HEALTHWEST

Procedure

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Prepared by:

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Subject: Clozaril/Clozapine Treatment System (CTS) Procedure

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I. PURPOSE:

To establish procedures for prescribing, monitoring, administering, and documenting the use of Clozaril/Clozapine as mandated by the FDA Clozapine Risk Evaluation & Mitigation Strategy (REMS) Program, Department of Community Health, and American Psychiatric Association Guidelines and Standards of Practice.

II. APPLICATION:

This procedure applies to all HealthWest employees, programs, contract physicians, physician assistants (PA), and nurse practitioners (NP) who prescribe, monitor, administer, and document Clozaril/Clozapine therapy.

III. DEFINITIONS/BACKGROUND INFORMATION:

A. Clozaril/Clozapine Treatment System (CTS) consists of doctors, PA, NP, pharmacists, medical testing laboratories; the individual's assigned Supports Coordinator (SC) and Registered Nurse Care Manager (RN Care Manager), individual receiving services, and support staff. Together they make sure the necessary weekly/biweekly/monthly blood testing is done, results are checked, and the correct number of Clozaril/Clozapine tablets is provided to the individual for each weekly/biweekly/monthly interval the individual is involved in Clozaril/Clozapine therapy.

B. Clozapine REMS: A strategy to manage known or potential risks associated with a drug or group of drugs, and is required by the FDA for Clozaril/Clozapine to ensure that the benefits of the drug outweigh the risk of severe Neutropenia.

C. Neutropenia: A blood disorder that occurs when a certain type of white blood cell count (WBC) called Neutrophils is not made or not enough of them are made. This makes it harder for the body to fight infection.

D. HealthWest Clozaril/Clozapine Clinic: A clinic occurring at a HealthWest location that the individual attends to receive medication monitoring by an RN, ANC draw by the laboratory, and Clozaril/Clozapine dispensing by the pharmacy.

E. Clozapine REMS provides a centralized point of access for prescribers and pharmacies to certify before prescribing or dispensing Clozapine and to manage patients on Clozapine prescriptions.

## IV. PROCEDURES

Overview of Sections

A. Clozaril/Clozapine Pretreatment
B. Initiation of Active Clozaril/Clozapine Treatment
C. Transferring Inpatient Clozaril/Clozapine Individuals New to the Outpatient CTS
D. Active Clozaril/Clozapine Treatment
E. Discontinuation of Clozaril/Clozapine Treatment
F. Response to Abnormal ANC Count
G. Changing Clozaril/Clozapine Dosage Midweek
H. Continuation of Clozaril/Clozapine Treatment in Event of Hospitalization
I. Response to Individual's Failure to Comply with Clozaril/Clozapine Treatment Procedures
J. Individuals Receiving Services Vacations

### A. CLOZARIL/CLOZAPINE PRETREATMENT

Prescribers must all get certified. To certify, prescribers must:

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

2. Successfully pass the *Knowledge Assessment for Healthcare Providers*.

3. Complete and submit the one-time Clozapine REMS Prescriber Enrollment Form.

    a. Prescribers can allow designees to enroll patients and enter ANCs on their behalf. The term designee refers to any person who has been designated or requested to perform some duty or function on behalf of a prescriber. Designees must be certified in the Clozapine REMS Program before they can perform any duties or functions for their associated prescriber.

    b. Prescriber designees must enroll in the Clozapine REMS Program, and a certified prescriber must confirm the designee. Any medical professional prescribing Clozapine must enroll and become certified in the Clozapine REMS Program. A notification will be sent to the

prescriber when the designee enrolls. Before a designee can become certified, the prescriber will need to approve the person acting on his/her behalf. Once the designee has been approved, they will be able to engage in patient management through the Clozapine REMS Program website.

c. A designee can perform the following actions on behalf of the prescriber:

1) Enroll patients.

2) Report ANC lab results.

3) Manage patients and view patient lists.

d. Get certified online at www.Clozapinerems.com or call (844) 267-8678 for more information or to request materials.

4. Physician/PA/NP determines that the individual meets criteria for Clozaril/ Clozapine treatment listed below:

a. Clozaril/Clozapine is indicated in the treatment of severely ill, treatment-resistant psychotic individuals, i.e., "schizophrenic," "schizoaffective," "bipolar psychotic," or other psychotic conditions, who have had a substantiated diagnosis of psychosis for many years and have been treated with standard antipsychotic medication(s) in the past without positive response, either:

1) Because of insufficient effectiveness of other medications.

2) The inability to achieve an effective dose due to intolerable adverse effects from those drugs.

3) FDA Clozapine REMS Program APA *Guidelines and Standards of Practice* strongly recommend an individual be given at least two trials, each with a different antipsychotic medication, at an adequate dose and for an adequate duration, as defined by the *Guidelines for Pharmacological Treatment*, to establish ineffectiveness prior to starting Clozaril/Clozapine. Well-documented history may be employed to demonstrate this.

4) Individuals with symptoms of psychosis who meet any of the following criteria that are persistent and not amenable to conventional treatment must have such thoroughly documented by the physician/physician assistant/nurse practitioner in the clinical record:

a) Presence of drug-induced chronic abnormal movements.

b) Well-documented history of drug-induced chronic abnormal movements.

c) Presence of, or well-documented history of, Tardive Dyskinesia.

d) Presence of, or well-documented history of, Tardive Dystonia.

b. The physician/PA/NP/RN must inform the individual of their role in the Clozaril/Clozapine Treatment System. The individual must consent to and complete baseline screening as ordered by the physician/PA/ NP.

c. The individual must be able to follow through with the required blood tests. Use the patient counseling tool titled *What You Need to Know about Clozapine & Neutropenia: A Guide for Patients and Caregivers.* Review this information with patients or their caregivers as often as needed to ensure they understand the risk of Neutropenia associated with Clozapine and the importance of ANC monitoring. Refer to Section 17 of the *Clozapine Prescribing Information* for additional important counseling messages for your Clozapine patients.

d. You may choose not to provide *What You Need to Know about Clozapine and Neutropenia: A Guide for Patients and Caregivers* to the patient or caregiver if you do determine that the patient's adherence to Clozapine treatment will be negatively impacted by providing it.

5. Physician/PA/NP/RN notifies SC of recommendation to initiate Clozaril/ Clozapine treatment.

a. If a SC is not assigned, Physician/PA/NP/RN notifies the primary worker who will contact the Access Program requesting authorization of Supports Coordination Services. Every individual who is treated with Clozaril/Clozapine must have a SC or designated support staff.

b. SC is required to have Clozaril/Clozapine training by a HealthWest RN Care Manager, to review and familiarize themselves with Clozaril/ Clozapine Treatment System (CTS) procedures.

c. The RN Care Manager will verify insurance provider using Health Plan Benefits search and information, all of which should be sent to the pharmacy and lab with initial orders.

d. The SC will notify RN Care Manager of spend-down information.

e. RN will use ECR data to verify identifiers that are required by Clozapine REMS such as date of birth and zip code.

6. Rechallenge check is completed:

a. Inquire about a patient's Clozaril/Clozapine history before enrolling the patient; please call the Clozapine REMS Program at 844-267-8678 for assistance or go to the website at www.Clozapinerems.com to view the history profile.

b. Per FDA requirements, if a patient and/or their caregiver or guardian will not provide the required information, the patient will not be able to receive Clozaril/Clozapine therapy.

c. Physician/designee enrolls consumer in the Clozapine REMS via online or Clozapine REMS Patient Enrollment Form or fax. Complete a Clozapine REMS Patient Enrollment Form.

7. Initial lab work is completed (pretreatment begins). Required laboratory testing prior to initiation and during therapy:

a. Prior to initiating treatment with Clozapine, a baseline ANC must be obtained within seven (7) days of anticipated start of Clozaril/Clozapine usage. The baseline ANC must be at least 1500/µL for the General Population, and at least 1000/µL for patients with documented Benign Ethnic Neutropenia (BEN).

b. Case Manager/RN coordinates sending the individual to the lab for the initial blood draw.

c. RN notifies the designated clerical person of the individual's pretreatment status.

d. RN sends the Health Plan Benefits report to the pharmacy and lab for all new Clozaril consumers.

e. Lab releases results to HealthWest addressed to physician within twenty-four (24) hours. They are distributed to RN who reviews and communicates results to physician. The lab report is initialed/commented on by physician and turned in for filing.

f. If the lab report is obtained verbally from the lab, the RN will note the results on Laboratory Telephone Report (Form MO12) and have the physician initial the form.

8. If ANC is above 1500/µL for the General Population and at least 1000/µL for BEN patients, physician/RN may continue with Clozaril/Clozapine pretreatment procedures.

9. If ANC is less than 1499/µL for BEN, physician must document his/her decision to retest and/or evaluate the cause of the condition (Clozaril/Clozapine treatment cannot start).

10. If ANC is less than 999/µL for BEN, obtain at least two baseline ANCs before initiating treatment.

B. INITIATION OF ACTIVE CLOZARIL/CLOZAPINE TREATMENT

1. Physician/designee enrolls consumer in Clozapine REMS.

2. You can enroll a General Population consumer patient one of two ways:

   a. By signing into the Clozapine REMS Program website at www.Clozapinerems.com and enrolling the patient online.

   b. By downloading the Clozapine REMS Patient Enrollment Form from the Clozapine REMS Program website at www.Clozapinerems.com, and faxing the completed form to 844-404-8876. HealthWest has all Clozaril forms in the H-drive for each HealthWest prescriber.

3. For patients with Benign Ethnic Neutropenia (BEN), prescribers would indicate BEN status as part of the enrollment process on the Clozapine Program website. Phone enrollment is only available for the General Population consumers. General population patients and BEN patients can also be enrolled via fax.

4. If another prescriber has previously treated the patient with Clozapine, you must enroll the patient with a HealthWest prescriber by completing and submitting the Clozapine REMS Patient Enrollment Form to the Clozapine REMS Program (online or by fax) to access the patient's ANC History. If you cannot find the patient online, contact the REMS Program at (844) 267-8678 for assistance or re-enroll the patient.

5. Certified physicians and designees can add ANC lab values for the enrolled consumer using the following steps:

   a. Sign into the Program website and navigate to your My Dashboard page using the button in the upper right corner of the page.

   b. Within our list of patients, select the "Add Lab" option from the actions drop-down list for the appropriate patient.

   c. Within the lab form, fill in the requested information and submit the form.

6. The patient's treatment status and monitoring frequency will automatically be set by the system.

7. RN/SC has individual receiving treatment/guardian sign an Authorization to Exchange Information allowing HealthWest to communicate with the lab and pharmacy, Clozapine REMS Program, and the specific brand of Clozaril/Clozapine manufacturer.

8. RN/SC interviews the individual, obtaining a list of all medications he/she is currently taking.

a. This list, with the individual's name, is forwarded to the pharmacy to be entered into their computer. Medications that will suppress bone marrow function will be identified by the pharmacy.

b. In the event of a potential medication interaction, the pharmacy will notify the RN, by telephone, at the time of review.

c. Physician/PA/NP and RN confer. Clozaril/Clozapine is not to be used with other medications that suppress bone marrow function. The physician/PA/NP must document in a progress note the presence or absence of any contraindicated medications being taken by or prescribed for the individual receiving services.

9. Physician/PA/NP/RN/case manager communicates with the individual/ guardian to complete the following:

a. Briefing of individual/guardian regarding Clozaril/Clozapine procedures.

b. *A Guide for Patients and Caregivers: What do I tell my Patients about Clozapine?* This guide is found on the Clozapine REMS website at www.Clozapinerems.com.

c. Use the patient counseling tool titled "*What You Need to Know about Clozapine and Neutropenia: A Guide for Patients and Caregivers*." Review this information with patients or their caregivers as often as needed to ensure they understand the risk of Neutropenia associated with Clozapine and the importance of ANC monitoring. Refer to Section 17 of the Clozapine prescribing information for additional important counseling messages for your Clozapine patients.

1) You may choose not to provide "*What you Need to Know about Clozapine and Neutropenia: A Guide for Patients and Caregivers"* to the patient or caregiver if you determine that the patient's adherence to Clozapine treatment will be negatively impacted by providing the guide.

d. Clozaril/Clozapine teaching sheet.

e. Consent for Use of Psychotropic Medications (Form C148).

f. If Tardive Dyskinesia is present, Consent Form: Patient with Tardive Dyskinesia (Form C153).

g. Prescriptions for starting dose of Clozaril/Clozapine.

10. Physician/PA/NP issues a standing order for weekly White Blood Cell and Absolute Neutrophil Count testing by the lab. RN will forward this order to the appropriate lab. Tests must be done weekly for at least six (6) months on all new Clozaril/Clozapine individuals.

11. Physician/PA/NP/RN completes Clozapine REMS ANC Reporting Form. A copy is retained and filed in the individual's chart, and a copy is forwarded to the pharmacy with the current lab results.

12. RN notifies designated HealthWest clerical staff that the individual is about to begin active Clozaril/Clozapine treatment. The following information is placed on the Clozaril Master List:

    a. Name

    b. Medicaid Recipient ID Number or other insurance provider information.

    c. Prescribing physician and HealthWest program.

    d. Brand of Clozaril/Clozapine.

    e. RN Care Manager and Case Manager assigned.

    f. Date of birth.

    g. Clozaril group.

13. The designated clerical staff transmits copies of the revised Clozaril Master List to HealthWest staff, RN Care Managers, Pharmacy, and lab as it is revised.

14. RN/designated HealthWest staff will forward the following to the pharmacy by 3:00 p.m. the Tuesday of the week due so that the individual's seven (7)-day supply of Clozaril/Clozapine is available for prompt pick up the next morning.

    a. Clozapine REMS ANC Reporting Form with current lab attached.

    b. The prescription for the individual's titration of Clozaril/Clozapine with Health Plan Benefits report attached.

15. The SC prepares and processes a Treatment Plan Addendum to modify the individual's existing PCP to include Clozaril/Clozapine treatment.

16. The RN takes and records vital signs (including weight) weekly for one (1) month and then monthly unless otherwise indicated. Abnormal results will be rechecked in accordance with the Clozapine REMS chart for recommended monitoring frequency and clinical decisions by ANC level.

17. The SC/designated staff coordinates the individual reporting to the Clozaril/Clozapine clinic or lab and pharmacy as needed.

    a. Blood is drawn at the designated location.

b. The individual receives a Clozaril/Clozapine Blood Draw Confirmation Slip to present to the pharmacy for medication pick-up to pick up a one (1)-week supply of Clozaril/Clozapine.

C. TRANSFERRING INPATIENT CLOZARIL/CLOZAPINE INDIVIDUALS NEW TO THE OUTPATIENT CTS

1. In the event Clozaril/Clozapine treatment is initiated for an individual while hospitalized, the assigned case manager will facilitate transfer to the HealthWest outpatient CTS. If a SC is not assigned, the HealthWest Hospital Liaison will process a referral for case management and monitor the individual and treatment procedures until a case manager is assigned.

2. The Case Manager/Hospital Liaison arranges for the individual to be seen by the HealthWest physician/PA/NP within the week of discharge and forward discharge information the day of the discharge and the most recent lab to the Care Manager or RN Care Manager. A HealthWest prescription will be obtained for WBC/ANC and Clozaril/Clozapine, and the RN Care Manager will establish protocol in accordance with what was started inpatient.

3. The RN enrolls consumer in the Clozapine REMS Program under HealthWest prescriber and submits online with the most recent lab or fax enrollment form.

D. ACTIVE CLOZARIL/CLOZAPINE TREATMENT

1. The frequency of monitoring WBC and ANC results, per the current FDA (Food and Drug Administration) recommendations, will be followed as is dictated in the *Clozapine and the Risk for Neutropenia: A Guide for Healthcare Providers* found on the website www.clozapinerems.com.

2. The lab ensures delivery and Clozapine REMS Program ANC results for all HealthWest Clozaril/Clozapine individuals to the appropriate HealthWest location on Wednesdays, no later than 2:00 p.m.

3. ANC results and Clozapine REMS ANC Reporting Form will be reviewed by the RN and initialed by the physician before being submitted for filing.

4. RN completes ANC Reporting Form by the appropriate Tuesday prior to the individual's Wednesday clinic. A ninety (90)-day order for Clozaril/Clozapine may be submitted to the pharmacy for a one-, two- or four-week supply if no change in dosage is anticipated. A new prescription must be written minimally every ninety (90) days and submitted to the pharmacy.

5. Designated HealthWest staff faxes a copy of the ANC Reporting Form and a copy of lab results to the pharmacy no later than Friday of the clinic date.

6. The physician/PA/NP sees the individual for medication reviews as needed, minimally every ninety (90) days. Clozaril/Clozapine dosage is adjusted as needed.

7. Prescriptions for increases or decreases in Clozaril/Clozapine are phoned or faxed to the pharmacy and documented in the clinical record according to HealthWest policy. The pharmacy is requesting that any time we increase the Clozaril dose in between dispense dates, we are to do a Clozaril prescription to bridge until the actual dispense due date for the regularly scheduled Clozaril clinic.

8. On the appropriate Wednesday, the individual proceeds to the designated lab and pharmacy or clinic location for blood draw and medication. If the individual is not capable of doing this independently, they will be escorted by a HealthWest staff or home staff person.

9. The RNs that conduct the weekly HealthWest Clozaril Clinic will be responsible for monitoring the individual's vital signs, assessing for medication effectiveness/side effects, and providing support. Monitoring will occur monthly unless otherwise indicated. Any abnormal vital signs will result in repeat monitoring in one (1) week. Generally, Clozapine treatment should be interrupted, as a precautionary measure, in any patient who develops a fever of 101.3 degree F or greater, and the ANC should be obtained.

10. RN is responsible for communicating changes to the lab and pharmacy. If additional routine laboratory work has been ordered, the RN will notify the lab so the draw can coincide with the scheduled WBC/ANC draw.

11. During the first week of Clozaril/Clozapine treatment, the individual's status is changed from "pretreatment" to "active treatment." The RN communicates status change(s) to the designated clerical staff prior to the next Tuesday. Status changes(s) are reflected on the Clozapine REMS ANC Reporting Form.

12. A designated clerical person is responsible for the updating of all information on the HealthWest Clozaril/Clozapine list. This list will be used by lab and pharmacy personnel to identify registered individuals who have failed to come in for their blood test or medication.

13. Designated clerical person sends a copy of the Clozaril/Clozapine list to all direct care HealthWest Staff, and to RN Care Managers to review. They will notify the clerical person if there are any discrepancies.

14. Active Clozaril/Clozapine individuals transferring from programs within HealthWest will require:

    a. A telephone call from the previous program nurse to the new program nurse regarding the transfer.

    b. The current Clozaril/Clozapine order and current labs faxed to the new program nurse.

    c. The new program nurse calling the designated clerical staff, laboratory, and pharmacy as needed.

15. The physician/PA/NP will write an order to change the frequency of WBC and ANC monitoring to every two (2) weeks for six (6) months after six (6) months of therapy has been completed if WBC and ANC results have remained normal.

    a. The RN will notify the lab and pharmacy of the change in monitoring frequency.

    b. Pharmacy will provide a two-week supply of medication to the individual.

16. The physician/PA/NP will write an order. The Clozapine REMS ANC Reporting Form will reflect change and enter change information online within twelve (12) months of treatment and ANC results have remained normal.

    a. The RN will notify the lab and pharmacy of the change in monitoring frequency.

    b. The pharmacy will supply a one (1)-month supply of medication to the individual.

E. DISCONTINUATION OF CLOZARIL/CLOZAPINE TREATMENT

1. Physician/PA/NP/RN informs the pharmacy of medication discontinuation with an order, and notifies the lab with an order the same day the Clozaril/Clozapine discontinuation is to start.

    a. When termination is planned, a gradual reduction over a one- to two-week period is recommended. The pharmacy will be advised of the last planned dose. The discontinuation order from the HealthWest prescriber will reflect the taper. The RN Care Manager will ensure the order is transmitted to and understood by the entire care team.

    b. The method of treatment discontinuation will vary depending on the patient's last ANC. Abrupt treatment discontinuation is necessary for moderate to severe Neutropenia that is suspected to have been caused by Clozapine.

    c. Remember to report the decision to discontinue Clozapine for a patient to the Clozapine REMS Program. You can do this one of three ways:

        1) By signing into the Clozapine REMS Program website at www.Clozapinerems.com.

        2) By calling the Clozapine REMS Program contact center at (844) 267-8678.

3) By completing the "Patient Update – Change Treatment Status" section of the ANC Lab Reporting Form and faxing it to the Clozapine REMS Program at (844) 404-8876.

d. When the individual's medical condition requires abrupt discontinuation, the RN and the prescribing physician/PA/NP will be notified if there are recurrences of psychiatric symptoms and/or withdrawal symptoms.

e. For some patients who experience, or have experienced, moderate Clozapine-related Neutropenia (ANC less than 1000/µL) or severe Clozapine-related Neutropenia (ANC less than 500/µL), the risk of serious psychiatric illness from discontinuing Clozapine may be greater than the risk of rechallenge. This may be relevant for patients with severe schizophrenic illness who have no treatment option other than Clozapine. In making the decision to rechallenge a patient, consider:

1) A hematology consultation.

2) The ANC ranges defined in the full prescribing information.

3) A discussion with the patient and his or her caregiver about the benefits and risks of Clozaril/Clozapine rechallenge the severity and characteristics of the neutropenia episode.

f. Prescribers may choose to continue Clozapine treatment in patients with ANCs less than 1000/µL in the General Population; however, the prescribers should follow the treatment recommendations carefully to determine if the benefits of continuing Clozaril/Clozapine treatment outweigh the risks.

g. If treatment is interrupted < 30 days, continue monitoring schedule as before. If treatment is interrupted > 30 days, continue monitoring as if a new patient. This is for General Population & BEN Population patients.

2. The RN sends an order to the lab indicating the four (4) post Clozaril dates that ANC must be done; then discontinue after the last date.

3. The RN continues to see the individual four (4) weeks following discontinuation of Clozaril, whether abrupt or gradual, to monitor and record vitals, monitor for withdrawal symptoms, assess physical and psychiatric condition, and provide support. Monitor patients carefully for the recurrence of psychotic symptoms and symptoms related to cholinergic rebound such as profuse sweating, headache, nausea, vomiting, and diarrhea.

4. For abrupt Clozapine discontinuation for a reason unrelated to Neutropenia, continuation of the existing ANC monitoring is recommended for General Population patients until their ANC is ≥ 1500/µL and for patients with BEN until their ANC is ≥ 1000/µL or above their baseline.

5. The individual continues to go to the lab weekly for four (4) weeks following discontinuation to have blood drawn for WBC/ANC counts. A confirmation slip for the ANC blood draw is not needed. Depending on the individual's ANC, more frequent blood testing may be ordered as outlined in Clozapine REMS treatment recommendations.

6. The lab delivers/faxes the ANC results to the appropriate HealthWest location the day it is drawn. The assigned RN reviews and communicates results to the prescribing physician via the Clozapine REMS ANC Reporting Form, indicating change in treatment status for each of the four (4) weeks following discontinuation. Change in treatment status may also be reported to Clozapine REMS via phone call or online. The Physician/PA/ NP will initial the results before filing.

7. After four (4) weekly ANCs, the RN instructs the designated clerical staff to remove the individual's name from the Clozaril/Clozapine list.

8. If the individual is not cooperative in obtaining a blood test after discontinuation, repeated attempts should be made to seek the individual's cooperation. The danger should be explained and documented. In the case of incompetent individuals, the guardian should be advised of the situation. Individuals may not be forced to comply.

F. RESPONSE TO AN ABNORMAL ANC COUNT (See Attachment A)

1. Mild Neutropenia: If an individual's ANC is between 1000/µL and 1499/µL:

   a. For General Population, the lab is to contact the HealthWest RN involved that working day.

   b. For BEN Population, Mild Neutropenia is normal range. Continue Patient's "Normal BEN Range" for ANC monitoring interval.

   c. For General Population patients the RN and Physician/PA/NP review the ANC results. (See Attachment A)

   d. Continue treatment.

   e. The Physician/PA/NP and RN develop and implement, within forty-eight (48) hours, a plan for monitoring the individual and document decision to maintain or reduce the dosage of Clozaril/Clozapine.

      1) For General Population patients, physician orders ANC to be done three (3) times weekly until ANC is 1500/µL) or greater. Once the ANC is equal to or greater than 1500/µL, the consumer's last "Normal Range" ANC monitoring interval may be reinstated.

      2) The RN monitors the individual's physical condition and records vitals as ordered by the Physician/PA/NP. Results are reviewed with the Physician/PA/NP.

3) RN will inform the SC and/or treatment team of the abnormal test results and monitoring plan.

4) SC/RN communicates this information to the individual and, if necessary, accompanies him/her to the lab for blood draws. The risk and symptoms of infection will be explained to the individual and others (family/care provider). The individual will be instructed to immediately report to the treatment team if they develop any symptoms of infection.

5) Primary care physician will be kept informed of the individual's status by the RN.

6) Recommend hematology consultation.

2. Moderate Leukopenia and Moderate Granulocytopenia: If the General Population individual's ANC is 500/µL to 999/µL.

a. The lab immediately notifies a HealthWest RN.

b. The RN and Physician/PA/NP review the ANC results.

c. Physician/PA/NP and RN develop, implement, and document (within 24 hours) a plan for monitoring the individual.

1) For the General Population recommend hematology consultation.

2) For the General Population interrupt treatment for suspected Clozapine-induced Neutropenia. The RN completes the Clozapine ANC Reporting Form and notifies the pharmacy and Clozapine REMS either online, by fax, or by phone.

"On hold" is checked for the individual's Clozaril/Clozapine status, ensuring that the pharmacy will stop dispensing Clozaril/Clozapine to this individual until ordered to resume by the Physician/PA/NP.

3) Daily ANC test must be ordered until the patient's ANC ≥ 1500/µL.

4) Once ANC is ≥ equal to or greater than 1500/µL, return to patient's last "normal range" ANC monitoring interval.

5) Resume Clozaril/Clozapine treatment once ANC normalizes ≥ 1500/µL with titrating order from HealthWest prescriber.

6) For the BEN Population recommend hematology consultation and continue Clozaril/Clozapine treatment.

7) For BEN Population, labs must be done three (3) times weekly until ANC is ≥ 1000/µL or patient's known baseline. Check ANC weekly for four (4) weeks, and then return to patient's last "normal BEN range" ANC monitoring interval.

8) RN will inform the SC and/or treatment team of the abnormal test results and monitoring plan.

9) SC/RN notifies the individual of the Clozaril/Clozapine status change and ensures that the individual stops taking his/her Clozaril/Clozapine. The risk and symptoms of infection will be explained to the individual and others (family/care provider) by RN. The individual will be instructed to report immediately to the treatment team if they develop any symptoms of infection.

10) SC/designated staff accompanies the individual to the lab for all prescribed blood draws as necessary.

11) The RN monitors the individual's physical condition, taking and recording vitals as ordered by the Physician/PA/NP. Results are reviewed with the Physician/PA/NP.

12) Primary care physician will be kept informed of the individual's status by the RN.

13) The RN completes the Clozapine ANC Reporting Form and notifies the pharmacy & Clozapine REMS either online, by fax, or by phone.

"On hold" is checked for the individual's Clozaril/Clozapine status ensuring that the pharmacy will <u>stop dispensing</u> Clozaril/Clozapine to this individual until ordered to resume by the Physician/PA/NP.

3. <u>Severe Leukopenia and Severe Granulocytosis</u>: Total ANC count is less than 500/µL for the General Population and less than 500/µL for the BEN Population.

a. Lab notifies HealthWest RN or Physician/PA/NP immediately. The HealthWest Emergency Line, (231)722-4357, is used for contacting the RN on call after hours, on holidays, or weekends.

b. Physician and RN review results and inform SC or designated staff person that Clozaril/Clozapine <u>must</u> be discontinued immediately for suspected Clozapine-induced Neutropenia. The Physician/PA/NP writes an order indicating discontinuation.

c. RN/SC or designated staff person contacts the individual at once and ensures that he/she discontinues Clozaril/Clozapine immediately.

d. The Physician/PA/NP orders appropriate monitoring procedures until ANC are at least four (4) weeks from day of discontinuation as follows:

1) For General Population patients, daily lab until ANC is ≥ 1000/µL.

2) For General Population patients ANC weekly until ANC is ≥ 1500/µL.

3) For the General Population, do not rechallenge unless prescriber determines the benefits outweigh risks. If patient is rechallenged, resume treatment as a NEW patient under "normal range" monitoring once the ANC is ≥ 1500/µL.

4) The physician/PA/NP must request medical consult with the primary care physician and appropriate medical referral(s) within 24 hours.

5) Physician/RN/PA/NP monitors the individual's physical/psychiatric condition.

e. RN notifies the pharmacy by telephone within twenty-four (24) hours that the individual has discontinued Clozaril/Clozapine treatment.

f. RN communicates status change to the designated clerical person. Treatment status is changed from "active" to "discontinued."

g. The RN flags the individual's record with a drug-sensitization warning of Allergic Agranulocytosis secondary to Clozaril/Clozapine.

h. All further steps outlined in Section E above, Discontinuation of Clozaril/ Clozapine Treatment, Paragraphs 1 through 8, are to be followed.

i. Physician/PA/NP/RN must communicate with the individual's primary care physician regarding the risk of infection. Recommend hematology consultation.

1) The physician/PA/NP must request medical consult with the primary care physician and appropriate medical referral(s) within 24 hours.

2) Physician/RN/PA/NP monitors the individual's physical/psychiatric condition.

4. Authorizing continuation of Clozaril/Clozapine when the ANC is less than 1000/µL for General Population or less than 500/µL for BEN Population.

a. A prescriber may authorize Clozapine treatment to continue.

b. This authorization is called a treatment rationale; it requires the prescriber to confirm that the benefits of continuing Clozaril/Clozapine treatment outweigh the risks of developing severe Neutropenia.

c. For reporting a treatment rationale:

1) The Clozapine REMS Program will alert the prescriber if an ANC is provided that is below the recommended thresholds for a patient. Clozapine will not be dispensed to the patient unless the prescriber provides a treatment rationale to authorize continued treatment.

2) The Clozapine REMS Program will change the treatment status of a patient with a low ANC to "interrupted" or "discontinued," and according to the recommendations in the prescribing information.

3) If the prescriber wishes to continue Clozaril/Clozapine treatment, the prescriber must change the patient's treatment status to "active," and confirm that the benefits of continuing Clozapine treatment outweigh the risks of developing severe Neutropenia (i.e., the treatment rationale).

4) Prescribers must confirm treatment continuation by faxing a signed Clozapine ANC Lab Reporting form to Clozapine REMS with a completed Treatment Rationale section.

5) After the prescriber provides the treatment rationale, the Clozapine REMS Program will issue a Pre-Dispense Authorization (PDA), which allows the outpatient pharmacy to dispense Clozaril/ Clozapine.

6) Information provided in the Clozapine REMS Program is not a substitute for appropriate documentation. Documentation to be in the patient's medical record regarding the prescriber's decision to continue, interrupt or discontinue Clozapine treatment.

5. Report suspected adverse events directly to the Clozapine REMS Program via phone. You may also report adverse event information to the FDA MedWatch Reporting System by phone at (800) FDA-1088, or by mail using Form 3500A, available at www.fda.gov/medwatch.

6. For Hospice patients (i.e., terminally ill patients with an estimated life expectancy of six months or less), the prescriber may reduce the ANC monitoring frequency to once every six months, after a discussion with the patient and his/her caregiver. The individual treatment decisions should weigh the importance of monitoring ANC in the context of the need to control psychiatric symptoms and the patient's terminal illness.

G. CHANGING CLOZARIL/CLOZAPINE DOSAGE MID-WEEK

1. Physician/PA/NP/RN/staff confer.

2. Physician/PA/NP determines that a specific change in dosage is needed.

3. Physician/PA/NP/RN phones in the new prescription to the pharmacy. The verbal order is documented according to HealthWest policy, and prescription copy is faxed to the pharmacy with “new” or “change” written on the fax to alert the pharmacist.

4. The rationale for the change is appropriately documented in the chart by the Physician/PA/NP/RN, signed by the Physician/PA/NP (or verbal order form), in case of a verbal order. [ENTERED IN OC]

5. The SC or designated staff contacts the individual the same working day and picks up the change in prescription of Clozaril/Clozapine and takes it to the individual with specific instructions on when to take it. (The individual, if able, may pick up the medication once notified by the RN or SC to do so.)

6. The RN communicates with the pharmacy regarding the midweek dosage change. In the event of a decrease, the pharmacy is to be instructed to reduce the individual’s next weekly supply of Clozaril/Clozapine by a corresponding number of pills. ******* (The individual is not to accumulate a supply of this medication.)

H. CONTINUATION OF CLOZARIL/CLOZAPINE TREATMENT IN EVENT OF HOSPITALIZATION

1. Psychiatric Hospitalization (Except KPH):

   a. HealthWest Physician/PA/NP/RN/SC/Case Manager alerts hospital staff of the individual’s medication needs and communicates relevant information.

   b. RN informs lab, pharmacy, and designated HealthWest clerical staff of the transfer. The clerical staff will update the individual’s Clozaril/Clozapine status change to "on hold/interrupted" on the next Clozaril/Clozapine List.

   c. Upon discharge, the SC/RN facilitates transfer back to the HealthWest Outpatient CTS. At the time of discharge, the hospital physician will provide a current Clozaril/Clozapine prescription and current WBC/ANC count results. SC responsible for getting the information on the day of discharge.

      1) If an individual is discharged on a weekday, the individual/ designated staff must report the same day to the pharmacy to pick up the change in his/her weekly prescription which will carry him/her until the following Wednesday.

2) An individual discharged over a weekend will be provided enough Clozaril/Clozapine by the hospital to last until the next working day. The first working day following discharge, the individual or designated staff will report to the pharmacy to pick up the remainder of his/her weekly prescription which will carry him/her until the following Wednesday.

3) If an individual was on Clozaril/Clozapine prior to admission to the hospital, the individual will turn in medication to RN/SC for appropriate disposal by a Health Care Professional.

d. SC arranges for the individual to be seen by a HealthWest physician/ PA/NP within seven (7) days of discharge.

e. The RN notifies the designated clerical staff of the individual's outpatient status on the day of discharge. The clerical staff will update the individual's Clozaril/Clozapine status change to "active treatment" on the next Clozaril/Clozapine List.

2. Kalamazoo Psychiatric Hospital (KPH):

a. Emergency Services (ES) staff alerts HealthWest's Kalamazoo Psychiatric Hospital (KPH) Liaison that the individual is receiving Clozaril/Clozapine.

b. ES notifies the individual's HealthWest RN of the admission, and this information is updated on the "Clozaril List," and the pharmacy is notified.

c. RN consults with the HealthWest KPH Liaison and forwards copies of the previous Clozaril prescribing information to the KPH Liaison.

d. When a Clozaril/Clozapine individual is to be discharged from KPH, the HealthWest Liaison must notify the HealthWest Program that will be responsible for his/her treatment after appropriate placement is found.

e. HealthWest Liaison obtains the results of the current WBC/ANC count from KPH. If a new WBC/ANC is required, HealthWest staff will facilitate arrangements to have the WBC/ANC count completed by the appropriate lab.

f. The HealthWest RN will complete the Clozapine Patient Enrollment Form on the day of discharge and fax it to Clozapine REMS (fax number (844) 404-8876) or submit the data online to Clozapine REMS website at www.Clozapinerems.com.

g. It should be noted that an individual cannot be released from KPH with more than a two (2)-week supply of Clozaril/Clozapine. Arrangements by the KPH Liaison for securing this medication in the community will have to be made quickly. The individual must

be seen, depending on the amount of medication dispensed, by a HealthWest Physician within seven (7) to fourteen (14) days of discharge.

3. Medical Hospitalization

a. HealthWest Physician/PA/NP/RN consults with the individual's private physician and communicates relevant medication information (with the exception of a life-threatening situation, the SC/RN/Physician/PA/NP must obtain the individual/guardian's written authorization to release information prior to disclosure).

b. If the treating Physicians/PA/NP elects to continue Clozaril/Clozapine, SC and/or designated HealthWest staff will facilitate a transfer to the Hospital Inpatient CTS.

c. Procedures outlined in Section H.1. (Items b through e) are followed with hospital medical staff.

I. RESPONSE TO INDIVIDUAL FAILURE TO COMPLY WITH CLOZARIL/ CLOZAPINE TREATMENT PROCEDURES

1. The individual fails to see the RN for scheduled vital sign monitoring appointments.

a. The RN will notify the SC or designated staff of the individual's missed appointment.

b. SC/designated staff promptly attempts to contact the individual to determine the reason for lack of compliance, and then confers with the Physician/PA/NP/RN.

c. If Clozaril/Clozapine is to be continued, the SC/designated staff requests the individual come in to see the RN and then directs him/her to the lab and pharmacy, if necessary.

d. If the individual cannot be located within three (3) days after the missed appointment, serious consideration must be given to temporarily suspend Clozaril/Clozapine treatment.

e. If the decision is to discontinue treatment due to lack of compliance, follow the procedures outlined in Section E.

2. Failure to Report to Lab/Clinic for Blood Draw.

a. If the individual fails to show for the clinic blood draw, their Clozaril/ Clozapine should be returned to the pharmacy. Pharmacy will notify RN by 5:00 p.m. on the day the Clozaril refill is due.

b. The RN will notify IHC lab of all Clozaril no-shows on the clinic day of the no-show. All delinquent and repeat Clozaril labs will be done at the IHC HealthWest lab. All repeat labs are done after

12:00 p.m. only, per directive of HealthWest prescribers, at HealthWest IHC lab. All delinquent Clozaril labs are done at the HealthWest IHC lab also.

3. Individual Fails to Pick Up Clozaril/Clozapine from Pharmacy after Blood Draw.

   a. After 12:00 p.m. on Wednesday, the pharmacy will contact the RN.

   b. Follow Paragraph 1 above (Items b through e) as appropriate.

4. Individual is not Taking Medications as Prescribed.

   a. RN confers with the Physician/PA/NP and SC/designated staff.

   b. Immediately following consultation, SC/designated staff contacts the individual to discuss/assess problems with medication compliance.

   c. Physician/PA/NP, RN, and SC confer to determine whether to continue or suspend Clozaril/Clozapine treatment. Treatment recommendations are documented in the record.

J. INDIVIDUALS RECEIVING SERVICES VACATIONS

1. If the individual is out of town for three (3) weeks or less after the first six (6) months of treatment but before twelve (12) months of treatment, RN is to contact the pharmacy for the appropriate amount of Clozaril/Clozapine.

2. Transfer to an existing Clozaril/Clozapine Treatment System if the individual is not able to appear for more than three (3) weeks and has not been on Clozaril treatment for more than twelve (12) months.

   a. The individual/guardian must notify the RN or SC two (2) to four (4) weeks in advance when planning to leave town on a vacation longer than three (3) weeks. If the individual must leave town on short notice (one to two days), the individual/guardian must notify the RN or SC as soon as possible, prior to leaving. The individual will need to provide an outline of his/her travel plans, giving destinations and expected arrival times, etc.

   b. The RN/SC will need to check with the individual's Health Plan regarding prior authorization needs. Michigan Medicaid will cover Clozaril/Clozapine costs while an individual is on vacation in other states only when prior authorization from the appropriate Health Care Plan has been obtained. Vacations of less than one (1) month are recommended, as the length of time outside of the state may affect Medicaid eligibility.

   c. The RN, Physician/PA/NP and SC confer. Consultation and recommendation for ensuring compliance with the

Clozaril/Clozapine treatment regimen over vacation are documented by the SC.

d. The RN phones the Clozaril REMS at (844) 267-8678.

e. The SC obtains from the individual/guardian separate Authorizations to Exchange Information for the participating CTS(s) allowing the RN/SC to communicate specific Clozaril/Clozapine treatment information.

f. To obtain authorization for out-of-state pharmacy coverage, the RN phones appropriate Health Care Plan.

g. The following information will need to be provided to the representative of the Health Plan:

1) Out-of-state physician's name and telephone number;

2) Out-of-state pharmacy's name and telephone number;

3) The dosage that the individual is taking;

4) Dates of service while the individual is out-of-state/town;

5) And, if available, the prescription numbers.

h. The Health Plan's Office of Prior Authorization will call the out-of-state pharmacy directly to authorize coverage.

i. Obtaining out-of-state laboratory services while the individual is covered by Michigan Medicaid does not require prior authorization. The laboratory must be willing to accept Michigan Medicaid as full payment. If not, the individual may need to pay the full amount or the difference of the cost of the required laboratory services. The individual may also attempt to find another laboratory willing to accept Michigan Medicaid. The laboratory bills Michigan Medicaid directly. The contact phone number is (517) 335-5477 and the fax number is (517) 335-5570.

j. If the individual is indigent, the SC must contact HealthWest Access and obtain authorization for payment of laboratory, pharmacy and HealthWest services.

k. The SC/RN shares the plan for out-of-state/town Clozaril/Clozapine services with the individual. The final plan should be available in writing for the individual.

l. The RN must notify the designated clerical staff the Tuesday before the vacation starts in order to change the individual's Clozaril status to "on vacation."

m. The SC/RN is to call the out-of-state/town CTS to confirm that the individual has followed through as arranged. If the individual has not followed through, the SC/RN will attempt to contact the individual.

n. The RN/SC instructs the individual to call the RN or SC immediately if he/she cannot follow through with the plan while on vacation.

o. If appropriate, the RN/SC will assist the individual with developing an alternative plan.

p. Depending on their functioning/compliance level, individuals may be able to set up their own Clozaril/Clozapine travel plans with minimal assistance from staff.

3. Continuing with HealthWest Outpatient CTS while the individual is vacationing (use when this option is easier, or no other CTS is available):

a. Follow Paragraph J above.

b. Locate via long distance phone a medical lab with fax capability in the city in which the individual is going to vacation.

c. Secure the following:

1) Directions to the lab.

2) Hours of operation.

3) Cost of WBC.

4) Fax number.

5) Fee for faxing WBC results to HealthWest.

d. The SC obtains an Authorization to Exchange Information for the participating lab, allowing the Physician/PA/NP/RN/SC to communicate specific Clozaril/Clozapine information.

e. HealthWest Physician/PA/NP or RN phones in an order for a WBC/ANC, gives lab the HealthWest fax number and name of staff to receive the results, and documents this according to Agency policy.

f. The RN/SC shares the plan for out-of-state/town Clozaril/Clozapine services with the individual; the final plan should be available in writing for the individual.

V. ATTACHMENTS:

ATTACHMENT A: RECOMMENDED MONITORING FREQUENCY AND CLINICAL DECISIONS BY ANC LEVEL

## VI. FORMS:

| | |
|---|---|
| M012 | LABORATORY TELEPHONE REPORT |
| C148 | CONSENT FOR USE OF PSYCHOTROPIC MEDICATIONS |
| C153 | CONSENT FORM – PATIENT WITH TARDIVE DYSKINESIA |

# Attachment A

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

## RECOMMENDED MONITORING FREQUENCY AND CLINICAL DECISIONS BY ANC LEVEL

| ANC LEVEL | TREATMENT RECOMMENDATION | ANC MONITORING |
|---|---|---|
| Normal Range for a New Patient<br>GENERAL POPULATION<br>●ANC ≥ 1500/µL<br><br>BEN POPULATION<br>●ANC ≥ 1000/µL<br>●Obtain at least two baseline ANC levels before initialing treatment. | ●Initiate treatment<br>●If treatment interrupted:<br><30 days, continue monitoring as before<br>≥30 days, monitor as if new patient.<br><br>●Discontinuation for reasons other than neutropenia. | ●Weekly from initiation to 6 months.<br>●Every 2 weeks from 6 to 12 months.<br>●Monthly after 12 months.<br><br>●See Section 2.4 of the full Prescribing information. |
| Mild Neutropenia<br>(1000 – 1499/µL)* | GENERAL POPULATION<br>●Continue treatment.<br><br>BEN POPULATION<br>●Mild Neutropenia is normal range for BEN population, continue treatment.<br>●Obtain at least 2 baseline ANC levels before initiating treatment.<br><br>●Discontinuation for reasons other than Neutropenia. | GENERAL POPULATION<br>●3 times weekly until ANC ≥ 1500/µL.<br>●Once ANC ≥ 1500/µL return to patient's last "Normal Range" ANC monitoring interval.**<br><br>BEN POPULATION<br>●Weekly from initiation to 6 months.<br>●Every 2 weeks from 6 to 12 months.<br><br>●See Section 2.4 of the full Prescribing information. |
| Moderate Neutropenia<br>(500 – 999/µL)* | GENERAL POPULATION<br>●Recommend hematology consultation.<br>●Interrupt treatment for suspected Clozapine-induced Neutropenia.<br>●Resume treatment once ANC normalizes to ≥ 1000/µL. | GENERAL POPULATION<br>●Daily until ANC ≥ 1000µL, then<br>●3 times weekly until ANC ≥ 1500µL.<br>●Once ANC ≥ 1500µL check ANC weekly for 4 weeks then return to patient's last "Normal Range" ANC monitoring interval.** |
| | BEN POPULATION<br>●Recommend hematology consultation.<br>●Continue treatment. | BEN POPULATION<br>●3 times weekly until ANC ≥ 1000µL or ≥ patient's known baseline.<br>●Once ANC ≥ 1000µL 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<br>(<500/µL)* | GENERAL POPULATION<br>●Recommend hematology consultation.<br>●Interrupt treatment for suspected Clozapine-induced Neutropenia.<br>●Do not rechallenge unless prescriber determines benefits outweigh risks. | GENERAL POPULATION<br>●Daily until ANC ≥ 1000µL<br>●3 times weekly until ANC ≥ 1500µL.<br>●If patient rechallenged, resume treatment as a new patient under "Normal Range* monitoring once ANC ≥ 1500µL. |
| | BEN POPULATION<br>●Recommend hematology consultation.<br>●Interrupt treatment for suspected Clozapine-induced Neutropenia.<br>●Do not rechallenge unless prescriber determines benefits outweigh risks. | BEN POPULATION<br>●Daily until ANC ≥ 500µL.<br>●3 times weekly until ANC ≥ patients established baseline.<br>●If patient rechallenged, resume treatment as a new patient under "Normal Range" monitoring once ANC ≥ 1000/µL or at patient's baseline. |

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.