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Disclaimer

This manual is based upon the evidence based, expert consensus recommendations presented in the article:


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. A critical component of all the algorithms in TMAP is measurement and documentation of target symptoms with quantitative scales.

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). 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.

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

- At baseline and throughout treatment, the patient should be evaluated for possible psychosocial interventions. Psychosocial rehabilitation programs oriented toward improving patients' adaptive functioning are the mainstay of nondrug treatment for schizophrenia. These programs may include basic living skills, social skills training, basic education, work programs, and supported housing.

- Use of the algorithms assumes 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 schizophrenia and the substance abuse disorder must be implemented in order to obtain optimal positive patient outcomes.

- Brief symptom ratings (PSRS, BNSA) should be completed at each medication visit so that medication treatment decisions are guided by objective data.

- Adequate documentation should be completed for each algorithm stage and treatment choice (i.e., critical decision points). If algorithm stages are skipped or if treatment is different from the algorithms, the rationale should be adequately documented.

- The frequency of clinic visits should be adequate to monitor for symptom changes and adverse effects, to adjust doses as necessary to achieve an optimum therapeutic trial, and change regimens when suboptimal clinical response is observed after regimen optimization.

- 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.

- All patients with schizophrenia who achieve a satisfactory clinical response (minimal positive symptoms and preferably remission) should continue treatment indefinitely as maintenance treatment.

- 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 Schizophrenia Medication Algorithm

Visit Frequency: While medications are being actively adjusted, patients should be seen every 2 weeks. As medications are stabilized and patients exhibit stable, positive response, visit intervals can be gradually lengthened to every 4 weeks. When patients achieve a stable response, visit frequency can be scheduled for every 8-12 weeks, as individually determined. Additional patient contact (e.g., by telephone) may be necessary to provide optimal care for a symptomatic patient.

Assessment Frequency: The 4-Item Positive Symptoms Rating Scale (PSRS) and the Brief Negative Symptom Assessment (BNSA) should be completed at each medication visit.

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 Schizophrenia after review of symptom patterns and severity on the Process Measures Graph, as well as any medication side effects and tolerability. The goals of treatment are symptomatic remission (or minimal positive symptoms), return of psychosocial functioning, and prevention of relapse and recurrence.

As much as possible, patients should receive an adequate trial of each antipsychotic. Patients need at least four weeks of therapeutic doses of an antipsychotic (excluding clozapine) before they can be classified as “non-responders” to the medication. Clozapine requires more time, up to three months. Assessing the full effects of an antipsychotic can take 12 weeks or longer. During acute relapses, multi-week trials of agents are difficult to sustain. However, failure to respond to an antipsychotic in 1-2 weeks should not eliminate it from future consideration as a possibly effective agent. Another trial may be worthwhile under more symptomatically stable circumstances.

Evaluations: At each medication visit, a physician will assess core symptom severity, overall functional impairment, and side effect severity. The provider/physician can complete the PSRS, BNSA and have the patient complete the global self-rating of symptom severity and side effects.

Medication Doses: Appropriate dosage ranges for medications used in the algorithms are included in Appendix C. Doses outside of the 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 ratings. 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.
Schizophrenia Algorithm

Choice of antipsychotic (AP) should be guided by considering the clinical characteristics of the patient and the efficacy and side-effect profiles of the medication. Further steps can be taken depending on clinical features or history of antipsychotic failures, and advancing to a new stage should be justified by history of past response.

Stage 1: First Episode Schizophrenia**
Trial of a single SGA
(ARIPPIRAZOLE, OLANZAPINE, QUETIAPINE, RISPERIDONE, or ZIPRASIDONE)

- Partial or Non-response

Stage 2
Trial of a single SGA or FGA
(not SGA tried in Stage 1)

- Partial or Non-response

Stage 3
CLOZAPINE

- Partial or Non-response

Stage 4
CLOZAPINE +
(FGA, SGA or ECT)

- Non-response

Stage 5
Trial of a single agent
FGA or SGA
(not tried in Stages 1 or 2)

Stage 6
Combination Therapy
E.g. SGA + FGA, combination of SGAs, (FGA or SGA) + ECT, (FGA or SGA) + other agent (e.g. mood stabilizer)*

Consider earlier trial of clozapine in patients with a history of recurrent suicidality, violence, or comorbid substance abuse. Persistence of positive symptoms > 2 years warrants and > 5 years requires a clozapine trial, independent of number of preceding antipsychotic trials.

Inconsistent results in RCTs

Value in clozapine failures not established

Case reports, no controlled studies of combinations in long term treatment of schizophrenia

* If patient is inadequately adherent at any stage, the clinician should assess contributing factors and consider a long-acting antipsychotic preparation, such as risperidone microspheres, haloperidol decanoate or fluphenazine decanoate.

** A treatment refractory evaluation should be performed to reexamine diagnosis, substance abuse, medication adherence, and psychosocial stressors. Cognitive Behavioral Therapy and other psychosocial augmentations should be considered.

©Whenever a second medication is added to an antipsychotic (other than clozapine) for the purpose of improving psychotic symptoms, the patient is considered to be in Stage 6.

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Schizophrenia Algorithm

The medications algorithms were designed with the objectives of optimizing long-term safety and tolerability, and achieving full symptom remission. The recommendations contained in the algorithm are based on the evidence available at the time of their development. When evidence is not available to guide algorithm development, expert consensus drives algorithm recommendations.

First-Episode vs. Multi-Episode Schizophrenia

The schizophrenia treatment algorithm is applicable both to patients with first-episode schizophrenia and chronic, multi-episode schizophrenia. While evidence suggests that individuals with a first-episode of schizophrenia are more likely to respond to lower doses of antipsychotic and may be more susceptible to certain antipsychotic side effects, no specific recommendations regarding dosage or side effects was made by the consensus panel. The majority opinion of the consensus panel is that second generation antipsychotic medications are favored as initial treatment for first-episode schizophrenia.

Medication Change Criteria

Medication changes should only be considered after evaluation of tolerability, efficacy, and safety. As much as possible, patients should receive an adequate trial of each antipsychotic. Patients need at least four weeks of a therapeutic dosage of an antipsychotic (excluding clozapine) before they can be classified as “non-responders” to the medication. Clozapine requires more time, up to three months. Assessing the full effects of an antipsychotic can take 12 weeks or longer. During acute relapses, multi-week trials of agents are difficult to sustain. However, failure to respond to an antipsychotic in 1-2 weeks should not eliminate it from future consideration as a possibly effective agent. Another trial may be worthwhile under more symptomatically stable circumstances.

Medication Serum Concentrations:

If lithium or valproate is utilized in Stage 6, serum concentrations should be obtained in order to assist in the evaluation of medication response and tolerability. It is recommended that within 2 weeks after initiating lithium (Li) or valproate (VPA), the patient be receiving the minimum target dose. If possible, a serum concentration should be obtained approximately 5-7 days (~5 half-lives) after reaching the initial target dose (i.e. about 2-3 weeks after starting the trial). Further dosage adjustments should be made based on efficacy and tolerability, with medication serum concentration being used as needed to inform an evaluation of efficacy and tolerability. Target serum concentrations are provided in Appendix C. Keep in mind that these recommendations are based on data from studies in acute mania. No therapeutic blood levels have been established for use of these agents as augmentation treatments in schizophrenia.

Monitoring Atypical Antipsychotics:

Routine health monitoring is essential to detection and management of side effects that may result from treatment with antipsychotic medications. As the use of atypical antipsychotic medications has become increasingly more widespread, several health implications have been recognized through case reports, post-marketing surveillance, and pharmacopeiemiological studies. Some antipsychotic
medications have been associated with weight gain, dyslipidemia, hyperglycemia, and altered EKG findings. In addition, significant research suggests that patients with schizophrenia may be more likely to experience certain health conditions, such as diabetes, even in the absence of medication-related risk factors. Based on this information, the Texas public health system has adopted the Mount Sinai Conference health monitoring guidelines. These guidelines include recommendations for monitoring the physical health of patients receiving antipsychotic medications, including recommendations for routine monitoring of metabolic side effects such as weight gain, diabetes, and hyperlipidemia. The Mt. Sinai Conference monitoring guidelines can be accessed using the following citation:


**Co-Occurring Substance Abuse**

It is common for individuals with schizophrenia to have a co-occurring substance abuse disorder. In these cases, it is extremely important that both disorders are appropriately treated in order to maximize the likelihood of a beneficial treatment outcome. The most common substances abused by patients diagnosed with schizophrenia are alcohol, marijuana and cocaine. Nicotine use is also extremely common among patients diagnosed with schizophrenia. Clozapine has demonstrated the most significant and consistent positive effect on outcomes in patients with schizophrenia and a co-occurring substance use disorder. As such, the consensus panel recommends that clozapine treatment be considered earlier in patients with a co-occurring substance use disorder.
Description of Algorithm Stages

This section of the manual explains the rationale behind the sequence of stages in the Schizophrenia Algorithm and highlights changes made at the Schizophrenia Algorithm Update Conference in June 2006.

Stage 1

Stage 1 is treatment for patients with new onset schizophrenia and includes monotherapy with a second-generation antipsychotic. Medication choices at Stage 1 include monotherapy with aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone.

Once adequate dose titration and treatment duration are achieved, decide how well the patient has responded to the chosen treatment.

If there is a full response, continue the treatment. If there is no response or a partial response after adequate dose titration and treatment duration, then go to Stage 2. However, if the patient has a history of comorbid substance abuse, suicidality, or violence, consider moving to Stage 3.

Stage 2

Stage 2 consists of monotherapy with one of the second-generation antipsychotics not tried during Stage 1 or with a first-generation antipsychotic. If the patient achieves full response, continue with the prescribed treatment. If there is no response, or a partial response, after adequate dose titration and treatment duration, go to Stage 3.

Stage 3

Clozapine is the Stage 3 treatment for schizophrenia. Clozapine is the only antipsychotic that has shown superiority over other antipsychotic agents in reducing psychotic symptoms. It is effective in treatment-resistant schizophrenia and in patients having a history of comorbid substance abuse, suicidality, or violence. Persistence of positive symptoms > 2 years warrants and > 5 years requires a clozapine trial, independent of number of preceding antipsychotic trials.

If clozapine does not provide a full response after adequate dose titration and treatment duration, an evaluation should be performed to reexamine the diagnosis and check for substance abuse, medication adherence, and psychosocial stressors. Cognitive behavioral therapy or psychosocial augmentation should also be considered before moving to Stage 4.

Stage 4

Stage 4 treatment includes clozapine plus one of the following:

A first-generation antipsychotic
A second-generation antipsychotic
Electroconvulsive therapy

If there is not a full response after adequate dose titration and treatment duration with any combination pharmacotherapy, move to Stage 5.
Stage 5
Stage 5 treatment consists of monotherapy with a first-generation or second-generation antipsychotic that was not tried at Stages 1 or 2.

The value of Stage 5 treatment in clozapine failures has not been established. If there is partial or no response after adequate dose titration and treatment duration, move to Stage 6.

Stage 6
Stage 6 treatment consists of combination therapy with a second-generation plus a first-generation antipsychotic, a combination of second-generation antipsychotics, a first-generation or second-generation antipsychotic plus electroconvulsive therapy, or a first-generation or second-generation antipsychotic plus another agent such as a mood stabilizer.

The recommendations at Stage 6 are based on case reports, as there have been no controlled studies of combinations in the long-term treatment of schizophrenia.
Tactics and Critical Decision Points (CDPs) for the Treatment of Schizophrenia

Stages 1, 2, 4, 5 and 6

<table>
<thead>
<tr>
<th>Critical Decision Point</th>
<th>Clinical Status</th>
<th>Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0 (CDP # 1)</td>
<td>Symptomatic</td>
<td>♦ Assess patient; choose a treatment stage and initiate a medication regimen from that stage; adjust dose to therapeutic dose within one week.</td>
</tr>
<tr>
<td>Week 5 (CDP # 2)</td>
<td>Full Response</td>
<td>♦ Continue current dose as maintenance treatment.</td>
</tr>
<tr>
<td></td>
<td>Partial Response</td>
<td>♦ Continue current dose.</td>
</tr>
<tr>
<td></td>
<td>No Response</td>
<td>♦ Consider increasing dose if medication tolerability is good.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>♦ Consider the next stage.</td>
</tr>
<tr>
<td>Week 8 (CDP # 3)</td>
<td>Full Response</td>
<td>♦ Continue current dose as maintenance treatment.</td>
</tr>
<tr>
<td></td>
<td>Partial Response</td>
<td>♦ Continue current dose.</td>
</tr>
<tr>
<td></td>
<td>No Response</td>
<td>♦ Consider increasing dose if medication tolerability is good.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>♦ Consider the next stage.</td>
</tr>
<tr>
<td>Week 12†§ (CDP # 4)</td>
<td>Full Response</td>
<td>♦ Continue current dose as maintenance treatment.</td>
</tr>
<tr>
<td></td>
<td>Partial Response</td>
<td>♦ Consider the next stage.</td>
</tr>
</tbody>
</table>

† Partial responders at week 12 should be titrated to doses at the upper end of the therapeutic range before a change in stages is considered.
‡ ≥ 20% improvement in positive symptoms by week 12 supports continued treatment for another 12 weeks, with dose titration as clinically warranted.
Tactics and Critical Decision Points (CDPs) for the Treatment of Schizophrenia

Stage 3
Clozapine Monotherapy

<table>
<thead>
<tr>
<th>Critical Decision Point</th>
<th>Clinical Status</th>
<th>Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0 (CDP # 1)</td>
<td>Symptomatic</td>
<td>♦ Initiate clozapine. Titrate to therapeutic dose within one month.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>♦ Adjust dose as needed during interim visits.</td>
</tr>
<tr>
<td>Week 16 (CDP # 2)</td>
<td>Full Response</td>
<td>♦ Continue current dose as maintenance treatment.</td>
</tr>
<tr>
<td></td>
<td>Partial Response</td>
<td>♦ Assess serum concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>No Response</td>
<td>♦ Assess serum concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td>Week 28 (CDP # 3)</td>
<td>Full Response</td>
<td>♦ Continue current dose as maintenance treatment.</td>
</tr>
<tr>
<td></td>
<td>Partial Response</td>
<td>♦ Assess serum concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>No Response</td>
<td>♦ Consider the next stage.</td>
</tr>
</tbody>
</table>
Process Measures: Evaluation of Patient Response

**Response**
Response criteria are shown below.

**RESPONSE CRITERIA**

<table>
<thead>
<tr>
<th>STAGE 1</th>
<th>Positive symptom score ≤ 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>STAGE 2</td>
<td>Positive symptom score ≤ 6</td>
</tr>
<tr>
<td>STAGE 3</td>
<td>&gt; 20% decrease in positive symptoms</td>
</tr>
<tr>
<td>STAGE 4</td>
<td>&gt; 20% decrease in positive symptoms</td>
</tr>
<tr>
<td>STAGE 5</td>
<td>&gt; 20% decrease in positive symptoms</td>
</tr>
<tr>
<td>STAGE 6</td>
<td>&gt; 20% decrease in positive symptoms</td>
</tr>
</tbody>
</table>

Generally speaking, symptoms respond to antipsychotics in somewhat different time frames. Agitation, sleep, and appetite often respond during the first 1-2 weeks, whereas personal hygiene and basic interpersonal socialization may be slower to respond (2-3 weeks), and psychotic symptoms can gradually decrease over 2-6 weeks or longer. Residual symptoms may continue to improve at 6-12 weeks. Chronic patients may show slower responses of all symptoms.

Negative symptoms are no longer included in the response criteria, as little evidence exists on which to base realistic goals for negative symptom improvement. Compared to the older agents, the newer medications are thought to be “better” for negative symptoms but this superiority may be explained by the newer agents’ reduced propensity to cause EPS (which can lead to secondary negative symptoms). Several factors (depression, environmental deprivation, positive symptoms) can contribute to negative symptoms, and medications may have little effect on core negative symptoms.

This in no way implies that negative symptoms are not important and do not need to be measured. On the contrary, recent findings indicate that negative and cognitive symptoms have more of an impact on patients’ functional status than the positive symptoms of schizophrenia. At each medication visit, clinicians should perform the PSRS, BNSA, and assessments of “other symptoms,” such as mood lability, anxiety, agitation, etc. and incorporate all findings into the clinical decision-making process.

**Partial Response**

A partial response at any stage of the algorithm is a basis for continuing the patient in that stage, up to the maximum recommended amount of time for that stage. At Critical Decision Points (CDPs), there is the option of changing the antipsychotic dose for partial responders. This is not a requirement, however. For many patients, further duration of treatment may be all that is needed. There are, unfortunately, no empirical guidelines for deciding when this is the case. Generally, prior time to achieve a response in a particular patient is helpful in judging when that patient is likely to
respond to the current treatment. In summary, a partial responder in Stages 1-2 has > 20% improvement in positive symptoms, but his/her absolute positive symptom score exceeds 6. In Stages 3 - 6, partial response is a clinical judgment that the patient whose symptoms have improved by less than 20% is “better.” It is not clinically meaningful to try to use scale score changes of less than 20% to distinguish between partial responders and non-responders.

Non-Response

At any stage, before concluding that a patient is a non-responder to an antipsychotic, the clinician should consider causes of non-response that would indicate a course of action other than changing to a new antipsychotic. Included in this list are:

1. Medication non-adherence
2. Incorrect diagnosis
3. Substance abuse
4. Side effects
5. Psychosocial stressors
6. Undiagnosed or uncorrected general medical problem such as diabetes, hypertension, hypothyroidism, and anemia
Process Measures: Evaluation of Patient Response

Positive Symptom Rating Scale (PSRS) and Brief Negative Symptom Assessment (GNSA)

Patients with a diagnosis of schizophrenia or schizoaffective disorder should be evaluated at every visit using the Positive Symptom Rating Scale, or PSRS, and the Brief Negative Symptom Assessment, or BNSA.

**PSRS**
The 4-item PSRS assesses positive symptoms of schizophrenia (suspiciousness, unusual thought content, hallucinations, and conceptual disorganization). These items are from the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962) and the expanded version of the BPRS (Lukoff, et al. 1993), both of which have been shown to be valid and reliable. For the 4-item PSRS the items are ranked on a scale of: N/A = Not Assessed, 1 = Not Present, 2 = Very Mild, 3 = Mild, 4 = Moderate, 5 = Moderately Severe, 6 = Severe, 7 = Extremely Severe. The interview takes 5 minutes or less to complete.

**BNSA**
The BNSA is a 4-item instrument utilized to assess a subset of DSM-IV negative symptoms (Alogia, Amotivation, Flat Affect, and Asociality). The items are based on items from the Negative Symptom Assessment developed by Alphs et al. (1989) and the Scale for the Assessment of Negative Symptoms (SANS) developed by Andreasen (1981). The BNSA provides quick assessment of distinct negative symptoms, and scoring is based largely on observation. The items are scored on a scale of 1 through 6, and the instrument takes less than five minutes to administer.

Clinicians can use the same scoring sheet to record scores from both the PSRS and the BNSA.

*A copy of these scales 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, insomnia, agitation, anxiety, level of interest, appetite, energy level). 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.
Patient Self-Ratings

Patient global ratings are recorded on the Clinical Record Form at the beginning of each visit. These ratings should apply to the symptoms and side effects the patient has experienced during the past week, and are rated on a 10-point scale (from “no symptoms” to “extremely severe”).

- **Core Symptoms**: The provider should ask the patient to make a global rating of symptoms he/she has experienced in the past week.

- **Overall Side Effect Severity**: The provider should ask the patient to make a global rating of side effects he/she has experienced in the past week.
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 medication unused in the Algorithm for Treatment of Schizophrenia.

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

A trial period off antipsychotics may be reasonable for some patients early in the course of illness. This, an individualized decision, depends on a number of factors that do not lend themselves to an algorithmic approach. Although research shows increased relapse rates among patients in discontinuation studies, only minimal guidance is provided regarding this treatment decision in patients who responded well to antipsychotics early in the course of their illness and have maintained a complete remission for a prolonged time period (e.g., > 2 yrs). Thus, the schizophrenia algorithm contains no guidelines for antipsychotic medication discontinuation, which is anticipated to be a rare event in the typical mental health clinic patient population.

Medication Maintenance

The evidence overwhelmingly favors the conclusion that, for most patients, maintenance antipsychotic medication is a key aspect of successful treatment, in preference to discontinuation or intermittent treatment. Less clear is what the maintenance dose of antipsychotic medication should be for any individual patient. A common clinical aphorism is that the maintenance dose should be the lowest that will keep the patient relatively symptom free. However, very low doses of maintenance medication are clearly less effective for a proportion of patients than doses in the usual range. Moreover, schizophrenia is an illness of natural exacerbations and remissions. Doses that are just sufficient during periods when the illness is quiescent are likely to be inadequate during periods when an exacerbation threatens. That is to say, the optimal maintenance dose is likely to be somewhat higher than the dose which prevents symptoms under the best of circumstances. On the other hand, too high a maintenance dose elevates side effect risks without therapeutic gain.
Documentation

Treatment with the Schizophrenia algorithm 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 SCZ algorithm is:

1. Past and current psychoactive medications and response

2. Primary current diagnosis. (Please note that these algorithms were developed for patients diagnosed with schizophrenia)

3. Core symptoms

4. Other symptoms

5. Side effects (to evaluate tolerability)

6. Response to treatment: overall functioning, PSRS & BNSA scores, patient self-report of symptom severity and side effects

Outpatient Documentation

Forms:

1. 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.

   CRFs may vary in format, but all should contain the minimum data specified
   Appendix F.

2. Process Measures Graphs: The Process Measures Graphs are optional instruments for noting the assessment scores that are recorded at each visit. A new graph is begun if the patient changes algorithm stages. The graphs will give the physician an “at a glance” reference for noting changes or trends in process measures scores as well as for anticipating Critical Decision Points. In order to be useful for decision making, the physician must see the graph at each visit. It can also be useful to show the graph to the patient or family member, thus visually demonstrating the improvement that has occurred since the patient started treatment. Copies of the Process Measures Graphs are included in Appendix A.

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 (ICF): 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.
3. Patient Algorithm: An individual patient's medication history obtained from patient interview and chart review can be recorded on a "Patient Algorithm", and, when kept up to date, will provide a quick reference for determining a patient's placement in the treatment algorithm.

**Inpatient Documentation**

**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:**

2. Inpatient Intake Form

3. Inpatient Contact Form
Modifications for Inpatient Use

Patients who have been hospitalized for symptoms of schizophrenia 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 algorithm recommends that clinicians see patients every two weeks when a new medication is started, approximately every four weeks while the patient is adjusting to the medication, and no less often than every 3 months once the patient is stable. Of course, opportunities to evaluate the patient and make clinical decisions and medication adjustments 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 treatment. Therefore, critical decision points to evaluate the need for mood stabilizer dosage adjustment or medication change can be made at shorter intervals. In general, if a patient is tolerating usual effective doses of an antipsychotic, dose titration should occur on a weekly basis if needed. Inpatient physicians should fill out a clinical record form for each patient on a weekly basis as well.

Accelerated movement to advanced treatment stage – Admission to a psychiatric unit is almost always due to acute circumstances, such as imminent danger to self or others, grave disablement, and/or a marked exacerbation of symptoms. The necessity of an inpatient admission signals that a change in treatment should be considered and each admission should trigger a thorough evaluation of algorithm staging. Rarely, a patient is admitted for his or her “first break,” and these patients will be started in Stage 1. Far more often the patient has an extensive medication history, and the admitting clinician assumes that the current medication is not working and advances the patient to the next stage of the algorithm. However, before changing a stage, the clinician should evaluate the following four factors:

1. Has the patient been taking the medication? Non-adherence is a major issue in most chronic diseases. Medication does nothing if not taken and, in order to produce maximum benefits, must be taken as directed. Explore this with the patient. Re-starting the current medication may be the best treatment.

2. Is substance abuse a problem? Drug abuse can cause acute and chronic psychiatric symptoms which often remit (albeit slowly) when the abuse stops. Always evaluate for symptoms of withdrawal and, if present, help the patient through the withdrawal period before staging the patient in the algorithm. Keep in mind that patients may resort to drugs of abuse to alleviate medication side effects, especially neurological ones.

3. Is the patient dealing with psychosocial stresses, such as housing problems, family difficulties, and/or employment uncertainties? If so, the treatment team needs to do what it can to help the patient resolve the problem(s), and a change in medication may not be beneficial. However, a medication change is probably warranted if the clinician determines that increased symptomatology was one of the major causes of the patient’s psychosocial problem(s).

4. If a patient has not demonstrated at least partial response in positive symptoms after 2-3 weeks treatment, with appropriate dose titration, then the clinician should consider a change in algorithm stage.
Use of adjunctive medications – Patients with schizophrenia frequently have co-existing symptoms of agitation, aggression, excessive anxiety, or insomnia. Inpatient treatment may necessitate the use of adjunctive medications for these symptoms. Refer to Appendix D.

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 unsuccessful. 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 prescriptions. The trend toward brief stays further aggravates the problem by forcing clinicians to discharge patients before they are completely 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 behind treatment decisions and outline the expected treatment plan. This would include detailing expected changes in medications, such as, “I expect Mr. Doe’s lorazepam (Ativan®) for agitation to be discontinued once agitation has either subsided or is adequately controlled with continued treatment of his antipsychotic medication (olanzapine).” This intent needs to be communicated to outpatient treating clinicians.

   Use of uniform documentation among all clinicians involved in a patient’s care assists in addressing this, and the TMAP documentation system is an example of such an effort. Additionally, 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.

   Similarly, it is important that clinicians treating patients in the hospital receive documentation of the care provided in the clinic in a timely fashion. Delays in the communication of outpatient treatment information to the inpatient physician may result in inappropriate treatment regimens and prolonged times to symptom stabilization and discharge. Once again, the use of uniform documentation systems can facilitate this process.

2. **Ensure that patients leave the hospital with enough medication to see them through to the first follow-up appointment.** If administrative policies prevent adequate supplies of medication from being dispensed, these policies need to be challenged.

3. **Establish communication between the inpatient and outpatient treatment teams.** Physicians working in both the inpatient and outpatient arenas need to get to know one another and brainstorm methods to improve coordination of care between the two settings. Three possible strategies for improving communication are:

   i. Have a team member (on each side) coordinate and follow-up on transfers.

   ii. Organize quarterly meetings with key inpatient and outpatient staff members.

   iii. Designate individuals in the respective organizations responsible for communicating patient information to clinicians in the other treatment setting. In the clinic, this may include methods to communicate information to hospital clinicians during the night and on weekends.

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 Transition

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

- Administration Manual, 4-item Positive Symptom Rating Scale (PSRS) and Brief Negative Symptom Assessment (BNSA)

- PSRS and BNSA Score Sheet

- Process Measures Graphs

- Scoring Criteria for Clinician- and Patient-Rated Overall Symptom and Side Effect Ratings
4-ITEM POSITIVE SYMPTOM RATING SCALE (PSRS)
(Version 5.0)

SCALE ITEMS AND ANCHOR POINTS

1. **SUSPICIOUSNESS**: Expressed or apparent belief that other persons have acted maliciously or with discriminatory intent. Include persecution by supernatural or other nonhuman agencies (e.g., the devil). Note: Ratings of “3” or above should also be rated under Unusual Thought Content.

   *Do you ever feel uncomfortable in public? Does it seem as though others are watching you? Are you concerned about anyone’s intentions toward you? Is anyone going out of their way to give you a hard time, or trying to hurt you? Do you feel in any danger?*

   *[If patient reports any persecutory ideas/delusions, ask the following]:

   *How often have you been concerned that [use patient’s description]? Have you told anyone about these experiences?*

   1. **Not Present**

   2. **Very Mild**
   
   Seems on guard. Reluctant to respond to some “personal” questions. Reports being overly self-conscious in public.

   3. **Mild**
   
   Describes incidents in which others have harmed or wanted to harm him/her that sound plausible. Patient feels as if others are watching, laughing, or criticizing him/her in public, but this occurs only occasionally or rarely. Little or no preoccupation.

   4. **Moderate**
   
   Says others are talking about him/her maliciously, have negative intentions, or may harm him/her. Beyond the likelihood of plausibility, but not delusional. Incidents of suspected persecution occur occasionally (less than once per week) with some preoccupation.

   5. **Moderately Severe**
   
   Same as 4, but incidents occur frequently, such as more than once per week. Patient is moderately preoccupied with ideas of persecution OR patient reports persecutory delusions expressed with much doubt (e.g., partial delusion).

   6. **Severe**
   
   Delusional – speaks of Mafia plots, the FBI, or others poisoning his/her food, persecution by supernatural forces.

   7. **Extremely Severe**
   
   Same as 6, but the beliefs are bizarre or more preoccupying. Patient tends to disclose or act on persecutory delusions.
2. **UNUSUAL THOUGHT CONTENT**: Unusual, odd, strange or bizarre thought content. Rate the degree of unusualness, not the degree of disorganization of speech. Delusions are patently absurd, clearly false or bizarre ideas that are expressed with full conviction. Consider the patient to have full conviction if he/she has acted as though the delusional belief were true. Ideas of reference/persecution can be differentiated from delusions in that ideas are expressed with much doubt and contain more elements of reality. Include thought insertion, withdrawal and broadcast. Include grandiose, somatic and persecutory delusions even if rated elsewhere. Note: If Suspiciousness is rated "6" or "7" due to delusions, then Unusual Thought Content must be rated a "4" or above.

*Have you been receiving any special messages from people or from the way things are arranged around you? Have you seen any references to yourself on TV or in the newspapers?*

*Can anyone read your mind?*

*Do you have a special relationship with God?*

*Is anything like electricity, X-rays, or radio waves affecting you?*

*Are thoughts put into your head that are not your own?*

*Have you felt that you were under the control of another person or force?*

*[If patient reports any odd ideas/delusions, ask the following]:*

*How often do you think about [use patient's description]?*

*Have you told anyone about these experiences? How do you explain the things that have been happening [specify]?*

1. **Not Present**

2. **Very Mild**
   Ideas of reference (people may stare or may laugh at him), ideas of persecution (people may mistreat him). Unusual beliefs in psychic powers, spirits, UFOs, or unrealistic beliefs in one's own abilities. Not strongly held. Some doubt.

3. **Mild**
   Same as 2, but degree of reality distortion is more severe as indicated by highly unusual ideas or greater conviction. Content may be typical of delusions (even bizarre), but without full conviction. The delusion does not seem to have fully formed, but is considered as one possible explanation for an unusual experience.

4. **Moderate**
   Delusion present but no preoccupation or functional impairment. May be an encapsulated delusion or a firmly endorsed absurd belief about past delusional circumstances.

5. **Moderately Severe**
   Full delusion(s) present with some preoccupation OR some areas of functioning disrupted by delusional thinking.

6. **Severe**
   Full delusion(s) present with much preoccupation OR many areas of functioning are disrupted by delusional thinking.

7. **Extremely Severe**
   Full delusions present with almost total preoccupation OR most areas of functioning are disrupted by delusional thinking.
3. **HALLUCINATIONS**: Reports of perceptual experiences in the absence of relevant external stimuli. When rating degree to which functioning is disrupted by hallucinations, include preoccupation with the content and experience of the hallucinations, as well as functioning disrupted by acting out on the hallucinatory content (e.g., engaging in deviant behavior due to command hallucinations). Include "thoughts aloud" ("gedankenlautwerden") or pseudohallucinations (e.g., hears a voice inside head) if a voice quality is present.

*Do you ever seem to hear your name being called?*
*Have you heard any sounds or people talking to you or about you when there has been nobody around?*
* [If hears voices]: What does the voicevoices say? Did it have a voice quality?*
*Do you ever have visions or see things that others do not see? What about smell — odors that others do not smell?*

[If the patient reports hallucinations, ask the following]:

*Have these experiences interfered with your ability to perform your usual activities/work?*
*How do you explain them? How often do they occur?

1. **Not Present**
2. **Very Mild**
   While resting or going to sleep, sees visions, smells odors, or hears voices, sounds or whispers in the absence of external stimulation, but no impairment in functioning.
3. **Mild**
   While in a clear state of consciousness, hears a voice calling the subject's name, experiences non-verbal auditory hallucinations (e.g., sounds or whispers), formless visual hallucinations, or has sensory experiences in the presence of a modality-relevant stimulus (e.g., visual illusions) infrequently (e.g., 1-2 times per week) and with no functional impairment.

4. **Moderate**
   Occasional verbal, visual, gustatory, olfactory, or tactile hallucinations with no functional impairment OR non-verbal auditory hallucinations/visual illusions more than infrequently or with impairment.

5. **Moderately Severe**
   Experiences daily hallucinations OR some areas of functioning are disrupted by hallucinations.

6. **Severe**
   Experiences verbal or visual hallucinations several times a day OR many areas of functioning are disrupted by these hallucinations.

7. **Extremely Severe**
   Persistent verbal or visual hallucinations throughout the day OR most areas of functioning are disrupted by these hallucinations.
4. **CONCEPTUAL DISORGANIZATION**: Degree to which speech is confused, disconnected, vague or disorganized. Rate tangentiality, circumstantiality, sudden topic shifts, incoherence, derailment, blocking, neologisms, and other speech disorders. Do not rate content of speech.

1. **Not Present**

2. **Very Mild**
   Peculiar use of words or rambling but speech is comprehensible.

3. **Mild**
   Speech a bit hard to understand or make sense of due to tangentiality, circumstantiality, or sudden topic shifts.

4. **Moderate**
   Speech difficult to understand due to tangentiality, circumstantiality, idiosyncratic speech, or topic shifts on many occasions OR 1-2 instances of incoherent phrases.

5. **Moderately Severe**
   Speech difficult to understand due to circumstantiality, tangentiality, neologisms, blocking, or topic shifts most of the time OR 3-5 instances of incoherent phrases.

6. **Severe**
   Speech is incomprehensible due to severe impairments most of the time. Many PSRS items cannot be rated by self-report alone.

7. **Extremely Severe**
   Speech is incomprehensible throughout interview.

Sources of information (check all applicable):

- Patient
- Parents/Relatives
- Mental Health Professionals
- Chart

Explain here if validity of assessment is questionable:

- Symptoms possibly drug-induced
- Underreported due to lack of rapport
- Underreported due to negative symptoms
- Patient uncooperative
- Difficult to assess due to formal thought disorder
- Other

Confidence in assessment:

- 1 = Not at all
- 5 = Very confident
BRIEF NEGATIVE SYMPTOM ASSESSMENT SCALE (version 5.0)
Items adapted from NSA and SANS

1. PROLONGED TIME TO RESPOND (a measure of Alogia): Observed throughout communication with
the patient. After asking the patient a question, he or she pauses for inappropriately long periods
before initiating a response. Delay is considered a pause if it feels as though you are waiting for a
response or if you consider repeating the question because it appears that the patient has not heard
you. He or she may seem "distant," and sometimes the examiner may wonder if he has even heard
the question. Prompting usually indicates that the patient is aware of the question, but has been
having difficulty in developing his thoughts in order to make an appropriate reply. Rate severity on the
frequency of these pauses.

1 Normal
No abnormal pauses before speaking.

2 Minimal
Minimal evidence of inappropriate pauses (brief but not abnormally lengthy pauses
occur) may be extreme of normal

3 Mild
Occasional noticeable pauses before answering questions. Due to the length of the
pause, you feel the need to repeat yourself once or twice during the interview.

4 Moderate
Distinct pauses occur frequently (20-40% of responses).

5 Marked
Distinct pauses occur most of the time (40-80% of responses).

6 Severe
Distinct pauses occur with almost every response (80-100% of responses).

2. EMOTION: UNCHANGING FACIAL EXPRESSION; BLANK, EXPRESSIONLESS FACE (a measure
of Flat Affect): The patient's face appears wooden, mechanical, frozen. Facial musculature is
generally expressionless and unchanging. The patient does not change expression, or change is less
than normally expected, as the emotional content of discourse changes. Because of this, emotions
may be difficult to infer. Disregard changes in facial expression due to abnormal involuntary
movements, such as tics and tardive dyskinesia. The two dimensions of importance when making this
crating are degree of emotional expression and spontaneity.

1. Normal
Spontaneous displays of emotion occur when expected. Normal degree of expressiveness of
emotions is present.

2. Minimal
Spontaneous expressions of emotion occur when expected. However, there is a reduction in
degree or intensity of the emotions expressed. May be extreme of normal.

3. Mild
Spontaneous expressions of emotion occur infrequently. When emotions are expressed, there
is a reduction in degree or intensity displayed.
4. **Moderate**
   Obvious reduction in spontaneous expressions. Spontaneous expressions of emotion may occur very rarely during interaction and only when discussing topics of special interest or humor to the subject.

5. **Marked**
   Facial expression is markedly decreased. There are no spontaneous expressions of emotion unless prompted or coaxed by the interviewer.

6. **Severe**
   There are no expressions of emotion even when attempts are made to elicit an emotional response. The subject’s face remains blank throughout the interview.

3. **REDUCED SOCIAL DRIVE.** (a measure of Asociality): This item assesses how much the subject desires to initiate social interactions. Desire may be measured in part by the number of actual or attempted social contacts with others. If the patient has frequent contact with someone (e.g., family member) who initiates the contact, does the patient appear to desire the contact (i.e., would he or she initiate contact if necessary)? In making this rating, probe the desire to initiate social interactions, number of social interactions, and the ability to enjoy them.

   **Assessed by asking the patient questions like:**

   - How have you spent your time in the past week?
   - Do you live alone or with someone else?
   - Do you like to be around people?
   - Do you spend much time with others?
   - Do you have difficulty feeling close to others?
   - Who are your friends?
   - How often do you see them?
   - Did you see them this past week?
   - Have you called them on the phone?
   - When you get together, who decides what to do and where to go?
   - When you spend time with others, do you ask them to do something with you or do you wait until they ask you to do something?
   - Is anyone concerned about your happiness or well being?

1. **Normal**
   Normal desire to initiate and normal number of contacts. Social contacts are enjoyable.

2. **Minimal**
   Minimal reduction in either the desire to initiate social contacts or the number of social relationships. May initially seem guarded, but has the ability to establish relationships over time. Social relationships are enjoyable.

3. **Mild**
   Reduction in desire to initiate social contacts. The patient has few social relationships and these social contacts are enjoyable.

4. **Moderate**
   Obvious reduction in the desire to initiate social contacts. The patient has few relationships toward which he or she feels indifference. However, a number of social contacts are initiated each week.
5. Marked
Marked reduction in desire to initiate social contacts. The patient has very few relationships toward which he or she feels indifference. The patient does not initiate social contacts but may maintain a few contacts (such as with family).

6. Severe
Patient does not desire social contact. Actively avoids social interactions.

4. GROOMING AND HYGIENE (a measure of Amotivation): Observed during interaction with the patient. The patient displays less attention to grooming and hygiene than normal. The patient presents with poorly groomed hair, disheveled clothing, etc. Do not rate grooming as poor if it is simply done in what one might consider poor taste (e.g., wild hairdo or excessive makeup). In addition to observation, one must ask the patient about regularity of bathing, brushing teeth, changing clothes, etc. This is particularly important with outpatients, as the patient may present his or her best grooming and hygiene at their clinic visit. Two dimensions to keep in mind when making this rating are current appearance and regularity of grooming behaviors.

Assess the patient by asking questions like:

- How many times in the past week have you taken a shower or bath?
- How often do you change your clothes?
- How often do you shower and brush your teeth?

1. Normal
Patient is clean (e.g., showers every day) and dressed neatly.

2. Minimal
Minimal reduction in grooming and hygiene, may be at the extreme end of the normal range.

3. Mild
Apparently clean but untidy appearance. Clothing may be mismatched. Patient may shower less often than every other day, or may brush teeth less than everyday.

4. Moderate
There is an obvious reduction in grooming and hygiene. Clothes may appear unkempt, rumpled, or the patient may look as if he or she just got out of bed. The patient may go without showering or bathing for two days at a time. The patient may go for two days without brushing his/her teeth.

5. Marked
There is a marked reduction in grooming and hygiene. Clothing may appear dirty, stained, or very unkempt. The subject may have greasy hair or a body odor. The patient may go 3 days at a time without showering or 3 or 4 days without brushing his/her teeth.

6. Severe
Clothing is badly soiled. Patient has a foul odor. Patient may go more than 4 days in a row without showering or more than 4 days in a row without brushing his/her teeth. Poor hygiene may present a health risk.
SCORE SHEET for
4-ITEM POSITIVE SYMPTOM RATING SCALE AND
BRIEF NEGATIVE SYMPTOM ASSESSMENT

4-Item Positive Symptom Rating Scale

Use each item's anchor points to rate the patient.

1. Suspiciousness
   *NA  1 2 3 4 5 6 7

2. Unusual Thought Content
   NA  1 2 3 4 5 6 7

3. Hallucinations
   NA  1 2 3 4 5 6 7

4. Conceptual Disorganization
   NA  1 2 3 4 5 6 7  SCORE: _____

* NA - not able to be assessed

4-Item Negative Symptom Rating Scale

Use each item's anchor points to rate the patient.

1. Prolonged Time to Respond
   1 2 3 4 5 6

2. Emotion
   Unchanging facial expression, blank, expressionless face.
   1 2 3 4 5 6

3. Reduced Social Drive
   1 2 3 4 5 6

4. Poor Grooming and Hygiene
   1 2 3 4 5 6  SCORE: _____

Source of Information (check all applicable)

___ Patient
___ Parents/Relatives
___ Mental Health Professionals
___ Chart

Confidence in assessment
___1=Not at all -- 5=Very confident

Explain here if validity of assessment is questionable:
___ Symptoms possibly drug-induced
___ Underreported due to lack of rapport
___ Underreported due to negative symptoms
___ Patient uncooperative
___ Difficult to assess due to formal thought disorder
___ Other

The 4-Item PSRS was adapted from the Expanded Version of the BPRS developed by:

The Brief Negative Symptom Assessment was adapted from the Negative Symptom Assessment and the Scale for the Assessment of Negative Symptoms developed respectively by:
# Process Measures Graph I

## Maintenance

<table>
<thead>
<tr>
<th>Pt. Init:</th>
<th>ID#:</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Medication(s):</th>
<th>Date Initiated:</th>
</tr>
</thead>
</table>

**Algorithm Stage:** _____

Start new sheet when changing stages.

### Aims/Goals: Towards Week...

Prior to Resides (home and family)

<table>
<thead>
<tr>
<th>Weight</th>
<th>Date</th>
</tr>
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</table>

| Month | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 |
|-------|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|

**Response = 6 or below in stages 1 and 2**

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<tr>
<th>4</th>
<th>6</th>
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Sc
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: 512-735-TMAP (8627)
TMAP Email: info@WebTMAP.org
Appendix C: Medication Charts

Medications Included in Algorithms for Most Recent Episode of Schizophrenia

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

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## Appendix C: Medication Charts

### Antipsychotics, Second Generation

<table>
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<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
</table>
| Aripiprazole (Abilify)<sup>6</sup> | 10-15 mg/day  | None      | 10-30 mg/day         | 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-density lipoprotein (LDL), and high-density lipoprotein (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 (Section 9) 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/erectile disorders 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/erectile disorders 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                  | • Fluoxetine                | • Carbamazepine                |                                  |                                  |
|               | 5-10 mg/day   | 5 mg/wk   | 10-20 mg/day         | 30 mg/day<sup>2</sup> | Once daily | • Dizziness                  | • Dry mouth                  | • Fluvoxamine                | • Ketocanazole                | • Carbamazepine                |                                  |                                  |
| Olanzapine (Zyprexa)<sup>6</sup> | 50 mg/day     | 300 mg every 3-7 days | 300-800 mg/day | 800 mg/day          | Twice daily | • Glucose dysregulation                  | • Hyperlipidemia                | • Fluoxetine                | • Ketoconazole                | • Ketocanazole                | • Carbamazepine                | • Carbamazepine                |                                  |                                  |
| Quetiapine (Seroquel)<sup>6</sup> | 1-2 mg/day    | 1 mg every 2-3 days | 2-6 mg/day        | 16 mg/day<sup>2</sup> | Once daily | • Headache                  | • Hyperlipidemia                | • Fluoxetine                | • Phenytoin                  | • Ketocanazole                | • Carbamazepine                | • Phenytoin                  | • Erythromycin                |                                  |                                  |
| Risperidone (Risperdal)<sup>6</sup> | 10-15 mg/day  | None      | 30 mg/day           | 60 mg/day          | Once daily | • Insomnia                  | • Increased appetite            | • Garageol                   | • Phenytoin                  | • Perphenazine                | • Carbamazepine                | • Perphenazine                | • Paroxetine                  | • Phenytoin                  | • Erythromycin                |                                  |                                  |

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<sup>2</sup> The CATIE trial utilized olanzapine doses up to 30 mg/day.

<sup>3</sup> Use of risperidone > 6mg/day is associated with an increased risk of EPS.

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Schizophrenia Clinician's Manual

Updated: April 2008
# Appendix C: Medication Charts

## Antipsychotics, Second Generation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziprasidone Geodon®</td>
<td>40-80 mg/day</td>
<td>20-40 mg every 2-3 days</td>
<td>80 - 160 mg/day</td>
<td>160 mg/day</td>
<td>Once or twice daily</td>
<td>See Previous Page</td>
<td>Dizziness</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ECG changes</td>
<td>Diazepam</td>
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<td>EPS</td>
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<td>Rash</td>
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<td></td>
<td></td>
<td>Sedation</td>
<td>Quinidine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vomiting</td>
<td>Sotalol</td>
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<td></td>
<td></td>
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<td>Thioridazine</td>
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<td></td>
<td></td>
<td>Tricyclic antidepressants</td>
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<td></td>
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</tr>
<tr>
<td>Clozapine</td>
<td>12.5 mg/day</td>
<td>25 mg daily</td>
<td></td>
<td>300-900 mg/day</td>
<td>Twice daily</td>
<td>1) CBC as indicated by guidelines approved by the FDA in the product labeling.</td>
<td>Agranulocytosis</td>
<td>Barbiturates</td>
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<tr>
<td>Generic available</td>
<td></td>
<td>Day 2: 25 mg daily</td>
<td></td>
<td></td>
<td></td>
<td>2) Pregnancy test – as clinically indicated.</td>
<td>Excess salivation</td>
<td>Caffeine</td>
</tr>
<tr>
<td>Clozaril®</td>
<td></td>
<td>Day 3: 25 mg twice daily</td>
<td></td>
<td></td>
<td></td>
<td>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 dose is stable.</td>
<td>Fever</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Fazado®</td>
<td></td>
<td>Day 6: 25 mg at morning, 50 mg at evening</td>
<td></td>
<td></td>
<td></td>
<td>4) Fasting plasma glucose level or hemoglobin A1c - before initiating a new antipsychotic, then yearly.</td>
<td>Glucose dysregulation</td>
<td>Ceramazoline</td>
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<tr>
<td></td>
<td></td>
<td>Day 8: 50 mg twice daily</td>
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<td></td>
<td></td>
<td>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.</td>
<td>Hyperlipidemia</td>
<td>Erythromycin</td>
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<tr>
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<td></td>
<td>Day 10: 75 mg twice daily</td>
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<td></td>
<td></td>
<td>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 &gt; 130 mg/dl.</td>
<td>Increased appetite</td>
<td>Phenytoin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Day 12: 100 mg twice daily</td>
<td></td>
<td></td>
<td></td>
<td>6) Sexual function inquiry – inquire yearly for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males.</td>
<td>Myocarditis</td>
<td>Rifampin</td>
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<tr>
<td></td>
<td></td>
<td>Day 14: 125 mg twice daily</td>
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<td></td>
<td></td>
<td>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.</td>
<td>Orthostatic hypotension</td>
<td>Ritonavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Day 16: 150 mg twice daily</td>
<td></td>
<td></td>
<td></td>
<td>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.</td>
<td>Sedation</td>
<td>Smoking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Day 18: 100 mg at morning, 200 mg at evening</td>
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<td></td>
<td></td>
<td>8) Sexual function inquiry – inquire yearly for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males.</td>
<td>Seizures</td>
<td>SSRIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Day 20: 100 mg at morning, 200 mg at evening</td>
<td></td>
<td></td>
<td></td>
<td>9) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly</td>
<td>Tachycardia</td>
<td>St John's Wort</td>
</tr>
</tbody>
</table>

4 The presence of food can increase ziprasidone's absorption up to two-fold.

5 Eventual maintenance dose schedule is twice daily dosing, 1/3 dose in morning, 2/3 dose in the evening.

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## Antipsychotics, First Generation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Potency</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Chlorpromazine               | 50-100 mg/day | 50-200 mg/day| 300-1000 mg/day      | 1000 mg/day       | Three times daily | 1) Pregnancy test – as clinically indicated  
2) BMI measurement – when a new antipsychotic is initiated, at least 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, if possibly  
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 gynecomastia/galactorrhea, 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 gynecomastia/galactorrhea, 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 | Guanethidine  
Meperidine  
Paroxetine  
Pindolol  
Quinolones  
β-Blockers  
Ziprasidone |
| **Mid Potency**              |               |              |                      |                   |          |                              |              |                             |
| Loxapine                    | 20 mg/day     | 10-50 mg/day | 50-150 mg/day        | 160 mg/day        | Once or twice daily | See Previous Page | Babylirans  
General anesthetics  
Opiate agonists  
Radiopaque contrast agents  
Tricyclic antidepressants  
CNS depressants  
Anticonvulsants  
Tetracycline |
| Molindone                   | 50-75 mg/day | 25 mg/day    | 50-150 mg/day        | 225 mg/day        | 3-4 times daily |                             |              |                             |
| Mobar                                 | 4-8 mg/day     | 4-8 mg/day | 16-64 mg/day         | 64 mg/day         | Three times daily |                             |              |                             |
| Perphenazine                 | 5 mg          | 2.5-5 mg/day | 5-20 mg/day          | 20 mg/day         | Three times daily |                             |              |                             |
| Fluphenazine                 | 12.5-25 mg/IM every 1-3 weeks | 12.5 mg per injection | 6.25-50 mg/IM every 2-4 weeks | 100 mg IM (per 4 weeks) | Every 1-3 weeks |                             |              |                             |

6 The CATIE trial used doses up to 32mg/day.
7 Starting dose generally 1.2 times the patient's oral dose.

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## Appendix C: Medication Charts

### Antipsychotics, First Generation

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>2-5 mg/day</td>
<td>2-5 mg/day</td>
<td>2-20 mg/day</td>
<td>20 mg/day</td>
<td>1 - 3 times daily</td>
<td>9) Vision questionnaire — ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision — yearly</td>
<td>- Azole antifungals</td>
<td>• Azole antifungals</td>
</tr>
<tr>
<td>Generic available</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Carbamazepine &lt;br&gt; Rifabutin &lt;br&gt; Rifampin</td>
</tr>
<tr>
<td>Haldol D</td>
<td>25-50 mg IM every 2-4 weeks</td>
<td>N/A</td>
<td>50-200 mg IM every 2-4 weeks</td>
<td>450 mg (per 4 weeks)</td>
<td>Every 3-4 weeks</td>
<td>10) Ocular evaluations — yearly for patients older than age 40 years; every 2 years for younger patients</td>
<td>Guanethidine &lt;br&gt;&lt;br&gt;Alcohol &lt;br&gt; Cisapride &lt;br&gt; Guanethidine &lt;br&gt; Metizamide &lt;br&gt; Paroxetine</td>
<td></td>
</tr>
<tr>
<td>Haloperidol D</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Guanethidine &lt;br&gt;&lt;br&gt;Alcohol &lt;br&gt; Cisapride &lt;br&gt; Guanethidine &lt;br&gt; Metizamide &lt;br&gt; Paroxetine</td>
</tr>
<tr>
<td>Decanoate</td>
<td>5-10 mg every 3-7 days</td>
<td>5-10 mg every 3-7 days</td>
<td>15-50 mg every 3-7 days</td>
<td>50 mg/day</td>
<td>2-3 times daily</td>
<td></td>
<td></td>
<td>Guanethidine &lt;br&gt;&lt;br&gt;Alcohol &lt;br&gt; Cisapride &lt;br&gt; Guanethidine &lt;br&gt; Metizamide &lt;br&gt; Paroxetine</td>
</tr>
<tr>
<td>Thiothixene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Guanethidine &lt;br&gt;&lt;br&gt;Alcohol &lt;br&gt; Cisapride &lt;br&gt; Guanethidine &lt;br&gt; Metizamide &lt;br&gt; Paroxetine</td>
</tr>
<tr>
<td>Navane</td>
<td>2-5 mg every 3-7 days</td>
<td>2-5 mg every 3-7 days</td>
<td>5-20 mg every 3-7 days</td>
<td>40 mg/day</td>
<td>Twice daily</td>
<td></td>
<td></td>
<td>Guanethidine &lt;br&gt;&lt;br&gt;Alcohol &lt;br&gt; Cisapride &lt;br&gt; Guanethidine &lt;br&gt; Metizamide &lt;br&gt; Paroxetine</td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Guanethidine &lt;br&gt;&lt;br&gt;Alcohol &lt;br&gt; Cisapride &lt;br&gt; Guanethidine &lt;br&gt; Metizamide &lt;br&gt; Paroxetine</td>
</tr>
<tr>
<td>Stilazine</td>
<td>2-5 mg every 3-7 days</td>
<td>2-5 mg every 3-7 days</td>
<td>5-20 mg every 3-7 days</td>
<td>40 mg/day</td>
<td>Twice daily</td>
<td></td>
<td></td>
<td>Guanethidine &lt;br&gt;&lt;br&gt;Alcohol &lt;br&gt; Cisapride &lt;br&gt; Guanethidine &lt;br&gt; Metizamide &lt;br&gt; Paroxetine</td>
</tr>
</tbody>
</table>

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8 Starting dose generally 10-20 times the patient's oral dose. Dose of first injection should not exceed 100 mg.

9 The maximum volume per injection site should not exceed 3 mL.

10 Multiple injections can be given at 1-7 day intervals to provide total loading dose.
# Appendix C: Medication Charts

## Adjunctive Agents, Agitation/Insomnia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonazepam</td>
<td>0.25-2 mg</td>
<td>N/A</td>
<td>0.5-4 mg/day</td>
<td>20 mg/day</td>
<td>As needed</td>
<td></td>
<td></td>
<td>Sodium oxybate</td>
</tr>
<tr>
<td>Generic Available</td>
<td>twice daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phenothiazine</td>
</tr>
<tr>
<td>Klonopin®</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Carbamazepine</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Azole antifungals</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5-2 mg</td>
<td>N/A</td>
<td>1-8 mg/day</td>
<td>10 mg/day</td>
<td>As needed</td>
<td>1) Pregnancy Test – as clinically indicated</td>
<td>Dizziness</td>
<td>Antidepressives</td>
</tr>
<tr>
<td>Generic Available</td>
<td>Three times daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clonazepam</td>
</tr>
<tr>
<td>Ativan®</td>
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<td></td>
<td></td>
<td></td>
<td>Kava</td>
</tr>
<tr>
<td>Temazepam</td>
<td>7.5-30 mg</td>
<td>N/A</td>
<td>15-30 mg/day</td>
<td>30 mg/day</td>
<td>Once daily at bedtime</td>
<td></td>
<td></td>
<td>CNS depressants</td>
</tr>
<tr>
<td>Generic Available</td>
<td>at bedtime</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Kava</td>
</tr>
<tr>
<td>Restoril®</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Valerian</td>
</tr>
</tbody>
</table>

## Adjunctive Agents, Insomnia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eszopiclone</td>
<td>2-3 mg</td>
<td>N/A</td>
<td>2-3 mg/day</td>
<td>3 mg/day</td>
<td>Once daily at bedtime</td>
<td>1) Pregnancy Test – as clinically indicated</td>
<td>Altered taste</td>
<td>Pramipexole</td>
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<td>Lunesta®</td>
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<td>St. John's Wort</td>
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<td></td>
<td></td>
<td></td>
<td>CNS depressants</td>
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<td></td>
<td></td>
<td>Kava</td>
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<td>Valerian</td>
</tr>
<tr>
<td>Trazodone</td>
<td>25 mg</td>
<td>N/A</td>
<td>12.5 – 100 mg/day</td>
<td>400 mg/day</td>
<td>Once daily at bedtime</td>
<td>1) Pregnancy Test – as clinically indicated</td>
<td>Blurred vision</td>
<td>Digoxin</td>
</tr>
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<td>Generic available</td>
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<td>Anticonvulsants</td>
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<td>Desyrel®</td>
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<td>Antidepressives</td>
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<td>Barbitalus</td>
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<td>5-10 mg/day</td>
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<td>Dizziness</td>
<td>Protease inhibitors</td>
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<td>Zaleplon</td>
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<td>5-10 mg/day</td>
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<td>Once daily at bedtime</td>
<td>1) Pregnancy Test – as clinically indicated</td>
<td>Dizziness</td>
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<td>Protease inhibitors</td>
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<td>Kava</td>
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<td>Valerian</td>
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</table>

N/A = Not Applicable

Schizophrenia Clinician's Manual 44 Updated: April 2008
### Appendix C: Medication Charts

#### Adjunctive Agents, Aggression/Hostility

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
</table>
| Carbamazepine         | 200-800 mg/day| 200 mg/day every 2-4 days | 400-1600 mg/day      | 1600 mg/day        | 2 - 3 Times Daily  | 1) CBC with platelets - baseline and 1 to 2 weeks after each dose increase and as clinically indicated  
2) Hepatic function panel and electrolytes; baseline and as clinically indicated  
3) Pregnancy Test - as clinically indicated  
4) Carbamazepine Levels - 1-2 weeks after dose adjustment, then as clinically indicated  
Therapeutic Serum Concentration: 4-12 mcg/ml  
Frequency of Serum Level Monitoring:  
• Day 5-7  
• Weekly until stable  
• Every 3-6 months | • Ataxia  
• Diplopia  
• Dizziness  
• Dysarthria  
• GI upset  
• Hypotension  
• Leukopenia  
• Nystagmus  
• Rash  
• Sedation | • Antipsychotics  
• Benzodiazepines  
• Clomipramine  
• Corticosteroids  
• Divalproex  
• Erythromycin  
• Lamotrigine  
• Oral contraceptive pill  
• SSRIs  
• Tricyclic antidepressants  
• Warfarin  
• Induce its own metabolism. May require dose dose titration. |
| Valproic Acid, Divalproex Sodium | 500 - 1000 mg/day | 500 mg/day every 1-2 weeks | 750-2000 mg/day | 50 mg/kg/day | Once or twice daily | 1) CBC - with differential and platelet count - baseline then once (1) to two (2) weeks after each dose increase, and as clinically indicated  
2) Hepatic function panel - baseline and as clinically indicated  
3) Pregnancy Test - baseline and as clinically indicated  
4) Valproic acid level - 1-2 weeks after initiation and dose change, then as clinically indicated  
5) Serum creatinine and BUN at baseline and as clinically indicated  
Therapeutic Serum Concentration: 50-150 mcg/ml  
Frequency of Serum Level Monitoring:  
• Day 7-14  
• At dosage change  
• As clinically indicated | • Alopecia  
• Ataxia  
• Cognitive impairment  
• Dizziness  
• GI upset  
• Hepatitis  
• Pancreatitis  
• Poly cystic ovarian syndrome  
• Rash  
• Somnolence  
• Thromboembolism  
• Tremor  
• Weight gain | • Antipsychotics  
• Benzodiazepines  
• Carbamazepine  
• Lamotrigine  
• Lithium  
• MAOIs  
• Phenytoin  
• Tricyclic antidepressants  
• Warfarin |

1. Maximum daily dosage should be based upon the medication serum level in the individual patient in the context of clinical response and tolerability.
2. Recommended dose titration of lamotrigine for patients taking carbamazepine (or other enzyme-inducing drugs) and not taking divalproex: 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.
3. Therapeutic serum level monitoring of mood stabilizers should be drawn 12-hours after the last dose.
4. Recommended dose titration of lamotrigine for patients taking divalproex 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.

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### Appendix C: Medication Charts

#### Adjunctive Agents, Aggression/Hostility

<table>
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<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>900 mg/day</td>
<td>Check serum level at 3-4 days and adjust (linear kinetics)</td>
<td>900-2400 mg/day</td>
<td>3600 mg/day</td>
<td>Once or twice daily</td>
<td>1) EKG (mandatory for everyone – baseline, yearly and as clinically indicated)</td>
<td>• Acne</td>
<td>• ACE-inhibitors</td>
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<td>Generic</td>
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<td></td>
<td></td>
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<td></td>
<td>2) CBC – baseline, yearly and as clinically indicated</td>
<td>• Acute renal dysfunction</td>
<td>• Caffeine</td>
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<tr>
<td>Eskalith</td>
<td></td>
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<td></td>
<td></td>
<td>3) Thyroid studies – baseline; then TSH every 6 months and as clinically indicated</td>
<td>• Cognition</td>
<td>• NSAIDs</td>
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<td>Eskalith CR</td>
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<td>4) BUN, creatinine, glucose and electrolytes; baseline and as clinically indicated</td>
<td>• Diarrhea</td>
<td>• Osmotic diuretics</td>
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<td></td>
<td>5) UA – baseline and as clinically indicated</td>
<td>• Dizziness</td>
<td>• Theophylline</td>
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<td>6) Pregnancy test – as clinically indicated</td>
<td>• ECG changes</td>
<td>• Thiazide diuretics</td>
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<td>7) Lithium Levels – one week after initiation or dosage change and as clinically indicated</td>
<td>• GI upset</td>
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<td></td>
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<td>Therapeutic Serum Concentration(^{15}):</td>
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<td>0.6-1.5 mEq/L</td>
<td>• Nausea</td>
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<td></td>
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<td>Frequency of Serum Level Monitoring:</td>
<td>• Polyuria</td>
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<td></td>
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<td></td>
<td></td>
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<td>• Day 7</td>
<td>• Sedation</td>
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<td></td>
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<td>• As clinically indicated</td>
<td>• Tremor</td>
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<td></td>
<td>• Vitamin D</td>
<td>• Dihydropyridine calcium antagonists</td>
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<td></td>
<td></td>
<td></td>
<td>• Oral contraceptive pill</td>
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</table>

\(^{15}\) Maximum daily dosage should be based upon the medication serum level in the individual patient in the context of clinical response and tolerability.

\(^{16}\) Therapeutic serum level monitoring of mood stabilizers should be drawn 12-hours after the last dose. Therapeutic blood level recommendations based upon data for acute mania in bipolar disorder.
### Adjunctive Agents, Depression

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
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<tbody>
<tr>
<td>Citalopram</td>
<td>20 mg/day</td>
<td>10 mg</td>
<td>20 mg/day</td>
<td>60 mg/day</td>
<td>Once daily in the morning</td>
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<td></td>
<td>Clozapine, Cyclosporine, Linezolid, MAOIs, NSAIDs, Pimozide, St. John’s Wort, Sympathomimetics, Tramadol, Triptans</td>
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<tr>
<td>Available as Celexa®</td>
<td>10 mg every 2 weeks</td>
<td>10 mg</td>
<td>20 mg/day</td>
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<tr>
<td>Escitalopram</td>
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<td>10-20 mg/day</td>
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<td>Lexapro®</td>
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<td>20 mg/day</td>
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<tr>
<td>Fluoxetine</td>
<td>20 mg/day</td>
<td>10-20 mg</td>
<td>20 mg/day</td>
<td>40-80 mg/day</td>
<td>Once daily in the morning</td>
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<td>Carbamazepine, Clozapine, Cyclosporine, Hydantoins, Linezolid, MAOIs, NSAIDs, St. John’s Wort, Sympathomimetics, Thioridazine, Tramadol, Triptans, Tricyclic antidepressants</td>
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<tr>
<td>Available as Prozac®</td>
<td>10 mg every 4 weeks</td>
<td>20 mg</td>
<td>20 mg/day</td>
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## Appendix C: Medication Charts

### Adjunctive Agents, Depression

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<th>Drug</th>
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<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
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<tbody>
<tr>
<td>Fluvoxamine</td>
<td>50 mg/day</td>
<td>50-100 mg every 2 weeks</td>
<td>100-200 mg/day</td>
<td>300 mg/day</td>
<td>Once or twice daily</td>
<td>See Previous Page</td>
<td>• Carbamazepine</td>
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<tr>
<td>Generic</td>
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<td>Luvox®</td>
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<td>Paroxetine</td>
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<td>10-20 mg every 2 weeks</td>
<td>20-30 mg/day</td>
<td>40-60 mg/day</td>
<td>Once daily in the morning</td>
<td>See Previous Page</td>
<td>• Hydantoins</td>
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<td></td>
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<td>• MAOIs</td>
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<td>Paxil®</td>
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<td></td>
<td>• NSAIDs</td>
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<td>Paxil CR®</td>
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<td>• Ropivacaine</td>
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<tr>
<td>Sertraline</td>
<td>50 mg/day</td>
<td>50-100 mg every 2 weeks</td>
<td>50-100 mg/day</td>
<td>150-200 mg/day</td>
<td>Once daily in the morning</td>
<td>See Previous Page</td>
<td>• St. John's Wort</td>
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<tr>
<td>Generic</td>
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<td>• Tactine</td>
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<td>• Theophyllines</td>
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<td>• Tricyclic antidepressants</td>
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</tbody>
</table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Bupropion</strong></td>
<td>150 mg/day</td>
<td>150 mg/day at 3-7 days</td>
<td>225-300 mg/day (SR)</td>
<td>450 mg/day</td>
<td>Twice daily ≤ 150 mg/dose</td>
<td>1) Pregnancy test – as clinically indicated</td>
<td>• Constipation</td>
<td>• Carbamazepine</td>
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<td>Generic available</td>
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<td></td>
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<td></td>
<td>• Dry Mouth</td>
<td>• Cyclobenzapine</td>
</tr>
<tr>
<td>Wellbutrin SR®</td>
<td>200-300 mg/day (SR)</td>
<td></td>
<td>400 mg/day (SR)</td>
<td></td>
<td>Twice daily ≤ (SR)/200 mg/dose</td>
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<td>• Headache</td>
<td>• Linezolid</td>
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<td></td>
<td>• Insomnia</td>
<td>• MAOIs</td>
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<td></td>
<td></td>
<td>• Nausea</td>
<td>• Ritonavir</td>
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<td></td>
<td>• Seizures</td>
<td>• Tricyclic antidepressants</td>
</tr>
<tr>
<td><strong>Venlafaxine</strong></td>
<td>37.5 mg/day</td>
<td>37.5 - 75 mg/day every 5-7 days</td>
<td>150-225 mg/day (XR)</td>
<td>375 mg/day</td>
<td>Twice daily (XR)</td>
<td>1) Pregnancy test – as clinically indicated</td>
<td>• Anxiety</td>
<td>• Linezolid</td>
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<td>• Blood pressure</td>
<td>• MAOIs</td>
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<td>Effexor®®</td>
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<td></td>
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<td></td>
<td>• Decreased appetite</td>
<td>• St. John's Wort</td>
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<td>Effexor XR®®</td>
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<td>• Dizziness</td>
<td>• Sympathomimetics</td>
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<td></td>
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<td></td>
<td>• Dry Mouth</td>
<td>• Tramadol</td>
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<td>• Fatigue</td>
<td>• Triptans</td>
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<td>• Nausea</td>
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<td>• Somnolence</td>
<td></td>
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<td></td>
<td></td>
<td>• Sweating</td>
<td></td>
</tr>
<tr>
<td><strong>Duloxetine</strong></td>
<td>30-60 mg/day</td>
<td>None</td>
<td>60 mg/day</td>
<td>60 mg/day</td>
<td>Once or twice daily</td>
<td>1) Pregnancy test – as clinically indicated</td>
<td>• Alcohol</td>
<td>• Alcohol</td>
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<tr>
<td>Cymbalta®®</td>
<td></td>
<td></td>
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<td>• Linezolid</td>
<td>• Linezolid</td>
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<td></td>
<td>• MAOIs</td>
<td>• St. John's Wort</td>
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<td>• Sympathomimetics</td>
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<td></td>
<td>• Tofranil</td>
<td>• Tramadol</td>
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<td></td>
<td></td>
<td></td>
<td>• Triptans</td>
<td>• Triptans</td>
</tr>
<tr>
<td><strong>Mirtazapine</strong></td>
<td>15 mg/day</td>
<td>15 mg every 1-2 weeks</td>
<td>30 mg/day</td>
<td>60 mg/day</td>
<td>Once daily at bedtime</td>
<td>1) Pregnancy test – as clinically indicated</td>
<td>• Constipation</td>
<td>• Tricyclic antidepressants</td>
</tr>
<tr>
<td>Generic available</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Dizziness</td>
<td>• Tetracyclic Antidepressants</td>
</tr>
<tr>
<td>Remeron®®</td>
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<td></td>
<td></td>
<td>• Drowsiness</td>
<td>• MAOIs</td>
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<td></td>
<td></td>
<td>• Increased Appetite</td>
<td>• Sibutramine</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Weight Gain</td>
<td>• Clevidine</td>
</tr>
</tbody>
</table>

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## Appendix C: Medication Charts

### Adjunctive Agents, Depression

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration</th>
<th>Target Dose or Range</th>
<th>Maximum Daily Dose</th>
<th>Schedule</th>
<th>Patient Monitoring Parameters</th>
<th>Side Effects</th>
<th>Selected Drug Interactions</th>
</tr>
</thead>
</table>
| Phenelzine Nardil®                | 45 mg/day     | 15 mg/week| 60-90 mg/day         | 90 mg/day          | 2 - 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 | - Edema  
- Insomnia  
- Orthostatic Hypotension  
- Sexual Dysfunction  
- Weight Gain                                      | - Atomoxetine  
- Bupropion  
- Carbamazepine  
- Dextromethorphan  
- Insulin  
- Levodopa  
- Linezolid  
- Meperidine  
- SSRIs  
- St. John's Wort  
- Sulfonylureas  
- Sympathomimetics  
- Tramadol  
- Triptans  
- Tricyclic antidepressants  
- Tyramine foods  
- Venlafaxine |
| Tranylcypromine Generic available Parnate® | 20-30 mg/day | 10 mg/week | 20-40 mg/day         | 60 mg/day          | 2 - 3 Times Daily            | 2) Pregnancy test – as clinically indicated  
3) Blood pressure at baseline and during dosage adjustments and as clinically indicated. Therapeutic ranges for the lab used should be listed on the report | - Edema  
- Insomnia  
- Orthostatic Hypotension  
- Sexual Dysfunction  
- Weight Gain                                      | - Atomoxetine  
- Bupropion  
- Carbamazepine  
- Dextromethorphan  
- Insulin  
- Levodopa  
- Linezolid  
- Meperidine  
- SSRIs  
- St. John's Wort  
- Sulfonylureas  
- Sympathomimetics  
- Tramadol  
- Triptans  
- Tricyclic antidepressants  
- Tyramine foods  
- Venlafaxine |
| Amitriptyline Generic available Elavil® | 25-75 mg/day | 25-50 mg/day every 1-2 days | 150 mg/day         | 300 mg/day          | Once daily | 1) EKG – baseline and as clinically indicated  
2) Pregnancy test – as clinically indicated  
3) Blood levels as clinically indicated.  
- Amitriptyline + Nortriptyline: 120-250 ng/mL17 | - Blurred vision  
- Constipation  
- Dry mouth  
- Orthostatic hypotension  
- Sedation  
- Tachycardia  
- Urinary retention  
- Weight gain                                      | - Carbamazepine  
- Clometidine  
- Clonidine  
- Fluoxetine  
- Guanethidine  
- Linezolid  
- MAOIs  
- Paroxetine  
- Procainamide  
- Quinidine  
- Quinolones  
- Rifabutin  
- Rifampin  
- St. John's Wort  
- Sympathomimetics  
- Valproate  
- Ziprasidone |
| Desipramine Generic available Norpramin® Pertofran® | 25-75 mg/day | 25-50 mg/day every 1-2 days | 150 mg/day         | 300 mg/day          | Once daily | 1) EKG – baseline and as clinically indicated  
2) Pregnancy test – as clinically indicated  
3) Blood levels as clinically indicated.  
- Desipramine: 100-300 ng/mL17 | - Blurred vision  
- Constipation  
- Dry mouth  
- Orthostatic hypotension  
- Sedation  
- Tachycardia  
- Urinary retention  
- Weight gain                                      | - Carbamazepine  
- Clometidine  
- Clonidine  
- Fluoxetine  
- Guanethidine  
- Linezolid  
- MAOIs  
- Paroxetine  
- Procainamide  
- Quinidine  
- Quinolones  
- Rifabutin  
- Rifampin  
- St. John's Wort  
- Sympathomimetics  
- Valproate  
- Ziprasidone |
| Doxepin Generic available Sinequan® | 25-75 mg/day | 25-50 mg/day every 1-2 days | 150 mg/day         | 300 mg/day          | Once or Twice daily | 1) EKG – baseline and as clinically indicated  
2) Pregnancy test – as clinically indicated  
3) Blood levels as clinically indicated.  
- Doxepin + Nortriptyline: 150-250 ng/mL17 | - Blurred vision  
- Constipation  
- Dry mouth  
- Orthostatic hypotension  
- Sedation  
- Tachycardia  
- Urinary retention  
- Weight gain                                      | - Carbamazepine  
- Clometidine  
- Clonidine  
- Fluoxetine  
- Guanethidine  
- Linezolid  
- MAOIs  
- Paroxetine  
- Procainamide  
- Quinidine  
- Quinolones  
- Rifabutin  
- Rifampin  
- St. John's Wort  
- Sympathomimetics  
- Valproate  
- Ziprasidone |
| Nortriptyline Generic available Pamelor® Aventyl® | 25 mg/day | 25 mg/day every 2 days | 75 mg/day         | 200 mg/day          | Once daily | 1) EKG – baseline and as clinically indicated  
2) Pregnancy test – as clinically indicated  
3) Blood levels as clinically indicated.  
- Nortriptyline: 50-150 ng/mL17 | - Blurred vision  
- Constipation  
- Dry mouth  
- Orthostatic hypotension  
- Sedation  
- Tachycardia  
- Urinary retention  
- Weight gain                                      | - Carbamazepine  
- Clometidine  
- Clonidine  
- Fluoxetine  
- Guanethidine  
- Linezolid  
- MAOIs  
- Paroxetine  
- Procainamide  
- Quinidine  
- Quinolones  
- Rifabutin  
- Rifampin  
- St. John's Wort  
- Sympathomimetics  
- Valproate  
- Ziprasidone |

17 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.

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Appendix C: Medication Charts

ADDITIONAL REFERENCES FOR DRUG INFORMATION

- Drug Interactions – [http://medicine.iupui.edu/lockhart/](http://medicine.iupui.edu/lockhart/)
- Drug Product Labeling – see specific FDA approved drug prescribing information

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## Appendix D: Side Effect and Co-Existing Symptom Management

### Management of Associated or Co-Existing Symptoms in Schizophrenia

Benzodiazepines and other medications with abuse/dependence potential are best avoided in patients with prior history of substance abuse/dependence or who are at risk for substance abuse. Nonaddicting agents are preferred.

<table>
<thead>
<tr>
<th>Co-Existing Symptom</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| **Agitation/Excitement** | - Consider adjunctive medications, including as needed use of oral and intramuscular medications including benzodiazepines, typical antipsychotics, and atypical antipsychotics:  
  - Lorazepam 1-4 mg or clonazepam 0.5-2 mg may be used in treating acute agitation. In emergent situations where rapid reduction of agitation is necessary, lorazepam 1-2 mg given intramuscularly may be preferable to oral dosing. The dose may be repeated every 1-2 hours as needed, and onset of effect is generally seen within 15-30 minutes.  
  - Haloperidol 5 mg orally or intramuscularly may be given every 30-60 minutes until patient is calm.  
  - Atypical antipsychotics in intramuscular or oral formulations may be given on an as needed basis to control acute agitation. If oral dosing is used, doses should be initiated at the low end of the dosing range. Intramuscular olanzapine, risperidone oral solution, and intramuscular ziprasidone act more rapidly than their oral counterparts and their use may be warranted in cases where the patient cannot tolerate or does not respond to typical antipsychotic agents and/or benzodiazepines.  
    - Intramuscular olanzapine 2.5-10 mg, may repeat 2 hours after initial dose and 4 hours after second dose, with a maximum of 30 mg daily.  
    - Intramuscular ziprasidone 10-20 mg as needed to a maximum dose of 40 mg daily. The 10 mg dose may be given every 2 hours, and the 20 mg dose may be given every 4 hours.  
    - Intramuscular aripiprazole 5.25 – 9.75 mg as needed every two hours to a maximum of 30 mg daily.  
  - Risperidone oral solution is available in 1mg/mL.  
  - Failure of the first trial of pharmacotherapy should be followed by a second trial of an alternative agent above.  
  - After failure of multiple trials of agents to control acute agitation/excitement, consider moving treatment to the next algorithm stage. |
| **Persistent symptoms of Aggression/Hostility/Mood Lability** | - Lithium, valproate and carbamazepine are all therapeutic options for the management of aggression and hostility associated with acute exacerbations in schizophrenia.  
  - If there is no discernible change in the clinical picture after 1-3 weeks, the clinician should discontinue the adjuvant mood stabilizer and consider switching the patient to clozapine. |
| **Depression** | - Medication treatments for depression in schizophrenia are the same as those used in major depressive disorder.  
  - SSRIs, venlafaxine XR, bupropion SR/XL, duloxetine and mirtazapine are recommended as first line treatments. |
<table>
<thead>
<tr>
<th>Co-Existing Symptom</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| - 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 milk  
| Insomnia - Adjunctive medications:  
  - Zolpidem 5-10 mg once daily at bedtime.  
  - Zaleplon 5-20 mg (10 mg recommended dose) once daily at bedtime.  
  - Eszopiclone 2-3 mg once daily at bedtime.  
  - Benzodiazepine, such as temazepam 15-30 mg once daily at bedtime or lorazepam 0.5-2mg once daily at bedtime.  
  - Trazodone 25-100mg once daily at bedtime.  
  - Low-dose tricyclic antidepressant, such as amitriptyline 10-50 mg once daily at bedtime.  
- Brief, targeted cognitive therapy.
Management of Treatment-Emergent Side Effects in Schizophrenia

In general, treatment emergent side effects should be addressed first by dose reduction or medication switching. Prescribing medications for side effects may lead to new side effects. Benzodiazepines and other medications with abuse/dependence potential are best avoided in patients with prior history of substance abuse/dependence or who are at risk for substance abuse. Nonaddicting agents are preferred.

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| GI Upset    | - Nausea and diarrhea are usually transient side effects with antidepressants, and improvement should occur within 2-3 weeks after initiation or dose increases.  
- Administer medication with food and large quantities of liquid.  
- Consider lowering dose, if possible, or slowing the dose titration.  
- Persistent GI upset may require changing to an alternative medication or adding an adjunctive agent, such as an H₂ blocker (e.g., famotidine, ranitidine). |
| Tremor      | - Enhanced physiologic tremor – A fine tremor of approximately 8-10 Hz; made worse with outstretched hands.  
  - Check blood levels of medication, if applicable.  
  - Decrease dose, divide dose, or change to slow release preparation of the medication.  
  - Propranolol can be given at 20-30 mg three times a day.  
- Parkinsonian tremor – Coarse tremor at rest of approximately 4-6 Hz.  
  - See treatment recommendations under Extrapyramidal Symptoms (EPS) below. |
| Sedation    | - A thorough evaluation of sleep behaviors should be performed, including a patient assessment of sleep quality.  
- May try dosing medication at bedtime.  
- Decrease dose if possible.  
- Substitute a less sedating alternative medication.  
- 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. |
| Extrapyramidal Symptoms (EPS) – Parkinsonian Tremor, Akathisia, and Dystonia | - Usually seen with typical antipsychotics or higher doses of risperidone.  
- Parkinsonian tremor – coarse tremor at rest of approximately 4-6 Hz.  
  - Decrease dose, divide dosing, use bedtime dosing, or switch to alternate medication.  
  - Pharmacological treatments include benztropine 1-2 mg twice daily, diphenhydramine 25-50 mg two or three times daily, or propranolol 20-30 mg three times daily.  
- Akathisia may respond to propranolol 20-30 mg three times a day. If this is not effective, alternatives include clonidine 0.1 mg three times a day, lorazepam 1 mg two or three times a day, or clonazepam 0.5-1 mg twice a day.  
- Dystonic reactions can often be prevented by benztropine 1 mg two or three times a day for the first few days of antipsychotic therapy. Acute dystonic reactions are generally managed with benztropine 1-2 mg IM or lorazepam 1-2 mg IM. |
<table>
<thead>
<tr>
<th><strong>Side Effect</strong></th>
<th><strong>Recommendations</strong></th>
</tr>
</thead>
</table>
| Tardive Dyskinesia | - Prescribe typical antipsychotics in the lowest dose necessary for the shortest time possible. Mid-potency typical agents may be preferred if typical antipsychotic is selected.  
- Use atypical antipsychotic medications.  
- Consider clozapine which has an extremely low risk of TD.  
- Consider other treatment modalities, including ECT. |
| Neuroleptic Malignant Syndrome (NMS) | - Patients with a history of NMS should be educated about the need to stay well hydrated and avoid strenuous physical activity when outside during hot weather.  
- If the patient has been on a FGA, changing to a SGA is reasonable. |
| Sexual Dysfunction | - May consider switching to an alternative medication with lower propensity to cause sexual dysfunction.  
- If SSRI-induced sexual dysfunction, may consider adding bupropion 75-150mg daily.  
- Alternatives for the management of sexual dysfunction secondary to psychotropic medications is to add a selective phosphodiesterase (PDE) type 5 inhibitor. Use is contradicted with concurrent nitrates. Caution use with concomitant CYP3A4 inhibitors. Data available for use in females is limited to small, open label trials.  
  • Sildenafil 25-100mg one-half to 1 hour before sexual activity.  
  • Tadalafil 10-20mg one-half to 1 hour before sexual activity.  
  • Vardenafil 5-20mg one-half to 1 hour before sexual activity.  
- Other alternative is cyproheptadine 4-8 mg, given shortly before sexual intercourse. However, cyproheptadine is also a serotonin receptor antagonist, and frequent use in patients with affective symptoms should proceed with caution. |
<table>
<thead>
<tr>
<th><em>Side Effect</em></th>
<th><em>Recommendations</em></th>
</tr>
</thead>
</table>
| 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.  
|               | - If due to concomitant antidepressant use: reduce the dose of antidepressant, if possible.  
|               | - Try moving the dosing of the medication to the morning.  
|               | - Adjunctive medications:  
|               |   • Zolpidem 5-10 mg once daily at bedtime.  
|               |   • Zaleplon 5-20 mg (10 mg recommended dose) once daily at bedtime.  
|               |   • Eszopiclone 2-3 mg once daily at bedtime.  
|               |   • Benzodiazepine, such as temazepam 15-30 mg once daily at bedtime or lorazepam 0.5-2mg once daily at bedtime.  
|               |   • Trazodone 25-100mg once daily at bedtime.  
|               |   • Low-dose tricyclic antidepressant, such as amitriptyline 10-50 mg once daily at bedtime.  
|               | - Brief, targeted cognitive therapy. |

| Weight Gain   | - Exercise (walking, jogging, swimming) for at least 3 times weekly, and for at least 30 minutes each time. |
|---------------| - Diet:  
|               |   • Eat smaller portions of 3 meals per day.  
|               |   • Decrease excess fats (decrease fried foods, eat lean meats, increase vegetables, salads, and fruits).  
|               |   • Decrease excessive low nutritional content carbohydrate (soft drinks, desserts, candy, gravies, potatoes, white bread).  
|               | - Avoid snacking, and particularly no evening snacks. |
Appendix E: TMAP Publications


Appendix F: 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 PCS 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 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.