Antipsychotic Treatment Practice Guidelines

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Policy

It is the policy of the San Bernardino County (County) of Department of Behavioral Health to establish practice guidelines for the use of antipsychotic medications in the provision of client treatment.

Purpose

The DBH Antipsychotic Treatment Practice Guidelines are intended to provide guidance for providers, to increase the effectiveness and safety of antipsychotics use. These Guidelines are not intended to be comprehensive in scope and are not a substitute for clinical judgment. In making decisions about client care physicians must carefully consider the clinical characteristics and circumstances of each individual.

Treatment Principles

The following are treatment principles for the use of antipsychotic medications in client treatment when clinically appropriate:

1. **Use the Lowest Effective Dosage:** Antipsychotic medications should be prescribed and titrated to clinical efficacy or patient tolerance based on side effects, according to dosing guidelines, before concluding that a particular antipsychotic medication is ineffective. In order to minimize side effects, the lowest effective dose of antipsychotic medication should be utilized. In a few cases the most effective dose for a particular patient may be outside the FDA approved range. Some medication doses need to be lowered based on patient characteristics such as renal or hepatic impairment. Obtaining antipsychotic serum levels may be useful in guiding dosing, especially when patients seem to be non-responsive to typically efficacious doses of medication.
2. **Limit Antipsychotic Polypharmacy:** Use of more than one antipsychotic medication in a patient may sometimes be needed for acute stabilization of a condition. However, concurrent use of more than one antipsychotic medication for maintenance therapy should be avoided. Whenever it is clinically determined that a patient requires use of more than one antipsychotic medication for their condition, the clinical rationale should be clearly documented in the medical record.
3. **Treat for an Adequate Duration:** Antipsychotic medication should be prescribed for a sufficient time period (at least 6 weeks)—and at an adequate dosage (dose that is at least in the middle of the FDA approved range), before concluding that a particular antipsychotic medication is ineffective.

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Treatment Principles, continued

4. **Monitor for Side Effects:** All antipsychotic medications have the potential for side effects. Sometimes the side effects are severe and may lead a patient to self-discontinue the medication. Psychiatric providers should routinely assess for side effects from antipsychotic medication. In particular, regular close monitoring for metabolic side effects for second generation antipsychotics and neurological side effects (especially involuntary movements) for first generation medications is strongly encouraged. Completion of AIMS assessment annually is recommended for all patients on an antipsychotic medication.
5. **Monitor for Adherence:** Providers and patients tend to overestimate adherence rates for oral medications. Adequate adherence with oral psychopharmacotherapy should be assessed prior to concluding that a particular antipsychotic medication is not efficacious in a patient. Monitoring antipsychotic serum levels, using pill counts, and collateral report are some of the most effective means of adherence assessment. Due to high rates of non-adherence, the use of long-acting injecting antipsychotic medications should be considered and discussed with all patients diagnosed with schizophrenia or schizoaffective disorder.
6. **Monitor for Treatment Resistance:** Patients with schizophrenia or schizoaffective disorder who have failed two (2) or more adequate trials of antipsychotic medications have treatment-resistant schizophrenia. A trial of clozapine should be considered and discussed with all patients with treatment resistant schizophrenia or schizoaffective disorder. A trial of clozapine should be considered and discussed with all patients with schizophrenia or schizoaffective disorder who are at risk of suicide or exhibit suicidal thoughts or behaviors.

Diagnoses and Disorders

The following outlines the diagnoses and indications for prescribing antipsychotic medications:

1. **Schizophrenia and Schizophrenia Spectrum Disorders:** positive and negative psychotic symptoms.
2. **Bipolar Disorder:** mania, depression, with psychotic features, augmentation of antidepressant.
3. **Major Depressive Disorder:** depression with psychotic features, augmentation of antidepressant.
4. **Unspecified Psychosis:** overt psychotic symptoms.
5. **Psychosis Secondary to General Medical Condition:** psychotic symptoms related to underlying physical illness.

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Diagnoses and Disorders, continued

6. **Psychosis Secondary to Substance Use Disorder**: psychotic symptoms secondary to acute or chronic use of psychoactive substances.
7. **Autistic Spectrum Disorder:** psychotic symptoms and behaviors related to primary diagnosis.
8. **Delirium:** for shortest duration to control acute psychotic symptoms.
9. **Dementia:** as last resort for control of psychotic symptoms impacting quality of life after all behavioral interventions have documented failure.
10. **Treatment of Acute Psychomotor Agitation:** which may be present in any of the above conditions.

Antipsychotic Medications and Dosing

The following tables provide guidelines for usual dose ranges for maintenance of non-hospitalized patients (total dose per 24 hours, unless otherwise noted). Note that some medications require dosing at more frequent dosing intervals than once daily. Also note that dose ranges vary depending on the indication and patient characteristics (age, renal/hepatic impairment, other factors).

Checking antipsychotic serum levels (12-hour trough levels) can be helpful in guiding dosing, determining medication adherence, and when to decide that a patient has reached the 'point of futility' with treatment of a certain antipsychotic (i.e., that further dose increases of a medication are unlikely to produce any additional benefit).

To calculate the *expected* 12-hour antipsychotic trough level for patients taking all or most of their antipsychotic medication at bedtime multiply the prescribed dose by the Concentration-Dose Relationship factor. This will yield the *expected* serum level for that particular antipsychotic medication and dose. Due to wide population variation in metabolism, an initial low serum level may *not* indicate poor adherence. A second data point on the same dose will be of significant help in differentiating kinetic and adherence issues. Up to 30% variability in serum level in the same patient is expected. However, If a patient's antipsychotic dose is unchanged, but a >50% variability in serum levels is seen between two (2) separate serum levels, it is likely that the patient is not consistently adherent to their medication regimen.

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Antipsychotic Medications and Dosing, continued

Table 1 - FIRST GENERATION (TYPICAL, CONVENTIONAL ANTIPSYCHOTICS)

Medication	Daily Dosage Range	Oral Concentration-Dose Relationship	Therapeutic Threshold (ng/mL)	Point of Futility (ng/ml)
Chlorpromazine (Thorazine)	50 - 800 mg	0.06	3 - 30	100
Fluphenazine (Prolixin)	5 - 20 mg	Smoker 0.06; Non-smoker 0.08-0.10	1.0	4.0
Haloperidol (Haldol)	5 - 20 mg	0.78	2.0	18
Loxapine (Loxitane)	20 - 100 mg	0.22	3.8	18.4
Perphenazine (Trilafon)	8 - 24 mg	CYP 2D6 EM: 0.04; CYP 2D6 PM: 0.08	0.81	5.0
Pimozide (Orap)	0.5 - 10 mg			
Thioridazine (Mellaril)	50 - 800 mg			
Thiothixene (Navane)	5 - 30 mg	Smoker: 0.04; Non-smoker: 0.05	1.0	12
Trifluoperazine (Stelazine)	2 - 20 mg		1.0	2.3

EM: Extensive Metabolizer; PM: Poor metabolizer. Serum level data from Meyer and Stahl, The Clinical Use of Antipsychotic Plasma Levels, Cambridge Press, 2021.

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Antipsychotic Medications and Dosing, continued

Table 2 - SECOND GENERATION (ATYPICAL ANTIPSYCHOTICS)

Medication	Daily Dosage Range	Oral Concentration -Dose Relationship	Therapeutic Threshold (ng/mL)	Point of Futility (ng/ml)
Aripiprazole (Abilify)	2 - 30 mg	11.0	110	500
Asenapine (Saphris)	5 - 20 mg	5 mg BID: 0.15; 10 mg BID: 0.20	1.0	(Based on maximal licensed dose of 10 mg BID)
Asenapine (Secuado)	3.8 - 7.6 mg (patch)	0.53	1.0	(Based on maximal licensed dose of 7.8 mg/24 hours)
Brexpiprazole (Rexulti)	0.5 - 4 mg	CYP 2D6 EM: 18; CYP 2D6 IM: 46	36	(Based on maximal licensed dose of 4 mg QHS)
Cariprazine (Vraylar)	1.5 - 6 mg	1.91	5.6	(Based on maximal licensed dose of 6 mg QHS)
Clozapine (Clozaril)	12.5 - 900 mg	Female Smoker: 0.80; Female Non-smoker: 1.32; Male Smoker: 0.67; Male Non-smoker: 1.08	350	1000
Iloperidone (Fanapt)	12 - 24 mg			
Lumateperone (Caplyta)	42 mg			
Lurasidone (Latuda)	20 - 160 mg	0.18	7.2	(Based on maximal licensed dose of 160 mg QPM with meal)
Olanzapine (Zyprexa)	2.5 - 40 mg	Smoker: 1.43; Non-smoker: 2.0	23	150
Olanzapine/ samidorphan (Lybalvi)	5/10 - 20/10 mg			

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Antipsychotic Medications and Dosing, continued

Table 2 - SECOND GENERATION (ATYPICAL ANTIPSYCHOTICS) (continued),

Medication	Daily Dosage Range	Oral Concentration -Dose Relationship	Therapeutic Threshold (ng/mL)	Point of Futility (ng/ml)
Paliperidone (Invega)	3 - 12 mg	4.09	20	90
Quetiapine (Seroquel)	300 - 800 mg			
Risperidone (Risperdal)	0.5 - 8 mg	7.0 (total rispidone+9 OH)	15 (total rispidone+9 OH)	112 (total rispidone+9 OH)
Ziprasidone (Geodon)	40 - 200 mg			

Table 3 - LONG-ACTING INJECTABLE ANTIPSYCHOTICS

Medication	Dosage Range
Aripiprazole lauroxil (Aristada)	441, 662, or 882 mg q 4 weeks, 882 mg q 6 weeks, 1064 mg q 2 months
Aripiprazole lauroxil (Aristida Initio)	675 mg once at initiation of Aristada
Aripiprazole monohydrate (Abilify Maintena)	300 - 400 mg q 4 weeks
Fluphenazine (Prolixin) decanoate	12.5 - 100 mg q 2 weeks
Haloperidol (Haldol) decanoate	50 - 400 mg per month
Paliperidone palmitate 6-month injection (Invega Hafyera)	1,092 - 1,560 mg q 6 months
Paliperidone palmitate 1-month injection (Invega Sustenna)	39 - 234 mg q 4 weeks
Paliperidone palmitate 3-month injection (Invega Trinza)	273 - 819 mg q 3 months
Risperidone intramuscular injection (Risperdal Consta)	25 - 50 mg q 2 weeks
Risperidone subcutaneous injection (Perseris)	90 - 120 mg q 1 month

Table 4 - TREATMENTS FOR TARDIVE DYSKINESIA

Medication	Daily Dosage Range
Deutetrabenazine	6 - 48 mg
Valbenazine	40 - 80 mg

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Side Effects, Safety Issues and Monitoring

The following outlines common side effects and safety issues associated with antipsychotic medications:

Acute Neurologic Side Effects
All antipsychotics may cause acute neurologic side effects, including akathisia, dystonia, and parkinsonism. Medications with anticholinergic properties may be utilized to counter the acute neurologic adverse effects which can be induced by antipsychotic medications. Anticholinergic medications include amantadine, benztropine, diphenhydramine, and trihexyphenidyl. Chronic use of anticholinergic medications for this indication should be avoided, to avoid occurrence of adverse effect. When clinically necessary, amantadine is the preferred anticholinergic for chronic use., mirtazapine) for the treatment of acute akathisia.

Chronic Neurologic Side Effects
Chronic exposure (3 or more months) to dopamine antagonists, including antipsychotic medications, may lead to tardive disorders, marked primarily by persistent, abnormal involuntary movements that have a delayed onset. The most common tardive disorder is tardive dyskinesia (TD). The Abnormal Involuntary Movement Scale (AIMS) should be administered regularly (at least annually) for detection and monitoring for TD. The occurrence of TD is generally higher in first generation antipsychotic medications than second generation antipsychotics. Clozapine is thought to have the lowest risk of TD amongst all antipsychotic medications. Prevention—by using the minimum effective dose of an antipsychotic medication—remains the most effective way to manage TD. In patients who develop TD, healthcare providers should educate the patient about TD, as well as the benefits and risks of adjustments to the current antipsychotic medication (including discontinuation and change to a different antipsychotic medication), discontinuation of antipsychotic medication altogether, and available treatments that may reduce TD symptoms. . In patients who develop TD and who clinically need to continue antipsychotic medication, a trial of clozapine trial may be warranted. Additionally, in moderate or severe TD, the use of a vesicular monoamine transporter 2 (VMAT2) inhibitor, such as valbenazine or deutetrabenazine, should be considered.

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Side Effects, Safety Issues and Monitoring, continued

Gastrointestinal Side Effects
Constipation may develop due to antipsychotic or anticholinergic medication. Reducing anticholinergic medications, change in antipsychotic, or use of laxative agents should be considered. California Department of State Hospitals constipation protocol is included in Appendix 1.

Pregnancy and Lactation
Studies on the use of antipsychotic medications in pregnant patients is limited. Regarding atypical antipsychotics, available data have not indicated significant teratogenic risks with this class of medications. Regarding typical neuroleptics, studies do not suggest significant teratogenic risks with high or medium potency agents. Some studies suggest a higher risk of congenital malformations following first trimester exposure to low-potency neuroleptics. In 2011, the FDA mandated changes to drug labels for all antipsychotic medications advising that neonates exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. Newborns of patients who took antipsychotic medication in the third trimester may experience withdrawal symptoms. Information regarding the use of antipsychotics in patients who breastfeed is limited, and especially lacking for newer antipsychotic medications. Most antipsychotics are present in breastmilk. Lower potency, typical antipsychotics (such as chlorpromazine) have been associated with sedation and developmental delay in infants who are breastfed. If a patient intends to breastfeed, olanzapine may be considered a preferred option, due to low levels of secretion into breastmilk. Limited data also indicates that the secretion of risperidone and quetiapine in breastmilk is low, and adverse events in the infant appear to be rare. Patients of childbearing age/potential should be counseled on the possible risks associated with fetal exposure to antipsychotic medications, along with the risks of untreated psychiatric illness in pregnant patients, so an informed decision can be made by the patient. Similarly, nursing patients should be counseled on the benefits of antipsychotic treatment, weighed against the possible risks to the infant

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Side Effects, Safety Issues and Monitoring, continued

Metabolic Side Effects
Antipsychotic medications (particularly atypical antipsychotics) are known to increase the risk of metabolic syndrome, including central adiposity, dyslipidemia (in particular elevated triglycerides and reduced HDL cholesterol), high blood glucose, hypertension, and obesity. Healthcare providers should monitor vital signs and labs, including glucose and lipid panel. Providers should educate patients abouts these effects and refer patients to their primary care provider for further assessment and monitoring. Providers may also consider prescribing medications to reduce metabolic side effects.

Hepatic and Renal Impairment
Consult individual medication prescribing information for antipsychotic medication use in individuals with significant hepatic or renal impairments. Antipsychotics are generally not dialyzable.

Physical and Lab Assessment
When prescribing antipsychotic medication, healthcare providers are encouraged to consult the APA Practice Guideline for "Treatment of Patients with Schizophrenia" for suggested physical and laboratory assessments on patients receiving this class of medication.

Endocrine Side Effects
Hyperprolactinemia is a common side effect of antipsychotic medications, especially those with high antagonism of D2 receptors. (e.g., haloperidol, paliperidone, and risperidone). Symptoms can include gynecomastia, galactorrhea, headaches, menstrual irregularities, infertility, and sexual side effects. Prolactin levels should be monitored in patients with new onset symptoms suggesting hyperprolactinemia, and first addressed with dosage reduction, change in antipsychotic medication, or antipsychotic discontinuation. Second-line options include adjunctive use of aripiprazole or use of a dopamine agonist medication.

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Side Effects, Safety Issues and Monitoring, continued

Cardiovascular Side Effects
QTc interval prolongation is a common side effect of antipsychotic medications but is often not clinically significant. In rare cases, however, QTc prolongation may result in ventricular arrhythmia or Torsades de Pointes (TdP). QTc is considered prolonged when >450ms for males and >470ms for females. Several antipsychotics ,including chlorpromazine, haloperidol, pimozide, and thioridazine, have substantial evidence that they prolong the QTc interval and are associated with TdP when used as directed. Cardiology consultation is not routinely indicated when prescribing medications that have the potential to prolong the QTc interval in patients without cardiac risk factors. However, consultation may be considered in patients with known cardiovascular disease and 1 or more risk factors for TdP. Consultation with cardiology should be pursued when a patient has marked QTc prolongation (>500ms), a sudden increase in QTc interval (>60ms), or when a patient is co-administered/co-prescribed multiple medications with high risk of QTc prolongation. In situations where a patient develops new onset cardiac symptoms, such as palpitations, syncope, or dizziness, prompt consultation with cardiology should be pursued.

Suggested Physical and Laboratory Assessments for Patients with Schizophrenia

From APA Practice Guideline for Treatment of Patients With Schizophrenia (2020), the following table outlines the suggested physical and laboratory assessments for patients with schizophrenia:

Assessments to monitor physical status and detect concomitant physical conditions		
	Initial or Baseline Assessment	**Follow-up Assessment**
Vital Signs	Pulse, blood pressure	Pulse, blood pressure, temperature as clinically indicated
Body weight and height	Body weight, height, BMI	BMC every visit for 6 months and at least quarterly thereafter
Hematology	CBC, including ANC	CBC, including ANC if clinically indicated (e.g., patients treated with clozapine)
Blood chemistries	Electrolytes, renal functions tests, liver function tests, TSH	As clinically indicated
Pregnancy	Pregnancy test for women of childbearing potential	

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Suggested Physical and Laboratory Assessments for Patients with Schizophrenia, continued

Assessments to monitor physical status and detect concomitant physical conditions, cont.,		
	Initial or Baseline Assessment	**Follow-up Assessment**
Toxicology	Drug toxicology screen, if clinically indicated	Drug toxicology screen, if clinically indicated
Electrophysiological studies	EEG, if indicated on the basis of neurological examination or history	
Imaging	Brain imaging (CT or MRI, with MRI being preferred), if indicated on the basis of neurological examination or history	
Genetic testing	Chromosomal testing, if indicated on the basis of physical examination or history, including developmental history	
Assessments related to other specific side effects of treatment		
Diabetes	Screening for diabetes risk factors, fasting blood glucose	Fasting blood glucose or hemoglobin A1c at 4 months after initiating a new treatment and at least annual thereafter
Hyperlipidemia	Lipid panel	Lipid panel at 4 months after initiating a new treatment and at least annual thereafter
Metabolic syndrome	Determine whether metabolic syndrome criteria are met	Determine whether metabolic syndrome criteria are met at 4 months after initiating a new treatment and at least annual thereafter
QTc prolongation	ECG before treatment with chlorpromazine, droperidol, iloperidone, pimozide, thioridazine, or ziprasidone or in the presence of cardiac risk factors	ECG with significant change in dose of chlorpromazine, droperidol, iloperidone, pimozide, thioridazine, or ziprasidone or with the addition of other medications that can affect QTc interval in patients with cardiac risk factors or elevated baseline QTc intervals

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Suggested Physical and Laboratory Assessments for Patients with Schizophrenia, continued

Assessments to monitor physical status and detect concomitant physical conditions, cont.,		
Hyperprolactinemia	Screening for symptoms of hyperprolactinemia Prolactin level, if indicated on the basis of clinical history	Screening for symptoms of hyperprolactinemia at each visit until stable, then yearly if treated with an antipsychotic known to increase prolactin Prolactin level, if indicated on the basis of clinical history
Antipsychotic-induced movement disorders	Clinical assessment of akathisia, dystonia, parkinsonism, and other abnormal involuntary movements, including tardive dyskinesia Assessment with structured instrument (e.g., AIMS, DISCUS) if such movements are present	Clinical assessment of akathisia, dystonia, parkinsonism, and other abnormal involuntary movements, including tardive dyskinesia, at each visit Assessment with a structured instrument (e.g., AIMS, DISCUS) at a minimum every 6 months in patients at high risk of tardive dyskinesia and at least every 12 months in other patients as well as if a new onset or exacerbation of preexisting movements is detected at any visit

Use of Clozapine

Clozapine is the most effective medication for treatment-resistant schizophrenia and for schizophrenia-associated suicide prevention. Healthcare providers may refer to the Department of Behavioral Health Clinical Practice Guideline: Clozapine for detailed guidelines on this medication

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Use of Clozapine, continued

A trial of clozapine should be considered:

1. After failure to achieve adequate response to two adequate trials of antipsychotic medications.
2. To reduce suicidal behavior in patients with schizophrenia or schizoaffective disorder.
3. In individuals that are developing tardive disorders.
4. In individuals who are requiring antipsychotic polypharmacy for adequate stabilization.

The essentials of clozapine treatment include:

1. Adequate monitoring of Absolute Neutrophil Count according to the Clozapine Risk Evaluation and Mitigation Strategy (REMS) program.
2. Slow titration to minimize cardiovascular and other side effects including orthostasis and sedation.
3. Treatment with the lowest effective dose to provide adequate symptom reduction.
4. Monitoring of bowel function to prevent treatment related constipation.
5. Monitoring for potential seizures related to clozapine.
6. Monitoring of cardiovascular side effects including myocarditis and cardiomyopathy.
7. Regular monitoring of clozapine and norclozapine serum levels to guide dosing and monitor adherence.
8. Reduction and retitration of clozapine if doses are missed more than 2 consecutive days.
9. Monitoring and treatment of excessive salivation (sialorrhea).
10. Frequent blood chemistry monitoring to detect metabolic related disturbances

Related Policy or Procedure

DBH Standard Practice Manual:

- Antidepressant Prescribing Guidelines (MDS2035)
- Sedative Hypnotics Prescribing Guidelines (MDS2037)
- Mood Stabilizer Prescribing Guidelines (MDS2038)

Reference(s)

APA Practice Guideline for Treatment of Patients With Schizophrenia (2020)

Appendix 1 Antipsychotic Treatment Practice Guidelines: Constipation Management Protocol for Clozapine Treated Patients (or Others on Severely Constipating Medications)

Background

Clozapine treated patients are at significant risk for ileus primarily due to its potent anticholinergic properties.[1] While the average colonic transit time (CTT) in adults is 24 hours, for clozapine treated patients not on laxatives the median CTT is over 4 times longer (110 hours).[2] Even with use of maximal doses of each of the three common classes of laxatives (docusate; osmotic; stimulant) the median CTT remains elevated at 62 hours. This appendix provides evidenced based recommendations for managing medication related constipation.

Note: Citations appear in the form of superscript numbers throughout. The corresponding citations can be found in the *Reference* Section at the end of this Appendix.

Non-pharmacological Interventions [3-5]

The following list outlines nonpharmacological interventions for Clozapine users:

A. Encourage physical activity. Being sedentary promotes constipation. Daily moderate exercise, e.g., walking for 20 minutes, has shown the greatest benefit.
B. Encourage adequate fluid intake. Dehydration increases water resorption from the bowel, thereby hardening stool further. This is especially important during hot summer months.
C. Encourage intake of fruits and vegetables, as adequate dietary fiber promotes bowel regularity.
D. Encourage patients to report any substantial changes in bowel habits, stool consistency or color, blood in the stool, or development of straining, incomplete evacuation, or hard stools.

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Appendix 1 Antipsychotic Treatment Practice Guidelines: Constipation Management Protocol for Clozapine Treated Patients (or Others on Severely Constipating Medications), Continued

Minimize Medication Related Causes of Constipation
6-11

The following list provides guidance for minimizing medications with related causes of constipation:

A. Where feasible, minimize or discontinue anticholinergic medications, as they prolong transit time, promote drying of stool, and increase risks of constipation, fecal impaction, or bowel obstruction. This includes antiparkinsonians (e.g., benztropine, diphenhydramine, trihexyphenidyl), and nonpsychiatric medications (e.g., oxybutynin, tolterodine, darifenacin, solifenacin, trospium, glycopyrrolate). The use of anticholinergic agents with clozapine doubles the ileus risk.
B. **DO NOT USE** bulk laxatives (psyllium). When slowed transit times are present, they may add to constipation mass, risk of fecal impaction and bowel obstruction.
C. **Iron and opioids:** If the patient is not iron deficient or suffering from iron-deficiency anemia, avoid use of iron supplements as they promote constipation. In those with anemia consider holding iron during the initial 4-6 weeks of clozapine titration, and then add back slowly with careful monitoring of bowel habits. Opioids as much as possible should be stopped prior to clozapine initiation as these agents are profoundly constipating.
D. Other medications associated with constipation include antiepileptics, diuretics, calcium channel blockers, cholinolytics, and serotonin antagonists (e.g., antiemetics). The effects of these agents are not as great as for anticholinergics, iron or opioids, but removal or modifying medications where possible may lessen the severity of constipation.

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Appendix 1 Antipsychotic Treatment Practice Guidelines: Constipation Management Protocol for Clozapine Treated Patients (or Others on Severely Constipating Medications), Continued

PRN Recommended Bowel Regimen
12-14

The following steps outline Pro re nata (PRN) Recommended Bowel Regimen:

Step	Treatment Intervention
1.	Applies to anyone with a constipation history or who is started on potentially constipating medications. Give docusate 250 mg BID at the beginning of treatment (e.g., when starting clozapine), with rescue PRN medication (e.g., magnesium citrate 150 ml or magnesium hydroxide 30 ml q two days PRN lack of bowel movement).
2.	If step 1 is not adequate, then add one osmotic laxative, e.g., polyethylene glycol 17 gms qam or lactulose 30 ml BID. Polyethylene glycol 3350 (Miralax) is generally superior to lactulose. (Lactulose is reserved for the treatment of hyperammonemia.)
3.	If steps 1 and 2 are not adequate to alleviate constipation, then add one stimulant laxative. Options include sennosides starting at 17.2 mg qhs (max 34.4 mg BID) or bisacodyl starting at 5 mg qhs (max 30 mg per day).
4.	If steps 1-3 fail to adequately control constipation, then add one secretogogue (see Table 1). If the secretory laxative is effective, it may be possible to taper off the stimulant laxative and then the osmotic laxative.

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Appendix 1 Antipsychotic Treatment Practice Guidelines: Constipation Management Protocol for Clozapine Treated Patients (or Others on Severely Constipating Medications), Continued

Basic Information on Intestinal Secretogogues

Table 1 - Basic Information on Intestinal Secretogogues [15-20]

Name	Mechanism	Staring Dose	Max Dose	Comments
Lubiprostone (Amitiza®)	Prostaglandin E1 analog	8 mcg BID	24 mcg BID	Give with food and water. No drug interactions. (Adverse effects can include nausea, abdominal pain, distention, diarrhea, dehydration, and rectal bleeding.
Linaclotide (Linzess®)	Guanylate cyclase-C agonist	145 mcg qd	290 mcg qd	Give > 30 min before 1st meal. No drug interactions. (Adverse effects can include diarrhea, dehydration, hypokalemia, and rectal bleeding.)
Plecanatide (Trulance®)	Guanylate cyclase-C agonist	3 mg qd	3 mg qd	No drug interactions. (Adverse effects can include diarrhea, dehydration, hypokalemia, and rectal bleeding.)
Prucalopride (Motegrity®)	5HT4 agonist	2 mg qd	2 mg qd	No drug interactions. (Adverse effects can include headache, abdominal pain, nausea, diarrhea, abdominal distention, dizziness. Monitor for worsening depressive symptoms or emergence of suicidal thoughts/behavior.)

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Appendix 1 Antipsychotic Treatment Practice Guidelines: Constipation Management Protocol for Clozapine Treated Patients (or Others on Severely Constipating Medications), Continued

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Appendix 1 Antipsychotic Treatment Practice Guidelines: Constipation Management Protocol for Clozapine Treated Patients (or Others on Severely Constipating Medications), Continued

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