**SUMMARY**

**Goals**
- No interruption clozapine therapy unless absolutely necessary
- Very close monitoring during clozapine initiation, titration, and dose reduction
- Appropriate clozapine titration
- Adequate therapeutic trial of clozapine
- Clear identification of primary and secondary clozapine prescribers
- Adherence with required statewide monitoring (using CCHCS/DHCS clozapine patient registry*) for all patients

**ALERTS**
- Fall in Absolute Neutrophil Count (ANC)
- Fever
- Constipation / abdominal pain
- Dizziness / fainting
- Chest pain / dyspnea / fatigue
- Significant tachycardia or arrhythmia
- New or increased seizures
- Eosinophilia

**DIAGNOSTIC CRITERIA/EVALUATION**

**Clozapine Indications**
- Patients who meet DSM-IV TR or DSM V criteria for diagnosis of schizophrenia.
- Patients with refractory schizophrenia or schizoaffective disorder, especially with suicidality or intermittent suicidality.
- Treatment-resistant bipolar disorder which has failed at least 2-3 combinations of antipsychotics, mood stabilizers and other neuroleptics (e.g., lithium, valproic acid, carbamazepine, oxcarbazepine).
- Any significant tardive dyskinesia (pronounced, often permanent, extrapyramidal symptoms).
- Psychosis in those with Parkinson’s disorder for whom quetiapine is not effective or causes too many side effect

**TREATMENT**

**Pretreatment Considerations**
Patients considered for clozapine therapy shall be admitted to a designated CDCR clozapine initiation facility for evaluation, acceptance, and initiation of clozapine treatment. (Currently these institutions are SAC, CMF, SQ, CIW, and CCWF).

Prescriber shall:
- Ensure no contraindications to clozapine.
- Verify baseline ANC ≥1500/μl for general population or ≥1000/μl for patients with Benign Ethnic Neutropenia (BEN)
- Obtain medication informed consent (unless the patient is under PC-2602 [involuntary MH treatment court order]).
- Obtain required baseline monitoring data (see Monitoring page 3).
- Ensure reporting of initial and ongoing ANC to Clozapine Risk Evaluation and Mitigation Strategy (REMS) program.
- Consider prophylactic bowel regimen to prevent potentially serious or life-threatening constipation (see pages 10-12).
- Consider prophylactic anticonvulsant medication in patients with history of seizures who are not currently on anticonvulsant medication. (Carbamazepine should be avoided due to neutropenia risk).
- Place a Medical Hold, as required, for patients on clozapine.

**CLOZAPINE RISK EVALUATION AND MITIGATION STRATEGY (REMS) PROGRAM**
- The Clozapine REMS program is an FDA-mandated program implemented by the manufacturers of
clozapine to provide a centralized point of access for pharmacists and prescribers to minimize the risk of clozapine-associated neutropenia.

- Starting October 12, 2015 prescribers, pharmacies, and patients must be enrolled with this new program for the prescribing, dispensing, and use of clozapine. The Clozapine REMS Program can be accessed at: www.clozapinerems.com or by calling 1-844-267-8678.
- Prior to dispensing clozapine, pharmacies must verify ANC is current and acceptable for each patient or verify the prescriber has authorized continuation of clozapine therapy by providing the treatment rationale for patients with ANC <1000/µL.
- ANC is used exclusively for patient monitoring. WBC counts are no longer accepted by the REMS program, although a prescriber may wish to consider additional monitoring.
- Patients with Benign Ethnic Neutropenia can now be treated with clozapine and have a separate monitoring algorithm.
- Prescribers can continue clozapine treatment for patients with ANC <1000/µL if prescribers believes the benefits of clozapine therapy outweigh the risk of severe neutropenia.
- Patients may be rechallenged with clozapine if the prescriber determines the risk of psychiatric illness is greater than the risk of severe neutropenia.

*CCHCS/DHCS MENTAL HEALTH PATIENT REGISTRY
Go to Lifeline → Health Care Operations → Quality Management → External Links: QM Portal → Patient Registries Header → Mental Health Registry (also named Psychotropic Medication Monitoring Registry) → Clozapine patients identified under CLOZ header.