

ST. CLAIR COUNTY COMMUNITY MENTAL HEALTH AUTHORITY

ADMINISTRATIVE PROCEDURES

Date Issued: 03/20

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SECTION Drugs and Medications	SUBJECT Clozaril (Clozapine) Clinic		
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I. APPLICATION:

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

II. PURPOSE STATEMENT:

St. Clair County Community Mental Health Authority (SCCCMHA) shall 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 this document, refer to Clozapine REMS Program at <https://www.clozapinerems.com/CpmgClozapineUI/home.u>. Furthermore, St. Clair Community Mental Health Authority (SCCCMHA), shall 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 administrative procedures 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.
- 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.

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C. Clozaril (Clozapine): An atypical anti-psychotic used for treatment resistant schizophrenia, and reducing suicidal behaviors in patients with schizophrenia or schizoaffective disorder which typically have not responded to traditional pharmacologic 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).~~

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E.D. 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 <https://www.clozapinerems.com/CpmgClozapineUL/home.u>.

F.E. REMS Program (Clozapine Risk Evaluation and Mitigation Strategy): Clozapine can induce neutropenia which is a reduced number of neutrophils and can be life-threatening. 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.F. WBC (White Blood Cell Count): Total number of white blood cells (leukocytes) in 1 cubic millimeter of peripheral venous blood specimen.

IV. STANDARDS:

INDIVIDUAL SELECTION

- A. 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 neutropenia).

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- 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/~~Registered~~ Nurse

2. Acquires written Informed Consent and: ~~p~~Provides oral/written educational information related to Clozaril, by providing access to the video "Is It Time to Consider Clozaril, and by providing the handout, ~~—~~"A Guide for patients and Caregivers: What You Need to Know about Clozapine and Neutropenia". ~~This~~which is available to be downloaded from the website. Nurse or prescribers must register patient into the Clozapine REMS before prescribing and baseline ANC entered.

Contractual Pharmacy

3. ~~Enters~~ electronically ~~the~~enters individual beginning Clozaril into ~~the~~ Clozapine REMS Program and receives Predispense Authorization (PDA) before Clozapine can be dispensed. A PDA is an electronic code that indicates the Clozapine REMS program has verified:
 - a. The prescriber is certified in the Clozapine REMS Program.
 - b. The pharmacy is certified in the Clozapine REMS Program.
 - c. The patient is enrolled in the Clozapine REMS Program.
 - d. The ANC is current (results are within 7 days of dispensing) 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.

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5. Records the results of the baseline WBC and ANC count on the individual's WBC and ANC History (Form #110) 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 completed within 7 days of dispensing.
 - c. Copy of insurance/Medicaid card or other approved payment method.

Psychiatrist/Nurse Practitioner

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

Clozaril Nurse

8. Ensures individuals and assigned case managers 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. Maintains Clozaril order ~~is maintained~~ in the electronic file.
3. Assesses individual during Clozaril clinic as to tolerance and side effects associated with Clozaril.

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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.

~~scheduled blood draw.~~

5. 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. Discusses 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, **if Clozaril treatment is stopped for two (2) days or more.**

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Case Manager/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.

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

Clinician/Case Manager

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

Clozaril Nurse

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

D. Termination Of Clozaril Treatment

Psychiatrist

1. Writes the order to discontinue Clozaril in the EHR.

Case Manager/Registered Nurse

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

Clozaril Nurse

3. Documents discontinuation of Clozaril on individual's Nursing Progress/~~Contaet~~ Note.
4. Directs individual/caregiver that a post CBC/Diff is required to assure individual is not experiencing post Clozaril neutropenia. Once lab results are available they are entered into the Clozaril Registry.
5. Ensures that the contractual pharmacy has received electronic script for discontinuation of Clozaril.

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VI. REFERENCES:

- A. Clozaril REMS
<https://www.clozapinerems.com/CpmgClozapineUI/home.u>
- B. Clozaril & Risk of Neutropenia: A Guide for Health Care Providers
https://www.clozapinerems.com/CpmgClozapineUI/remss/pdf/resources/Clozapine_REMS_A_Guide_for_Healthcare_Providers.pdf

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VII. EXHIBITS:

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

VIII. REVISION HISTORY:

Dates issued 09/90; 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.

EXHIBIT A

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).

EXHIBIT B

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

CLOZAPINE REMS
The Single Shared System for Clozapine
No Blood, No Drug™



Before starting treatment with clozapine, the baseline ANC must be:

- at least 1500/ μ L for the general population
- at least 1000/ μ L for patients diagnosed with BEN

During treatment, monitor ANC regularly as described in [Table 1](#) below.

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

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

^{*} Confirm all initial reports of ANC less than 1500/ μ L (ANC < 1000/ μ L for BEN patients) with a repeat ANC measurement within 24 hours
^{**} if clinically appropriate

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

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

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

** If clinically appropriate