

### 3.3 PARAMETERS FOR THE USE OF ANTIPSYCHOTIC MEDICATIONS

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#### I. GENERAL PARAMETERS FOR USE

A. **Definition:** Antipsychotic medications in this parameter include:

phenothiazines, haloperidol, thiothixene, loxapine; and selected newer antipsychotic medications: aripiprazole (Abilify), asenapine (Saphris), brexpiprazole (Rexulti), cariprazine (Vraylar), clozapine (Clozaril), iloperidone (Fanapt), lurasidone (Latuda), olanzapine (Zyrex), quetiapine (Seroquel), paliperidone (Invega), risperidone (Risperdal), and ziprasidone (Geodon).

B. **Essential Use:** Antipsychotic medications should almost always be tried in the acute treatment of individuals with a diagnosis of schizophrenia or schizoaffective disorder if positive or negative symptoms are present, or have been present in the last year, and no contraindications to their use exist.

C. **Optional Use:**

1. Antipsychotic medications may be continued in individuals with a diagnosis of schizophrenia or schizoaffective disorder who are asymptomatic for greater than one year if the risks of relapse outweigh the risks and discomfort of medication use.
2. Antipsychotic medications may be tried in individuals with diagnoses other than schizophrenia or schizoaffective disorder in which psychotic symptoms (including negative symptoms) are present.
3. Antipsychotic medications may be used to treat mania in bipolar disorder, manic phase, or mixed type; and prophylactically to decrease the likelihood of developing mania during antidepressant treatment for bipolar disorder, depressed phase; and as prophylaxis against developing further mood episodes for bipolar disorder in partial or complete remission.
4. Specific antipsychotic medications (aripiprazole, brexpiprazole, olanzapine, and quetiapine) may be used to augment a sub-optimal antidepressant response to antidepressant medications when changing the type or dose of the antidepressant is not clinically indicated.
5. Specific antipsychotic medications (aripiprazole and risperidone) may be used for the treatment of irritability associated with autistic spectrum disorders.
6. Lurasidone and quetiapine may be used for the treatment of bipolar disorder, depressed phase.

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**II. MULTIPLE CONCURRENT ANTIPSYCHOTIC MEDICATIONS**

- A. Excepting the circumstances described below, when two antipsychotics may be prescribed simultaneously, only one antipsychotic medication should be used at any one time. The reason for concurrent dosing should be well documented in the clinical record.
- B. During brief (= or <90 days) transition from one to another
  - 1. When one of two antipsychotic medications is being used as a sleeping aid, and using the antipsychotic being used as a sleeping aid as monotherapy is poorly tolerated or ineffective for target symptoms.
  - 2. When successive trials of all appropriate monotherapy with available newer antipsychotic medications at appropriate dose and duration have been unsuccessful.
- C. Prior to initiating concurrent treatment with 2 or more newer antipsychotic medications for individuals who have not responded to treatment with single newer antipsychotic medications, a trial of clozapine should be considered and initiated unless there are significant contraindications that have clearly been documented as such in the clinical record.
- D. Whenever 2 or more antipsychotics are prescribed simultaneously, reasons for this polypharmacy and estimated duration should be periodically (at least every 90 days) and fully documented in the clinical record.

**III. SELECTION OF ANTIPSYCHOTIC MEDICATIONS**

- A. Antipsychotic medications should be selected based upon the following:
  - 1. Side effect profiles that appear best suited for a given history and presentation,
  - 2. Contraindication or lack of availability of other antipsychotic medications, and
  - 3. Current stabilization on a particular antipsychotic medication.
- B. No more than six months should elapse before a different antipsychotic medication is tried in individuals whose target symptoms persist and are clinically significant after an adequate dose of a current antipsychotic medication is reached.
- C. An antipsychotic medication with a low incidence of extrapyramidal side effects should be substituted if clinically significant parkinsonism, dystonia, or akathisia is present and cannot be effectively managed by lowering the dose of the current antipsychotic medication, or by adding anti- Parkinsonian agents.
- D. If no contraindications to clozapine are present and the client agrees, it should be substituted in instances in which tardive dyskinesia has occurred, and an ongoing need for further antipsychotic medication use persists.
- E. In cases in which tardive dyskinesia is present and clozapine is contraindicated or refused, and an ongoing need for further antipsychotic medication use persists, another antipsychotic medication with a low incidence of extrapyramidal side effects should be substituted.

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**IV. ADDITIONAL PRECAUTIONS WITH THE USE OF ANTIPSYCHOTIC MEDICATIONS**

- A. **Black Box Warning:** Because of concerns that treatment of older adults with dementia-related psychosis treated with antipsychotic drugs may be at an increased risk of death, the reason for selection and consideration of the risk of these medications in such an individual should be documented in the clinical record.
- B. **Contraindications:** Because of the relatively greater risks of sedation, cardiac arrhythmias, and metabolic disturbances, and the availability of antipsychotics with fewer such risks, chlorpromazine and thioridazine should no longer be used, except in unusual situations that are adequately documented in the clinical record at least every 90 days.

**V. USE OF CLOZAPINE**

- A. **Essential Use:**
  - 1. Clozapine should be tried if symptoms persist and are clinically significant more than 6 months after adequate trials of at least two other newer antipsychotic medications, and there are no contraindications to such treatment.
  - 2. Clozapine should be tried if there is tardive dyskinesia that does not stabilize or reverse with switch to other antipsychotic medications with a low incidence of extrapyramidal side effects.
- B. **Optional Use:** Clozapine may be tried for individuals with psychotic disorders who have persistent suicidal ideation or behaviors that have not been significantly diminished while using other antipsychotic medications.
- C. **Special Considerations:**
  - 1. Clozapine use and clinical documentation should be compliant with FDA mandated standards for registration, linkages, monitoring, and reporting. Please also see section VI. [www.clozapinerems.com](http://www.clozapinerems.com)
  - 2. Program practices should support the proper use of clozapine by:
    - i. Ensuring that program staff participating in clozapine use have a complete understanding of clozapine FDA prescribing and monitoring requirements.
    - ii. Ensuring that clozapine continuation is consistent with Medi-Cal guidelines which require significant improvement if patients are continued on clozapine past 24 weeks. (Clinicians may use the BPRS to document their improvement.)
    - iii. Ensuring that if severe tardive dyskinesia is the reason for initiating clozapine treatment, substantial reduction in AIMS Global Score, with no deterioration in clinical condition, should be recorded to document the rationale of the treatment risk.
    - iv. Meeting the requirements of the clozapine REMS registry.
    - v. Having protocols in place for the review and record keeping of clients approved for clozapine.
    - vi. Using an appropriate informed consent from the client for clozapine, which lists specific risks, and
    - vii. Obtaining the indicated release from the client to share information with the clozapine REMS registry.

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**VI. USE OF LONG ACTING ANTIPSYCHOTIC MEDICATIONS**

**A. Essential Use:**

1. Use of long acting injectable (LAI) antipsychotic medications should be limited to individuals with current non-adherence to antipsychotic medication as reported by client or others, leading to treatment failure as evidenced by hospitalizations, incarceration, or clinical non-response.
2. LAI antipsychotic medications should not be used concurrently with oral antipsychotic medications except during time limited (less than 60 days) switch over from oral to injectable medication.
3. Specific LAI antipsychotic medications should be used only within programs that have the capacity to provide the necessary clinical and logistical support required by those medications. They include:
  - viii. Long acting injectable risperidone (Risperdal CONSTA).
  - ix. Support for refrigeration and tracking.
  - x. Olanzapine LAI (Zyprexa Relprevv) not currently on formulary. If used, enrollment in Zyprexa Relprevv Risk Evaluation and Mitigation Strategy (REMS) registration and monitoring program for post injection delirium/sedation (PDSS) syndrome.  
<https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm>

**B. When prescribing Long Acting Injectable (LAI) Risperidone (Consta), the following guidelines should be used:**

1. The program site should have compliant refrigeration capacity. The refrigerator should be in a secured, locked area (e.g., medication room) and used only for medications. Note: the temperature should be monitored. Risperdal Consta is stable outside of refrigeration for a period of 7 days. Unused dosages may be used for other clients as long as the client is approved for using Consta.
2. The program site should have arrangements for delivery of Consta by a Pharmacy compliant with refrigeration requirements. Consta should be delivered under cold storage, in an ice chest.
3. If a client is insured, the program should confirm that health plan will cover the cost of medication.
4. The client should be prescribed oral risperidone **ONLY** (no other antipsychotic in addition to Consta) during the period of initiation. Also, once the client is stable on Consta, (3 weeks) no additional antipsychotic be given, with the exception of short term oral risperidone when the Consta dosage increased is anticipated.
5. Reasons for use include either of the following:
  - i. Current non-adherence to newer antipsychotic medication as reported by the client or another, leading to treatment failure as evidenced by hospitalizations, incarceration, or clinical non-response.
  - ii. For a client stabilized on decanoate antipsychotic medication (haloperidol or fluphenazine), when there is ongoing evidence of likely non-adherence with oral medication and/or treatment recommendations and the risk of tardive dyskinesia outweighs the risks of destabilization by the medication switch.

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**VII. ANTIPSYCHOTIC DOSAGES**

- A. The lowest effective dose of antipsychotic medication should be used in order to promote comfort and safety and to minimize the risks of EPS, tardive dyskinesia, and other untoward effects.
- B. An adequate trial with a daily dose within the usual range for a specific antipsychotic medication should be attempted before using higher doses. Use of higher doses should be associated with appropriately increased monitoring of target symptoms and untoward effects and should not be continued for longer than 90 days in the absence of clinical improvement.
- C. **Clozapine:** An adequate trial with a daily dose (after titration) between 150 and 600 mg. should be attempted before using higher doses. Doses above 900 mg. daily have not been shown to be clearly more effective and, therefore, should be used only after obtaining a clozapine plasma level that establishes compliance, and documentation of rationale and estimated duration of trial. [ClozapineREMS.com](http://ClozapineREMS.com)
- D. **Olanzapine:** An adequate trial with a daily dose between 10 and 20 mg. should be attempted before using higher doses. Doses above 40 mg. daily have not been shown to be clearly more effective and, therefore, should not be used without documentation of rationale and estimated duration of trial. Olanzapine should not be used to treat dementia-related psychosis in older adults due to a higher reported incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, in this population.
- E. **Quetiapine:** An adequate trial with a daily dose between 150 and 800 mg. should be attempted before using higher doses. Doses above 900 mg. daily have not been shown to be clearly more effective and, therefore, should not be used without documentation of rationale and estimated duration of trial. Quetiapine should not be used solely for the purpose of sedation, in the absence of other indications.
- F. **Risperidone:** An adequate trial with a daily dose between 2 and 6 mg. should be attempted before using higher doses. Doses above 12 mg. daily have not been shown to be clearly more effective and, therefore, should not be used without documentation of rationale and estimated duration of trial.
- G. **Ziprasidone:** An adequate trial with a dose of 40 mg. b.i.d. should be attempted before using higher doses. Doses above 80 mg. b.i.d. have not been shown to be clearly more effective and therefore require clinical documentation of reasoning. Safety above 100 mg. b.i.d. has not been established and such use, therefore, requires additional justification.
- H. **Aripiprazole:** An adequate trial with a daily dose between 10 and 20 mg. should be attempted before using higher doses. Doses above 30 mg. daily have not been shown to be clearly more effective and, therefore, should not be used without documentation of rationale and estimated duration of trial.
- I. **Asenapine:** An adequate trial of 5mg. sublingually b.i.d. for schizophrenia and 10 mg. sublingually for bipolar disorders should be attempted before using higher dosages.

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- J. **Iloperidone:** Iloperidone should be initiated only when antipsychotic medications with a side effect profile with lower incidence of prolongation of the QTc are contraindicated or not effective. An adequate trial of 6-12 mg. b.i.d. should be attempted before using higher dosages.
- K. **Lurasidone:** An adequate trial with a daily dose of between 40 and 160 mg. for schizophrenia or 20-120 mg. for bipolar disorder should be attempted before using higher dosages.

**VIII. GENERAL HEALTH-RELATED ASSESSMENT AND MONITORING FOR INDIVIDUALS RECEIVING ANTIPSYCHOTIC MEDICATIONS**

Antipsychotic medication should be initiated and maintained only in circumstances that permit adequate general health-related assessment and monitoring that is consistent with DMH Parameters, [3.7 General Health-Related Monitoring, Consultation and Interventions](#)

**IX. NON-ADHERENCE WITH ANTIPSYCHOTIC MEDICATIONS**

- A. Assessment and interventions for non-adherence with antipsychotic medication involve clinical, social, and ethical considerations, and should involve close collaboration between the clinician, the individual being prescribed antipsychotic medication, and family and other involved individuals.
- B. In situations in which individuals are non-adherent with assessment and monitoring recommendations, continued treatment with antipsychotic medications should be consistent with DMH Parameters for Non-Adherence: Medication Non- Compliance.