. Additionally, time may be spent addressing particular clinical or therapeutic issues. The length of each teleconference may vary depending on the type/number of questions, with a maximum time limit of 60 minutes. Please call the Office of the Medical Director (512/206-4511) for schedule information.

**TIMA** Texas Implementation of Medication Algorithms  
**QUICK INVENTORY OF DEPRESSIVE SYMPTOMATOLOGY (SELF-REPORT)**  
**(QIDS-SR)**

NAME: \_\_\_\_\_ TODAY'S DATE \_\_\_\_\_

Please circle the one response to each item that best describes you for the past seven days.

1. Falling Asleep:

- 0 I never take longer than 30 minutes to fall asleep.
- 1 I take at least 30 minutes to fall asleep, less than half the time.
- 2 I take at least 30 minutes to fall asleep, more than half the time.
- 3 I take more than 60 minutes to fall asleep, more than half the time.

5. Feeling Sad:

- 0 I do not feel sad
- 1 I feel sad less than half the time.
- 2 I feel sad more than half the time.
- 3 I feel sad nearly all of the time.

2. Sleep During the Night:

- 0 I do not wake up at night.
- 1 I have a restless, light sleep with a few brief awakenings each night.
- 2 I wake up at least once a night, but I go back to sleep easily.
- 3 I awaken more than once a night and stay awake for 20 minutes or more, more than half the time.

3. Waking Up Too Early:

- 0 Most of the time, I awaken no more than 30 minutes before I need to get up.
- 1 More than half the time, I awaken more than 30 minutes before I need to get up.
- 2 I almost always awaken at least one hour or so before I need to, but I go back to sleep eventually.
- 3 I awaken at least one hour before I need to, and can't go back to sleep.

4. Sleeping Too Much:

- 0 I sleep no longer than 7-8 hours/night, without napping during the day.
- 1 I sleep no longer than 10 hours in a 24-hour period including naps.
- 2 I sleep no longer than 12 hours in a 24-hour period including naps.
- 3 I sleep longer than 12 hours in a 24-hour period including naps.

## **TIMA** Texas Implementation of Medication Algorithms

Please complete either 6 or 7 (not both)

### 6. Decreased Appetite:

- 0 There is no change in my usual appetite.
- 1 I eat somewhat less often or lesser amounts of food than usual.
- 2 I eat much less than usual and only with personal effort.
- 3 I rarely eat within a 24-hour period, and only with extreme personal effort or when others persuade me to eat.

### 7. Increased Appetite:

- 0 There is no change from my usual appetite.
- 1 I feel a need to eat more frequently than usual.
- 2 I regularly eat more often and/or greater amounts of food than usual.
- 3 I feel driven to overeat both at mealtime and between meals.

Please complete either 8 or 9 (not both)

### 8. Decreased Weight (Within the Last Two Weeks):

- 0 I have not had a change in my weight.
- 1 I feel as if I've had a slight weight loss.
- 2 I have lost 2 pounds or more.
- 3 I have lost 5 pounds or more.

### 9. Increased Weight (Within the Last Two Weeks):

- 0 I have not had a change in my weight.
- 1 I feel as if I've had a slight weight gain.
- 2 I have gained 2 pounds or more.
- 3 I have gained 5 pounds or more.

### 10. Concentration/Decision Making:

- 0 There is no change in my usual capacity to concentrate or make decisions.

- 1 I occasionally feel indecisive or find that my attention wanders.
- 2 Most of the time, I struggle to focus my attention or to make decisions.
- 3 I cannot concentrate well enough to read or cannot make even minor decisions.

# **TIMA** Texas Implementation of Medication Algorithms

## 11. View of Myself:

- 0 I see myself as equally worthwhile and deserving as other people.
- 1 I am more self-blaming than usual.
- 2 I largely believe that I cause problems for others.
- 3 I think almost constantly about major and minor defects in myself.

## 12. Thoughts of Death or Suicide:

- 0 I do not think of suicide or death.
- 1 I feel that life is empty or wonder if it's worth living.
- 2 I think of suicide or death several times a week for several minutes.
- 3 I think of suicide or death several times a day in some detail, or I have made specific plans for suicide or have actually tried to take my life.

## 13. General Interest:

- 0 There is no change from usual in how interested I am in other people or activities.
- 1 I notice that I am less interested in people or activities.
- 2 I find I have interest in only one or two of my formerly pursued activities.
- 3 I have virtually no interest in formerly pursued activities.

## 14. Energy Level:

- 0 There is no change in my usual level of energy.
- 1 I get tired more easily than usual.
- 2 I have to make a big effort to start or finish my usual daily activities (for example, shopping, homework, cooking or going to work).
- 3 I really cannot carry out most of my usual daily activities because I just don't have the energy.

## 15. Feeling slowed down:

- 0 I think, speak, and move at my usual rate of speed.
- 1 I find that my thinking is slowed down or my voice sounds dull or flat.
- 2 It takes me several seconds to respond to most questions and I'm sure my thinking is slowed.
- 3 I am often unable to respond to questions without extreme effort.

## 16. Feeling restless:

- 0 I do not feel restless.
- 1 I'm often fidgety, wringing my hands, or need to shift how I am sitting.
- 2 I have impulses to move about and am quite restless.
- 3 At times, I am unable to stay seated and need to pace around.

To Score:

1. Enter the highest score on any 1 of  
the 4 sleep items (1-4) \_\_\_\_\_  
\_\_\_\_\_
  2. Item 5 \_\_\_\_\_  
\_\_\_\_\_
  3. Enter the highest score on any 1  
appetite/  
weight item (6-9) \_\_\_\_\_  
\_\_\_\_\_
  4. Item 10 \_\_\_\_\_  
\_\_\_\_\_
  5. Item 11 \_\_\_\_\_  
\_\_\_\_\_
  6. Item 12 \_\_\_\_\_  
\_\_\_\_\_
  7. Item 13 \_\_\_\_\_  
\_\_\_\_\_
  8. Item 14 \_\_\_\_\_  
\_\_\_\_\_
  9. Enter the highest score on either of  
the 2 psychomotor items (15 and  
16) \_\_\_\_\_  
\_\_\_\_\_
- TOTAL SCORE (Range 0-27)** \_\_\_\_\_  
\_\_\_\_\_



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**EL INVENTARIO RÁPIDO DE SINTOMATOLOGÍA DE LA DEPRESIÓN (REPORTE PERSONAL)  
(QIDS-SR)**

NOMBRE: \_\_\_\_\_ LA FECHA DE HOY: \_\_\_\_\_

Por favor marque la respuesta en cada sección que mejor describa los últimos siete días.

**1. SUEÑO:**

- 0 Nunca tomo más tiempo que 30 minutos para dormirme.
- 1 Tomo al menos 30 minutos para dormirme, no me toma más de la mitad del tiempo.
- 2 Tomo por lo menos 30 minutos para dormirme, esto me pasa la mayoría de las veces.
- 3 Tomo más que 60 minutos para dormirme, esto me pasa la mayoría de las veces.

**2. DORMIR DURANTE LA NOCHE:**

- 0 No me despierto durante la noche.
- 1 Tengo un sueño ligero inquieto, y a veces me despierto cada noche.
- 2 Me despierto por lo menos una vez cada noche, pero vuelvo a dormirme fácilmente.
- 3 Despierto más de una vez cada noche y me quedo despierto por 20 minutos o más, la mayoría de las veces.

**3. DESPERTARSE DEMASIADO TEMPRANO:**

- 0 La mayoría del tiempo, despierto no más que por 30 minutos antes de que yo necesite levantarme.
- 1 Más de la mitad del tiempo, despierto por más de 30 minutos antes de que yo necesite levantarme.
- 2 Casi siempre me despierto por lo menos por una hora aproximadamente antes de que yo necesite levantarme, pero me vuelvo a dormir al rato.
- 3 Despierto por lo menos una hora antes de que yo necesite levantarme , y no puedo volver a dormir.

**4. EL DORMIR DEMASIADO:**

- 0 Duermo no más que 7-8 horas por noche, sin tomar una siesta durante el día.
- 1 Duermo no más que 10 horas incluyendo siestas durante un período de 24 horas.
- 2 Duermo no más que 12 horas incluyendo siestas durante un período 24 horas.
- 3 Duermo más que 12 horas, incluyendo siestas durante un período de 24 horas.

**5. EL SENTIRSE TRISTE:**

- 0 No me siento triste.
- 1 Me siento triste menos de la mitad del tiempo.
- 2 Me siento triste más de la mitad del tiempo.
- 3 Me siento triste casi todo el tiempo.

**6. EL APETITO DISMINUIDO:**

- 0 No hay cambio en mi apetito usual.
- 1 Frecuentemente como algo menos ó en menor cantidades de alimento que lo usual.
- 2 Como mucho menos que lo usual y solamente con esfuerzo personal.
- 3 Como raramente durante un período de 24 horas, y solamente con esfuerzo personal extremo o cuando otros me persuaden que coma.

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**7. EL AUMENTO DE APETITO:**

- 0 No hay cambio en mi apetito usual.
- 1 Siento una necesidad de comer más frecuentemente que lo usual.
- 2 Como regularmente más frecuentemente y/o mayores cantidades de alimento que lo usual.
- 3 Me siento conducido a sobrealimentarme tanto en la hora de comer como entre comidas.

**8. EL PESO DISMINUSIÓN (Durante las Dos Últimas Semanas):**

- 0 No he tenido un cambio en mi peso.
- 1 Siento como si he tenido una pérdida de peso ligera.
- 2 He perdido 2 libras o más.
- 3 He perdido 5 libras o más.

**9. EL PESO AUMENTO (Durante las Dos Últimas Semanas):**

- 0 No he tenido un cambio en mi peso.
- 1 Siento como si he tenido una ganancia de peso ligera.
- 2 He ganado 2 libras o más.
- 3 He ganado 5 libras o más.

**10. LA CONCENTRACIÓN Y EL HACER DECISIONES:**

- 0 No hay cambio en mi usual capacidad de concentrarme o de hacer decisiones.
- 1 Me siento ocasionalmente indeciso ó encuentro que mi atención es muy poca.
- 2 La mayoría del tiempo, lucho por concentrar mi atención o para hacer decisiones.
- 3 No puedo concentrarme bastante bien para leer o no puedo hacer hasta decisiones menores.

**11. LO QUE PIENSO DE MI MISMO:**

- 0 Me veo con tanto mérito e igualmente meritorio como la otra gente.
- 1 Me culpo más que lo usual.
- 2 Creo ampliamente que provoco problemas para otros.
- 3 Pienso casi constantemente acerca de defectos mayores y menores en mi mismo.

**12. LOS PENSAMIENTOS DE MUERTE O DE SUICIDIO:**

- 0 No pienso en el suicidio o la muerte.
- 1 Considero que la vida no tiene sentido y me pregunto se ésta vida tiene valor.
- 2 Pienso en el suicidio o la muerte varias veces por semana por varios minutos.
- 3 Pienso en el suicidio o la muerte varias veces al día con bastante detalle, ó he hecho planes específicos para suicidarme ó he realmente intentado terminar mi vida.

**13. INTERÉS GENERAL:**

- 0 No hay cambio en general de la manera que me siento interesado en otros y en actividades.
- 1 Noto que estoy menos interesado en la gente o en actividades.
- 2 Encuentro que estoy interesado solamente en uno o dos actividades que anteriormente yo hacia.
- 3 Tengo virtualmente no interés en actividades que yo anteriormente hacia.

## 14. EL NIVEL DE ENERGÍA

- 0 No hay cambio en mi usual nivel de energía.
- 1 Me canso más fácilmente que lo usual.
- 2 Tengo que hacer un esfuerzo grande para comenzar ó acabar mis usuales actividades diarias (por ejemplo, compras, tarea, cocinar o yendo a trabajar).
- 3 Realmente no puedo llevar a cabo la mayoría de mis usuales actividades diarias porque precisamente no tengo la energía.

## 15. SENTIRSE MAS LENTO QUE LO USUAL

- 0 Pienso, hablo, y me muevo tan rápido como antes.
- 1 Encuentro que mi pensamiento es mas lento o mi voz suena sin ánimo y aburrida.
- 2 Me toma varios segundos para responder a la mayoría de las preguntas y yo estoy seguro que mi pensamiento está demasiado lento.
- 3 Me siento frecuentemente incapaz de responder a las preguntas a menos que haga un esfuerzo extremo.

## 16. SENTIRSE INQUIETO

- 0 No me siento inquieto.
- 1 Estoy frecuentemente inquieto, escurro mis manos, o necesito cambiar donde estoy sentado.
- 2 Tengo impulsos de estar moviéndome y me siento bastante inquieto.
- 3 A veces me siento incapaz de permanecer sentado y necesito pasearme de un lado al otro.

To Score:

- 1. Enter the highest score on any 1 of the 4 sleep items (1-4) \_\_\_\_\_
- 2. Item 5 \_\_\_\_\_
- 3. Enter the highest score on any 1 appetite/weight item (6-9) \_\_\_\_\_
- 4. Item 10 \_\_\_\_\_
- 5. Item 11 \_\_\_\_\_
- 6. Item 12 \_\_\_\_\_
- 7. Item 13 \_\_\_\_\_
- 8. Item 14 \_\_\_\_\_
- 9. Enter the highest score on either of the 2 psychomotor items (15 and 16) \_\_\_\_\_
- TOTAL SCORE (Range 0-27)** \_\_\_\_\_