

# Clozapine Care Guide

February 2022



CALIFORNIA CORRECTIONAL  
HEALTH CARE SERVICES

*Information contained in the Care Guide is not a substitute for a health care professional's clinical judgment. Evaluation and treatment should be tailored to the individual patient and the circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to "Disclaimer Regarding Care Guides" for further clarification. <https://cchcs.ca.gov/clinical-resources/>*

## SUMMARY

### GOALS

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- ✓ Identify patients for whom clozapine is indicated
- ✓ Individualized titration and adequate therapeutic trial
- ✓ Close monitoring during all phases of treatment (using California Correctional Health Care Services/Division of Health Care Services [CCHCS/DHCS] clozapine patient registry)
- ✓ Minimize interruptions in treatment
- ✓ Recognize and manage common and uncommon adverse effects

### ALERTS

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- ◆ Absolute neutrophil count (ANC) < 500/mcL
- ◆ Constipation, particularly with abdominal pain and/or nausea/vomiting
- ◆ Fever in the first 6-8 weeks of treatment
- ◆ Chest pain/dyspnea/fatigue
- ◆ Dizziness or syncope
- ◆ New or increased seizures
- ◆ Acute rise in clozapine plasma level, particularly to  $\geq 1000$  ng/ml

### DIAGNOSTIC CRITERIA

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- Treatment-resistant Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) schizophrenia or schizoaffective disorder
- Treatment-resistance is defined as the failure to respond adequately to at least two antipsychotic trials, one of which consisted of a second-generation or third-generation agent
- A trial consists of treatment with a standard therapeutic dose of an antipsychotic for a duration of at least four to six weeks. Ideally, there should be evidence of medication adherence, e.g., therapeutic plasma drug levels
- Patients with schizophrenia or schizoaffective disorder characterized by persisting suicidality or chronic aggression
- Patients with treatment-resistant or mixed bipolar disorder
- Patients with a tardive syndrome or drug-induced parkinsonism who require on-going treatment with an antipsychotic
- Psychosis in patients with Parkinson's disease
- Primary polydipsia in patients with severe mental illness, particularly if associated with symptomatic hyponatremia (water intoxication)
- Mental disorders, including personality disorders, which include impulsive aggression or violence against others or self
- Patients admitted to California Department of Corrections and Rehabilitation (CDCR) already taking clozapine and who are stable on clozapine should be continued on clozapine

### BASELINE REQUIREMENTS

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- Pretreatment
- Patient Housing and Clozapine Initiation: Clozapine can be utilized in the following settings:
  - Psychiatric Inpatient Programs (PIP)
  - At approved institutions
  - At levels of care and institutions that obtain approval from the Statewide Chief of Psychiatry
- Prescriber Responsibilities:
  - Ensure no contraindications to clozapine (See pages 2-3)

- Obtain medication informed consent unless there is a court order for involuntary medication
  - Register with Clozapine Risk Evaluation and Mitigation Strategy Program (REMS) (See below)
  - Obtain baseline monitoring data (See page 4)
  - Assess bowel function carefully (See pages 13-14)
  - Contact the Primary Care Provider (PCP) to have a Medical Hold placed for patients on clozapine
  - Registration with Clozapine REMS
  - The Clozapine REMS program is an FDA mandated program that provides a centralized point of access for pharmacists and prescribers in order to minimize the risk of clozapine-associated severe neutropenia (ANC < 500/mcL)
  - Prescribers, pharmacies, and patients must be enrolled per the most updated REMS guidelines before prescribing or dispensing clozapine. Go to: [www.clozapinerems.com](http://www.clozapinerems.com) or call 1-844-267-8678
    - The system tracks patients, identifying those who have developed severe neutropenia
    - Patients with Benign Ethnic Neutropenia (BEN) are identified on enrollment allowing application of appropriate ANC monitoring algorithm
  - For terminally ill patients in hospice care, a waiver application can be obtained from and submitted to the REMS program. If approved, ANC and other lab monitoring requirements may be suspended.
- Prior to dispensing clozapine, pharmacies must verify the ANC is current, with appropriate monitoring for the range, or that the prescriber has provided rationale for continuing treatment for general population patients with an ANC < 1000/mcL or rechallenging patients with severe neutropenia.