TEXAS MEDICATION ALGORITHM PROJECT

PROCEDURAL MANUAL

MAJOR DEPRESSIVE DISORDER ALGORITHMS

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Major Depressive Disorder Algorithms Procedural Manual
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Disclaimer

This manual is based upon the evidence based, expert consensus recommendations as presented in: Trivedi MH, Crismon ML, Fava M, et al. The Texas Medication Algorithm Project (TMAP): Update to the Algorithm for the Treatment of Major Depressive Disorder. (publication pending).

The manual also reflects the experiences of the TMAP team in conducting the research evaluating use of the algorithms, as well as in implementing the algorithms in public mental health systems. These algorithms reflect the state of knowledge, current at the time of publication, on effective and appropriate care as well as clinical consensus judgments when research-based 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) may not apply to all patients, and each must be adapted and tailored to each individual patient. The authors bear no responsibility for the use and/or modification of these guidelines by third parties. The provision of clinical care, including recommendations contained in these or other guidelines, in whole or in part, is entirely the responsibility of the clinician.

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Overview of the Texas Medication Algorithm Project

Algorithms facilitate clinical decision making by providing clinicians 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 assertively treat the severely and persistently mentally ill (SPMI) population may enhance patient outcomes while improving the utilization of crisis/hospital services and improving 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 an algorithm-driven disease management program 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 I disorder (BDI), and major depressive disorder (MDD).A best practice treatment has been defined as a series of treatment steps that guides physicians in determining medication treatment plans, thereby generating the best outcome for each individual consumer. The algorithms consist of both treatment strategies (recommended sequential medication regimen options) and treatment tactics (recommended options for optimal use of a medication regimen in a given patient). Equal attention should be given to the treatment tactics as to the strategies.

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. Phase 3 evaluated the clinical and economic impact of medication treatment algorithms for MDD, SCZ, and BDI in comparison with Treatment As Usual (TAU). For bipolar disorder, results from each of these phases has been published (please refer to Appendix F for a list of publications).

Implementation of the algorithms on a system wide basis was the next step in offering high quality care to the SPMI patient population in the public mental health sector. This rollout was referred to as Texas Implementation of Medication Algorithms (TIMA) (Phase 4 of TMAP) in order to distinguish it from the research phases of TMAP. However, in order to retain name identity, TMAP is once again being used for the program. The rollout began with the training of physicians and support personnel in algorithm implementation.

Continued revision 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.

* State public mental health services are now provided as a component of the Texas Department of State Health Services (DSHS).

For additional information regarding the development of the most current Bipolar I Disorder Algorithms, please refer to the article: Trivedi MH, Crismon ML, Fava M, et al. The Texas Medication Algorithm Project (TMAP): Update to the Algorithm for the Treatment of Major Depressive Disorder. (publication pending).

Clinical Management

- At baseline and throughout treatment, the patient should be evaluated for possible psychosocial interventions, including evidence based psychotherapy.

- Appropriate use of these treatment algorithms requires that the clinician has made a thorough evaluation and an accurate diagnosis. If a patient completes trials of two stages of the algorithm without observable positive outcomes, the patient should be re-evaluated for accuracy of diagnosis and the occurrence of co-occurring general medical and mental disorders, including substance abuse.

- If co-occurring substance abuse is present, concomitant treatment of both the depression and the substance abuse disorder must be implemented in order to obtain positive patient outcomes.

- The TMAP panel strongly recommends the use of measurement-based care for the treatment of MDD. Measurement of symptom severity (e.g., the Quick Inventory of Depressive Symptoms), side effects, and global functioning should be completed at each visit so that treatment decisions are guided by objective data.

- The ultimate goals of treatment for depression are to achieve remission, return to optimal levels of psychosocial functioning, and to prevent relapse and recurrence of depression.

- Adequate documentation should be completed for each algorithm stage and decision point. If algorithm stages are skipped or if treatment diverges from the algorithm guidelines, the rationale should be adequately documented.

- The frequency of clinic visits should be adequate to implement treatment tactics including monitoring for symptom changes and adverse effects, adjusting doses as necessary to achieve an optimum therapeutic trial, and changing regimens when suboptimal clinical response is observed after regimen optimization.

- All patients with major depressive disorder without psychotic features who achieve symptom remission should continue treatment at the same does for at least 6 to 9 months. After recovery, maintenance phase therapy should be considered, as appropriate based on risk for recurrence of depression.

- When a choice exists between brand, generic, or different formulations (e.g., slow release) of a recommended medication, always initiate treatment with the form that is likely to be best tolerated by the patient, which will lead to enhanced adherence with treatment. Careful attention should be given to adequate dose and duration of treatment for each chosen regimen.

- If medication acquisition cost is a consideration in medication selection, these decisions should be addressed within a specific treatment stage. If all other things are equal (i.e., efficacy, safety, tolerability), then a less expensive medication regimen within a specific algorithm stage may be considered.

At-a-Glance
Major Depressive Disorder Medication Algorithms

Visit Frequency: The TMAP panel recommends visits at week 2, 4, 6, 9, and 12 when entering the treatment algorithm for MDD. Patients who present with suicidal ideation and/or severe functional impairment may require more frequent visits, either in office or via telephone contact.

Assessment Frequency: At each visit a physician assessment of core symptom severity, overall functional impairment, and side effect severity should be conducted. In addition, a symptom-based rating scale (such as the QIDS-SR_{16} or QIDS-C_{16}) should be administered.

Criteria for Medication Change: Medication changes are made after evaluation of tolerability, efficacy across multiple symptom domains, and safety. Clinicians should consult the Tactics and Critical Decision Points for the Treatment of Major Depressive Disorder after review of symptom patterns and severity on the $QIDS_{16}$, as well as any medication side effects and tolerability. The goals of treatment are full symptomatic remission, return of psychosocial functioning, and prevention of relapses and recurrences. Any symptoms, even those in the mild to moderate range, warrant consideration of tactics that may further optimize response. Response criteria using the $QIDS_{16}$ is as follows:

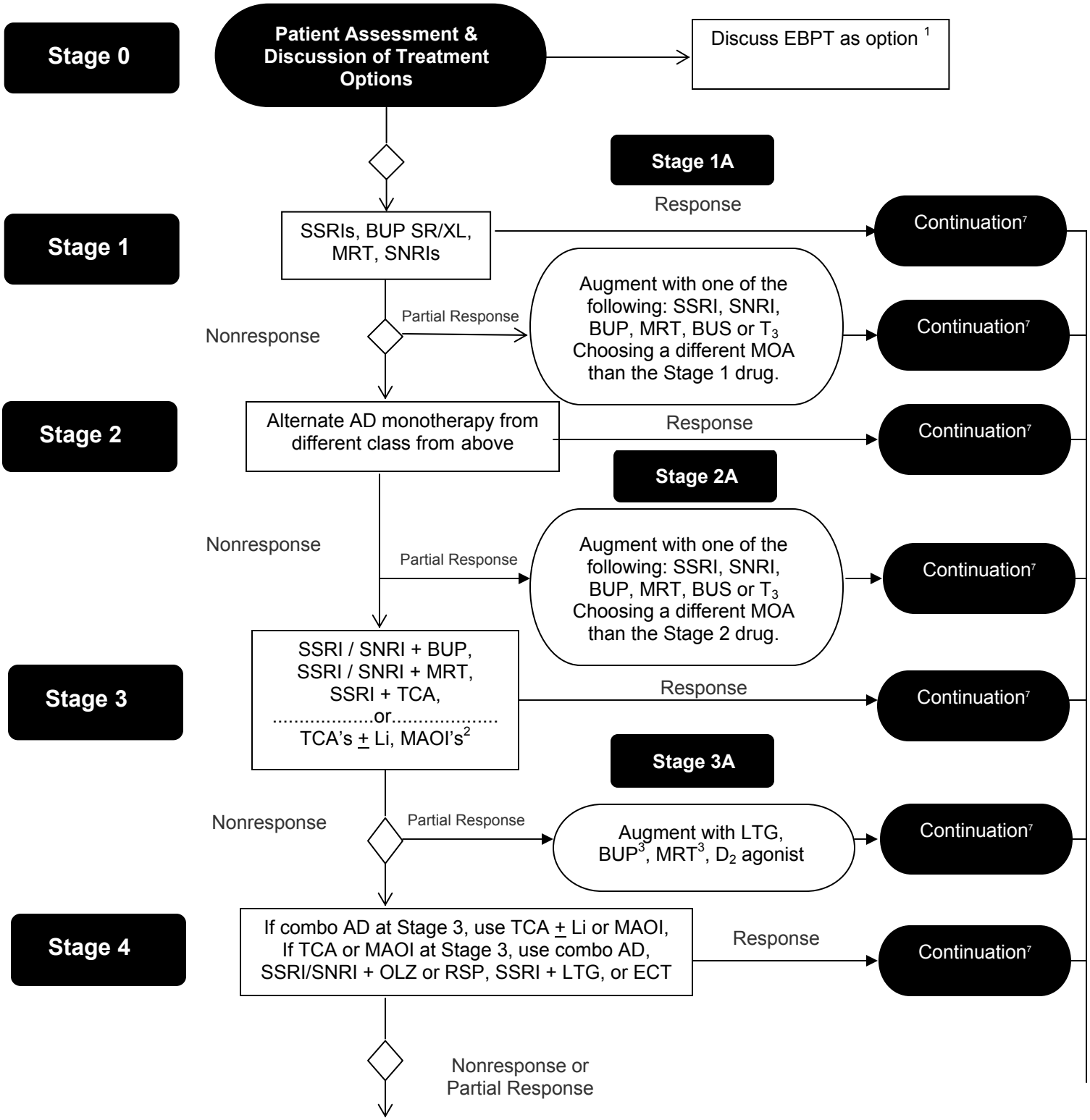
Nonresponse	($QIDS_{16} \geq 9$)
Partial response	($QIDS_{16} = 6$-8)
Full response/remission	($QIDS_{16} \leq 5$)

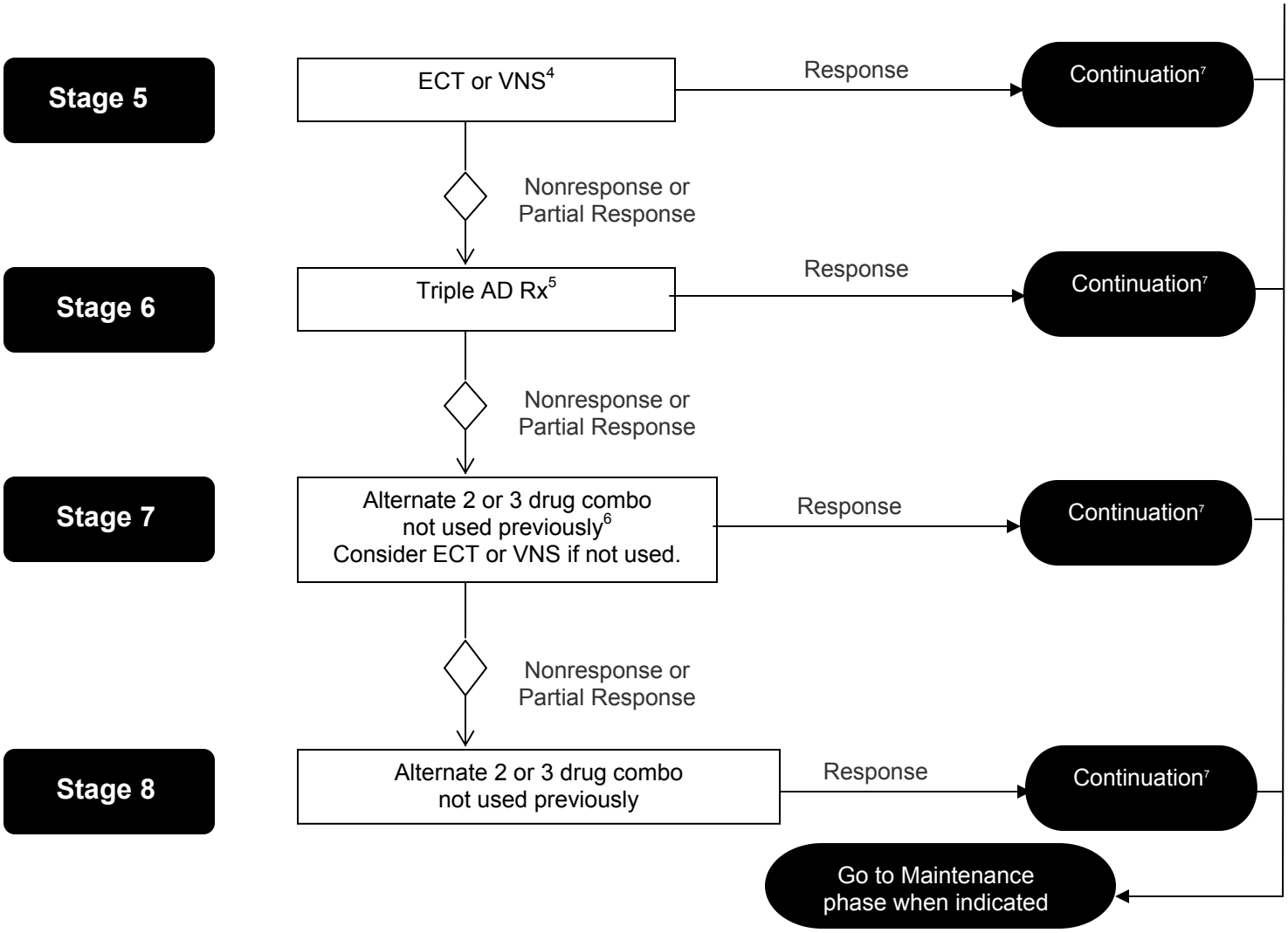
Medication Switching: When switching between antidepressant medications, it is generally recommended to use a cross-tapering strategy.

Medication Doses: Appropriate dosage ranges for medications used in the algorithms are included in *Appendix C.* Doses outside of these accepted ranges should have a chart note indicating "change from algorithm recommended" and documentation of rationale for change. Doses above the usual therapeutic range should be time limited (e.g., 4-6 weeks), and response to this dose evaluated using the brief clinical rating scales. If improvement has not occurred with the higher than usual dosage in this time frame, then treatment should be changed to the next treatment stage.

Documentation: Uniform documentation is an important component of the algorithm program. Clinical rating scale information, response to treatment, prescribed medications, and the rationale for changing medications should be clearly documented on the Clinical Report Form.

Algorithm for the Treatment of Major Depressive Disorder





[1] EBPT = Evidence based psychotherapy. EBPT is an option before starting pharmacotherapy or in combination with pharmacotherapy at any stage in the algorithm.

[2] TCAs ± Li or MAOIs should be considered over combination tx, unless tolerability, prior response, or patient preference otherwise.

[3] Use MRT as an augmenting agent if a SSRI/SNRI + BUP is used in stage 3; use BUP as an augmenting agent if a SSRI/SNRI + MRT is used in stage 3.

[4] If VNS chosen, it augments pharmacotherapy.

[5] Use agents with different MOA; use agents with response in the past (even minimal); choose among SSRIs, SNRIs, BUP, MRT, TCAs, MAOIs, AAPs, LTG, Li.

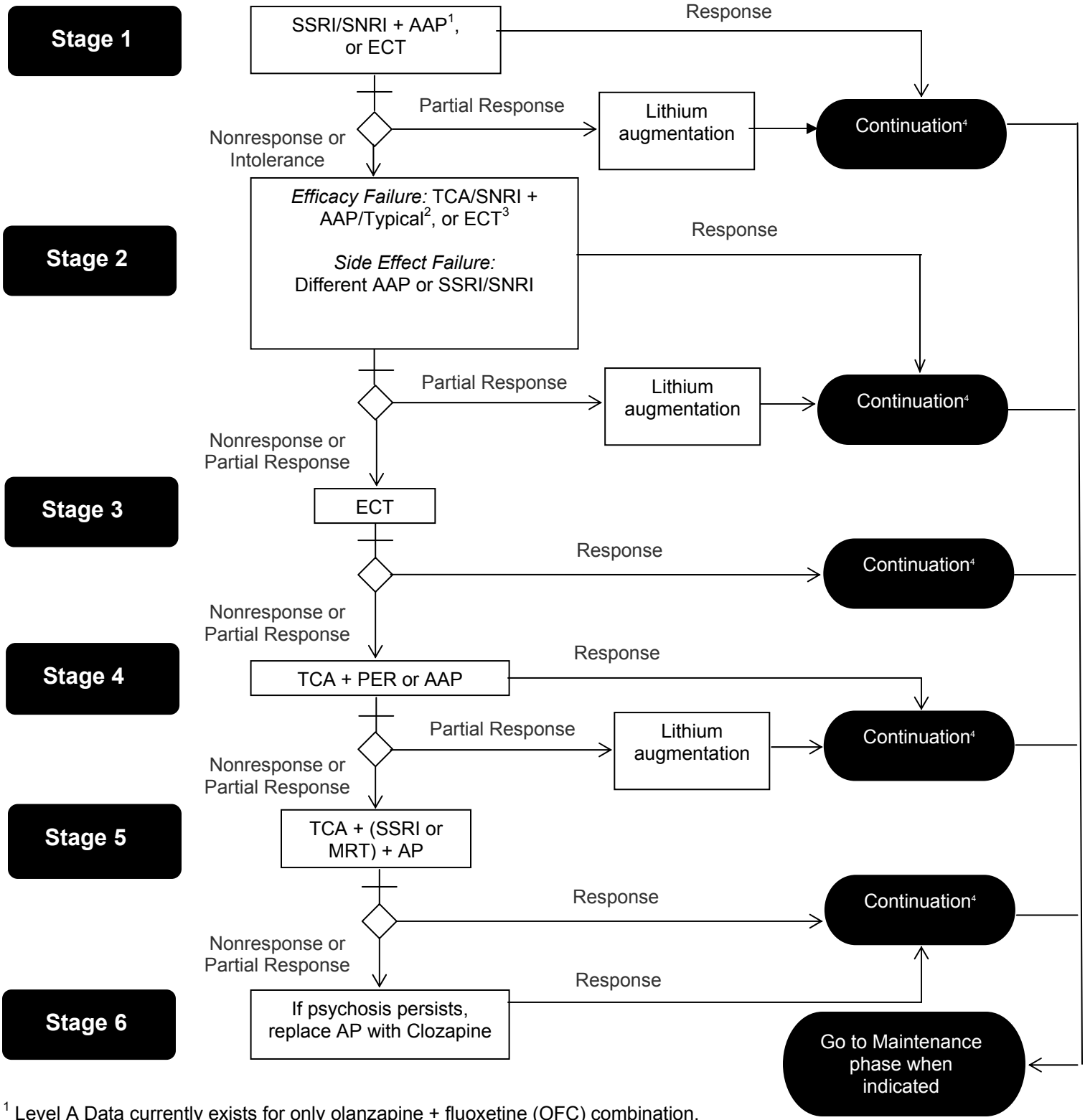
[6] Use agents with a different MOA; use agents with response in the past; If not previously used, consider ECT or VNS here.

[7] Continuation phase treatment should include treatment 6-9 months after remission of symptoms with antidepressant(s) that achieved symptom remission.

Abbreviations

AD=antidepressant
AAP=atypical antipsychotic
BUP SR/XL = bupropion SR/XL
BUS=buspirone
EBPT=evidence based psychotherapy
ECT = electroconvulsive therapy
Li = lithium
LTG = lamotrigine
MAOI=monoamine oxidase inhibitor
MOA=mechanism of action
MRT=mirtazapine
OLZ = olanzapine
RIS = risperidone
SNRI=serotonin-norepinephrin reuptake inhibitor
SSRI=selective serotonin reuptake inhibitor
T_3= liothyronine
TCA=tricyclic antidepressant

Algorithm for the Treatment of Major Depressive Disorder with Psychotic Features



[1] Level A Data currently exists for only olanzapine + fluoxetine (OFC) combination.
[2] If an atypical agent proved to lack efficacy in Stage 1, clinicians may choose to use a typical agent in Stage 2
[3] If a patient suffers from continuing/worsening psychosis or suicidality for ≥ 2 weeks, the ALGO strongly suggests ECT.
[4]Continuation phase treatment should include treatment for 4 months on antipsychotic and lifetime treatment on antidepressant.

Major Depressive Disorder Algorithms

The recommendations for treatment of major depressive disorder (MDD) consist of two algorithms, one for MDD without psychotic features and one for MDD with psychotic features. Compared to past versions of the algorithms, this version includes a broader range of augmentation options as well as an earlier use of combination treatments for nonpsychotic depression. In addition, the MDD with psychotic features algorithm has undergone signification revision.

The treatment algorithms discussed in this manual are intended to be step-by-step medication treatment recommendations. While the focus of the treatment algorithms, and this manual, are pharmacotherapy, evidence-based psychotherapy should be considered and discussed with patients with nonpsychotic depression. The treatment algorithms are evidence-based to the extent that evidence is available to guide treatment decisions. Where clinical data is found to be lacking, expert consensus opinion drives the treatment recommendations. The algorithms are designed to be flexible, and suitable for use in both inpatient and outpatient settings.

It should be emphasized that these algorithms do not serve as a substitute for clinical judgement, but rather are meant to provide a systematic approach to pharmacological treatment of MDD. Appropriate use of these treatment algorithms requires that the clinician has made a thorough evaluation and an accurate diagnosis. Depending on the patient history, severity of depressive and/or psychotic symptoms, and co-morbid conditions, individuals may enter the algorithm at different states. If a patient completes trials of two stages of the algorithm without observable positive outcomes, the diagnosis should be re-evaluated, with special attention to screening for bipolar depression. The presence of co-occurring general medical and mental disorders, including substance abuse, should also be continuously re-evaluated.

Depression commonly co-occurs with other psychiatric disorders (e.g. anxiety disorders, nicotine dependence, etc.) and presence of comorbid psychiatric conditions may favor the choice of one particular medication over another. While it seems logical and parsimonious to choose an agent that might be effective for both depression as well as other comorbid disorders, no prospective study has explored whether consideration of comorbid disorders in the choice of a specific antidepressant improves treatment overall outcomes. Choosing an agent based on FDA-approved indications is suggested for the monitoring and treatment of anxiety disorders, eating disorders, OCD, and other conditions.

The ultimate goals of treatment for depression are to achieve remission, return to optimal levels of psychosocial functioning, and to prevent relapse and recurrence of depression. The TMAP panel strongly recommends the use of measurement-based care during treatment for MDD. Measures of symptom severity (e.g. the Quick Inventory of Depressive Symptoms), side effects and global functioning can be extremely beneficial tools to help guide treatment.

Monitoring Atypical Antipsychotics

Routine health monitoring is an essential part of managing side effects that may result from certain pharmacologic treatments. Atypical antipsychotics are one class of medications that have evidence supporting their use in the treatment of psychotic and nonpsychotic major depressive disorder. As use of this class of medications has continued to expand in the treatment of psychiatric illnesses, several health implications have been recognized through post-marketing surveillance. Taking into account these findings, the Texas public health system recently adopted the Mount Sinai Conference monitoring guidelines (Marder SR, et al. *American Journal of Psychiatry* 2004;161:1334- 49.) Although these recommendations are for patients with schizophrenia, they apply to any patient taking an antipsychotic medication. Similar recommendations have also been developed by a joint task force of the American Psychiatric Association and the American Diabetes Association (American Diabetes Association, American Psychiatric Association, American Association of Clinical Endrocrinologists, et al. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004;27:596-601. and American Diabetes Association, American Psychiatric Association, American Association of Clinical Endrocrinologists, et al. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. J Clin Psychiatry 2004;65:267-272.)

Co-Occurring Substance Abuse

When depression co-occurs with alcohol or other substance abuse, it is critical to treat both the substance abuse as well as the mood disorder. Treatment of only one of the two disorders results in clinical outcomes inferior to appropriately treating the two disorders concomitantly. Most importantly, the clinician should not wait until the patient is abstinent from substances before beginning appropriate treatment for the major depressive disorder. Although adequate evidence regarding the comparative efficacy of antidepressants in the dual-diagnosis population is lacking, the safety profile of SSRI medications would seem to favor their use in these patients.

Description of Algorithm Stages

Algorithm for Treatment of Major Depressive Disorder

Stage 0.
Stage 0 involves patient assessment and discussion of treatment options. Evidence-based psychotherapy should be discussed as an option with every patient, either as a sole treatment or in combination with pharmacotherapy. Patients should be encouraged to engage in a healthy lifestyle, including exercising regularly and engaging in proper nutrition. Nutritional supplementation with omega-3 fatty acids and folate in women should be considered, and can be added at any stage of the algorithm.

Stage 1.
Stage 1 includes antidepressant monotherapy. Medications recommended at this stage include selective serotonin reuptake inhibitors (SSRIs) (fluoxetine, paroxetine, sertraline, citalopram and escitalopram), serotonergic noradrenergic reuptake inhibitors (SNRIs) (venlafaxine and duloxetine), bupropion and mirtazapine. All these antidepressants are considered similar in regards to efficacy in treatment-naïve patients. As such, treatment selection should be based upon individual patient characteristics (comorbidities, concomitant medication, individual or strong family history of response to a particular medication) and patient preference. The antidepressants available at Stage 1, while generally considered equally effective, differ significantly in their side effect profiles and potential for drug interactions. All of the antidepressants included in Stage 1 can be administered once daily, with the exception of bupropion SR at doses exceeding 150 mg/day. Nefazodone, tricyclics (TCAs), and monoamine oxidase inhibitors (MAOIs) are not included at stage 1 due to concerns over safety and tolerability.

Stage 1A.
Stage 1A is an augmentation stage for patients who display partial response to stage 1 treatment. Augmentation of stage 1 antidepressant treatment increases the likelihood of achieving remission without losing the clinical improvements seen in Stage 1. The augmentation agent chosen should have a different mechanism of action than the Stage 1 antidepressant to which it is added. Recommended augmentation strategies include addition of bupropion (BUP), mirtazipine (MRT), lithium (Li), liothyronine (T3) or buspirone (BUS) to an SSRI or SNRI from stage 1; or, if the stage 1 treatment is bupropion or mirtazapine, it is appropriate to add an SSRI or SNRI at stage 1A.

Stage 2.
Patients who do not respond or tolerate Stage 1 treatment should enter Stage 2 of the algorithm. Stage 2 offers the same medications as in Stage 1, but the panel recommends that a different class of antidepressant (i.e., a medcation with a different mechanism of action) should be tried. Even though evidence for switching from one SSRI to another shows about the same remission rate as switching to an antidepressant of another class, consensus was reached on moving to another class for tactical reasons, i.e., not arriving at combination antidepressant treatment in Stage 3 without having tried antidepressants with different mechanisms.

Stage 2A.
Stage 2A is an augmentation stage for patients who display partial response to stage 2 treatment. Augmentation choices recommended in Stage 2A are the same as those in Stage 1A and include BUP, MRT, Li, T3, BUS, SSRI, or SNRI; however, if a patient was also treated with an augmentation agent in Stage 1A, an alternate augmenting approach should be used in Stage 2A.

Stage 3.
Stage 3 involves the use of combination treatment and is indicated for patients who did not respond or did not tolerate medications prescribed at Stage 2. Combination treatments included in this stage are SSRI/SNRI + BUP, SSRI/SNRI + MRT, SSRI + TCA, and SSRI + atypical antipsychotic (AAP). MAOI monotherapy and TCA treatment (either as a monotherapy or in combination with lithium) are also introduced as a treatment alternative in Stage 3. Because of tolerability and safety issues, TCAs and MAOIs are not recommended until stage 3 even though strong evidence supports their efficacy (Level A). The use of lithium augmentation with TCAs may also be considered (Level A). Both clinical evidence and the panel's consensus opinion suggests that TCAs with or without lithium augmentation and MAOIs should be considered prior to combination treatments, however this is tempered by tolerability, prior response, and patient preference.

As noted above, Stage 3 introduces AAPs as a treatment alternative. Although the AAPs are associated with significant side effects, strong efficacy data support the use of olanzapine (Level A) risperidone (Level B) and aripiprazole (Level A) as augmenting agents in depression. Note that the risk for metabolic side effects such as weight gain, hyperglycemia and hypercholesterolemia is highest for olanzapine compared with other atypical antipsychotics. All atypical antipsychotics are associated with a small risk of tardive dyskinesia (TD) as well. All patients receiving AAPs should be evaluated regularly for development of TD with an instrument such as the Abnormal Involuntary Movement Scale (AIMS), and these evaluations should be documented in the clinical record form (CRF). Other important recommendations for monitoring of AAP treatment are noted in the medication charts included as Appendix C.

Stage 3A.
Partial responders at Stage 3 may have their antidepressant therapy augmented by lamotrigine (LTG), BUP, MRT, or dopaminergic agonists (e.g., pramipexole) (Level B evidence). If the combination used in Stage 3 includes an AAP, a dopamine agonist (D_2 agonist) should not be used as an augmentation strategy in Stage 3A. If the antidepressant combination used in Stage 3 includes MRT, BUP should be used as an augmenting agent. If the antidepressant combination used in Stage 3 includes BUP, MRT should be used as the augmenting antidepressant.

Stage 4.
If a TCA (± Li) or a MAOI was used in Stage 3, an alternative Stage 3 approach should be tried (SSRI/SNRI+BUP/MIR or SSRI+TCA/AAP). Alternatively, if a combination treatment (SSRI/SNRI + BUP/MRT/TCA/AAP) was been used in Stage 3, a TCA (± Li) or a MAOI should be used. Electroconvulsive therapy (ECT) is also introduced as a Stage 4 treatment alternative. Level A data support the use of ECT in the treatment. In fact, initial treatment with ECT should be considered in some depressed patients with significant suicidal features. Since cognitive side effects may be of concern over time with ECT, the length of treatment should be no longer than 1 or 2 treatments after symptoms have gone into remission or have not shown further improvement. The patient should receive 6 to 10 treatments before being considered treatment-resistant. A maximum of 20 treatments is recommended by the panel.

Stage 5.
Stage 5 includes patients who did not improve clinically during Stage 4 due to unsatisfactory symptom improvement or inability to tolerate side effects. Stage 5 also includes partial responders at Stage 4, and patients whose previous treatment history or current clinical features suggest that prior stages are not appropriate. Stage 5 treatment recommends the use of ECT (Level A evidence), or vagus nerve stimulation (VNS) (Level B evidence), combined with antidepressant treatment. VNS is

not considered a treatment for acute depression. Antidepressant therapy should be prescribed during VNS treatment and after ECT treatment.

Stage 6.
At this point in the algorithm, very little evidence exists to guide treatment. As such, stages 6-8 are based on expert opinion and the consensus of the TMAP panel. Stage 6 includes patients who did not improve clinically during Stage 5 due to unsatisfactory symptom improvement or inability to tolerate side effects. Stage 6 also includes partial responders at Stage 5, patients whose previous treatment history or current clinical features suggest that prior stages are not appropriate, and patients who refused ECT and/or VNS as treatment options.

At this stage, triple antidepressant therapy is considered, although evidence for this approach is lacking. Triple antidepressant therapy should be tailored to minimize the risk for drug-drug interactions and to include medications with different mechanisms of action. Examples of recommended combinations of medications in Stage 6 include: 1) and SSRI/SNRI + MRT + BUP; 2) and SSRI/SNRI + MRT + Li; 3) an SSRI + BUP + AAP.

Stage 7.
An alternate 2 or 3 drug combination not previously used should be considered at this stage. ECT or VNS combined with antidepressant treatment should also be considered if not used previously for the current episode of depression.

Stage 8.
Stage 8 is essentially the same as Stage 7 with yet another alternate 2 or 3 drug combination not used in Stages 6 and 7. ECT, VNS plus antidepressant treatment, an MAOI, or a TCA (with or without Li) should be considered if not used previously for the current episode.

Algorithm for Treatment of Major Depressive Disorder with Psychotic Features

Stage 1.
Entry into the algorithm implies that the patient has received a comprehensive evaluation and a diagnosis of major depressive disorder with psychotic features. It is critical that treatment address both the depressive and psychotic symptoms of the illness. The first stage of the algorithm should be used for patients experiencing a first episode of psychotic depression or for those who responded to a Stage 1 regimen during a previous episode. Combination of an antidepressant and an antipsychotic is more efficacious than either one alone.

The options at Stage 1 consist of any SSRI or SNRI plus any atypical antipsychotic agent, or ECT (Level A data). Although this stage allows clinicians to choose any SSRI or SNRI and any AAP, current evidence favors the use the olanzapine and fluoxetine combination (OFC) (Level A evidence). The rationale behind including other antidepressant and antipsychotic agents is based on potential tolerability and side effect concerns with OFC. Although Level A evidence supports the use of a TCA with an antipsychotic in psychotic depression, that combination is not recommended at this stage because of the safety and tolerability concerns with the TCAs.

Stage 1A.
Stage 1A is an augmentation stage for patients who partially responded to Stage 1 treatment. Lithium is recommended as an augmenting agent in Stage 1A (Level B evidence).

Stage 2.
Patients who do not experience appropriate clinical response during Stage 1 because of inadequate improvement of depressive or psychotic symptoms, or because of side effect intolerance should progress to Stage 2 in the algorithm. Patients may also enter the algorithm at Stage 2 initially if their history of response during a previous episode of psychotic depression included a treatment option in Stage 2. If treatment failure at Stage 1 was due to side effects, Stage 2 options consist of using a different SSRI/SNRI or a different atypical antipsychotic (not clozapine). If lack of efficacy was the cause of treatment failure at Stage 1, a TCA or a SNRI should be combined with an antipsychotic. At Stage 2, clinicians have the option to institute an older, typical antipsychotic if the AAP used in Stage 1 was inefffective. If either clinical severity or the presence of significant suicidality warrants, ECT should also be considered if not already tried in Stage 1.

Given the severity of illness associated with psychotic depression, including the risk of suicide, safe, efficacious, and prompt treatment is essential. The clinician should closely monitor psychosis and the presence of suicidal ideations, using clinical judgment to guide treatment emergencies. It is the panel's consensus that if a patient is suffering from persistent or worsening psychosis or suicidal ideation (lasting for 2 weeks or more), immediate treatment with ECT is recommended. This addendum is not based upon evidence, but rather, upon expert consensus and the clinician's ethical obligation to provide prompt relief to patients suffering from psychosis/suicidal ideation.

Stage 2A.
Stage 2A is an augmentation stage indicated for patients who exhibit partial response to medication or ECT at Stage 2. As in Stage 1A, lithium is recommended as an augmenting agent at this stage (level B evidence).

Description of Algorithm Stages

Stage 3.
Stage 3 is indicated for patients that did not respond to Stage 2 options due to inadequate symptom improvement or inability to tolerate side effects. Stage 3 also includes patients who only partially responded to Stages 2 or 2A, or whose previous treatment history or current clinical features suggest that prior stages are not appropriate. ECT (level A evidence) should be offered at this point, if not used in prior stages. Since cognitive side effects may be of concern over time with ECT, the length of treatment should be no longer than 1 or 2 treatments after symptoms have gone into remission or have not shown further improvement. The patient should receive 6 to 10 treatments before being considered treatment-resistant. A maximum of 20 treatments is recommended.

Stage 4.
Stage 4 is indicated for patients who did not achieve remission during Stage 3 or were unable to tolerate Stage 3 treatment. Stage 4 also includes patients whose previous treatment history or current clinical features suggest that prior stages are not appropriate. The Stage 4 treatment recommendation is a TCA combined with either perphenazine or an atypical antipsychotic. The best evidence exists for use of perphenazine, olanzapine, or risperidone combined with a TCA (level A evidence). Other atypical antipsychotics have efficacy for the treatment of psychotic symptoms and have a significantly lower risk of tardive dyskinesia compared to first generation antipsychotics, which makes them suitable options at this stage. Clozapine is again excluded at Stage 4 due to concerns regarding safety and tolerability.

Stage 4A.
Stage 4A is an augmentation stage indicated for patients who exhibit partial response to medication at Stage 4. As in the other augmentation sub-stages, lithium is recommended as the augmenting agent.

Stage 5.
Stage 5 is indicated for patients who did not achieve adequate symptom improvement with Stage 4 and patients whose treatment history or current clinical features suggest that prior stages are not appropriate. At this stage, a 3 drug combination consisting of a TCA+SSRI/SNRI/MIR+AP is recommended. Level A and B evidence support the use of these different treatments in psychotic depression.

Stage 6.
Stage 6 is indicated for patients with inadequate response to Stage 5, and for which psychosis persists. Stage 6 also includes patients whose treatment history or current clinical features suggest that prior stages are not appropriate. At this stage, the antipsychotic used by the patient should be replaced by clozapine (level C evidence). Safety and tolerability issues led the consensus panel to restrict the use of clozapine to Stage 6.

Tactics and Critical Decision Points

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. Treatment within both the non-psychotic depression algorithm and the psychotic depression algorithm follow the same set of CDPs. During treatment, at each CDP the physician should assess the patient and make a decision to either continue or change treatment based on improvement in symptoms and tolerability. Note: Patients start at CDP # 1 at the beginning of each new stage or treatment. If tolerability is good, patients should receive an adequate dose and duration trial before moving to the next algorithm stage in patients with inadequate improvement.

Critical Decision Points involve a consideration of response among all domains, symptom improvement, tolerability, and safety. Evaluate the pattern and severity of symptoms by reviewing the QIDS responses or score sheet (please refer to *Appendix A* for score sheet). The Tactics and Critical Decision Points for treatment of the depressed patient allow for clinician judgment and choice in determining where to make adjustments to medications responsive to the individual patient's presentation.

Visit Frequency
The frequency of physician offices visits should be individualized for each patient. The TMAP panel recommends that, in general, a patient starting or switching to a new medication should be seen every two weeks until they are stable. For some patients who present with suicidal ideation or severe functional impairment, more frequent interaction may be necessary. In addition, a small percentage of patient's may be at increased risk for self-injurious or suicidal behavior during the initial period of medication treatment. For this reason, it is recommended that contact be made during the early phase of treatment, prior to the first follow-up visit. This contact does not necessarily have to occur face-to-face, and may consist of a telephone call to patient in the first week of treatment to evaluate for the presence of activation, suicidal ideation, or self-injurious behavior.

Adequate Medication Trial
An adequate trial of an antidepressant should generally last 8-12 weeks. In the absence of side-effects or tolerability issues, the dosage of medication should be increased every 2-3 weeks until either: a) remission is achieved; b) the maximum dosage of the medication is achieved; c) treatment-emergent side effects limit dosage titration. In cases where no response to treatment is appreciated after 4-6 weeks, the clinician and patient may wish to progress to the next stage of the algorithm or alternatively titrate through the dosage range of the medication. In cases where partial response is noted, it is generally most appropriate to titrate medication dosage or attempt an augmentation trial. Inability for the patient to tolerate a medication due to side effects should lead to consideration of dosage reduction or medication switch. When a patient displays a sustained remission of depressive symptoms, it is appropriate for the patient to enter continuation phase treatment.

Switching Medications
When a patient fails to respond to an antidepressant medication, or when intolerable side-effects necessitate, a switch in antidepressant medication may be warranted. Medication switches may be within-class (e.g. SSRI to SSRI) or between-class (e.g. SSRI to SNRI). A variety of strategies can be used when it is necessary to switch antidepressant medications; however, regardless of the switch strategy employed, the goal is to perform the medication switch in a manner that minimizes side effects and has a low risk of worsening depressive symptoms. Strategies for switching from one medication to another are included in *Appendix E*.

Tactics and Critical Decision Points

Tactics and Critical Decision Points (CDPs)
for the Treatment of Major Depressive Disorder

Critical Decision Point (CDP)	Clinical Status		Plan
Week 0 (CDP #1)	QIDS-C_{16} ≥ 9	Symptomatic	• Initiate medication; adjust dose to lower end of therapeutic dose range or serum level.
Week 2 (CDP #2)	QIDS-C_{16} ≤5	Remission	• Continue current dose.
	QIDS-C_{16} = 6-8	Partial Response	• Gradually increase dose as tolerated.
		SEs intolerable	• Continue current dose and address SEs. • Decrease dose and continue for 2 additional weeks. • Switch to another antidepressant
	QIDS-C_{16} ≥9	Nonresponse	• Gradually increase dose as tolerated.
		SEs intolerable	• Decrease dose and continue for 2 additional weeks. • Switch to another antidepressant.
Week 4 (CDP #3)	QIDS-C_{16} ≤5	Remission	• Continue current dose.
	QIDS-C_{16} = 6-8	Partial Response	• Continue current dose. • Consider increasing dose.
		SEs intolerable	• Continue current dose and address SEs. • Switch to another antidepressant.
	QIDS-C_{16} ≥9	Nonresponse	• Increase dose. • Switch to another antidepressant.
		SEs intolerable	• Switch to another antidepressant.

Tactics and Critical Decision Points

Critical Decision Point (CDP)	Clinical Status		Plan
Week 6 (CDP #4)	QIDS-C_{16} ≤5	Remission	• Continue current dose.
	QIDS-C_{16} = 6-8	Partial Response	• Increase/maximize dose. • Use augmentation.
		SEs intolerable	• Continue current dose and address SEs. • Switch to another antidepressant.
	QIDS-C_{16} ≥9	Nonresponse	• Use augmentation. • Switch to another antidepressant.
		SEs intolerable	• Switch to another antidepressant.
Week 9 (CDP #5)	QIDS-C_{16} ≤5	Remission	• Continue current dose.
	QIDS-C_{16} = 6-8	Partial Response	• Increase dose. • Use augmentation. • Switch to another antidepressant.
	QIDS-C_{16} ≥9	Nonresponse or SEs intolerable	• Switch to another antidepressant.
Week 12 (CDP #6)	QIDS-C_{16} ≤5	Remission	• Go to follow-up phase.
	QIDS-C_{16} = 6-8	Partial Response	• Switch to another antidepressant. • Increase dose and reevaluate in 2 weeks.[a]
	QIDS-C_{16} ≥9	Nonresponse or SEs intolerable	• Switch to another antidepressant.

If after 12 weeks the patient has not remitted, but the clinician feels that 2 more weeks of treatment would be beneficial, treatment may be extended.

QIDS-C_{16}, 16-item Quick Inventory of Depressive Symptomatology – Clinician-rated; SEs, side effects

Process Measures: Evaluation of Patient Response

Quick Inventory of Depressive Symptomatology (QIDS)

The QIDS is a depression rating scale based on the nine DSM-IV criterion symptom domains. The QIDS is available in both clinician-rated (QIDS-C) and self-rated versions (QIDS-SR). Both versions consist of 16 items and ask the patient to report the severity of their depressive symptoms over the last week. Each item on the QIDS is scored from 0-3, with a higher score indicating more severe symptom severity. There are 4 questions related to sleep, 4 questions related to appetite/weight and 2 questions related to psychomotor agitation. The other 6 domains of depressive symptoms have 1 question each. For the sleep, appetite, and psychomotor agitation items, only the highest score across all domain items is scored. Therefore, the total possible score on the QIDS instruments ranges from 0-27, with increasing score indicating more severe depression.

The QIDS instruments have demonstrated high reliability and validity. In addition, both versions are sensitive to treatment effects and can be useful tools to aid in evaluation of treatment response. The QIDS-SR can be easily completed while the patient is waiting to be seen by the clinician. The clinician-rated version of the QIDS takes approximately 5-7 minutes to complete and score.

A copy of this scale and the scoring sheet can be found in Appendix A.

Clinician Ratings

Each of the symptom clusters is rated on a 10-point scale (from “no symptoms” to “extremely severe”). The rating is based on impression of the patient at this visit, as well as information about the patient’s clinical status during the week prior to the visit.

- **Core Symptoms:** Based upon all available information, clinician impression of the presence and severity 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 impressions for each of the specific “other symptoms” listed (irritability, mood lability, agitation, aggression, anxiety, fatigue, level of interest). Under “other,” specify and rate any other symptoms that are 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.

The 0-10 rating scale is described in Appendix A.

Medications and Dosing

Please refer to *Appendix C* for summary of recommended doses, titration schedules, maximum recommended doses, side effects, monitoring parameters, and drug interactions for medications used in the Algorithm for the Treatment of Major Depressive Disorder or the Algorithm for the Treatment of Major Depressive Disorder with Psychotic Features.

Appendix D contains recommendations for dealing with treatment-emergent side effects as well as co-existing symptoms.

Overlap and Taper Guidelines are outlined in *Appendix E.*

Continuation Treatment

Continuation phase treatment

The purpose of continuation phase treatment is to bridge the patient between achieving remission to recovery from their episode of depression. Patients who remit with pharmacotherapy during acute phase treatment should continue their medication for AT LEAST 6 to 9 months after symptom remission. Medication treatment during this phase should be continued at the same dosage that produced therapeutic response. The TMAP panel recommends that clinic visits should occur at least once every 3 months at this point.

Patients who responded to acute phase therapy with ECT should receive antidepressant medication during continuation phase. Antidepressant selection should be based on patient specific factors, such as history of prior response. Lithium may also be used as an augmentation medication during continuation phase treatment following ECT. Maintenance ECT should be considered in patients who acutely responded to ECT but are experiencing a relapse during the continuation phase despite other treatments (level B evidence).

Maintenance Treatment

Maintenance phase treatment

Recurrence rates among patients with a history of major depression are high. It has been estimated that approximately 50% of patient will experience a recurrence of depression after an initial episode without long-term treatment, and the risk of recurrence increases with each subsequent episode of depression. By the third episode of depression, it is estimated that 90% of patients will experience recurrence without maintenance antidepressant treatment.

Based on the evidence showing a high risk of recurrence in patients with a history of MDD, the TMAP panel recommends that all patients who experience three or more major depressive episodes should be maintained on antidepressant medication for a course of preventive therapy. Maintenance medication should be prescribed at the same dose that produced symptom remission. The duration of maintenance phase treatment varies between 1 year and lifetime, depending on risk factors for recurrence and patient preference.

Maintenance treatment should be considered for some patients at high risk for recurrent depression after only two episodes of major depression. Patients with chronic depression (current episode >2 years), a co-morbid anxiety disorder, post-traumatic stress disorder, or a serious personality disorder may also benefit from maintenance antidepressant treatment. Other co-morbidities such as substance abuse, an eating disorder, or those with serious ongoing stressors may also warrant longer term treatment. Patients experiencing a first episode of MDD without psychotic features should be evaluated for slow tapering and discontinuation of antidepressant medication at the end of the continuation phase, rather than proceeding with maintenance treatment.

Transition to Maintenance Treatment – Psychotic Depression

Continuation Treatment

Continuation phase treatment

Patients who remit with pharmacotherapy during acute phase treatment should continue their antidepressant medication indefinitely after symptom remission. Antidepressant treatment during this phase should be continued at the same dosage that produced therapeutic response. Antipsychotic medication should be continued for at least 4 months following response and then, if clinically indicated, may be tapered and discontinued. If either depressive or psychotic symptoms begin to re-emerge, the antipsychotic may need to be re-started and continued for a longer or perhaps indefinite course.

Patients who responded to acute phase therapy with ECT should receive antidepressant medication during continuation phase. Antidepressant selection should be based on patient specific factors, such as history of prior response. Maintenance ECT should be considered in patients who acutely responded to ECT but are experiencing a relapse during the continuation phase despite other treatments.

Maintenance Treatment

Maintenance phase treatment

Very little research is available to guide clinical decision making in regards to appropriate maintenance treatment for major depression with psychotic features. The consensus opinion of the TMAP panel is that patients who have experienced a major depressive episode with psychotic features should receive lifetime maintenance treatment with an antidepressant, at full therapeutic dose associated with response.

Documentation

Treatment with the major depressive disorder (MDD) algorithms utilizes uniform documentation developed by TDSHS and the TMAP team, and modified for use by various centers. The critical information from patient history needed for implementation of the MDD algorithms is:

1. Past and current psychoactive medications and response.
2. Primary current diagnosis. (Please note that these algorithms were developed for patients diagnosed with Major Depressive Disorder, either with or without psychotic features.)
3. Core symptoms.
4. Other symptoms.
5. Side effects (to evaluate tolerability).
6. Response to treatment: overall functioning, QIDS scores, patient self-report of symptom severity and side effects.

Outpatient Documentation

Required Forms:

Outpatient Clinic Visit Clinical Record Form (CRF): The CRF should be completed at each visit in which a clinician or other clinician is evaluating response to treatment. Please note that all patients will have a stage entered for the principal treatment algorithm.

e.g. Patient is on Stage 3A of the Algorithm for the Treatment of Major Depressive Disorder.

Stage: 3A

CRFs may vary in format, but all should contain the minimum data specified in *Appendix G*. A template CRF is also included.

Optional Forms: If these forms are not used, then an alterative uniform documentation process should be used to record this important information.

1.) Outpatient Intake Form

2.) 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 the physician or other clinical personnel.

Inpatient Data Collection

Required Forms:

1.) Inpatient Clinic Visit Clinical Record Form: Complete as usual. See instructions above for "Outpatient Clinic Visit Clinical Record Form" for detailed example.

Optional Forms:

1.) Inpatient Intake Form

2.) Inpatient Contact Form

Modifications for Inpatient Use

Patients who have been hospitalized with a diagnosis of major depressive disorder require prompt interventions to achieve stabilization and discharge. It is likely that a clinician may make the following modifications to the TMAP algorithms to achieve these goals.

Adjustment to Critical Decision Points – The critical decision points are set at 2-week intervals, assuming outpatient treatment. Of course, opportunities to evaluate the patient and make clinical decisions and medication adjustments may happen on an expedited schedule when the patient is an inpatient. Although psychotropic medications do not work faster when a patient is hospitalized, the clinician does have an ongoing opportunity to evaluate the patient's response to and tolerance of treatment. Therefore, critical decision points to evaluate the need for antidepressant dosage adjustment or medication change can be made at shorter intervals.

Accelerated movement to advanced treatment stage –In depression, symptoms may improve slowly, but assuming appropriate dose titration, the clinician should consider a change in algorithm stage if there has been no improvement in depressive symptoms within four weeks and adequate medication doses.

Use of adjunctive medications – Symptoms of anxiety or insomnia may necessitate the use of adjunctive medications for these symptoms. Although it is anticipated that adjunctive medications may be used more commonly in the hospital, their use is still typically time limited, and this intent needs to be communicated to the outpatient treating clinician. For example, at the time of discharge, include instructions for follow-up procedures, including intended taper of short-term medications. Providing the outpatient clinician with the last 1 or 2 inpatient CRFs can be extremely helpful in communicating clinical information.

Inpatient to Outpatient Transition

The transition between inpatient and outpatient care is often problematic. Most inpatient clinicians have dealt with the frustration of discharging a patient only to see him or her return to the hospital within a few weeks as a result of not receiving outpatient follow-up and/or not filling or taking prescriptions. Brief hospital stays may further aggravate the problem because patients are discharged before they are truly stabilized. By the same token, outpatient clinicians must constantly revise their treatment plans when their long-term treatment intentions are not followed by the inpatient physician. The following three strategies may improve transitions between the two treatment settings:

1. **Document the treatment plan.** It is imperative that all clinicians document the rationale for treatment decisions and outline the expected treatment plan. This includes detailing expected changes in medications. Inpatient clinicians may want to start notes to their outpatient colleagues with "transfer" rather than "discharge" (I am 'transferring' the acute care of this patient…) because the former term implies a continuation of care while the latter suggests a disruption.

2. **Ensure that patients leave the hospital with enough medication** to see them through to the first follow-up appointment. Administrative policies should not prevent patients from receiving adequate medication to last until the first outpatient clinician appointment.

3. **Establish communication between the inpatient and outpatient treatment teams**. Clinicians working in both arenas should get to know each other and brainstorm about ways to improve coordination between the two settings. Two possible strategies for improving communication are (1) having a team member (on each side) whose job it is to coordinate and follow-up on transfers and (2) organizing regular meetings with key inpatient and outpatient staff members.

4. **Use of clinical report form (CRF):** If the clinician documents pharmacotherapy care on the CRF, then a transfer of copies of the last 1 or 2 completed CRF's to the clinician assuming care of the patient can be helpful in communicating the treatment the patient has received as well as the clinical status the last time the patient was seen.

Outpatient to Inpatient Treatment

Communication and transition in care is equally important when a patient is admitted to the hospital. The outpatient treating clinician should be contacted when patients are hospitalized, and copies of the last two CRFs should be FAXed to the hospital. The outpatient clinician should be asked about the patient's response to medication and potential reasons for illness exacerbation. It should not necessarily be assumed that a patient relapsed because of medication treatment failure. Not taking medications appropriately and alcohol or other substance use are common factors leading to hospitalization. These, as well as other factors (e.g., family or other environmental stress), should be considered in deciding whether to continue the patient on the same medication regimen being used in the outpatient setting or to move to a new treatment stage.

Appendix A: Process Measures

- Quick Inventory of Depressive Symptoms-Clinician Rated (QIDS-C)
- Quick Inventory of Depressive Symptoms-Self-Rated (QIDS-SR)
- Quick Inventory of Depressive Symptoms-Scoring Sheet
- Scoring Criteria for Physician- and Patient-Rated Overall Symptom and Side Effect Ratings

Quick Inventory of Depressive Symptomatology (Clinician-Rated)

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QIDS-C16 ANSWER SHEET

For office use only:

☐ Spanish ☐ By phone ☐ Ad hoc visit ☐ update **QC**

Patient ID _____ Date ___/___/____ (MM / DD / YYYY)

Level ___

Week in level ___

1. Sleep Onset Insomnia:

- ☐ 0 Never takes longer than 30 minutes to fall asleep.
- ☐ 1 Takes at least 30 minutes to fall asleep, less than half the time.
- ☐ 2 Takes at least 30 minutes to fall asleep, more than half the time.
- ☐ 3 Takes more than 60 minutes to fall asleep, more than half the time.

2. Mid-Nocturnal Insomnia:

- ☐ 0 Does not wake up at night.
- ☐ 1 Restless, light sleep with few awakenings.
- ☐ 2 Wakes up at least once a night, but goes back to sleep easily.
- ☐ 3 Awakens more than once a night and stays awake for 20 minutes or more, more than half the time.

3. Early Morning Insomnia:

- ☐ 0 Less than half the time, awakens no more than 30 minutes before necessary.
- ☐ 1 More than half the time, awakens more than 30 minutes before need be.
- ☐ 2 Awakens at least one hour before need be, more than half the time.
- ☐ 3 Awakens at least two hours before need be, more than half the time.

4. Hypersomnia:

- ☐ 0 Sleeps no longer than 7-8 hours/night, without naps.
- ☐ 1 Sleeps no longer than 10 hours in a 24 hour period (include naps).
- ☐ 2 Sleeps no longer than 12 hours in a 24 hour period (include naps).
- ☐ 3 Sleeps longer than 12 hours in a 24 hour period (include naps).

Enter the highest score on any 1 of the 4 sleep items (1-4 above):

☐ 0
☐ 1
☐ 2
☐ 3

= page total

CRC ID _____

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QIDS-C16 ANSWER SHEET

☐ update QC

Patient ID |_|_|_|_|_|_|_|_|_| Date |_|_|/|_|_|/|_|_|_|_| (MM / DD / YYYY)

Level |_|_|

Week in level |_|_|

5. Mood (Sad):

☐ 0 Does not feel sad.

☐ 1 Feels sad less than half the time.

☐ 2 Feels sad more than half the time.

☐ 3 Feels intensely sad virtually all of the time.

Rate either 6 or 7 (not both)

6. Appetite (Decreased):

☐ 0 No change from usual appetite.

☐ 1 Eats somewhat less often and/or lesser amounts than usual.

☐ 2 Eats much less than usual and only with personal effort.

☐ 3 Eats rarely within a 24-hour period, and only with extreme personal effort or with persuasion by others.

- OR -

7. Appetite(Increased):

☐ 0 No change from usual appetite.

☐ 1 More frequently feels a need to eat than usual.

☐ 2 Regularly eats more often and/or greater amounts than usual.

☐ 3 Feels driven to overeat at and between meals.

Rate either 8 or 9 (not both)

8. Weight (Decrease) Within the Last Two Weeks:

☐ 0 Has experienced no weight change.

☐ 1 Feels as if some slight weight loss has occurred.

☐ 2 Has lost 2 pounds or more.

☐ 3 Has lost 5 pounds or more.

- OR -

9. Weight (Increase) Within the Last Two Weeks:

☐ 0 Has experienced no weight change.

☐ 1 Feels as if some slight weight gain has occurred.

☐ 2 Has gained 2 pounds or more.

☐ 3 Has gained 5 pounds or more.

Enter the highest score on any 1 of the 4 appetite/weight change items (6-9 above):

☐ 0
☐ 1
☐ 2
☐ 3

+ item 5 = |_|_| page total

QIDS-C16 ANSWER SHEET

☐ update QC

Patient ID _____ Date ___/___/____ (MM/DD/YYYY)

Level ___

Week in level ___

10. Concentration/Decision Making:

- ☐ 0 No change in usual capacity to concentrate and decide.
- ☐ 1 Occasionally feels indecisive or notes that attention often wanders.
- ☐ 2 Most of the time struggles to focus attention or make decisions.
- ☐ 3 Cannot concentrate well enough to read or cannot make even minor decisions.

11. Outlook (Self):

- ☐ 0 Sees self as equally worthwhile and deserving as others.
- ☐ 1 Is more self-blaming than usual.
- ☐ 2 Largely believes that he/she causes problems for others.
- ☐ 3 Ruminates over major and minor defects in self.

12. Suicidal Ideation:

- ☐ 0 Does not think of suicide or death.
- ☐ 1 Feels life is empty or is not worth living.
- ☐ 2 Thinks of suicide/death several times a weeks for several minutes.
- ☐ 3 Thinks of suicide/death several times a day in depth, or has made specific plans, or attempted suicide.

13. Involvement:

- ☐ 0 No change from usual level of interest in other people and activities.
- ☐ 1 Notices a reduction in former interests/activities.
- ☐ 2 Finds only one or two former interests remain.
- ☐ 3 Has virtually no interest in formerly pursued activities.

14. Energy / Fatigability:

- ☐ 0 No change in usual level of energy.
- ☐ 1 Tires more easily than usual.
- ☐ 2 Makes significant personal effort to initiate or maintain usual daily activities.
- ☐ 3 Unable to carry out most of usual daily activities due to lack of energy.

___ = **page total (total items 10-14)**

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QIDS-C16 ANSWER SHEET

☐ update QC

Patient ID |_|_|_|_|_|_|_|_|_| Date |_|_| / |_|_| / |_|_|_|_|
MM DD YYYY

Level |_|_|
Week in level |_|_|

15. Psychomotor Slowing:

- ☐ 0 Normal speed of thinking, gesturing, and speaking.
- ☐ 1 Patient notes slowed thinking, and voice modulation is reduced.
- ☐ 2 Takes several seconds to respond to most questions; reports slowed thinking.
- ☐ 3 Is largely unresponsive to most questions without strong encouragement.

16. Psychomotor Agitation:

- ☐ 0 No increased speed or disorganization in thinking or gesturing.
- ☐ 1 Fidgets, wrings hands, and shifts positions often.
- ☐ 2 Describes impulse to move about and displays motor restlessness.
- ☐ 3 Unable to stay seated. Paces about with or without permission.

Enter the highest score of either of the 2 psychomotor items (15 or 16 above):

☐ 0
☐ 1
☐ 2
☐ 3

= page total

|_|_| **17. QIDS-C16 = sum of page totals (range: 0-27)**

Quick Inventory of Depressive Symptomatology (Self-Rated)

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.

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.

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.

Please complete <u>either</u> 6 <u>or</u> 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 <u>either</u> 8 <u>or</u> 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.

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.

<u>To Score</u>:

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) _____

QIDS-SR Scoring Criteria

Normal	**≤ 7**
Mild	**8 – 12**
Moderate	**13 – 16**
Moderate to Severe	**17 - 20**
Severe	**21 +**

Physician- and Patient-Rated Overall Symptom and Side Effect Ratings

Symptom and Side Effect Sheet

Depression

Circle that number that best describes how much a problem your symptoms were:

0 1 2 3 4 5 6 7 8 9 10

Not a problem — Moderate — Extreme or severe problem

List the most bothersome symptoms in the last week:

-
-
-

Things I did for me: _____

_____

Circle that number that best describes how much a problem your side effects were:

0 1 2 3 4 5 6 7 8 9 10

Not a problem — Moderate — Extreme or severe problem

List the most bothersome side effects in the last week:

-
-
-

Things I did that helped: _____

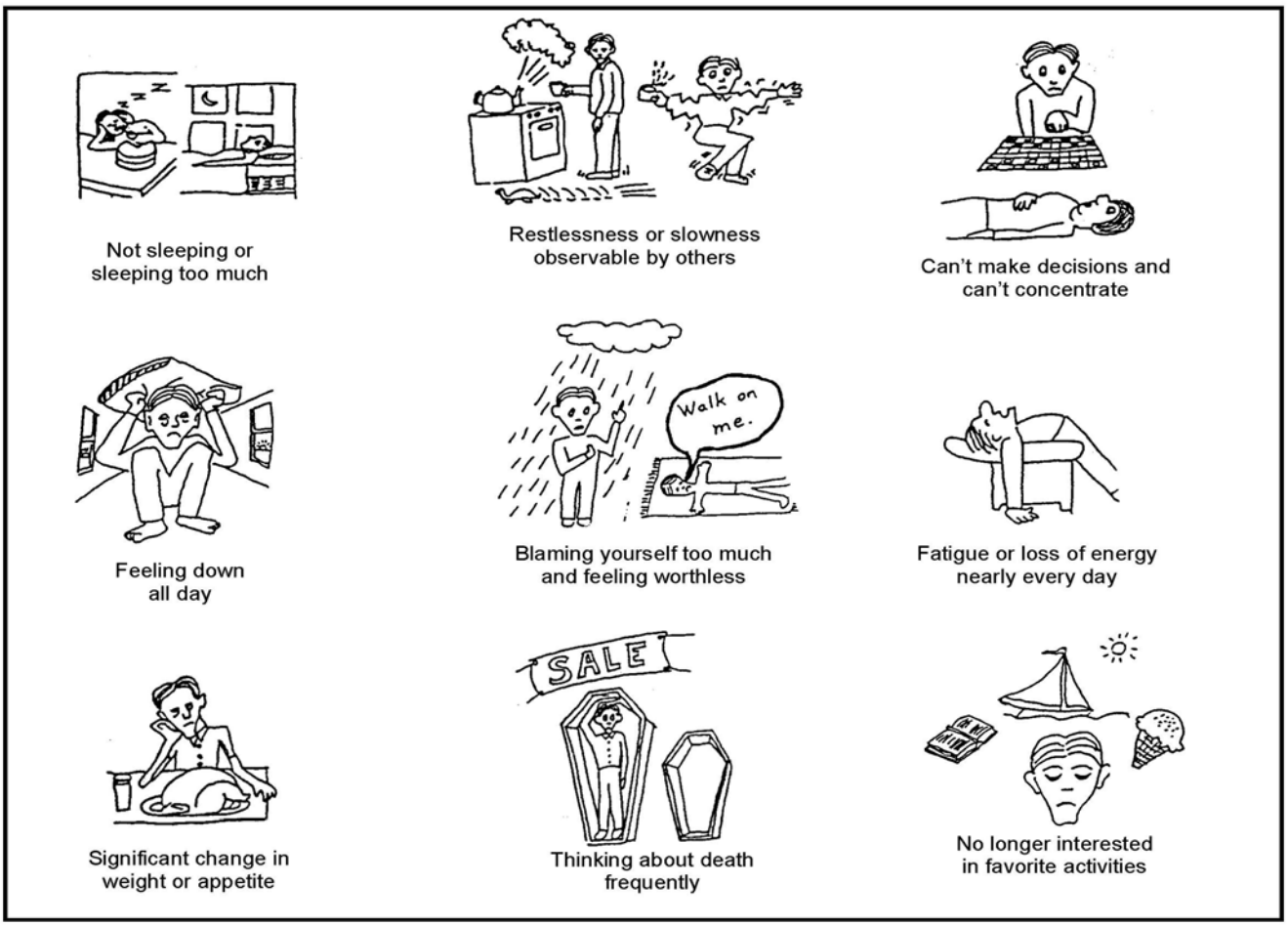
_____

List medications that you are currently taking:

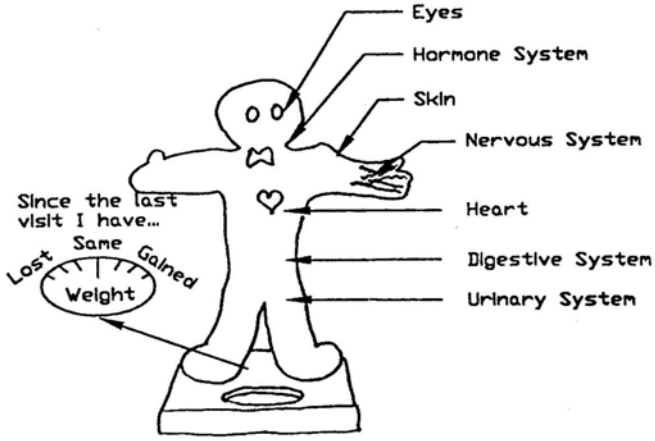
1.
2.
3.
4.

About how long have you been taking each medication? Weeks Months Years

SYMPTOMS



Medications can cause side effects in many parts of the body. Some may go away in time, others can be treated by your doctor.



Ask your doctor about side effects that need to be reported immediately!

Illegal drugs and alcohol may increase the side effects of medications or keep them from working.

Appendix B: Communications

TMAP Information
The University of Texas at Austin
College of Pharmacy PHR 5.110
1 University Station A1910
Austin, TX 78712

TMAP Phone: 512-232-5986
TMAP Fax: 877-735-TMAP (8627)
TMAP Email: info@WebTMAP.org

Appendix C: Medication Charts

Medications Included in Algorithm for the Treatment of Major Depressive Disorder or the Algorithm for the Treatment of Major Depressive Disorder with Psychotic Features

(Please refer to the Physicians' Desk Reference, FDA approved product labeling, or other sources for more complete information.)

Appendix C: Medication Charts

Antidepressants, SSRI								
Drug	**Starting Dose**	**Titration**	**Initial Target Dose**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Citalopram Generic available Celexa®	20 mg/day	10 mg/day every 2 weeks	20-40 mg/day	60 mg/day	Once daily	1) Pregnancy test – as clinically indicated 2) Monitor for emergence of suicidal ideation or behavior	• Agitation • Constipation • Diarrhea • Dizziness • Dry Mouth • Fatigue • Headache • Insomnia • Loss of appetite • Nausea • Nervousness • Sexual Dysfunction • Somnolence • Sweating	• Clozapine • Cyclosporine • Linezolid • MAOIs • NSAIDs • Pimozide • St. John's Wort • Sympathomimetics • Tramadol • Triptans
Escitalopram Lexapro®	10 mg/day	10 mg/day every 2 weeks	10-20 mg/day	20 mg/day	Once daily			• Cyclosporine • Linezolid • MAOIs • NSAIDs • St. John's Wort • Sympathomimetics • Tramadol • Triptans
Fluoxetine Generic available Prozac®	20 mg/day	10-20 mg/day every 4 weeks	20-40 mg/day	80 mg/day	Once daily			• Carbamazepine • Clozapine • Cyclosporine • Hydantoins • Linezolid • MAOIs • NSAIDs • St. John's Wort • Sympathomimetics • Thioridazine • Tramadol • Triptans • Tricyclic antidepressants

Appendix C: Medication Charts

Antidepressants, SSRI								
Drug	**Starting Dose**	**Titration**	**Initial Target Dose**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Fluvoxamine Generic available Luvox®	50 mg/day	50-100 mg/day every 2 weeks	100-200 mg/day	300 mg/day	1-2 times daily	1) Pregnancy test – as clinically indicated 2) Monitor for emergence of suicidal ideation or behavior	• Agitation • Constipation • Diarrhea • Dizziness • Dry Mouth • Fatigue • Headache • Insomnia • Loss of appetite • Nausea • Nervousness • Sexual Dysfunction • Somnolence • Sweating	• Carbamazepine • Clozapine • Cyclosporine • Grapefruit • Hydantoins • Linezolid • MAOIs • Methadone • NSAIDs • Ropivacaine • St. John's Wort • Sympathomimetics • Tacrine • Theophyllines • Thioridazine • Tizanidine • Tramadol • Triptans • Tricyclic antidepressants
Paroxetine Generic available Paxil® Paxil CR®	20 mg/day	10-20 mg/day every 2 weeks	20-40 mg/day	50 mg/day	Once daily			• Cyclosporine • Linezolid • MAOIs • NSAIDs • Phenothiazines • St. John's Wort • Sympathomimetics • Tramadol • Triptans • Tricyclic antidepressants
Sertraline Generic available Zoloft®	50 mg/day	50-100 mg/day every 2 weeks	50-150 mg/day	200 mg/day	Once daily			• Carbamazepine • Clozapine • Cyclosporine • Grapefruit • Hydantoins • Linezolid • MAOIs • NSAIDs • Phenothiazines • Pimozide • St. John's Wort • Sympathomimetics • Tramadol • Triptans • Tricyclic antidepressants

Appendix C: Medication Charts

Antidepressants, SNRI								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Venlafaxine Generic available Effexor Effexor XR®	37.5 mg/day	37.5 – 75 mg/day every week	150 mg/day	375 mg/day	1-2 times daily	1) Pregnancy test – as clinically indicated. 2) Blood pressure prior to initiating treatment, during dosage titration, and as clinically necessary 3) Monitor for emergence of suicidal ideation or behavior	• Anxiety • Decreased Appetite • Dizziness • Dry Mouth • Fatigue • Insomnia • Nausea • Somnolence • Sweating	• Linezolid • MAOIs • St. John's Wort • Sympathomimetics • Tramadol • Triptans
Duloxetine Cymbalta®	30-60 mg/day	30 mg/day at 1-2 weeks	60 mg/day	60 mg/day	1-2 times daily	1) Pregnancy test – as clinically indicated 2) Blood pressure prior to initiating treatment, during dosage titration, and as clinically indicated 3) Hepatic function testing – baseline and as clinically indicated 4) Monitor for emergence of suicidal ideation or behavior		• Alcohol • Linezolid • MAOIs • St. John's Wort • Sympathomimetics • Thioridizine • Tramadol • Triptans

Antidepressants, Other								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Bupropion Generic available Wellbutrin SR® Wellbutrin XL®	150 mg/day	150 mg/day at 3-7 days	300 mg/day	400 mg/day (SR) 450 mg/day(XL)	Twice daily (SR) Once daily (XL)	1) Pregnancy test – as clinically indicated 2) Monitor for emergence of suicidal ideation or behavior	• Constipation • Dry Mouth • Headache • Insomnia • Nausea • Seizures	• Carbamazepine • Cyclosporine • Linezolid • MAOIs • Ritonavir • Tricyclic Antidepressants
Mirtazapine Generic Available Remeron®	15 mg/day	15 mg/day every 1-2 weeks	15-30 mg/day	45 mg/day	Once daily at bedtime	1) Pregnancy test – as clinically indicated 2) Weight 3) Hepatic function testing – baseline and as clinically indicated 4) Lipid panel – baseline and as clinically indicated 5) Fasting blood gluocse – baseline and as clinically indicated 6) Monitor for emergence of suicidality	• Constipation • Dry mouth • Increased appetite • Nausea • Sedation • Weight gain	• Alcohol • Linezolid • MAOIs • SSRIs • St. John's Wort • Tramadol

Appendix C: Medication Charts

Antidepressants, MAOI								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Phenelzine Nardil®	45 mg/day	15 mg/day every 2-3 weeks	45-60 mg/day	90 mg/day	3 times daily	1) Blood chemistries with emphasis on hepatic and renal functions; baseline, yearly and as clinically indicated during prolonged or high dose therapy 2) Pregnancy test – as clinically indicated 3) Blood pressure at baseline and during dosage adjustments and as clinically indicated. 4) Monitor for emergence of suicidal ideation or behavior	• Edema • Insomnia • Orthostatic Hypotension • Sexual Dysfunction • Weight Gain	• Atomoxetine • Bupropion • Carbamazepine • Dextromethorphan • Insulins • Levodopa • Linezolid • Meperidine • SSRIs • SNRIs • St. John's Wort • Sulfonylureas • Sympathomimetics • Tramadol • Triptans • Tricyclic Antidepressants • Tyramine Foods
Tranylcypromine Generic Available Parnate®	30 mg/day	10 mg/day every 2-3 weeks	20-40 mg/day	60 mg/day	2 - 3 times daily			
Selegeline[2] EMSAM®	6 mg/day	3mg/day at intervals no less than every 2 weeks	6 mg/day	12 mg/day	Once daily	1) Pregnancy test – as clinically indicated 2) Blood pressure at baseline and during dosage adjustments and as clinically indicated. 3) Monitor for emergence of suicidal ideation or behavior	• Application site reactions • Diarrhea • Dry mouth • Headache • Insomnia	

[2] Transdermal Delivery System

Appendix C: Medication Charts

Antidepressants, Tricyclic								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Amitriptyline Generic available Elavil®	25-75 mg/day	25-50 mg/day every week	150 mg/day	300 mg/day	1-2 times daily	1) EKG – baseline and as clinically indicated 2) Pregnancy test – as clinically indicated 3) Liver function test – baseline 4) Blood levels as clinically indicated. **Amitriptyline + Nortriptyline: 120-250 ng/mL	• Blurred Vision • Constipation • Dry Mouth • Orthostatic Hypotension • Sedation • Tachycardia • Urinary Retention • Weight gain	• Carbamazepine • Ciimetidine • Clonidine • Fluoxetine • Guanethidine • Linezolid • MAOIs • Paroxetine • Procainamide • Quinidine • Quinolones • Rifabutin • Rifampin • St. John's Wort • Sympathomimetics • Valproate • Ziprasidone
Desipramine Generic available Norpramin® Pertofrane®	50-75 mg/day	25-50 mg/day every week	150-200 mg/day	300 mg/day	1-4 times daily	1) EKG – baseline and as clinically indicated 2) Pregnancy test – as clinically indicated 3) Liver function test – baseline 4) Blood levels as clinically indicated. ** Desipramine: 125-300 ng/mL		
Doxepin Generic available Sinequan®	50-75 mg/day	25-50 mg/day every week	75-150 mg/day	300 mg/day	1-3 times daily	1) EKG – baseline and as clinically indicated 2) Pregnancy test – as clinically indicated 3) Liver function test – baseline 4) Blood levels as clinically indicated. **Doxepin + Nordoxepin: 150-250 ng/mL		
Imipramine Generic available Tofranil® Tofranil-PM®	5-100 mg/day	25-50mg/day every week	100 mg/day	300 mg/day	1-4 times daily	1) EKG – baseline and as clinically indicated 2) Pregnancy test – as clinically indicated 3) Liver function test – baseline 4) Blood levels as clinically indicated. ** Imipramine + Despiramine: 125-250 ng/mL		
Nortriptyline Generic available Pamelor® Aventyl®	25-50 mg/day	25 mg/day every week	75 mg/day	150 mg/day	1-2 times daily	1) EKG – baseline and as clinically indicated 2) Pregnancy test – as clinically indicated 3) Liver function test – baseline 4) Blood levels as clinically indicated. ** Nortriptyline: 50-150 ng/mL		

** Therapeutic drug monitoring of tricyclic antidepressants can be performed after 5-7 days of consistent dosing. Dose adjustments made to achieve 12-hour blood levels within a therapeutic range.

Appendix C: Medication Charts

Augmentation Agents								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Buspirone Generic available BuSpar®	15 mg/day	15 mg/day every week	20-60 mg/day	60 mg/day	2-3 times daily	1) Pregnancy test – as clinically indicated	• Dizziness • Drowsiness • Headache • Nausea	• Alcohol • Furazolidone • Procarbazine • MAOIs • SNRIs • SSRIs • Grapefruit juice
Lamotrigine Lamictal®	25 mg/day*	25 mg/day for 2 weeks, then increase to 50 mg/day for 2 weeks, then 100 mg/day for 1 week*	50-100 mg/day*	200 mg/day	1-2 times daily	1) Renal function test – baseline and as clinically indicated 2) Hepatic function test – baseline, yearly and as clinically indicated 3) Pregnancy Test – as clinically indicated	• Ataxia • Dizziness • Headache • Nausea • Rash • Somnolence • Stevens Johnson Syndrome	• Carbamazepine† • Divalproex‡
Lithium Generic available Eskalith® Eskalith® CR	300 mg/day	150mg/day every 1-2 weeks	600-900 mg/day	Based on the medication serum level in the individual patient in the context of clinical response and tolerability	1-2 times daily	1) EKG – baseline , yearly and as clinically indicated 2) CBC – baseline, yearly and as clinically indicated 3) Thyroid studies – baseline; then TSH every 6 months and as clinically indicated 4) BUN, creatinine, glucose and electrolytes; baseline and as clinically indicated 5) UA – baseline and as clinically indicated 6) Pregnancy test – as clinically indicated 7) Lithium Levels – one week after initiation or dosage change and as clinically indicated Target serum concentration: 0.4-0.6mEq/L	• Acne • Acute renal dysfunction • Cognition • Diarrhea • Dizziness • ECG changes • GI upset • Hypothyroidism • Nausea • Polyuria • Sedation • Thirst • Tremor • Weight gain	• ACE-Inhibitors • Caffeine • NSAIDs • Osmotic diuretics • Theophylline • Thiazide diuretics

*Recommended dosing in absence of enzyme inhibiting or inducing agents.

Liothyronine (T_3) Cytomel®	25 mcg/day	None	25-50 mcg/day	50 mcg/day	Once daily	1) Thyroid function test – baseline and as clinically indicated	• Diarrhea • Headache • Irritability • Nervousness • Sweating • Tachycardia	• Anticoagulants • Hypoglycemics • Oral Contraceptives • Tricyclic Antidepressants
Pramipexole Mirapex®	0.375 mg/day	0.375 mg/day every week	.375-1 mg/day	1.5 mg/day	Three times daily	1) Hepatic function test – baseline, yearly and as clinically indicated 2) Pregnancy Test – as clinically indicated	• Constipation • hypotension • Insomnia • Impulse control • Nausea • Psychosis • Psychomotor agitation • Somnolence	• Alcohol • Cimetidine • Diltiazem • Dopamine antagonists • Ranitidine • Triamterene • Verapamil
Ropinirole Requip®	0.25 mg/day	0.25 mg/day every week	0.25 -1.5 mg/day	2 mg/day	Once daily at bedtime	1) Hepatic function test – baseline, yearly and as clinically indicated 2) Pregnancy Test – as clinically indicated	• Constipation • hypotension • Insomnia • Impulse control • Nausea • Psychosis • Psychomotor agitation • Somnolence	• Dopamine antagonists • Cimetidine • Metoclopramide

† Recommended dose titration of lamotrigine for patients taking carbamazepine (or other enzyme-inducing drugs) and not taking valproate:
50mg daily for weeks 1 & 2;
100 mg daily (in divided doses) for weeks 3 & 4;
200 mg daily (in divided doses) for week 5;
300 mg daily (in divided doses) for week 6;
up to 400 mg daily (in divided doses) for week 7 and thereafter.

‡ Recommended dose titration of lamotrigine for patients taking valproate or other forms of valproic acid:
25 mg every other day for weeks 1 & 2;
25 mg daily for weeks 3 & 4;
50 mg daily for week 5;
100mg daily for week 6 and thereafter.

Appendix C: Medication Charts

Atypical Antipsychotics								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Aripiprazole Abilify®	Aug: 10 mg/day Psychosis: 15 mg/day	5-15 mg/day	Aug: 10-15mg/day Psychosis: 15-30 mg/day	Aug: 15mg/day Psychosis: 30 mg/day	Once daily	1) Pregnancy test – as clinically indicated 2) BMI measurement – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated and quarterly when the antipsychotic dose is stable. 3) Fasting plasma glucose level or hemoglobin A1c – before initiating a new antipsychotic, then yearly. If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly. 4) Lipid screening [total cholesterol, low-and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl 5) EKG – before initiating treatment with ziprasidone (Geodon ®) and subsequently if the patient demonstrates symptoms (e.g., syncope) associated with QT interval prolongation. 6) Sexual function inquiry – inquire yearly for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males. If a patient is receiving an antipsychotic known to be associated with Prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly. 7) Prolactin level – if there is evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males. 8) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase 9) Tardive dyskinesia evaluation – every 6 months. For high-risk patients (including the elderly) every 3 months. 10) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly. 11) Ocular evaluations – yearly for patients older than age 40 years; every 2 years for younger patients	• Agitation • Constipation • EPS • Insomnia • Nausea • Somnolence	• Carbamazepine • Fluoxetine • Ketoconazole • Paroxetine • Quinidine • St John's wort
Olanzapine Zyprexa®	Aug: 5-10 mg/day Psychosis: 5-10 mg/day	5 mg/day	Aug: 10-20 mg/day Psychosis: 10-20 mg/day	Aug: 20 mg/day Psychosis: 20mg/day	Once daily		• Constipation • Dizziness • Dry Mouth • Glucose Dysregulation • Hyperlipidemia • Increased Appetite • Sedation • Weight Gain	• Carbamazepine • Fluvoxamine • Rifampin • Smoking • St. John's Wort
Quetiapine Seroquel®	Aug: 100 mg/day Psychosis: 100 mg/day	100 mg/day x 3 days, then 200 mg/day	Aug: 150-400 mg/day Psychosis: 400-800 mg/day	Aug: 400 mg/day Psychosis: 800 mg/day	1-2 times daily		• Cataract Formation • Dry Mouth • Glucose Dysregulation • Headache • Hyperlipidemia • Increased Appetite • Orthostatic Hypotension • Sedation • Weight Gain	• Erythromycin • Fluconazole • Ketoconazole • Phenytoin • St. John's Wort • Thioridazine • Valproate
Risperidone Risperdal®	Aug: 0.25-0.5 mg/day Psychosis: 1-2 mg/day	1-2 mg/day	Aug: 0.5-2 mg/day Psychosis: 4-6 mg/day	Aug: 3mg/day Psychosis: 6 mg/day	1-2 times daily		• EPS • Glucose Dysregulation • Galactorrhea • Hyperlipidemia • Menstrual irregularity • Orthostatic Hypotension • Prolactin Elevation • Sedation • Sexual dysfunction • Tardive Dyskinesia • Weight Gain	• Carbamazepine • Cimetidine • Fluoxetine • Paroxetine • Phenytoin • Rifampin • Tricyclic Antidepressants

Appendix C: Medication Charts

Atypical Antipsychotics								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Ziprasidone Geodon®	Aug: 20mg/day Psychosis: 40 mg/day	20-40 mg/day	Aug: 20-160 mg/day Psychosis: 80-160 mg/day	Aug: 160mg/day Psychosis: 160 mg/day	Twice daily	See previous page	• Dizziness • ECG Changes • EPS • Rash • Sedation • Vomiting	• Carbamazepine • Diuretics • Moxifloxacin • Quinidine • Sotalol • Thioridazine • Tricyclic Antidepressants
Clozapine Generic available Clozaril® Fazaclo®	Aug: Not suggested Psychosis: 12.5-25 mg/day	25 mg/day every 2-3 days	Aug: Not suggested Psychosis: 100-400 mg/day	Aug: Not suggested Psychosis: 900 mg/day	1 - 3 times daily	1) CBC as indicated by guidelines approved by the FDA in the product labeling. 2) Pregnancy test – as clinically indicated 3) BMI measurement – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated, and quarterly when the antipsychotic does is stable. 4) Fasting plasma glucose level or hemoglobin A1c - before initiating a new antipsychotic, then yearly. If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly. 5) Lipid screening [total cholesterol, low-and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl 6) Sexual function inquiry – inquire yearly for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males. If a patient is receiving an antipsychotic known to be associated with Prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly. 7) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase. 8) Tardive Dyskinesia evaluation – every 12 months. For high risk patients (including the elderly), every 6 months. 9) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly 10) Ocular evaluations – yearly for patients older than age 40 years; every 2 years for younger patients	• Agranulocytosis • Excess Salivation • Fever • Glucose Dysregulation • Hyperlipidemia • Increased Appetite • Myocarditis • Orthostatic Hypotension • Sedation • Seizures • Tachycardia • Weight Gain	• Barbiturates • Caffeine • Carbamazepine • Cimetidine • Erythromycin • Phenytoin • Rifampin • Ritonavir • Smoking • SSRIs • St John's Wort

Appendix C: Medication Charts

Antipsychotics, Typical								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Low Potency						1) Pregnancy test – as clinically indicated 2) BMI measurement – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated, and quarterly when the antipsychotic dose is stable 3) Fasting plasma glucose level or hemoglobin A1c – before initiating a new antipsychotic, then yearly If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly 4) Lipid screening [total cholesterol, low-and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl 5) Sexual function inquiry – inquire yearly for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males. If a patient is receiving an antipsychotic known to be associated with Prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly 6) Prolactin level – if there is evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males. 7) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase 8) Tardive dyskinesia evaluation – every 6 months For high risk patients (including the elderly), every 3 months.	• Constipation • Dry mouth • EPS • Orthostatic hypotension • Photosensitivity • Sedation • Tachycardia • Tardive dyskinesia	
Chlorpromazine *Generic available* Thorazine®	300 mg/day	100-200 mg/day	400-1000 mg/day	2000 mg/day	Three times daily			• Guanethidine • Meperidine • Paroxetine • Pindolol • Quinolones • Beta-Blockers • Ziprasidone
Mid Potency								
Perphenazine *Generic available* Trilafon®	6-8 mg/day	4-8 mg/day	24 mg/day	64 mg/day	Three times daily			• Paroxetine • Quinolones
High Potency								
Fluphenazine *Generic available* Prolixin®	2.5 mg	2.5-5 mg/day	2.5-20 mg/day	40 mg/day	Three times daily			• Guanethidine • Paroxetine • Quinolones

Appendix C: Medication Charts

Antipsychotics, Typical								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Fluphenazine D *Generic available* Prolixin Decanoate®	12.5-25 mg IM every 1-3 weeks[3]	12.5 mg per injection	6.25-50 mg IM every 2-4 weeks	100mg IM (per 4 weeks)	Every 1-3 weeks	9) Vision questionnaire –ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly 10) Ocular evaluations – yearly for patients older than age 40 years; every 2 years for younger patients See Previous Page	See Previous Page	• Guanethidine • Paroxetine • Quinolones
Haloperidol *Generic available* Haldol®	2 mg/day	2-5 mg/day	2-20 mg/day	40 mg/day	1 - 3 times daily			• Azole antifungals • Carbamazepine • Rifabutin • Rifampin
Haloperidol D *Generic available* Haldol Decanoate®	25-50 mg IM every 2-4 weeks[4,5,6]	N/A	50-200 mg IM every 2-4 weeks	450 mg (per 4 weeks)	Every 3-4 weeks			• Azole antifungals • Carbamazepine • Rifabutin • Rifampin

[3] Starting dose generally 1.2 times the patient's oral dose
[4] The maximum volume per injection site should not exceed 3 mL.
[5] Multiple injections can be given at 1-7 day intervals to provide total loading dose.
[6] Starting dose generally 10-20 times the patient's oral dose. Dose of first injection should not exceed 100 mg.

Appendix C: Medication Charts

Adjunctive Treatments, Insomnia								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Zolpidem *Generic Available* Ambien® Ambien CR®	5-10 mg/day CR: 6.25-12.5 mg/day	N/A	5-10 mg/day CR: 6.25-12.5 mg/day	10 mg/day CR: 12.5 mg/day	Once daily at bedtime	1) Pregnancy test – as clinically indicated	• Confusion • Dizziness • Drowsiness • Hallucinations • Headache • Somambulism	• Alcohol • Protease Inhibitors • St. John's Wort • Pramipexole • Benzodiazepine • Barbituates
Zaleplon Sonata®	5-10 mg/day	N/A	5-10 mg/day	20 mg/day	Once daily at bedtime	1) Pregnancy test – as clinically indicated	• Confusion • Dizziness • Drowsiness • Hallucinations • Headache • GI upset	• Alcohol • Benzodiazepine • Barbituates • Cimetidine • St. John's Wort • Pramipexole
Eszopiclone Lunesta®	2 mg/day	N/A	2 mg/day	3 mg/day	Once daily at bedtime	1) Pregnancy test – as clinically indicated	• Confusion • Dizziness • Drowsiness • Dry Mouth • Hallucinations • Headache • Unpleasant taste	• Alcohol • Benzodiazepine • Barbituates • Cimetidine • St. John's Wort • Pramipexole
Trazodone *Generic Available* Deseryl®	50-100 mg/day	N/A	50-200 mg/day	200 mg/day	Once daily at bedtime	1) ECG: baseline and as clinically indicated 2) LFTs: baseline and as clinically indicated 3) serum creatinine/BUN: baseline and as clinically indicated 4) thyroid function tests (TFTs): baseline and as clinically indicated	• Confusion • Dizziness • Blurred vision • Constipation • GI upset • Headache • Hypotension • Nausea • Priapism	• Linezolid • MAOIs • SSRIs • SNRIs • St. John's Wort • TCAs • Tramadol

Appendix C: Medication Charts

Adjunctive Treatment, Fatigue or Excessive Somnolence								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Modafanil Provigil®	200mg/day	N/A	200 mg/day	400 mg/day	Once daily in the morning	1) CBC with differential: baseline and as clinically indicated 2) Hepatic function tests: baseline and as clinically indicated	• Anorexia • Anxiety • Headache • Insomnia • Irritability • Nausea Nervousness • Tachycardia	• Aripiprazole • Cimetidein • Clozapine • Grapefruit juice • MAOIs • Stimulants • Oral contraceptives

Adjunctive Treatments, Sexual Dysfunction								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Bupropion *Generic available* Wellbutrin SR® Wellbutrin XL®	75-150 mg/day	N/A	75-150 mg/day	400 mg/day (SR) 450 mg/day(XL)	Twice daily (SR) Once daily (XL)	1) Pregnancy test – as clinically indicated 2) Monitor for emergence of suicidal ideation or behavior	• Constipation • Dry Mouth • Headache • Insomnia • Nausea • Seizures	• Carbamazepine • Cyclosporine • Linezolid • MAOIs • Ritonavir • Tricyclic Antidepressants
Sildenafil Viagra®	50 mg/day	N/A	25-100mg/day	100 mg/day	1 hour prior to sexual activity	None	• Dyspepsia • Dizziness • Headache • Flushing • Priapism	• Nitrates • Cimetidine • Clarithromycin • Fluoxetine • Grapefruit juice • Ketoconazole
Tadalafil Cialis®	10 mg/day	N/A	5-20 mg/day	20 mg/day	1 hour prior to sexual activity	None	• Dyspepsia • Dizziness • Headache • Flushing • Priapism	• Nitrates • Cimetidine • Clarithromycin • Fluoxetine • Grapefruit juice • Ketoconazole
Vardenafil Levitra®	10 mg/day	N/A	5-20 mg/day	20 mg/day	1 hour prior to sexual activity	None	• Dyspepsia • Dizziness • Headache • Flushing • Priapism	• Nitrates • Cimetidine • Clarithromycin • Fluoxetine • Grapefruit juice • Ketoconazole

Appendix C: Medication Charts

Adjunctive Treatment, Anxiety								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Clonazepam *Generic available* Klonopin®	0.25 mg/day	N/A	1-2 mg/day	4 mg/day	1-2 times daily	1) Pregnancy test – as clinically indicated	• Ataxia • Confusion • Dizziness • Dependence • Drowsiness • Fatigue	• Alcohol • Barbituates • Erythromycin • Fluoxetine • Protease inhibitors • St. John's Wort • Tramadol • TCAs
Lorazepam *Generic Available* Ativan®	2-3 mg/day	N/A	2-3 mg/day	10 mg/day	2-4 times a day or as needed	1) Pregnancy test – as clinically indicated	• Ataxia • Confusion • Dizziness • Dependence • Drowsiness • Fatigue	• Alcohol • Barbituates • Tramadol • TCAs
Buspirone *Generic available* BuSpar®	15 mg/day	15 mg/day every week	20-60 mg/day	60 mg/day	2-3 times daily	1) Pregnancy test – as clinically indicated	• Dizziness • Drowsiness • Headache • Nausea	• Alcohol • Furazolidone • Procarbazine • MAOIs • SNRIs • SSRIs • Grapefruit juice

Nutritional Supplements								
Drug	**Starting Dose**	**Titration**	**Target Dose or Range**	**Maximum Daily Dose**	**Schedule**	**Patient Monitoring Parameters**	**Side Effects**	**Selected Drug Interactions**
Omega-3 Fatty Acids	EPA 1 g/day*	N/A	EPA 1-2 g/day*	EPA 4 g/day	1-3 times daily	None	• Nausea • G/I upset • Diarrhea	• Anticoagulants • Platelet inhibitors • antihypertensives
Folic Acid	500 mcg/day	N/A	500 mcg/day	1 mg/day	Once daily	None	• GI upset	• Cholestyramine • Colestipol • Sulfsalazein
Methylfolate Deplin ®	7.5 mg/day	N/A	7.5 mg/day	7.5 mg/day	Once daily	None	• GI upset	• Cholestyramine • Colestipol • Sulfsalazine

* Dosages reported here are based on EPA content. Omega-3 fatty acid supplements may contain primarily EPA, DHA or a combination of EPA and DHA. When a combination product is used, the ratio of EPA:DHA should ideally be >1.

Appendix C: Medication Charts

Additional References for Drug Information

- *AHFS Drug Information 2006*, American Society of Health-System Pharmacists, Bethesda, MD, 2006.
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- Drug Product Labeling – see specific FDA approved drug prescribing information
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Appendix D. Side Effect and Co-Existing Symptom Management

Treatment-Emergent Side Effects

In general, treatment emergent side effects should be addressed first by dose reduction or medication switching. Prescribing medications for side effects is not optimal and may lead to the emergence of new side effects.

Side Effect	Comments/recommendations

Anxiety	• Initiation of antidepressant agents (and dose increases) may be associated with transient anxiety in some patients. Titrating medication slowly to the target dosage may be necessary for some patients.
	• Short-term adjunctive treatment with anxiolytic medication may be considered if anxiety symptoms are problematic.
	• Adjunctive medication options include:
	  ○ Short-term benzodiazepine treatment
	  ▪ Lorazepam: 2-3 mg/day, given 2-4 times daily
	  ▪ Clonazepam: 1-2 mg/day, divided once or twice daily
	  ○ Buspirone: 20-60 mg/day, divided two or three times daily
	  ○ Hydroxyzine: 25-50 mg every 4-6 hours as needed.

Discontinuation Syndrome	• Onset generally occurs within 1-3 days of discontinuation of antidepressant agents, and depends on the half-life of medication.
	• Discontinuation syndrome may occur in some patients who are intermittently adherent with their antidepressant medication, especially venlafaxine or paroxetine.
	• To minimize the risk and/or impact of discontinuation side-effects, antidepressant medications should generally be tapered prior to discontinuation. Discontinuation tapers should be individualized, but a good rule of thumb is that medication should be decreased by 10-20 percent every week over the course of 4-8 weeks. If intolerable discontinuation side effects occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose and slowing the taper rate may be considered.
	• Symptoms associated with the anti-depressant discontinuation syndrome include:
	  ○ Flu-like symptoms, malaise
	  ○ Headache
	  ○ Dizziness
	  ○ GI upset (nausea, diarrhea)
	  ○ Transient changes in mood, affect, appetite, and sleep
	  ○ Electric “shock-like” sensation in upper extremities
	  ○ Vivid dreams/nightmares
	  ○ Impaired concentration

Side Effect	Comments/recommendations

Extrapyramidal Symptoms (EPS)	• Most commonly seen with first generation antipsychotics, but may also be seen with second generation antipsychotics.
	• EPS include parkisonian tremor, akathisia and dystonia.
	• Parkinsonian tremor – Coarse tremor at rest of approximately 4-6 Hz.
	  ○ Treatment strategies
	  ▪ Decrease dose, divide dosing, use bedtime dosing, or switch to alternate antipsychotic medication.
	  ▪ Pharmacological treatments include:
	  • Benztropine: 1-2 mg twice daily
	  • Diphenyhydramine: 25-50 mg two or three times daily
	  • Amantadine: 100 mg two times daily
	• Akathisia is an unpleasant subjective feeling of inner restlessness
	  ▪ Decrease dose, divide dosing, or switch to alternate antipsychotic medication.
	  ▪ Pharmacological treatments include:
	  • Propranolol: 20-30 mg three times a day
	  • If propranolol is not effective, alternatives include clonidine, lorazepam or clonazepam.
	• Dystonic reactions are characterized by prolonged muscle spasms
	  ○ Benztropine 1 mg two or three times a day for the first few days of antipsychotic therapy may be effective for preventing dystonic reactions in individuals with a history of dystonic reactions to antipsychotic medications.
	  ○ Acute dystonic reactions are generally managed with benztropine 1-2 mg IM or lorazepam 1-2 mg IM.

GI Upset	• Nausea and diarrhea are usually transient side effects with antidepressants. Treatment-emergent nausea typically abates within the 1-2 weeks of treatment. • GI side effects may be improved by administration of medication with food and large quantities of liquid. • With some antidepressant medications (e.g. duloxetine) treatment-emergent nausea appears to be dose related. Lowering the total daily dosage, using BID instead of QD dosing, and slowly titrating to the target dosage may reduce the risk of treatment-emergent nausea. • Persistent GI upset may require changing to an alternative antidepressant medication, or the use of adjunctive agent (e.g. promethazine, ondansetron).

Side Effect	Comments/recommendations

Insomnia	• Promote good sleep hygiene:
	  ○ Encourage regular aerobic exercise at least four hours before bedtime.
	  ○ Avoid alcoholic beverages.
	  ○ Encourage regular sleep cycles.
	  ○ Eliminate noises and distracting lights.
	  ○ Engage in relaxing activities before bed (reading, sex, meditation, etc.).
	  ○ Try a glass of warm milk.
	• Consider reducing the dosage of antidepressant or consider morning administration if the patient is taking their medication at a time other than the morning.
	• Consider switching to a sedating antidepressant medication (e.g. mirtazapine) if appropriate.
	• Adjunctive medication options include:
	  ○ Zolpidem: 5-10 mg once daily at bedtime.
	  ○ Zolpidem CR: 6.25-12.5 mg once daily at bedtime
	  ○ Eszopiclone: 2-3 mg once daily at bedtime
	  ○ Trazodone: 25-100 mg once daily at bedtime

Fatigue/sedation	• A thorough evaluation of sleep behaviors should be performed, including a patient assessment of sleep quality.
	• Reduce the dose of antidepressant or consider administering medication at bedtime.
	• Consider switching to a less sedating alternative medication, if appropriate.
	• Adjunctive medications may be considered. However, in patients with psychosis, adjunctive treatment is not recommended as it may possibly worsen the course of the episode. Adjunctive medications may include:
	  ○ Modafinil: 100-200 mg given in the morning
	  ○ Stimulants, such as methylphenidate 20-80 mg daily, in single or divided doses.

Side Effect	Comments/recommendations

Sexual Dysfunction	• Sexual dysfunction is a common side effect with antidepressant medications, especially SSRIs and SNRIs.
	• In men sexual dysfunction may present as inability to achieve or maintain an erection or anorgasmia. In women, decreased libido and/or anorgasmia may be the presentation.
	• It is important to consider that sexual dysfunction, specifically decreased interest in sexual activity, is commonly associated with depression.
	• SSRIs and SNRIs are associated with higher rates of treatment-emergent sexual dysfunction than buproprion and mirtazapine.
	• If a patient experiences SSRI/SNRI-induced sexual dysfunction, switching to an alternative antidepressant with lower propensity to cause sexual dysfunction (e.g. bupropion) may be beneficial; however if the patient has had a robust response to antidepressant treatment it may be preferable to add low-dose buproprion or mirtazapine to current treatment rather than switch to a new treatment.
	• In some cases, use of a selective phosphodiesterase (PDE) type 5 inhibitor may be appropriate.
	  ○ Sildenafil: 25-100 mg one hour prior to intercourse
	  ○ Tadalafil: 5-20 mg one hour prior to intercourse
	  ○ Vardenafil: 5-20 mg one hour prior to intercourse

Weight Gain	• Weight gain during antidepressant treatment may be a side effect of medication, or may be associated with improved appetite with improvement in depressive symptoms.
	• Mirtazapine is especially associated with increased appetite and weight gain. If a patient taking mirtazapine experiences significant weight gain, consideration may be given to switching to an alternative antidepressant.
	• Exercise (walking, jogging, swimming) at least three times weekly, and for at least 30 minutes each time.
	• Diet:
	  ○ Eat smaller portions of three meals per day.
	  ○ Decrease excess fats (decrease fried food, eat lean meats, increase vegetables, salads, and fruits).
	  ○ Decrease excessive low nutritional content carbohydrate (soft drinks, deserts, candy, gravies, potatoes, white bread).
	  ○ Avoid snacking, and particularly, no evening snacks.

Associated or Co-Existing Symptoms

Associated or Co-Existing Symptom	Recommendations

Anxiety	• Anxiety is commonly associated with depression.
	• Medication Treatment options include:
	  o Benzodiazepine treatment
	  ▪ Lorazepam: 2-3 mg/day, given 2-4 times daily
	  ▪ Clonazepam: 1-2 mg/day, divided once or twice daily
	  o Buspirone: 20-60 mg/day, divided two or three times daily
	  o Hydroxyzine: 25-50 mg every 4-6 hours as needed.

Fatigue/sedation	• Fatigue, or more specifically anergia, is a common symptom associated with depression
	• Adjunctive medications may be considered to treat fatigue if symptoms do not respond to antidepressant treatment. However, in patients with psychosis, adjunctive treatment is not recommended as it may possibly worsen the course of the episode. Adjunctive treatments for fatigue include:
	  o Modafinil: 100-200 mg given in the morning
	  o Stimulants, such as methylphenidate 20-80 mg daily, in single or divided doses.

Insomnia	• Promote good sleep hygiene:
	  o Encourage regular aerobic exercise at least four hours before bedtime.
	  o Avoid alcoholic beverages.
	  o Encourage regular sleep cycles.
	  o Eliminate noises and distracting lights.
	  o Engage in relaxing activities before bed (reading, sex, meditation, etc.).
	  o Try a glass of warm milk.
	• Avoid prescribing any medications which may exacerbate insomnia.
	• Consider use of a sedating antidepressant medication (e.g. mirtazapine) if appropriate.
	• Adjunctive medication options include:
	  o Zolpidem: 5-10 mg once daily at bedtime.
	  o Zolpidem: CR 6.25-12.5 mg once daily at bedtime
	  o Eszopiclone: 2-3 mg once daily at bedtime
	  o Trazodone: 25-100 mg once daily at bedtime

Appendix E. Overlap and Taper Guidelines

Cross-tapering

Generally speaking, the best method to switch from one antidepressant medication to another involves cross-tapering of dosage over a period of days to weeks. This method involves lowering the dosage of the current antidepressant medication while simultaneously initiating the new medication at its starting dosage. Over a period of days to weeks, depending on the medications involved, the dosage of the medication to be discontinued, and the target dosage of the medication to be started, the old medication will be weaned while the new medication will be titrated to the target dosage. Cross-tapering attempts to minimize the risk of discontinuation side-effects and/or clinical worsening sometimes associated with abrupt discontinuation of antidepressant medications; however, cross-tapering may increase the risk for drug-interactions as well as create a situation where side-effect burden may increase. Cross-tapering may be especially beneficial when switching from a medication with a short half-life (e.g. paroxetine) to a new medication. Cross-tapering is also strongly recommended when switching from an SNRI to an SSRI, buproprion or mirtazapine.

Abrupt discontinuation and switch

In some cases, it is optimal to abruptly discontinue the old antidepressant and start the new medication without a cross-taper. For example, in cases of severe and intolerable side-effects, it may be preferred to discontinue the offending medication immediately and start a new medication. In addition, in some cases of a within-class medication switch (e.g. switching from citalopram to sertraline), a discontinuation and switch without a cross-taper period may be appropriate. Additionally, immediate discontinuation and switch is usually well-tolerated when switching from an SSRI to an SNRI (e.g. sertraline to duloxetine).

Switching to or from MAOI treatment

Due to the potential for significant drug-interactions and toxicity when MAOIs are combined with other antidepressants, a unique switch strategy is necessary when the antidepressant switch involves a MAOI. Generally speaking, a 2 week washout period is necessary when switching from an SSRI, SNRI, TCA, buproprion, or mirtazapine to a MAOI. Similarly, a 2 week washout period is necessary when switching from a MAOI to an SSRI, SNRI, TCA, buproprion, or mirtazapine. An exception to the 2 week rule exists when the medication involved in the MAOI switch is the SSRI fluoxetine. Due to the long half-life of fluoxetine, and its metabolite norfluoxetine, a 5 week washout period is recommended when switching from fluoxetine to a MAOI.

Discontinuation of Antidepressant Treatment

Antidepressant discontinuation syndrome (ADS) may occur following abrupt discontinuation of antidepressant therapy. ADS is characterized by flu-like symptoms, dizziness, insomnia, nervousness, nausea, agitation and anxiety. These discontinuation-emergent side effects are most commonly associated with paroxetine and venlafaxine, but may occur with any antidepressant medication. Slowly tapering the antidepressant dosage prior to discontinuation is recommended to minimize discontinuation-emergent adverse events. General recommendations are that the dose of antidepressant should be tapered no more rapidly than 25% per week. Tapering and discontinuation usually can be completed over a 2–3 month period. Before discontinuing treatment, patients should be educated concerning the signs and symptoms of recurrence of depressive symptoms, as well as symptoms associated with ADS.

Appendix F. TMAP Publications

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Appendix G. Minimum Data Set for Documentation

The following information should be entered on the Clinical Record Form at each patient visit:

1. **Patient identification information**
Indicate information required by the health care organization.

2. **Date**
Date of visit (month/day/year)

3. **Service activity code**
Service activity or billing code for this visit

4. **Physician/clinician code or identification**

5. **Duration of visit**
Record start and end times of visit (hour:minute am/pm).

6. **Current diagnoses**
Record the current psychiatric diagnoses using DSM IV-TR codes. Please place primary diagnosis first.

7. **Current algorithm**
Check box of the specific algorithm that is being used.

8. **Current stage in algorithm and weeks in this current stage**
Record current stage in algorithm at the beginning of this visit and how many weeks the patient has been in this stage.

9. **Vital signs**
Record current vital signs: weight, height, blood pressure, pulse rate.

10. **Most recent drug levels**
Most recent values (as applicable) with date

11. **Has patient taken medications as prescribed?**
Check appropriate box.

12. **Any other medications taken during the past week?**
Include any prescriptions, over-the-counter medications, or complementary medications taken in addition to medications prescribed by this physician.

13. **Patient global self report**
Record patient's results, including symptom severity and side effects.

14. **Clinical rating scales**
Record the scores of any and all appropriate clinical rating scales, including POS SX, NEG SX, QIDS (SR or C), BDSS, AIMS, and any others. Although only the total score is required for the Minimum Data Set, greater clinical utility is achieved by listing each item score for the scale or scales used. The individual rating scale items can be preprinted on the CRF if desired.

These items provide a global impression of the clinician's impression of the severity of each of these symptoms as observed at the visit as well as during the week prior to the visit.

For items 15 – 17, a scale of 0 – 10 should be used:

0 = No symptoms
5 = Moderate symptoms
10 = Extreme symptoms

15. **Core symptoms**

These are the severity of the core symptoms for the three adult disorders (Bipolar Disorder, Major Depressive Disorder, and Schizophrenia)for which algorithms have been developed: mania, depression, positive psychotic symptoms, and negative symptoms.

16. **Other symptoms**

These include other symptoms that are commonly seen in individuals with mental disorders and include: irritability, mood lability, agitation, anxiety, level of interest, appetite, energy, and insomnia. A space is left in case the clinician wishes to add additional symptoms that may be present in a given patient.

17. **Overall side effect severity**

Rate the overall level of side effect severity from all medications being taken by the patient.

18. **Suicidal or homicidal**

Indicate if the patient is presently suicidal or homicidal and, if yes, please comment in the progress note section.

19. **Overall functioning**

Rate from 0 – 10 (0 = Low and 10 = High) your overall impression of the patient's ability to function on a daily basis. Please note: this is not a GAF score, but the clinician's overall impression of how the patient has been functioning during the last week.

20. **Are serum concentrations needed?**

This provides a prompt for the clinician to order medication serum concentrations if they are needed. If yes, please specify in the progress note section.

21. **Rationale for diagnostic and other services**

The rationale for ordering diagnostic and other services should be clearly documented.

22. **Medication response**

Please indicate the patient's response to the medication since the beginning of the current stage. Check the box that applies. Please note that this is medication response and, depending on comorbidity and the patient's psychosocial situation, this may not necessarily represent the patient's overall improvement in mental health status.

23. **Rationale for change in medication**

If medication is being changed (including dose changes), please note rationale by checking all boxes that apply.

24. **Prescription information**

- This information should be completed regardless of whether a patient is getting a new prescription for ongoing medications.
- List all medications being taken by the patient for the core syndrome, other symptoms, or side effects.
- Indicate via check mark, if this is a new medication, continuation of a previous medication, or medication being discontinued at this visit.
- Provide the following information: dose, frequency, duration the medication is to be taken, titration (or tapering) schedule, and any other pertinent information describing the medication or use of this medication.
- Indicate via check mark the following:
  - S = Core symptoms
  - OS = Other symptoms
  - SE = Side effects of S or OS medications
  -

25. **Progress note**
Use the progress note to indicate additional information, assessments, or impressions not addressed elsewhere or to expand on information already given. This section should also address any variation from algorithm-based treatment. Clinics may use preprinted templates for this section if they wish.

26. **Next visit**
The treating clinician indicates the recommended number of weeks until the patient should return to the clinic. Clinic staff should record the actual date of the next scheduled visit.

27. **Signature and title**
Treating clinician should sign name and degree designation or title.