

ST. CLAIR COUNTY COMMUNITY MENTAL HEALTH AUTHORITYDate Issued: 09/90Date Revised: 12/91;07/94;09/97;08/05;08/07;08/09;08/11;  
11/12;11/13;11/14;11/15;11/16;01/18;01/19

Page 1

<b>CHAPTER</b> Health/Medical	<b>CHAPTER</b> 04	<b>SECTION</b> 001	<b>SUBJECT</b> 0085
<b>SECTION</b> Drugs and Medications	<b>SUBJECT</b> Clozaril (Clozapine) Clinic		
<b>WRITTEN BY</b> Pat McLellan and Peggy Lawton	<b>REVISED BY</b> Melissa Nicholson	<b>AUTHORIZED BY</b> Tracey Pingitore	

I. APPLICATION:

- SCCCMHA Providers & Sub-Contract Providers
- SCCCMHA Board
- Direct Operated Programs
- Community Agency Programs
- Residential Programs
- Specialized Foster Care
- SUD Providers

II. POLICY STATEMENT:

It shall be the policy of the St. Clair County Community Mental Health Authority (SCCCMHA) to ensure a coordinated management system regarding the prescribing and monitoring of the medication Clozaril (Clozapine). For all prescribing management and monitoring guidelines for the use of Clozaril also referred to as clozapine from this point forward in the policy, refer to Clozapine REMS Program at <https://www.clozapinerems.com/CpmgClozapineUI/home.u>. It shall be the policy of the St. Clair Community Mental Health Authority (SCCCMHA), to comply with the Clozapine REMS Program which is an FDA-mandated program implemented by the manufacturers of clozapine which is intended to assist Health Care Providers (HCP) ensure the safety of patients on clozapine. Clozapine REMS is a single shared registry with requirements for prescribers, pharmacists, patients and distributors. It shall always be the policy and directive that when prescribing clozapine, prescriber is to follow the requirements and guidelines set forth in the Clozapine REMS Program.

III. DEFINITIONS:

- A. ANC (Absolute Neutrophil Count): ~~Neutrophils are a type of white blood cell. Clozaril can induce neutropenia, which is a decrease in the absolute neutrophil count and can be life threatening, which is why scheduled lab monitoring is a requirement. The ANC is specified ( or it can be referred to as the PMN count, which is the polymorphonuclear count) in the listed results of the differential. It may also be calculated by multiplying the total WBC by the total percentage of neutrophils from the differential. aleculated by adding the number of segmented neutrophils and the number of basil neutrophils and multiplying the sum by the total WBC x (% neutrophil + % bands)/100. ANC will be used exclusively for patient monitoring (WBC's will no longer be accepted).~~
- B. Benign Ethnic Neutropenia (BEN): An ethnic-specific condition which results in a normally low baseline neutrophil count. Refer to the Clozaril REMS algorithm for the adjusted acceptable ANC guidelines. ~~-which can be treated with Clozapine and has separate ANC monitoring algorithm.~~

<b>CHAPTER</b> Health/Medical	<b>CHAPTER</b> 04	<b>SECTION</b> 001	<b>SUBJECT</b> 0085
<b>SECTION</b> Drugs and Medications	<b>SUBJECT</b> Clozaril (Clozapine) Clinic		

- C. Clozaril (Clozapine): An atypical anti-psychotic used ~~to treat for treatment resistant schizophrenia, and reducing suicidal behaviors in patients with schizophrenia or schizoaffective disorder certain individuals with an array of mental illnesses~~—which ~~have~~ typically have not responded to traditional pharmaco-therapeutic agents.
- D. Clozaril Monitoring Program: The monitoring program that is implemented through designated local laboratories and contractual pharmacies, and conforms to the protocols and standards as established by the Food and Drug Administration (FDA).
- E. Clozaril Nurse: A Registered Nurse assigned to monitor and execute a smooth, efficient and safe clinic for individuals receiving Clozaril. All nurses, pharmacists and prescribers must be certified in the REMS Program. To complete this go to [//www.clozapinerems.com/CpmgClozapineUL/home.u](http://www.clozapinerems.com/CpmgClozapineUL/home.u).
- F. REMS Program (Clozapine Risk Evaluation and Mitigation Strategy): Clozapine ~~can induce is associated with severe~~ neutropenia, which is a reduced number of neutrophils and can be life-threatening. ~~(absolute neutrophil count of less than 500/uL)~~. The requirements to prescribe, dispense, and receive clozapine are incorporated into a single shared program called the Clozapine Risk Evaluation and Mitigation Sharing Strategy (REMS). A REMS is a strategy to manage known or potential risks associated with a drug or group of drugs, and is required by the FDA for clozapine to ensure that the benefits of the drug outweigh the risk of severe neutropenia. The Clozapine REMS Program replaces the individual clozapine patient registries and the National Non-Rechallenge Master File (MMRMF).
- G. WBC (White Blood Cell Count): Total number of white blood cells (leukocytes) in 1 cubic millimeter of peripheral venous blood specimen.

#### IV. STANDARDS:

##### A. INDIVIDUAL SELECTION

Clozapine is an atypical antipsychotic indicated for treatment resistant schizophrenia or schizoaffective disorder, and in reducing suicidal behavior in patients with these diagnoses. Patients must be enrolled in the Clozapine REMS Program by the prescriber or prescribers certified designee.

- B. Individuals being considered for treatment with clozapine, should demonstrate unsatisfactory response to at least 2 typical or atypical anti-psychotic agents at prescribed doses and for a duration of time as determined by the treating psychiatrist, prior to being considered for Clozaril therapy.
- C. Before starting treatment with clozapine, the baseline ANC must be at least 1500/uL for the general population and at least 1000uL for patients diagnosed with BEN (benign ethnic

<b>CHAPTER</b> Health/Medical	<b>CHAPTER</b> 04	<b>SECTION</b> 001	<b>SUBJECT</b> 0085
<b>SECTION</b> Drugs and Medications	<b>SUBJECT</b> Clozaril (Clozapine) Clinic		

neutropenia).

- D. After initiation of treatment with Clozaril, the ANC counts need to be monitored as per guidelines in the Clozapine REMS which also provide recommendations for Clozapine long-term treatment

V. PROCEDURES:

A. Pre-Clozaril Treatment

**Psychiatrist**

1. Determines individual's appropriateness for Clozaril treatment and orders baseline laboratory test – CBC with differential. ANC must be within the stated ranges as put forth in the Clozaril REMS guidelines.

**Psychiatrist/Nurse**

2. Acquires written Informed Consent and provides oral/written and educational information written information related to on Clozaril, by providing access to the video “Is It Time to Consider Clozaril, and by providing the handout according to the policy on Psychotropic Medications and Informed Consent –#05-002-0010. Patient/and caregivers may be provided Clozaril Program authorized information entitled “A Guide for patients and Caregivers: What You Need to Know about Clozapine and Neurtropenia” which is available to be downloaded from the website. Patients and caregivers also must be offered the opportunity to view the video “Is it Time to Consider Clozaril”. Nurse or prescribers must register patient into the Clozapine REMS before prescribing and baseline ANC entered.

**Contractual Pharmacy**

3. Electronically enters individual beginning Clozaril in Clozapine REMS Program and receives Predispose Authorization (PDA) before Clozapine can be dispensed. A PDA is an electronic code that indicates the Clozapine REMS program has verified:
  - The prescriber is certified in the Clozapine REMS Program.
  - The pharmacy is certified in the Clozapine REMS Program.
  - The patient is enrolled in the Clozapine REMS Program.
  - The ANC is current and acceptable according to the patient's monitoring schedule, or the prescriber has authorized the continuation of Clozapine treatment.

**Clozaril Nurse**

4. Reviews pre-Clozaril baseline CBC/Diff results and links to prescriber.
5. Records the results of the baseline WBC and ANC count on the individual's WBC and ANC

<b>CHAPTER</b> Health/Medical	<b>CHAPTER</b> 04	<b>SECTION</b> 001	<b>SUBJECT</b> 0085
<b>SECTION</b> Drugs and Medications	<b>SUBJECT</b> Clozaril (Clozapine) Clinic		

History (Form #110) History (Form #110) from in the Clozaril nurse reference book. Enters lab data from each draw and within the required guideline frequencies in the Clozaril Registry. } Sends laboratory report to the individual's Pharmacy for dispense. SCCCMHA utilizes Genoa Pharmacy or Kroger Pharmacy if the individuals insurance does not allow Genoa to fill Clozaril.

6. Sends the following information to the contractual pharmacy at least 24 hours before Clozaril treatment is to start:
  - a) Ensure that contractual pharmacy has received original physician's order in written form or by electronic script.
  - b) Lab results.
  - c) Copy of insurance/Medicaid card or other approved payment method.

#### **Psychiatrist/Nurse Practitioner**

7. Prescribes Clozaril dosage titration. Clozaril titration schedule (Exhibit C) is available as guideline. Physician order is maintained in electronic file.

#### **Clozaril Nurse**

8. Ensures individuals and assigned casemanagers are aware of site, time, and day of the Clozaril Clinic.

### **B. Active Clozaril Treatment**

#### **Psychiatrist**

1. Reviews the medication at least every ninety (90) days or as clinically indicated. Prescribes Clozaril (Clozapine) with refills.

#### **Clozaril Nurse**

2. Clozaril order is maintained in electronic file. ~~Order to be reviewed after medication review.~~
3. Assesses individual during Clozaril clinic as to tolerance and side effects associated with Clozaril.
4. Reviews results of CBC (in accordance with Section IV. D.) and records WBC and ANC on individual's Clozaril record (form #110). Inputs results into Clozaril registry with each scheduled blood draw.

<b>CHAPTER</b> Health/Medical	<b>CHAPTER</b> 04	<b>SECTION</b> 001	<b>SUBJECT</b> 0085
<b>SECTION</b> Drugs and Medications	<b>SUBJECT</b> Clozaril (Clozapine) Clinic		

5. ~~Completes Clozapine WBC and ANC History (form#110) for necessary contractual pharmacy or supplies pharmacy with lab results.~~ Maintains electronic lab results in the individual's EHR.
6. Informs psychiatrist and individual's assigned treatment staff of abnormal laboratory results or any pertinent clinical information.
7. Discuss with provider/individual if emergency supply is needed; and obtains order from psychiatrist appropriate
8. Completes all the appropriate case record documentation. Completes a Progress/Contact Note for face-to-face contacts.

#### **Home Provider**

9. **If Clozaril** treatment is stopped for two (2) days or more, contacts the prescribing psychiatrist/nurse practitioner for dosing instructions.

#### **Casemanager/Home Provider**

10. Notifies Clozaril Nurse one (1) week in advance of individual's vacation plans if vacation is outside of St. Clair County and longer than two (2) weeks.

### **C. Individuals Placed In St. Clair County CMH During Clozaril Treatment**

#### **CMH Institutional Liaison, Placement Coordinator, or Outpatient Intake Clinician**

1. Notifies Clozaril nurse at least seven (7) days prior to placement to ensure a smooth transition for continued Clozaril therapy.
2. Provides the Clozaril nurse with the following information:
  - a. Social Security number,
  - b. Copy of insurance or Medicaid card,
  - c. Current Clozaril dosage with copy of current physicians order,
  - d. ANC counts from last four (4) blood tests,
  - e. List of other medications individual is currently receiving.
3. Requests CBC with Differential to be drawn on the day of discharge from previous Clozaril monitoring program (i.e., institution, OP labs, etc.).
4. Ensures laboratory results are faxed immediately to the Clozaril nurse.

<b>CHAPTER</b> Health/Medical	<b>CHAPTER</b> 04	<b>SECTION</b> 001	<b>SUBJECT</b> 0085
<b>SECTION</b> Drugs and Medications	<b>SUBJECT</b> Clozaril (Clozapine) Clinic		

- Ensures individual is placed into CMH system with a seven (7) day supply of Clozaril.

#### **Clinician/Casemanager**

- Ensures individual is seen by CMH contractual physician/psychiatrist within seven (7) days of placement or transfer into CMH system.

#### **Clozaril Nurse**

- Follows procedures as outlined in Section (V.B) ACTIVE CLOZARIL TREATMENT for the remaining steps.

### **D. Termination Of Clozaril Treatment**

#### **Psychiatrist**

- Writes the order to discontinue Clozaril in the EHR.

#### **Casemanager/Nurse**

- Receives notification of intent to discontinue Clozaril. Notifies caregiver, if applicable, that the medication is being discontinued.

#### **Clozaril Nurse**

- Documents discontinuation of Clozaril on individual's Progress/Contact Note. Enters post-Clozaril lab information into the registry
- ~~Ensures four (4) Directs individual/caregiver that a post CBC/Diff is required to assure individual is not experiencing post Clozaril -neutropenia. weekly laboratory tests (CBC) are obtained following the discontinuation of Clozaril. Once lab results are available they are entered into the Clozaril Registry.~~
- ~~Reviews the results of weekly CBC laboratory reports. Records WBC and ANC in individuals Clozaril WBC and ANC History (Form #110)~~
- ~~Completes Clozaril WBC and ANC History Form (Form #110) following each of the four (4) weekly post-Clozaril blood draws. Maintains third copy in central Clozaril file. (Only as needed per contractual pharmacy) Supply lab results to contractual pharmacies by copy of lab results.~~
- Ensure that contractual pharmacy has received electronic script for discontinuation of Clozaril.

<b>CHAPTER</b> Health/Medical	<b>CHAPTER</b> 04	<b>SECTION</b> 001	<b>SUBJECT</b> 0085
<b>SECTION</b> Drugs and Medications	<b>SUBJECT</b> Clozaril (Clozapine) Clinic		

~~8. Completes all the appropriate case record documentation, a Progress/Contact Note regarding consumer's post-Clozaril status/condition.~~

VI. REFERENCES:

~~None Available~~Clozaril REMS

VII. EXHIBITS:

- A. Clozaril (Clozapine) Titration Schedule
- B. Clozapine REMS Guidelines

**CLOZARIL (CLOZAPINE) TITRATION SCHEDULE**

CONSUMER NAME \_\_\_\_\_ CASE NO. \_\_\_\_\_ DATE \_\_\_\_\_

B.P. Sitting \_\_\_\_\_ B.P. Standing \_\_\_\_\_ Pulse \_\_\_\_\_ Resp. \_\_\_\_\_

**DOSAGE FOR FIRST WEEK**DAY 1 \_\_\_\_\_ TAKE ONE-HALF OF A 25 MG TABLET AT CLOZARIL CLINIC APPOINTMENT.  
(DAY & DATE)DAY 2 \_\_\_\_\_ TAKE ONE-HALF OF A 25 MG TABLET TWICE A DAY (MORNING & BEDTIME).  
(DAY & DATE)DAY 3 \_\_\_\_\_ TAKE ONE - 25 MG TABLET TWICE A DAY (MORNING & BEDTIME).  
(DAY & DATE)DAY 4 \_\_\_\_\_ TAKE ONE- 25 MG TABLET THREE TIMES A DAY (MORNING, AFTERNOON &  
(DAY & DATE) BEDTIME).DAY 5 \_\_\_\_\_ TAKE ONE - 25 MG TABLET IN THE MORNING AND ONE IN THE AFTERNOON.  
(DAY & DATE) TAKE TWO – 25 MG TABLETS AT BEDTIME.DAY 6 \_\_\_\_\_ TAKE ONE - 25 MG TABLET IN THE MORNING AND ONE IN THE AFTERNOON.  
(DAY & DATE) TAKE THREE – 25 MG TABLETS AT BEDTIME.DAY 7 \_\_\_\_\_ TAKE ONE - 25 MG TABLET IN THE MORNING AND ONE IN THE AFTERNOON.  
(DAY & DATE) TAKE FOUR – 25 MG TABLETS AT BEDTIME.**DOSAGE FOR SECOND WEEK**DAY 8 \_\_\_\_\_ TAKE ONE - 25 MG TABLET IN THE MORNING.  
(DAY & DATE) TAKE TWO - 25 MG TABLETS IN THE AFTERNOON.  
TAKE ONE - 100 MG TABLET AT BEDTIME.DAY 9 \_\_\_\_\_ TAKE ONE - 25 MG TABLET IN THE MORNING.  
(DAY & DATE) TAKE THREE - 25 MG TABLETS IN THE AFTERNOON.  
TAKE ONE - 100 MG TABLET AT BEDTIME.DAY 10 \_\_\_\_\_ TAKE ONE - 25 MG TABLET IN THE MORNING.  
(DAY & DATE) TAKE ONE - 100 MG TABLET IN THE AFTERNOON.  
TAKE ONE - 100 MG TABLET AT BEDTIME.DAY 11 \_\_\_\_\_ TAKE TWO - 25 MG TABLETS IN THE MORNING.  
(DAY & DATE) TAKE ONE - 100 MG TABLET IN THE AFTERNOON.  
TAKE ONE - 100 MG TABLET AT BEDTIME.DAY 12 \_\_\_\_\_ TAKE THREE - 25 MG TABLETS IN THE MORNING.  
(DAY & DATE) TAKE ONE - 100 MG TABLET IN THE AFTERNOON.  
TAKE ONE - 100 MG TABLET AT BEDTIME.DAY 13 \_\_\_\_\_ TAKE ONE - 100 MG TABLET THREE TIMES A DAY (MORNING, AFTERNOON &  
(DAY & DATE) BEDTIME).DAY 14 \_\_\_\_\_ TAKE ONE - 100 MG TABLET THREE TIMES A DAY (MORNING, AFTERNOON &  
(DAY & DATE) BEDTIME).



**Clozapine and the Risk of Neutropenia:**  
A Guide for Healthcare Providers

**Table 1: Recommended Monitoring Frequency and Clinical Decisions by ANC Level**

ANC Level	Treatment Recommendation	ANC Monitoring
<p><b>Normal Range for a New Patient</b> <b>GENERAL POPULATION</b></p> <ul style="list-style-type: none"> <li>ANC ≥ 1500/μL</li> </ul> <p><b>BEN POPULATION</b></p> <ul style="list-style-type: none"> <li>ANC ≥ 1000/μL</li> <li>Obtain at least two baseline ANC levels before initiating treatment</li> </ul>	<ul style="list-style-type: none"> <li>Initiate treatment</li> <li>If treatment interrupted:                             <ul style="list-style-type: none"> <li>&lt; 30 days, continue monitoring as before</li> <li>≥ 30 days, monitor as if new patient</li> </ul> </li> <li>Discontinuation for reasons other than neutropenia</li> </ul>	<ul style="list-style-type: none"> <li>Weekly from initiation to six months</li> <li>Every 2 weeks from 6 to 12 months</li> <li>Monthly after 12 months</li> <li>See Section 2.4 of the full Prescribing Information</li> </ul>
<p><b>Mild Neutropenia</b> (1000 - 1499/μL)*</p>	<p><b>GENERAL POPULATION</b></p> <ul style="list-style-type: none"> <li>Continue treatment</li> </ul> <p><b>BEN POPULATION</b></p> <ul style="list-style-type: none"> <li>Mild Neutropenia is normal range for BEN population, continue treatment</li> <li>Obtain at least two baseline ANC levels before initiating treatment</li> <li>If treatment interrupted                             <ul style="list-style-type: none"> <li>&lt; 30 days, continue monitoring as before</li> <li>≥ 30 days, monitor as if new patient</li> </ul> </li> <li>Discontinuation for reasons other than neutropenia</li> </ul>	<p><b>GENERAL POPULATION</b></p> <ul style="list-style-type: none"> <li>Three times weekly until ANC ≥ 1500/μL</li> <li>Once ANC ≥ 1500/μL return to patient's last "Normal Range" ANC monitoring interval**</li> </ul> <p><b>BEN POPULATION</b></p> <ul style="list-style-type: none"> <li>Weekly from initiation to six months</li> <li>Every 2 weeks from 6 to 12 months</li> <li>Monthly after 12 months</li> <li>See Section 2.4 of the full Prescribing Information</li> </ul>
<p><b>Moderate Neutropenia</b> (500 - 999/μL)*</p>	<p><b>GENERAL POPULATION</b></p> <ul style="list-style-type: none"> <li>Recommend hematology consultation</li> <li>Interrupt treatment for suspected clozapine induced neutropenia</li> <li>Resume treatment once ANC normalizes to ≥ 1000/μL</li> </ul> <p><b>BEN POPULATION</b></p> <ul style="list-style-type: none"> <li>Recommend hematology consultation</li> <li>Continue treatment</li> </ul>	<p><b>GENERAL POPULATION</b></p> <ul style="list-style-type: none"> <li>Daily until ANC ≥ 1000/μL, then</li> <li>Three times weekly until ANC ≥ 1500/μL</li> <li>Once ANC ≥ 1500/μL check ANC weekly for 4 weeks, then return to patient's last "Normal Range" ANC monitoring interval**</li> </ul> <p><b>BEN POPULATION</b></p> <ul style="list-style-type: none"> <li>Three times weekly until ANC ≥ 1000/μL or ≥ patient's known baseline</li> <li>Once ANC ≥ 1000/μL or patient's known baseline, check ANC weekly for 4 weeks, then return to patient's last "Normal BEN Range" ANC monitoring interval.**</li> </ul>
<p><b>Severe Neutropenia</b> (&lt; 500/μL)*</p>	<p><b>GENERAL POPULATION</b></p> <ul style="list-style-type: none"> <li>Recommend hematology consultation</li> <li>Interrupt treatment for suspected clozapine induced neutropenia</li> <li>Do not rechallenge unless prescriber determines benefits outweigh risks</li> </ul> <p><b>BEN POPULATION</b></p> <ul style="list-style-type: none"> <li>Recommend hematology consultation</li> <li>Interrupt treatment for suspected clozapine induced neutropenia</li> <li>Do not rechallenge unless prescriber determines benefits outweigh risks</li> </ul>	<p><b>GENERAL POPULATION</b></p> <ul style="list-style-type: none"> <li>Daily until ANC ≥ 1000/μL</li> <li>Three times weekly until ANC ≥ 1500/μL</li> <li>If patient rechallenged, resume treatment as a new patient under "Normal Range" monitoring once ANC ≥ 1500/μL</li> </ul> <p><b>BEN POPULATION</b></p> <ul style="list-style-type: none"> <li>Daily until ANC ≥ 500/μL</li> <li>Three times weekly until ANC ≥ patient's established baseline</li> <li>If patient rechallenged, resume treatment as a new patient under "Normal Range" monitoring once ANC ≥ 1000/μL or at patient's baseline</li> </ul>

\* Confirm all initial reports of ANC less than 1500/μL (ANC < 1000/μL for BEN patients) with a repeat ANC measurement within 24 hours

\*\* If clinically appropriate

