

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 current edition of DSM 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 Physician Coordinator 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 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 medication; quantity of medication prescribed is based upon lab review schedule.
 - d) ALL prescriptions written for clozapine will be written for **NO REFILLS**.
 - e) All individuals or their conservators prescribed clozapine will be provided the "FDA Patient Information Sheet on Clozapine" (*See Information Sheet*).
 - f) All individuals prescribed clozapine will be informed of the lab work (blood draw) requirements while on clozapine. All individuals prescribed clozapine, along with their treating psychiatrist, will sign the "Acknowledgment of Required Lab Work" form (*See Acknowledgment Form*).
5. Use of clozapine serum level-Routine ordering of clozapine serum level is not generally recommended. Considerations for ordering a level may include:
- a. Poor clinical response at typical/therapeutic dose.
 - b. When on concomitant agents (e.g. Enzyme inducers, enzyme inhibitors, etc.) that can potentially alter clozapine serum levels.
 - c. New starts-5 days after dose is titrated to 300mg.-400mg./day to ensure adequate trial of clozapine.
 - d. When a patient is having intolerable adverse effects at usual therapeutic doses.
6. Coordination with VCMC Inpatient Psychiatric, Medical and Surgical Units, Crisis Residential Treatment Center (CRT) and in-County Mental Health Rehabilitation Centers (MHRC) such as Casa de Salud
- a). At the time of discharge the staff at these facilities will contact the clozapine physician at the receiving facility.
 - b) In the event that a clozapine client is admitted at one of these facilities, 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 facility where the patient will receive follow up.
 - d) At discharge 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. (See attached document-Clozapine History)
7. 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.)

Ventura County Behavioral Health

CLOZAPINE HISTORY

(Required on all transferring clozapine patients)

1. Current dosage and dose form (dissolving or regular tablets);
2. How long on this dose?
3. Is this the maintenance dose, or is the patient undergoing titration?
4. Under which registry is the patient listed?
5. What is the interval of CBCs (7, 14, or 28 days)?
6. How long on this schedule?
7. Have there been any significant drops or other untoward events during the previous 12 months?
8. Is there evidence that clozapine is effective, and more effective than other antipsychotics?
9. Are copies of AT LEAST the last 4 CBCs sent? And copies of the most recent general labs (metabolic, thyroid, and lipids)?
10. Is the patient taking any other antipsychotics? If so, why?
11. If clozapine serum level was obtained-indicate rationale for ordering level, date ordered, result and any action taken.
12. How much medication is client being discharged with?

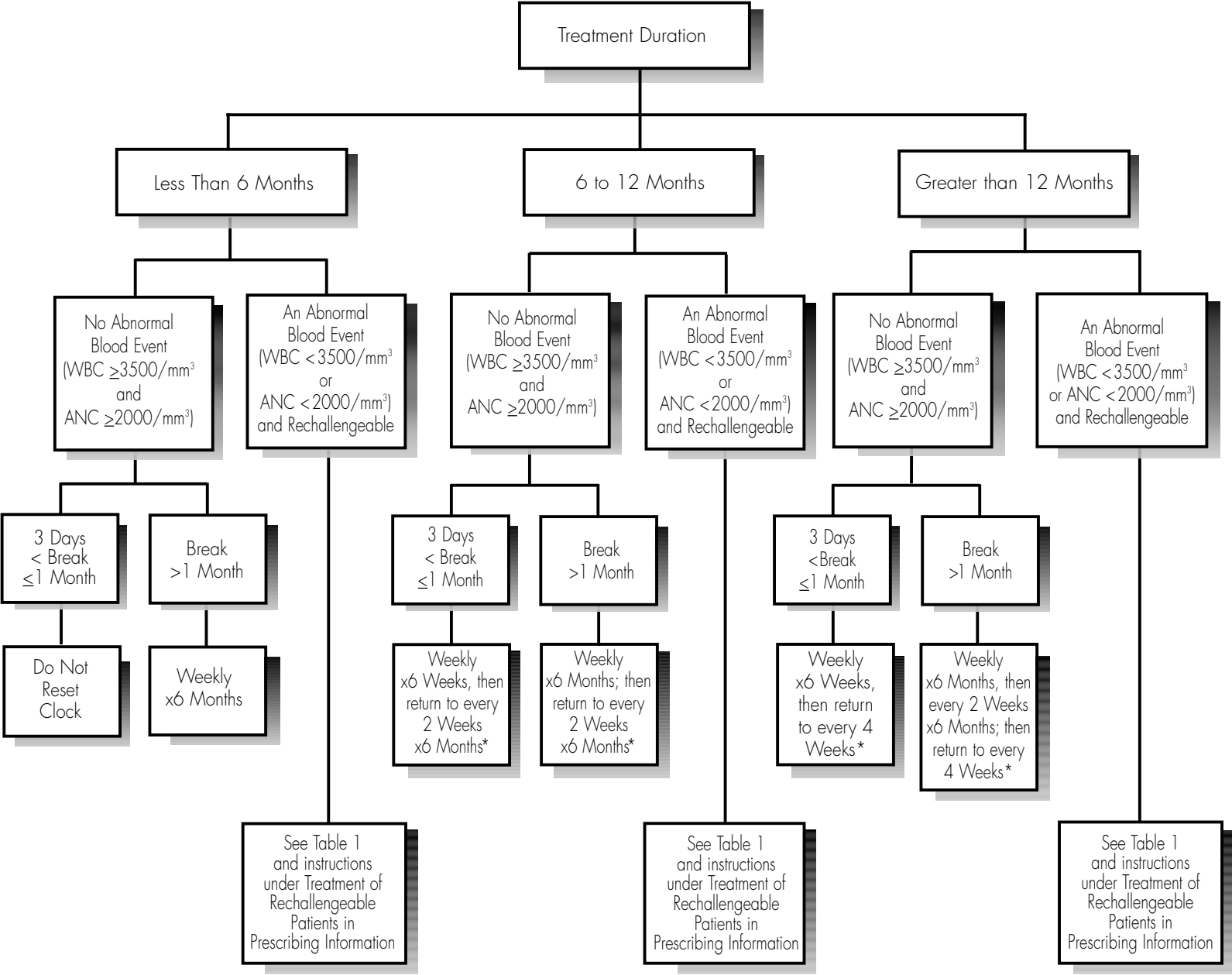
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Table 1: From Clozapine Package Insert: Frequency of Monitoring based on Stage of Therapy or Results from WBC Count and ANC Monitoring Tests

Situation	Hematological Values for Monitoring	Frequency of WBC and ANC Monitoring
Initiation of therapy	WBC $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$ 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 $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$	Every 2 weeks for 6 months
12 months of therapy	All results for WBC $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$	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 $\geq 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$
Substantial drop in WBC or ANC	Single Drop or cumulative drop within 3 weeks of WBC $\geq 3000/\text{mm}^3$ or ANC $\geq 1500/\text{mm}^3$	1. Repeat WBC and ANC 2. If repeat values are $3000/\text{mm}^3 \leq \text{WBC} \leq 3500/\text{mm}^3$ and ANC $< 2000/\text{mm}^3$, then monitor twice weekly
Mild Leukopenia ----- Mild Granulocytopenia	$3500/\text{mm}^3 > \text{WBC} \geq 3000/\text{mm}^3$ and/or $2000/\text{mm}^3 > \text{ANC} \geq 1500/\text{mm}^3$	Twice-weekly until WBC $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ then return to previous monitoring frequency
Moderate Leukopenia ----- Moderate Granulocytopenia	$3000/\text{mm}^3 > \text{WBC} \geq 2000/\text{mm}^3$ and/or $1500/\text{mm}^3 > \text{ANC} \geq 1000/\text{mm}^3$	1. Interrupt therapy 2. Daily until WBC $> 3000/\text{mm}^3$ and ANC $> 1500/\text{mm}^3$ 3. Twice-weekly until WBC $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ 4. May rechallenge when WBC $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ 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 $< 2000/\text{mm}^3$ and/or ANC $< 1000/\text{mm}^3$	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 $> 3000/\text{mm}^3$ and ANC $> 1500/\text{mm}^3$ • Twice weekly until WBC $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ • Weekly after WBC $> 3500/\text{mm}^3$
Agranulocytosis	ANC $\leq 500/\text{mm}^3$	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 $> 3000/\text{mm}^3$ and ANC $> 1500/\text{mm}^3$ • Twice weekly until WBC $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ • Weekly after WBC $> 3500/\text{mm}^3$

***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 $\geq 3,500/\text{mm}^3$ and all ANC values have been $\geq 2,000/\text{mm}^3$).

TRACKING PATIENTS: RESUMING MONITORING FREQUENCY
AFTER INTERRUPTION IN THERAPY



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

Clozapine Registry Phone Numbers

Company	Drug	Phone Number
Novartis	Clozaril	1-800-448-5938
TEVA	clozapine	1-800-507-8334
Jazz	Fazaclo, Clozapine ODT, Versacloz	1-877-329-2256
Mylan	clozapine	1-800-843-9915

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