

**Ventura County Medical Center & Ventura County Behavioral Health
Clinical Practice Guideline
for Prescribing and Monitoring Clozapine**

The contents of this clinical practice guideline are to be used as a guide. Healthcare professionals should use sound clinical judgment and individualize patient care. The CPG is not meant to be a replacement for training, experience, CME or studying the latest literature and drug information.

All patients prescribed clozapine are treated and monitored in a manner consistent with the Food and Drug Administration (FDA) requirements.

1. Indications for clozapine treatment.

- a) Treatment refractory schizophrenia-meets DSM-IV criteria of schizophrenia or schizoaffective disorder.
 - i) The patient has had at least two drug treatment trials with other antipsychotic agents.
 - ii) The patient has risk of or evidence of recurrent suicidal behavior in schizophrenia or schizoaffective disorder.
 - iii) Patients with tardive dyskinesia who require treatment with antipsychotics.

2. Relative contraindications for use of clozapine.

The Medical Director or Lead Psychiatrist is consulted if necessary.

- a) Previous hypersensitivity to clozapine.
- b) History of clozapine-induced agranulocytosis or severe granulocytopenia.
- c) Medical condition or drug associated with myeloproliferative disease or immunosuppression.
- d) Severe medical condition or other illnesses causing central nervous system depression or comatose states from any cause.
- e) Seizure Disorder
- f) History of Paralytic Ileus

3. Procedures completed by the prescribing psychiatrist or designee in order to prescribe clozapine.

- a) Determine what pharmacy the client will use.
- b) Contact pharmacy to determine what brand of clozapine is stocked.
- c) Register physician (if not already done) in the registry with brand of clozapine that the physician intends to prescribe (see phone list of Pharmaceutical Companies manufacturing clozapine).
- d) Obtain a rechallenge/authorization/registration number from the appropriate clozapine registry to verify patient eligibility to receive clozapine (*See phone list of Pharmaceutical Companies manufacturing clozapine*).
- e) Nursing staff records this number in the client record on the Physician Orders Sheet and in clozapine database (Outpatient).

4. Prescribing of clozapine

- a) All mandated blood monitoring is completed per FDA guidelines. (*See attached documents: 1) Frequency of Monitoring based on Stage of Therapy or Results from WBC Count and ANC Monitoring Tests and, 2) Resuming Monitoring Frequency after Interruption of Therapy.*)

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- b) Only psychiatrists authorized by the Medical Director are to write prescriptions for clozapine.
 - c) All clozapine prescriptions are written for a weekly, biweekly or 28 day supply of medications; quantity of medication prescribed is based upon lab review schedule.
 - d) ALL prescriptions written for clozapine will be written for **NO REFILLS**.
 - e) ALL prescriptions written in the outpatient clinic for clozapine will include the following:
 - i) Stamped with: "Please contact prescribing physician if patient has not picked up prescription by _____ (enter date)".
 - ii) For phone orders to the pharmacy in addition to the medication order, the nurse provides the most recent lab results and a date to contact the prescribing physician if the patient has not picked up the prescription.
 - f) All individuals prescribed clozapine will be provided the "FDA Patient Information Sheet on Clozapine" (*See Information Sheet*).
 - g) All individuals prescribed clozapine will be informed of the lab work (blood draw) requirements of maintenance on clozapine. All individuals prescribed clozapine, along with their treating psychiatrist, will sign the "Acknowledgment of Required Lab Work" form (*See Acknowledgment Form*).
 - h) Physician Procedures for Follow-up Appointment & Lab
Physician will provide client with a "Clozapine Client Appointment Schedule Slip" (*See Form*).
5. Coordination with VCMC Inpatient Psychiatric, Medical and Surgical Units
- a) Designated staff on the VCMC Inpatient Psychiatric Unit will contact the designated clozapine physician at the receiving VCBH Outpatient Clinic prior to the initiation of clozapine and at the time of discharge of the patient.
 - b) In the event that a client prescribed clozapine is hospitalized at the Inpatient Psychiatric, Medical or Surgical Unit(s), designated staff at these units will contact the outpatient psychiatrist by the next working day and confer with the outpatient team.
 - c) Patients are referred for clozapine treatment to the Clozapine Treatment Team (CTT) at the outpatient clinic where the patient will receive follow up.
 - d) At discharge from the Inpatient Psychiatric, Medical or Surgical Unit staff communicates with the outpatient clinic and provides information on the results of the last lab test completed and ensures patient receives an adequate supply of medication to last until the patient is able to be seen at the outpatient clinic.
- 6) VCBH Outpatient Clozapine Team Responsibilities
- a) Each Outpatient Adult Behavioral Health Clinic will adhere to the procedures described in the Clozapine Team Responsibilities - (VCBH Policy PH48.)

Clozapine Registry Phone Numbers

Company	Drug	Phone Number
Novartis	Clozaril	1-800-448-5938
TEVA	clozapine	1-800-507-8334
AZUR	Fazaclo	1-877-FAZA-CLO
Caraco	clozapine	1-866-828-2892
Mylan	clozapine	1-800-843-9915

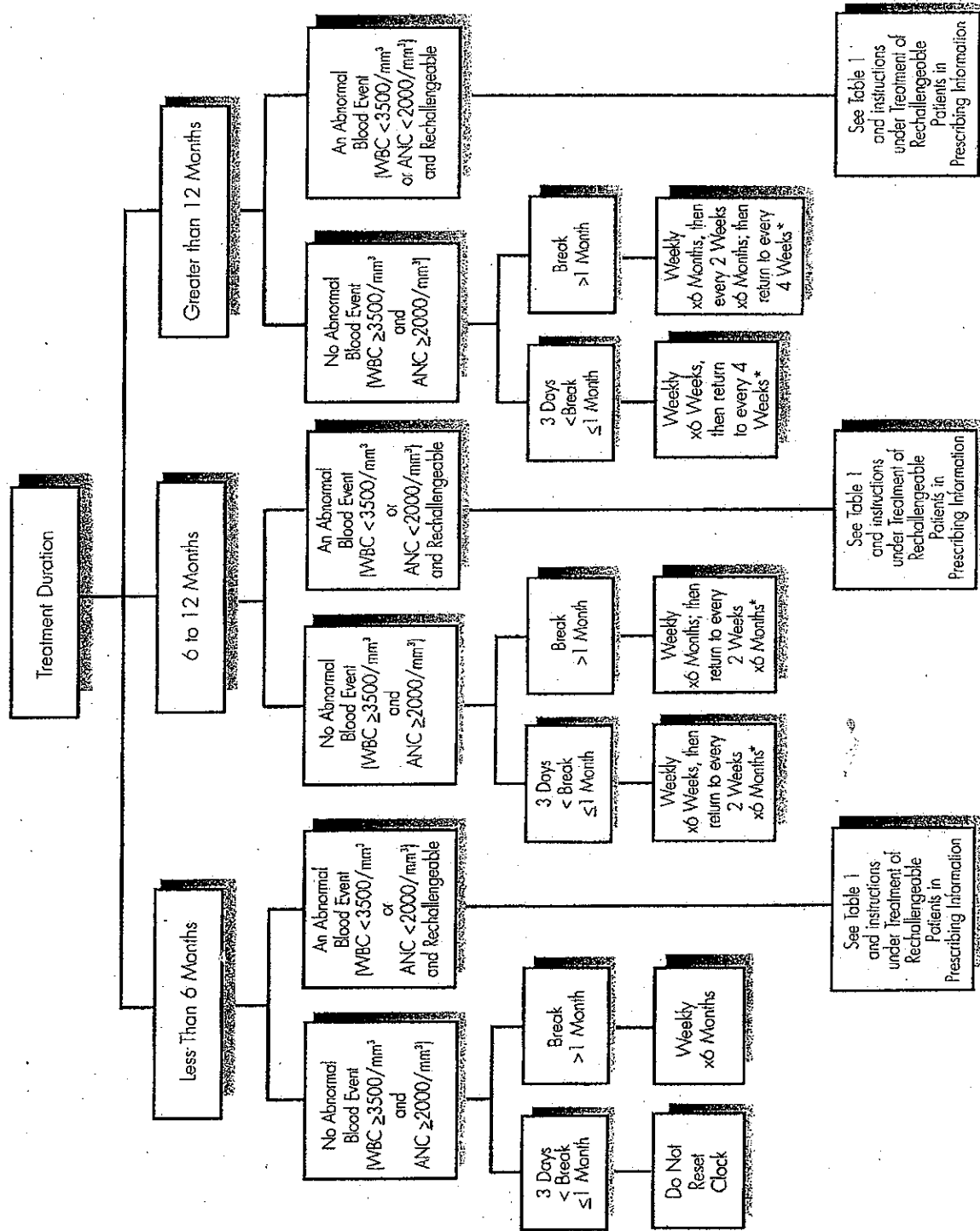
4/12/2010

Table 1: From Clozapine Package Insert: Frequency of Monitoring based on Stage of Therapy or Results from WBC Count and ANC Monitoring Tests

Situation	Hematological Values for Monitoring	Frequency of WBC and ANC Monitoring
Initiation of therapy	WBC \geq 3500/mm ³ and ANC \geq 2000/mm ³ Note: Do not initiate in patients with 1) history of myeloproliferative disorder or 2) clozapine induced agranulocytosis or granulocytopenia	Weekly for 6 months
6 months - 12 months of therapy	All results for WBC \geq 3500/mm ³ and ANC \geq 2000/mm ³	Every 2 weeks for 6 months
12 months of therapy	All results for WBC \geq 3500/mm ³ and ANC \geq 2000/mm ³	Every 4 weeks ad infinitum***
Immature forms present	N/A	Repeat WBC and ANC
Discontinuation of Therapy	N/A	Weekly for at least 4 weeks from day of discontinuation or until WBC \geq 3500/mm ³ and ANC $>$ 2000/mm ³
Substantial drop in WBC or ANC	Single Drop or cumulative drop within 3 weeks of WBC \geq 3000/mm ³ or ANC \geq 1500/mm ³	1. Repeat WBC and ANC 2. If repeat values are 3000/mm ³ \leq WBC \leq 3500/mm ³ and ANC $<$ 2000/mm ³ , then monitor twice weekly
Mild Leukopenia ----- Mild Granulocytopenia	3500/mm ³ $>$ WBC \geq 3000/mm ³ and/or 2000/mm ³ $>$ ANC \geq 1500/mm ³	Twice-weekly until WBC $>$ 3500/mm ³ and ANC $>$ 2000/mm ³ then return to previous monitoring frequency
Moderate Leukopenia ----- Moderate Granulocytopenia	3000/mm ³ $>$ WBC \geq 2000/mm ³ and/or 1500/mm ³ $>$ ANC \geq 1000/mm ³	1. Interrupt therapy 2. Daily until WBC $>$ 3000/mm ³ and ANC $>$ 1500/mm ³ 3. Twice-weekly until WBC $>$ 3500/mm ³ and ANC $>$ 2000/mm ³ 4. May rechallenge when WBC $>$ 3500/mm ³ and ANC $>$ 2000/mm ³ 5. If rechallenged, monitor weekly for 1 year before returning to the usual monitoring schedule of every 2 weeks for 6 months and then every 4 weeks ad infinitum
Severe Leukopenia ----- Severe Granulocytopenia	WBC $<$ 2000/mm ³ and/or ANC $<$ 1000/mm ³	1. Discontinue treatment and do not rechallenge patient 2. Monitor until normal and for at least four weeks from day of discontinuation as follows: • Daily until WBC $>$ 3000/mm ³ and ANC $>$ 1500/mm ³ • Twice weekly until WBC $>$ 3500/mm ³ and ANC $>$ 2000/mm ³ • Weekly after WBC $>$ 3500/mm ³
Agranulocytosis	ANC \leq 500/mm ³	1. Discontinue treatment and do not rechallenge patient 2. Monitor until normal and for at least four weeks from day of discontinuation as follows: • Daily until WBC $>$ 3000/mm ³ and ANC $>$ 1500/mm ³ • Twice weekly until WBC $>$ 3500/mm ³ and ANC $>$ 2000/mm ³ • Weekly after WBC $>$ 3500/mm ³

***Every 4 week monitoring requires clozapine treatment for at least 1 year, every 2 week monitoring for at least the past 6 months, and acceptable WBC and ANC values over the past year (i.e., all WBC counts have been \geq to 3,500/mm³ and all ANC values have been \geq 2,000/mm³).

TRACKING PATIENTS: RESUMING MONITORING FREQUENCY AFTER INTERRUPTION IN THERAPY



* Transitions to reduce frequency of monitoring only permitted if all WBC ≥ 3500 and ANC ≥ 2000.



Patient Information Sheet

Clozapine (marketed as Clozaril)

This is a summary of the most important information about Clozaril. For details, talk to your healthcare professional.

What is Clozaril?

Clozaril is a prescription medicine used to treat people with severe forms of schizophrenia that have not responded to or cannot take other treatments. Clozaril is also used to lower the risk of suicidal behavior in people with schizophrenia or schizoaffective disorder. Clozaril is not approved for use in children.

Who Should Not Take Clozaril?

You should not take Clozaril if:

- You are taking other medicines that can cause the same serious bone marrow side effects as Clozaril.
- You can ask your healthcare professional for a complete list of these medications.

What are The Risks?

The following are the risks and potential side effects of Clozaril therapy. However, this list is not complete.

- **Increased chance of death in elderly persons.** Elderly patients treated with atypical antipsychotics, such as Clozaril, for dementia had a higher chance for death than patients who did not take the medicine. Clozaril is not approved for dementia.
- **Agranulocytosis,** a potentially life-threatening reaction where the body's bone marrow does not produce enough white blood cells. Because of this risk, your healthcare professional must monitor your blood while you are taking Clozaril.
- **Seizures.** The risk of seizure is increased in people who have a history of seizures or other predisposing factors. Because of this risk you should not engage in any activity where you may suddenly lose consciousness, such as operating complex machinery, driving, swimming, climbing, etc.
- **Heart problems.** Clozaril can cause a condition called myocarditis, or swelling of the heart muscle. Some of the warning signs of myocarditis are tiredness, shortness of breath, rapid breathing, fever, chest pain, and irregular

heart beat. If these happen, call your healthcare professional right away.

- **Lowering of blood pressure** when you stand up. This may also lead to fainting. In rare instances, this has been associated with lung and/or heart collapse.

Clozaril and other antipsychotic medications can cause serious problems such as:

- **A life-threatening nervous system problem called neuroleptic malignant syndrome (NMS).** NMS can cause a high fever, stiff muscles, sweating, a fast or irregular heart beat, change in blood pressure, and confusion. NMS can affect your kidneys. NMS is a medical emergency. Call your healthcare professional right away if you experience these symptoms.
- **A movement problem called tardive dyskinesia (TD).** Call your healthcare professional right away if you get muscle movements that cannot be stopped.
- **High blood sugar and diabetes.** Patients with diabetes or who have a higher chance for diabetes should have their blood sugar checked often.
- **Other serious side effects may include** fever, blood clots in the lung, increased blood sugar, and liver disease.
- **The most common side effects include** drowsiness, increased salivation, rapid heart beat, dizziness, constipation, headache, shaking, and lightheadedness.

What Should I Tell My Healthcare Professional?

Before you start using Clozaril, tell your healthcare professional if you:

- have or had heart or lung problems
- have or had seizures
- have or had blood clots
- have or had diabetes or increased blood sugar
- have or had liver disease
- have or had glaucoma
- have or had stomach problems
- have or had prostate enlargement
- are trying to become pregnant, are already pregnant, or are breast-feeding
- drink alcohol
- smoke



Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
Druginfo@fda.hhs.gov



Patient Information Sheet

Clozapine (marketed as Clozaril)

Are There Any Interactions With Drugs or Foods?

Because certain other medications can interact with Clozaril, review all medications that you are taking with your health care professional, including those that you take without a prescription. You should not take Clozaril if you are taking other medicines that can cause the same serious bone marrow side effects as Clozaril.

Your healthcare professional may have to adjust your dose or watch you more closely if you take the following medications:

- certain medicines used to treat anxiety, called benzodiazepines
- certain medicines used to clear thoughts, called psychotropic drugs
- epinephrine
- phenytoin
- rifampin
- cimetidine

- erythromycin
- carbamazepine
- fluvoxamine
- paroxetine

Avoid drinking alcohol while taking Clozaril.

Is There Anything Else I Need to Know?

- Dizziness, and sometimes fainting, caused by a drop in blood pressure may happen with Clozaril, especially when you first start taking this medicine or when the dose is increased.
- Clozaril may impair judgment, thinking, or motor skills. You should be careful in operating machinery, including automobiles, until you know how Clozaril affects you.

Clozaril FDA Approved 1989
Patient Information Sheet Revised 09/2006



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Druginfo@fda.hhs.gov

VENTURA COUNTY BEHAVIORAL HEALTH DEPARTMENT
ACKNOWLEDGEMENT OF REQUIRED LAB WORK

Dear _____:

Please be aware that in all cases in which medication is prescribed, especially psychotropic medications, it is essential that you be in good physical condition and/or that there are no contraindications for your taking the medication as prescribed.

You have been prescribed Clozaril® (clozapine). This medication is different from most other medications, due to the requirement for a lab monitoring system. Prior to starting Clozaril® (clozapine), lab work (a blood draw) was taken in order to get your baseline and also to determine if you are a suitable candidate for this medication. This same lab work will continue as a monitoring tool, both while you are taking Clozaril® (clozapine), and will continue for a period of time, upon discontinuing Clozaril® (clozapine).

This lab work is necessary and is a requirement for being prescribed Clozaril® (clozapine).

By signing below, you are stating that you understand that you will be required to complete the required lab work. Initially this lab work must be completed every 7 days, and eventually, every 28 days. As your physician, I will let you know when your lab work is required, and will work with the rest of your treatment team to ensure your success in completing your required lab tests.

By signing below, you are also indicating that you have been provided a copy of the "Patient Information Sheet on clozapine (marketed as Clozaril®)"

- Yes I understand and agree to the lab Monitoring required for taking Clozaril® (clozapine)
- I have been provided a copy of the "Patient Information Sheet on clozapine (marketed as Clozaril®)"

Patient's Signature

Date:

Physician's Signature

Date

Ventura County Behavioral Health
Mental Health Services
Confidential Patient Information
Welfare and Institutions Code 5328 and
Evidence Code 1014

Clozaril® (clozapine) LAB
ACKNOWLEDGEMENT

Name:
ID#:
Site#: