SECTION 5, CHAPTER 11, POLICY 002-D

ATTACHMENT D – GUIDELINES FOR THE USE OF CLOZAPINE

A. Agency Requirements

1. In order for Clozapine to be utilized in a Yolo County Health and Human Services Agency (HHSA) behavioral health program, the provider shall maintain written policies and procedures for a Clozapine treatment program.

2. HHSA shall maintain guidelines for prescribing and monitoring Clozapine that are consistent with Clozapine REMS (Risk Evaluation and Mitigation Strategy) requirements and guidelines, as part of a Clozapine treatment program.

3. As part of an FDA-mandated program to help healthcare providers ensure the safety of clients on Clozapine, HHSA behavioral health prescribers and clinical nursing staff will participate in the Clozapine REMS (Risk Evaluation and Mitigation Strategy) Program. The Clozapine REMS Program includes the following key program requirements:

a. Prescribers

i. Must certify in the Clozapine REMS Program to prescribe Clozapine.

ii. Must enroll all patients in the Clozapine REMS Program.

iii. Must report client ANC levels to the Clozapine REMS Program for every prescription of Clozapine.

b. Nursing Staff

i. Register with Clozapine REMS Program to obtain certification as a designee for prescribers in order to register clients and enter lab results on Clozapine REMS.

c. Pharmacies

i. Must certify in the Clozapine REMS Program to dispense Clozapine.

ii. Must verify the prescriber is certified and the client is enrolled, prior to dispensing Clozapine.

iii. Must verify ANC is current and acceptable for each client, or the prescriber authorized the continuation of Clozapine treatment by providing the treatment rationale, prior to dispensing Clozapine.

d. Clients

i. Must be enrolled in the Clozapine REMS Program by the prescriber to receive Clozapine.

ii. Must comply with ANC testing requirements.

4. As with all new prescription medications, informed medication consent shall be obtained before initiating treatment with Clozapine. Clients who are to receive Clozapine should be notified of the following in a clearly documented manner:

a. The significant risk of developing agranulocytosis.

b. There is a significant risk of seizure during Clozapine treatment.

c. There is a risk of orthostatic hypotension, especially during the period of initial dose titration.

d. Clozapine will be made available only through the Clozapine REMS Program designed to ensure the required blood monitoring.

e. Weekly blood tests are required for at least the first six (6) months of treatment with Clozapine to monitor for the occurrence of agranulocytosis and neutropenia. Adjustments in frequency may be considered later, based upon response and lab results.

f. Clients are to immediately report the appearance of lethargy, weakness, fever, sore throat, malaise, mucous membrane ulceration or other possible signs of infection.

g. Clients are to avoid driving and any other potentially hazardous activity while beginning Clozapine until its effect on the client is known.

h. If a client stops taking Clozapine for more than two (2) days, the client should not start their medication at the same dosage, and should contact their physician for further instructions.

i. Clients should notify their physician if they are taking, or plan to take, any prescription or over-the-counter medications, drugs, or alcohol.

j. Clients should notify their physician if they become pregnant, or intend to become pregnant, during their therapy.

k. Clients should not breastfeed an infant if they are taking Clozapine.

5. HHSA behavioral health nursing staff will offer monthly Clozaril clinics to meet with those clients taking Clozapine in order to review lab results, side effects, compliance, and response.

6. HHSA behavioral health prescribers will follow-up with their clients prescribed Clozapine every one to three months, depending on titration and monitoring schedule. Clients will have more frequent follow-up with the prescriber when initiating Clozapine.

B. Prescribing Standards

1. HHSA prescribers must follow the complete manufacturer's recommendations and full prescribing information on Clozapine found on the current package insert.

2. **Indications for Clozapine Treatment**

   a. The client meets the DSM-V criteria for the diagnosis of Schizophrenia or Schizoaffective Disorder.

   b. The client has had at least two drug treatment trials, each with a different standard antipsychotic drug product, and carried out at an adequate dose for an adequate duration.

   c. The client is unable to achieve recommended antipsychotic dosages on other medication due to intolerable effects.

3. **Contraindications for Clozapine Treatment**

   a. History of serious hypersensitivity to clozapine or any other component of clozapine tablets.

   b. History of drug-induced blood dyscrasia.

   c. Severe debilitation.

   d. Uncontrolled seizure disorder.

   e. White blood cell count of less than 3500 per mm^3.

   f. History of myeloproliferative disorder.

4. **Reinstitution of Clozapine**

   a. Clozapine therapy may not be reinstituted in any client who has had a drop in white blood cell count below 3000 cells of granulocyte count below 1500 cells.

5. **Pre-Clozapine Work-up**

   a. Physical examination within the past 30 days.

   b. Blood pressure, supine and standing (orthostatic blood pressure).

   c. Oral temperature.

d. Pulse.

e. Electrocardiogram (EKG) within the past six months.

f. Hematologic measurements: Complete Blood Count (CBC) with differential, Comprehensive Metabolic Panel (CMP), Liver Function Tests (LFTs), and thyroid function tests.

g. Pregnancy test for females and, if indicated, appropriate contraceptives prescribed.

h. Check history of HIV testing.

6. Dispensing and Administering Clozapine

a. All procedures required by the manufacturer for physicians and pharmacists are to be followed, including the recommended dosages and titration schedules.

C. Monitoring

1. Laboratory Requirements and Hematologic Effects

a. CBCs with differential are drawn weekly from initiation to six (6) months; every two (2) weeks from 6 to 12 months; then monthly after 12 months.

b. If treatment is interrupted for less than 30 days, continue monitoring as before. If treatment is interrupted for 30 days or longer, monitor as if a new client.

c. If a client has an abnormal absolute neutrophil count (ANC), labs must be re-drawn. HHSA behavioral health prescribers and nursing staff will follow the "Clozapine REMS Monitoring Frequency and Clinical Decisions by ANC Level" chart, located at: https://www.clozapinerems.com/CpmgClozapineUI/rems/pdf/resources/ANC_Table.pdf

2. Other Effects

a. Clients vital signs should be closely monitored during initial titration periods and with dosage changes, and at each Clozaril clinic.

b. CMPs, LFTs, and thyroid tests should be repeated after six (6) months, twelve (12) months, and then annually.

c. In many cases, there may be a transition period during which Clozapine is increased and another antipsychotic is decreased. Prescribers should monitor clients closely and document the cross-titration.

d. Antidepressants should be prescribed only as a result of clear evidence of a major depression.

e. Immuno-suppressants should not be used with Clozapine.