

Division of Mental Health and Developmental Services
Policy #4.015 - Obtaining, Use, and Documentation of Formulary Approved
Medication including Clozapine (Clozaril)

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Policy: Formulary approved medications may be prescribed by all Division physicians who have been privileged to do so. Within the framework of professionally accepted standards of medical practice the choice of medication(s) prescribed is conditioned by certain parameters: the clinical condition of the patient, cost effectiveness, risk/benefits and desired outcomes. *In questions relating to the parameters, review by Division medical director will be final.*

Note: In all cases, the patient, guardian, patient advocate, or responsible physician may initiate an appeal process regarding medication(s).

Purpose: The purpose is to establish procedures for use and documentation of medications as prescribed components of the patient's multidisciplinary treatment throughout the Division. This includes Class I and Class II medications.

Definitions:

- Medication Consultation Form - is found in Appendix A and is to be completed according to the protocol specified in the Procedure Section of this policy.
- Class I Medications - Medications approved by the FDA for specific indications that require no special procedures associated with their use.
- Class II Medications - Medications approved by the FDA for specific indications which require a prior clinical failure of a Class I medication regimen and/or severe significant side effects and/or tardive dyskinesia caused by Class I medications.

Note: There is currently only one Class II medication available in the formulary Clozapine (Clozaril).

References: Local agency policies concerning: the agency formulary, maximum medication doses and regimes, controlled substances, prescriptions, and other agency policies regarding the use of medications and their procurement.

Procedures:

I. Class I Medications:

- A. Formulary restrictions for psychotropic medications for all new and existing patients are no longer in effect.
- B. The strategy to be utilized in the selection and utilization of appropriate medication for all patients is:
 - 1. Sound clinical judgment.
 - 2. Use of the "DECISION MATRIX IN THE USE OF ATYPICAL ANTIPSYCHOTICS" Attachment F.
 - 3. Use of the "DECISION MATRIX IN THE USE OF SSRIs" Attachment G.
 - 4. Appropriate continuing record documentation of patient education, efficacy and side effects.
 - 5. Adherence to any and all special FDA mandated prescribing policies.
 - 6. The use of a generic form of the drug chosen, if available, unless:
 - a) Otherwise determined special circumstances by the agency P & T Committee.
 - b) Justifiable clinical circumstances documented in the clinical record.
 - 7. All questions relating to selection and utilization will be reviewed by the Division medical director whose decision will be final.
- C. The "revised Medication Consultation Form (appendix A)" is to be used for:
 - 1. Non-formulary medications.
 - 2. Individual and daily doses of formulary-approved medications that are not within the FDA approved indications.
 - 3. Individual and daily doses of formulary-approved medications that exceed agency established approved maximums.
 - 4. Appeal by consumer, guardian, advocate or physician of any prescription written by a physician with the MHDS system. In the case of an appeal, the person initiating the appeal will fill in the appropriate section dealing with appeal process justifying the appeal. The completed appeal will be forwarded to the P & T Committee chairman or designee for committee review, comment and disposition. After completion, the appeal will be forwarded to the medical director or designee for review, comment and disposition.

Following appeal completion, the form will be forwarded to the pharmacy for processing.

Note: In all cases, the physician or patient or guardian advocate will be notified of the results of the appeal by the pharmacy.

II. Class II Medications, i.e., Clozapine (Clozaril):

- A. Clozapine is an atypical antipsychotic medication indicated for the management of severely ill schizophrenic patients who fail to respond adequately to other antipsychotic drug treatment. Because of the significant risk of agranulocytosis and seizure associated with its use. Clozapine should be used only in accordance with the schizophrenia algorithm. It is the intention of the Division to provide the fullest spectrum of psychiatric therapy available for the benefit of its patients, while ensuring simultaneously maximum possible safety for the patients under treatment.
- B. Clozapine may be prescribed in accordance with the protocols listed in this directive.
1. Clozapine is contraindicated in patients with myeloproliferative disorders, a history of Clozapine induced agranulocytosis, severe granulocytopenia, or patients receiving other marrow suppressing medication, particularly Carbamazepine, or severe central nervous system depression.
 2. All patients to be given a trial on Clozapine will have completed a "Clozapine Protocol Form" (Attachment A) by the prescribing physician and the pharmacy and a written consent form for treatment. A copy of each will be kept in the patient's chart and on file in the Pharmacy.
 3. Prior to the administration of Clozapine, the following screens must be performed:
 - a) A complete blood count must be obtained within seven (7) days of the first administration of Clozapine with a white blood cell count of $>3,500$.
 - b) The Pharmacist will complete the Clozaril Registration Form (Attachment B) for all authorized prescribers and will transmit the information to the Clozaril Registry or equivalent registry.
 - c) After the above conditions have been met the pharmacy will transmit information to the Clozaril registry, complete Clozaril WBC Monitoring Form or its equivalent (Attachment C). An "Authorization Code Number" will be obtained and entered on the "Clozapine Protocol Form" (Attachment A). A copy of the completed form will be returned to the prescriber who will then write a maximum seven (7) days prescription or order.
 4. Standing orders for weekly white blood cell counts must be sent to the lab before a prescription or order is sent to the pharmacy. Outpatients prescribed Clozapine will be registered with the agency laboratory or agency approved laboratory and after the initial order for WBC is written will be considered to have standing orders for weekly WBC's at the laboratory. These standing orders must be rewritten at least every six months. After six months of continuous Clozapine treatment the prescriber may elect to order laboratory testing for WBC at bi-weekly intervals if WBC counts remain acceptable during this period. The

Laboratory and the Pharmacy should both be notified if this is to occur, to prevent delays in dispensing.

5. The prescriber will review the weekly WBC and a copy of this review will be transmitted directly to the pharmacy. The pharmacy will transmit the WBC to the "Registry". The National Registry Reporting Form (Attachment C) may be used for this function but other means are acceptable. An acceptable WBC count will permit the patient to receive a maximum seven (7) day prescription or order.
 - a) An "acceptable WBC" value for patient on Clozapine is a total of WBC of greater than 3,500 with a neutrophil count over 1,500.
 - b) If the WBC falls below 3,500, or three successive WBCs show consistent decline of 3,000 (total) with a WBC remaining above 3,500, the prescriber must reconsider the Clozapine therapy and document in the chart this change in WBCs, along with the decision to continue or discontinue therapy; these parameters do not necessarily represent an absolute indication for stopping Clozapine therapy.
 - c) If the total WBC falls below 3,000 or the neutrophil count falls below 1,500, Clozapine therapy should be interrupted. WBC and differential counts should be performed daily and the patient should be carefully monitored for flu-like symptoms or other symptoms suggestive of infection.
 - d) Therapy may be resumed if no symptoms of infection develop and the WBC returns to levels above 3,000 and the neutrophil count returns to levels of above 1,500. However, in this event, twice-weekly WBCs and differential counts should continue until the total WBC returns to levels above 3,500. The attached Algorithm should be utilized to restart the medication (Attachment E).
 - e) Any WBC value of less than 2,000 or neutrophil count below 1,000 while on Clozapine is "unacceptable" and Clozapine therapy must be discontinued immediately and permanently. The patient should never again be re-tried on Clozapine. A hematology consultation is to be obtained immediately for further treatment recommendations.

6. Upon approval of Clozapine for therapy the Pharmacy will dispense the medication according to the following protocols.
 - a) Inpatients will have their medication supplied in the manner common to their medications, except that a patient must have an acceptable WBC result drawn within the seven (7) days preceding the current day's closing. No medication will be dispensed to a patient with an unacceptable WBC.
 - b) Outpatients will have their prescriptions filled in weekly or bi-weekly installments. The patient must have an acceptable WBC result drawn within the preceding seven (7) days or

- fourteen (14) days. No medication will be dispensed to a patient with an unacceptable WBC.
- c) The Pharmacy will transmit the information required weekly to the Registry.
7. When Clozapine is discontinued, four (4) weekly WBCs will be obtained after the drug is stopped and these will be reported to the prescriber. The information will also be sent weekly to the Registry.
8. When Clozapine is discontinued the psychiatrist will complete the top half of the "Discontinuation Form, or equivalent" (Attachment D) and forward it to the P & T Committee. The committee will send the form to the Medical Director who will sign it and send it to the Pharmacy. The Pharmacy will inform the Registry and send the original to Medical Records for filing in the patient's chart and retain a copy in the pharmacy.
- III. Each Division agency shall incorporate this policy into the agency policy manual.

ATTACHMENTS

- A. Clozapine Protocol Form
- B. Clozapine Registration Form
- C. Clozapine WBC Monitoring Form
- D. Clozapine Discontinuation Form
- E. Interrupted Therapy Algorithm Form
- F. Decision Matrix in the use of Atypical Antipsychotics
- G. Decision Matrix in the use of SSRIs



Administrator

Effective Date: 6/8/98
Date Revised: 2/28/03; 7/2/07
Date Approved by MHDS Commission:

CLOZARIL PROTOCOL FORM

Agency: _____

1. Psychiatrist

I request that Clozaril (Clozapine) be approved for therapeutic trial on _____
for the following clinical indications:

Patient is a severely ill schizophrenic who has experienced intolerable side effects and/or adverse reactions to:

- | | | |
|------------------------------------|------------------------------------|--------------------------------|
| <input type="checkbox"/> Haldol | <input type="checkbox"/> Thorazine | <input type="checkbox"/> _____ |
| <input type="checkbox"/> Mellaril | <input type="checkbox"/> Navane | <input type="checkbox"/> _____ |
| <input type="checkbox"/> Stelazine | <input type="checkbox"/> Prolixin | <input type="checkbox"/> _____ |

Patient is a severely ill schizophrenic whose symptoms have not been controlled adequately on a therapeutic regimen equivalent to six weeks of chlorpromazine at 1,000 mg. daily:

- | | | |
|------------------------------------|------------------------------------|--------------------------------|
| <input type="checkbox"/> Haldol | <input type="checkbox"/> Thorazine | <input type="checkbox"/> _____ |
| <input type="checkbox"/> Mellaril | <input type="checkbox"/> Navane | <input type="checkbox"/> _____ |
| <input type="checkbox"/> Stelazine | <input type="checkbox"/> Prolixin | <input type="checkbox"/> _____ |

- Patient is currently receiving Clozaril per accepted standards.
- Patient has Tardive Dyskinesia.
- The above named patient has been screened through the Clozaril National Registry using the Sandoz Clozaril Patient Safety Assurance Form and has been issued a "Rechallenge Clearance Authorization Code Number."

Authorization Code Number: _____ Signature _____ Date _____

2. Medical Clearance

- Patient has been screened:
- White Blood Cell Count is greater than 3,500
- White Blood Cell Count is less than 3,500
- Medical History shows no absolute contraindication
- Medical History is significant for _____

Signature _____ Date _____

3. Authorization

The Agency Clozaril Advisory Panel has reviewed the above information and patient record and

- Treatment with Clozaril per Agency Protocol is **AUTHORIZED**
- Treatment with Clozaril is **NOT AUTHORIZED**

Medical Director Signature _____ Date _____

REGISTRATION FORM B



CLOZAPINE Prescription Access System™

P.O. Box 4649, Star City, WV 26504-4649 • Toll-free Phone: 800-843-9915 • Toll-free Fax: 800-843-9916

- A. I am completely familiar with the Clozapine Prescribing Information, including WARNINGS concerning the risk of death associated with agranulocytosis and granulocytopenia.
- B. I understand that each of my patients must be enrolled in the CLOZAPINE Prescription Access System (CPAS) to reduce the potential of rechallenging patients at risk. Clozapine should not be prescribed before receiving a patient reclearance from the CLOZAPINE Prescription Access System. I agree to report all White Blood Cell (WBC) counts (normal and abnormal) to the pharmacy for submission to the CLOZAPINE Prescription Access System within 7 days of collection for weekly patients and within 14 days of collection for biweekly patients. Finally, I agree to notify the CLOZAPINE Prescription Access System promptly of all discontinued patients and submit the results of the 4 required weekly WBC counts after discontinuation of therapy.
- C. I understand that the CLOZAPINE Prescription Access System strongly recommends my enrollment of a local quality assurance committee to help ensure compliance with the Clozapine Prescribing Information requirements. The CLOZAPINE Prescription Access System will notify the physician and pharmacist of all issues regarding noncompliance.

The completion of this document demonstrates my intention to participate in the CLOZAPINE Prescription Access System. I have devised a plan for a Clozapine access group which meets the requirements of the Prescribing Information. Signing this form constitutes commitment on my part to ensure drug dispensing will be contingent upon receipt of WBC count test results and will be performed in compliance with the guidelines of the CLOZAPINE Prescription Access System.

Physician's Signature _____ Date / / M D Y Pharmacist's Signature _____ Date / / M D Y

PHYSICIAN (If registered with CLOZAPINE Prescription Access System, only DEA/ID number is required.)

Physician's DEA/ID Number

Physician's Name (Type or Print) & Title _____
 Address _____ City _____ State _____ Zip Code _____
 Phone Number _____

Associated Institution _____

PHARMACIST (If registered with CLOZAPINE Prescription Access System, only DEA/ID number is required.)

Pharmacy DEA/ID Number

Pharmacist's Name (Type or Print) & Title _____
 Pharmacy Name _____
 Address _____ City _____ State _____ Zip Code _____
 Phone Number _____ Fax Number _____

Wholesaler _____ Fax Number _____
 Address _____ City _____ State _____ Zip Code _____

PATIENT

Initials First Last Date of Birth M D Y Sex M/F Zip Code

Today's Date M D Y Race W Afr/A Hisp Asian Other Patient's Social Security #

New Patient? Patient Continuing Treatment? Y N If weekly testing, how many weeks without interruption or a treatment break >1 month? Check here to receive preprinted Patient-Specific WBC Count Reporting Forms (Form D).

Patient With Interrupted Treatment? If yes, Biweekly testing? Y N

PATIENT RECLEARANCE CODE IS Confirmed by: _____ Date: _____
 (Provided by CLOZAPINE Prescription Access System)



The Mylan Brand
CLOZAPINE

CLOZAPINE Prescription Access System™

P.O. Box 4649, Star City, WV 26504-4649 • Toll-free Phone: 800-843-9915 • Toll-free Fax: 800-843-9916

The completion of this document demonstrates my intention to participate in the CLOZAPINE Prescription Access System (CPAS) and to participate in a plan that ensures that drug dispensing will be contingent upon receipt of White Blood Cell (WBC) count test results. Completion of this form constitutes a continuing commitment to adhere to the guidelines outlined in the Clozapine Prescribing Information and the parameters of the CLOZAPINE Prescription Access System.

Please mark appropriate box

WEEKLY WBC MONITORING

BIWEEKLY WBC MONITORING

PATIENT

First Last
Initials

Patient's Reclearance Code

Patient's Social Security #
--

Patient's Treatment

Pretreatment

Active

Interrupted

Discontinued

Blood Draw Date

M D Y

Total WBC Count (per mm³) x 10³

. x 10³

Total ANC (per mm³)

(Optional)

Is WBC Count Acceptable for Dispensing?

Yes No

Today's Clozapine Dosage:

Total Mg/Day

Dispensed From:

Bottle

Unit Dose

Today's Date:

M D Y

PRESCRIBING REMINDERS:

Treatment should not be initiated if WBC count is <3500 (3.5 x 10³) per mm³

Please see full prescribing information for patients with interruption of Clozapine treatment

If subsequent WBC counts are <3500 (3.5 x 10³) per mm³ and ≥3000 (3.0 x 10³) per mm³ and ANC ≥1500/mm³, twice-weekly WBC counts with differential should be performed

If total WBC count is <3000 (3.0 x 10³) per mm³ and ≥2000 (2.0 x 10³) per mm³ or ANC <1500/mm³ and ≥1000/mm³, therapy should be interrupted and patient closely monitored

If total WBC count is <2000 (2.0 x 10³) per mm³ or ANC <1000/mm³, therapy should be discontinued and patient should never be rechallenged with Clozapine

PHYSICIAN (If registered with CLOZAPINE Prescription Access System, only DEA/ID number is required.)

Registered Physician

Covering Physician

Physician's DEA/ID Number

Physician's Signature

Registered Physician's Name (Type or Print) & Title

Covering Physician's Name

Address

()

Phone Number

City

()

Fax Number

State

Zip Code

PHARMACIST (If registered with CLOZAPINE Prescription Access System, only DEA/ID number is required.)

Pharmacist's Name (Type or Print) & Title

Pharmacy DEA/ID Number

Pharmacy Name

Address

()

Phone Number

City

()

Fax Number

State

Zip Code

CLOZARIL DISCONTINUATION FORM

Agency: _____

1. Psychiatrist

Patient Name: _____

Clozaril Start Date: _____

This patient has been on treatment with Clozaril (Clozapine) and therapy is now being terminated for the following reason(s):

- Noncompliance with medication
- Noncompliance with phlebotomy schedule
- Patient withdrew consent for treatment
- White Blood Cell Count less than 3,500
- White Blood Cell Count less than 2,000
- Clozapine related seizures
- Death (specify cause): _____
- Other (please specify): _____

Signature _____ Date _____

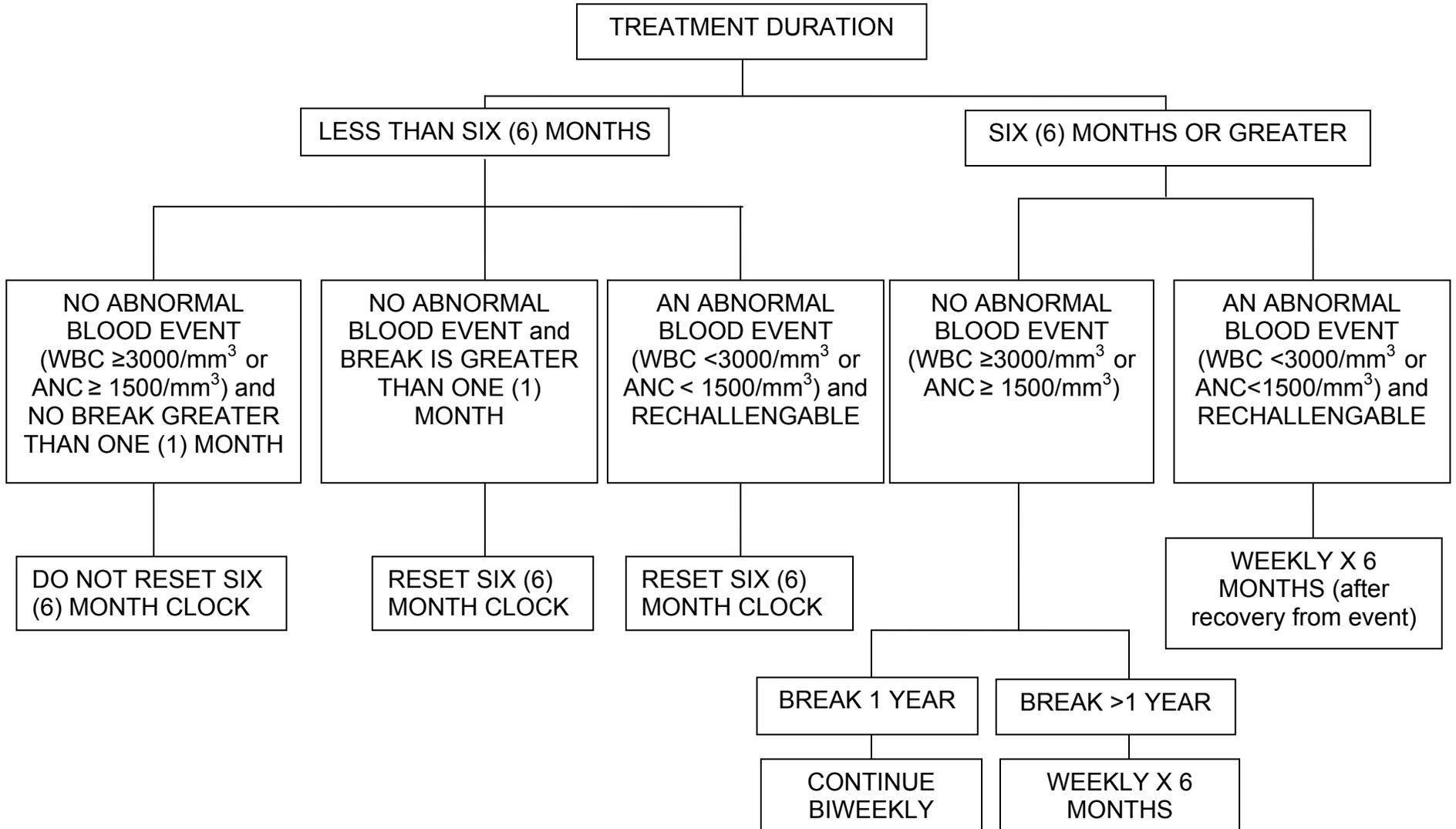
2. Agency Advisory Panel

The Agency Clozaril Advisory Panel has reviewed the above information and patient record.

- Authorization for treatment with Clozaril is **REVOKED**
- Clozaril National Registry has been notified of discontinuation.

Medical Director Signature _____ Date _____

INTERRUPTED THERAPY (WBC < 3000/mm³ ANC < 1500/mm³ FOR BI-WEEKLY MONITORING)



MHDS DECISION MATRIX IN THE USE OF ATYPICAL ANTIPSYCHOTICS

We are still in the process of completely adopting the NMAP (Nevada Medication Algorithm Project) in Schizophrenia, a variation of the TMAP. The TMAP (Texas Medication Algorithm Project) guidelines (algorithm) reflect the state of current knowledge on effective and appropriate care, as well as clinical consensus judgments. The TMAP authors further caution that the guidelines may not apply to all patients, but must be adapted and tailored to each individual patient. Proper use, adaptation modifications or decisions to disregard, in whole or in part, are entirely the responsibility of the clinician. The decision matrix denoted below follows the TMAP model, but with the incorporation of fiscal responsibility requirement. Fiscal responsibility is not a new concept in the optimal treatment of patients. It has always been implicit in the overall clinical responsibility of the clinician. Unfortunately it has not received as much attention as it merits. Because of the inevitable changes in scientific information and technology including the future availability of single source drugs in generic forms, it is imperative that periodic review resulting in the updating and revisions of the decision matrix be needed from time to time. Thus, the decision matrix will become a very dynamic concept that seeks to maximize and stabilize the clinical and fiscal positions of our patients and our organization. The medical staff will be involved in developing new decision matrices as they apply to different classes of drugs.

In the attached TMAP Antipsychotic Algorithm, the atypical antipsychotics referenced in Stages 1 to 3 are Olanzapine, Quetiapine and Risperidone. This was developed prior to the release of Ziprasidone. The modification in the MHDS system is as follows:

- Stage 1: Risperidone or Ziprasidone (Use in any order)
- Stage 2: Use the other in above
- Stage 3: Use Quetiapine or Olanzapine (Use in any order)
- Stage 4: Use the other in above
- Stage 5: Typical Antipsychotic
- Stage 6: Clozapine
- Stage 7: Augmentations

MHDS DECISION MATRIX IN THE USE OF SSRIs

We have not yet started orientation for the implementation of the NMAP (Nevada Medication Algorithm Project) Depression Algorithm. We are on schedule to adopt the principles of the guidelines. And, like in the use of atypical antipsychotics, we shall make modifications in the interest of our clinical and fiscal goals. Review the clinician's responsibility as denoted in the decision matrix for the use of atypical antipsychotics.

However, our establishment of a decision matrix in the class of SSRIs prepares us for such an implementation. In the TMAP (Texas Medication Algorithm Project) SSRIs feature in Stages 1, 2, and 3 of the algorithm. Monotherapy is recommended in those first 3 stages.

The modification in the MHDS (NMAP) system is as follows:

In considering the use of SSRIs, regardless of the Stage, the decision matrix is:

- Step 1: Fluoxetine
- Step 2: Lexapro
- Step 3: Celexa or Paxil or Zoloft