SECTION 2

Choosing the Right Neuroleptic for a Patient

F329 Guide to Surveyors – LTC Facilities

(I) Residents who have not used antipsychotic drugs are not given these drugs unless antipsychotic drug therapy is necessary to treat a specific condition as diagnosed and documented in the clinical record; and

(II) Residents who use antipsychotic drugs receive gradual dose reductions, and behavioral interventions, unless clinically contraindicated, in an effort to discontinue these drugs.

Psychosis is a common disorder in the elderly and the symptoms of psychosis may be lessened by antipsychotic medications. Many, i.e., 16% to 25% of all elders, will experience at least one psychotic episode in later life. Common causes of chronic psychosis in the elderly include dementia, depression, delirium, Parkinson's disease, schizophrenia, and manic depressive illness. Psychosis implies failure to distinguish internally generated perceptions from external reality as manifested by symptoms such as hallucinations or delusions. Hallucinations are internally generated sensory perceptions that lack an external sensory stimulus, e.g., hearing voices. These false perceptions often occur in impaired sensory modalities; e.g., auditory hallucinations in a patient with hearing impairment. Delusions are fixed false beliefs with no basis in fact. Delusions commonly include false ideas about stealing, infidelity, abandonment and abuse. Patients often recognize that hallucinations or delusions are unusual ideas and these elders will often deny symptoms. Delusional systems often have fragments of truth embedded in the beliefs. Psychosis requires treatment when symptoms produce patient distress or disruptive behavior. Some psychotic patients do not require medication and this treatment decision requires a careful assessment.

Psychotropic medications are drugs that alter thought, mood, behavior, or intellectual function. Neuroleptics are powerful, mind-altering psychotropic medications and the use of these drugs is carefully monitored by nursing home surveyors. Neuroleptics are divided into two groups: old or first generation, e.g, Haldol, Navane, Mellaril, and new or second generation, i.e., risperidone, olanzapine, quetiapine **(Tables 2-1 and 2-2)**. All old antipsychotic medications block the dopamine (D_2) receptor. New, second generation neuroleptics have a variety of neurochemical actions. Both first and second generation neuroleptics lessen psychotic symptoms in some patients such as hallucinations, delusions, disorganized thought, and symptoms of mania in some patients. There is no way to determine whether a patient will respond to these medications nor can a clinician predict which medication is best for a patient.

Table 2-1. New Antipsychotics and Available Preparations

Generic Name	Brand Name	Tablet	Liquid	Sol-Tab	Injectable
Clozapine	CLOZARIL	✓			
Olanzapine	ZYPREXA	✓		✓	✓
Quetiapine	SEROQUEL	✓			
Risperidone	RISPERIDAL	✓	✓	✓	✓
Ziprasidone	GEODON	✓			✓
Aripiprazole	ABILIFY	✓	✓	✓	✓

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Neuroleptic medications decrease symptoms or improve quality of life in 18% to 37% of symptomatic Alzheimer patients who reside in nursing homes. Most elderly schizophrenics require long-term prescription of these medications to avoid relapse. Implementation of the OBRA regulations resulted in a significant decrease in the use of psychoactive medications in long-term care facilities. OBRA regulations have diminished prescription of psychoactive medications as much as 36% but up to half of patients who undergo dose reduction will have significant symptom relapse requiring continued medication. Staff and physician education plays the greatest role in the success of a facility's neuroleptic dose reduction program. The prescription of neuroleptics involves six basic steps: (1) proper resident assessment, (2) determination of potential medication side effects, (3) choice of an appropriate medication, (4) titration to optimal dose, 5) continuous monitoring of clinical efficacy and side effects, and 6) assessment for dose reduction. Surveyors will want to see documentation for each step to be assured that appropriate psychopharmacology is employed after behavioral management was considered.

STEP 1: Assessment of Indication for Antipsychotic Therapy. The precise target symptoms for the medication should be defined and documented. Not all "psychotic" symptoms require medication. Hallucinations and delusions should not be treated unless they distress the patient or produce dangerous behaviors. For patients with distressing hallucinations or delusions, neuroleptics may provide significant symptomatic relief and reduction of disruptive behaviors that result from these symptoms. For example, the patient who attempts to flee because voices say that the patient will be killed, or residents who refuse food that they believe is poisoned. Inspectors want to see documentation of specific target symptoms for neuroleptics. Neuroleptic agents do not improve behavioral complications of cognitive deficits like amnesia, aphasia, and apraxia. For example, staff should not medicate a patient who repeats the same question because the resident does not remember the previous answer. Neuroleptic agents are not the first option for agitation, wandering, or disruptiveness. Physicians can sedate patients who pose a serious risk of harm or disrupt the unit after behavioral interventions fail; however, the staff must evaluate the patient and devise a long-term management plan beyond chemical restraints.

The PRN prescription of neuroleptics should be: (1) brief, (2) for specific acute psychiatric problems, or (3) utilized to assess need for increased medication. Patients who receive repeated doses of PRN neuroleptics need re-evaluation. Facilities that use large numbers of PRN medication may need reassessment of their behavior management program. Neuroleptics should not be used as sleeping pills.

STEP 2: Assessment for Side Effects. All antipsychotic medications have side effects. New, second generation medications have fewer side effects than first generation medications. Clinicians should avoid older, first generation neuroleptics in patients with Parkinson's disease, where there is a deficiency of brain dopamine.

STEP 3: Prescription of Appropriate Medication. The second generation antipsychotic medications should be used unless the clinician has a specific reason for using older, more toxic medications. The type, dose preparation, and schedule of a neuroleptic should be tailored for each patient. In general, elderly patients require 1/4 the dose of younger patients **(See Tables 2-3 and 2-4)**. The dose should vary according to the size and age of patients as well as other co-existing medical problems. Some side effects may provide a therapeutic advantage **(See Decision Tree 2-5 on Page 8)**.

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For example, psychotic patients who do not sleep at night can receive sedating neuroleptics at the hour of sleep to help them rest and also lessen their psychotic symptoms. Patients with progressive agitation in the afternoon or early evening; i.e., sundowning, can receive their first dose of medication one-hour before the symptoms generally commence, e.g., 4pm, and then a second dose later in the evening to help them sleep. Patients who struggle in the morning with activities of daily living (ADL's) can receive a small amount of medication upon awakening to help calm them for the ADL's. Clinicians should avoid polypharmacy and use one neuroleptic at a time. Do not add sedating drugs like Vistaril or Ativan to help "augment the neuroleptic." Depot preparations, e.g., Haldol decanoate, are injections that maintain blood levels for two or three weeks. Depot preparations can be used in severely non-compliant patients.

The availability of multiple new atypical antipsychotic medications provides clinicians with a broader range of choices for treating the psychotic patient. Six new "atypical" medications include ziprasidone, aripiprazole, clozapine, risperidone, olanzapine, and quetiapine **(See Table 2-2).** Clozapine can produce significant hematological and neurological complications, including aplastic anemia, seizures and severe orthostatic hypertension.

Table 2-2. Summary of Common Doses of Antipsychotic Medications Prescribed for Younger and Elderly Populations with Dementia*

Drug	Healthy/Adult Daily Dose	Frail/Elderly Daily Dose	Maximum OBRA Dose	Major Advisory
1st Generation				
Chlorpromazine	25-1000mg	10-200mg	75mg	Anticholinergic Side Effects
Thioridazine	25-500mg	10-250mg	75mg	Blackbox Cardiac Warning
Haloperidol	1.0-30mg	0.5-5.0mg	4mg	High potential for EPS/TD
Fluphenazine	1-20mg	1-5mg	4mg	High potential for EPS/TD
2nd Generation				
Clozapine	100-600mg	25-300mg		Black Box for Agranulocytosis
Risperidone	1-4mg	0.25-2.0mg	2mg	Dose-related EPS
Olanzapine	5-20mg	2.5-10mg	10mg	Sedation and Metabolic Issues
Quetiapine	25-800mg	25-200mg	200mg	Sedation and Hypotension Possible
Ziprasidone	20-160mg	20-80mg	NA	Cardiac QTc Warning
Aripiprazole	5-30mg	5-20mg	NA	Akathisia and/or withdrawal Dyskinesia Possible

***All drugs have an FDA Black Box warning for increased mortality in AD patients**

DOSAGE MUST BE ADJUSTED FOR EACH PATIENT

CONSENT PDR

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Primary care physicians should avoid the use of clozapine unless continuing mediation prescribed by a psychiatrist or under extraordinary circumstances **(Table 2-3).** Large studies are not available on the use of ziprasidone in the elderly and this medication has some potential to produce cardiac arrhythmias. Clinicians should consider common side effects including sedation, extrapyramidal motor symptoms, falls, and autonomic changes before prescription of all antipsychotics.

Risperidone and quetiapine are two, second generation drugs commonly prescribed by primary care clinicians. Risperidone is effective in elderly demented patients to a maximum dose of 2mg per day and works as well as old antipsychotics like Haldol. Risperidone can produce mild to moderate extrapyramidal symptoms including Parkinsonism and akathisia **(See Table 3-1)**. Risperidone provides good reduction of psychosis with minimal sedation. Seroquel is an antipsychotic that

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produces more sedation than olanzapine or risperidone but has the fewest extrapyramidal side effects. Seroquel functions like a low potency typical neuroleptic, e.g., Mellaril, which produces sedation and orthostatic hypotension. Seroquel or olanzapine can be used to treat Parkinsonian patients who exhibit psychotic symptoms. Most new medications have rapid onset but Olanzapine has a moderately long half life. Risperidone has an active metabolite that can accumulate in patients with poor renal function. Olanzapine is a second generation antipsychotic that is effective in many psychiatric disorders. Olanzapine may produce fewer extrapyramidal symptoms than risperidone but some patients can develop sedation or orthostatic hypotension. The smallest dose, i.e., 2.5mg, is sometimes high for some frail elders although this problem can be managed by dosing every other day **(See Table 2-2).**

Table 2-3. A Partial Summary of Common Side Effects Produced by Antipsychotic Medications in Persons with Dementia

Category of Side Effect	Symptom of Side Effect	First Generation Antipsychotic Medications at Greater Risk	Risk Level	Second Generation Antipsychotic Medications at Greater Risk	Risk Level	Comments for All Types of Medications
COGNITIVE	Confusion	Low Potency, e.g., chloropromazine	H	All equal	L	All medications at high dose
	Sedation	Low Potency, e.g., chloropromazine	H	Quetiapine	L	All medications at high dose
NEUROLOGICAL	Parkinsonism	High potency haloperidol	H	Risperdal	L	Quetiapine quite low
	Dystonia	High potency haloperidol	H	All equal	R	
	Tardive Dyskinesia	All Medications	H	All equal	I	
	Akathisia	High potency, e.g., haloperidol	H	Aripiprazole	I	
METABOLIC	Obesity	Some reported in all medications	M	Olanzapine and Clozapine	M	Monitor Weight
	Hyperglycemia	Some reported in all medications	M	Olanzapine and Clozapine	M	Aripiprazole and ziprasidone with low risk
	Dyslipidemia	Some reported in all medications	I, M	Clozapine	M	Monitor lipids with all medications
AUTONOMIC	Orthostatic hypotension	Low potency, e.g., chloropromazine	H	Seroquel, Clozapine	L	---
	Tachychardia	Low potency	I	Clozapine	L	---
NEUROLEPTIC MALIGNANT SYNDROME	Hypertension, Tachycardia, Hypothermia, Muscular Rigidity	All high potency, e.g., haloperidol	L	All equal	R	Rare in second generation medications
OTHER (drug-specific)	Cardiac QTc Prolongation	thioridazine	H	Ziprasidone	I	Most have minimal effect
	Agranulocytosis	All equal	L	Clozapine only	H	---
BLACK BOX	Black box for ↑ mortality in elderly with dementia	All Medications	L	All Medications	L	All drugs have a Black Box warning

H=high M=moderate L=low R=rare I=Inconclusive

Risperidone is available as a liquid while Olanzapine, risperidone and aripiprazole are available as wafers that dissolve on the tongue (**See Table 1).** These preparations are beneficial to non-compliant patients or residents with swallowing disorders. Cost is a significant issue, as the second generation antipsychotics are substantially more expensive than older medications.

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Some patients with chronic mental illness, e.g., schizophrenia, require long-acting, injectable medications like the depot preparations of Haldol and Prolixin. These intra-muscular preparations are safe in the elderly but all older medications can produce side effects **(See Table 2-4).**

Table 2-4. Summary of Injectable, Long-Acting Preparation (Depot Preparations) of Antipsychotic Medications for the Adult Patient with Dementia (Dosing Range in Milligrams – Given Every 2 Weeks)

Intramuscular Medication	IM Dose for Frail/Elderly (mg)	IM Dose for Young Healthy (mg)
Haloperidol (Haldol decanoate) *every two weeks*	12.5 to 25	12.5 to 75
Perphenazine (Prolixin decanoate) *every two weeks*	2.5 to 25	12.5 to 50
Risperdal Consta – *every two weeks*	25	25 to 50
Dose frequency may be increased with longer duration between injections, e.g., every 3 to 4 months.		

DOSING MUST BE ADJUSTED FOR EACH PATIENT

Step 4: Titration to Optimal Dose. The dosage of neuroleptics must be titrated upward until the desired clinical improvement is present or the patient develops unacceptable side effects. Dose adjustments should occur every one or two weeks to allow the patient to reach steady state. Psychotic symptoms usually improve over a 4-6 week period after reaching optimal doses. Clinicians should become familiar with the second generation medications as well as one high-potency, first generation medication, e.g., Haldol. First generation, low dose antipsychotics such as Mellaril or Thorazine, can produce significant side effects. The use of a limited formulary improves the clinician's knowledge about specific medications or side effects and simplifies the formulary for nursing staff **(See Tables 2-1 and 2-2).** Although the older medications are cheaper, clinicians should begin therapy with new antipsychotics.

The licensed professionals on the team must assess the effect of the medication on target symptoms every one to two weeks during dose titration. Nursing assistants should be encouraged to record behavioral observations on a daily basis. Physicians should review the effect of the antipsychotic medication every two to four weeks and dose titration should not occur more often than once a week to allow the patient to reach steady-state. Neuroleptics usually require two to six weeks to lessen psychotic symptoms. The starting and maximum doses vary by diagnosis, patient's body size, and medical morbidity. Frail dementia patients require low doses while healthy schizophrenics require more substantial doses.

Typical starting doses for demented patients include risperidone 0.25 to 0.5mgm per day and Seroquel 25-50mg per day. Maximum doses typically include risperidone 2mg per day and Zyprexa 10mg per day. Stable asymptomatic patients should be considered for dose reduction every 6 months. Serum

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levels are available to assess absorption and compliance, but blood levels do correlate to clinical improvement **(See Tables 2-3 and 2-4).**

STEP 5: Monitoring for Compliance Effectiveness and Safety.

Staff should assess clinical improvement produced by psychotropic medication. The resident should demonstrate reduction of target symptoms, improvement of behavior or enhanced quality of life. Medication should be changed or discontinued when the patient fails to improve after a reasonable time, e.g., six weeks to six months.

Some patients may not respond to the first prescribed medication. Clinicians should first determine whether adequate doses were prescribed and whether the patient took the medication. Psychotic patients frequently refuse or "cheek" medications, i.e., hold medications in mouth and later spit out the drugs. Mouth checks require a resident to open their mouth after swallowing medications for examination by staff. Liquid preparations are more difficult to check-- especially when followed by large amounts of juices. Clinicians must determine whether the old symptoms persist, e.g., hallucinations, or the staff has new additional problems they want corrected with medication, e.g., hallucinations improve but the patient still wanders. Intercurrent medical problems, e.g., UTI or environmental changes, may explain "therapy resistance". When the psychotic symptoms persist despite adequate doses, the clinician should consider switching to another new, second generation medication, e.g., switch from risperidone to olanzapine. Patients should be placed on old antipsychotics when the new medications have proven ineffective or contraindicated. The concurrent use of two or more antipsychotics is rarely indicated. A specialist should evaluate patients who take two different types of neuroleptics as this therapy constitutes excessive medication under nursing home survey standards. Safety issues are important, especially during the first six months of therapy **(See Table 2-5).**

Table 2-5. Important Side Effects Associated With Antipsychotic Medications In Older Patients with Dementia

Side Effect	Drug	Risk	Data	Ref.
Death	All	Slight	S	T1, T2
Stroke	All, but higher in old meds.	Slight	C	T3
Pulmonary embolism	All	Slight	C	T5
Hyperpro-lactinemia osteoporosis	Old > new	Unclear	C	T6, T7

Old=first generation S=substantial data C=controversial

Example of a Basic Neuroleptic Note: CASE #1. Mr. Jones has Alzheimer's disease with hallucinations and delusions. He becomes agitated every afternoon and attempts to flee because he claims the staff is "going to kill him." He is often up all night. Evaluation of the patient shows no medical cause for his symptoms. Patient has no orthostatic hypotension or excessive drowsiness. Behavioral management has failed to control problem.

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Plan: Patient will receive Seroquel 25mgm at 2 o'clock in the afternoon and 25mg at hs. Recreational therapist will program activities late in the afternoon or early evening. Clinical effect will be assessed in two weeks. Family was advised of potential side effects, including FDA Black Box warning. Family agrees that risk is worth potential benefit.

CASE #2. Ms. Brown has Alzheimer's disease and she is convinced that the staff is poisoning her. She will occasionally refuse to eat and bathe. Evaluation of the patient shows no medical causes for the delusion and no evidence of extrapyramidal symptoms. Behavioral interventions fail to improve compliance. Patient will receive 0.25mg of risperidone qhs for 14 days and then 0.5mg hs at day 15. Staff will reassess in one month for possible upward titration to a total of 2mg per day. Staff will distract patient when she begins to discuss delusional ideas; avoid arguing with Ms. Brown. Family was advised about potential risks, including FDA Black Box warning. Family agrees to medication.

These facilities are following the Ten Commandments of OBRA.

Ten Commandments of OBRA For Psychotropic Medication

1. Thou shalt know thy regulations.
2. Thou shalt not prescribe medications from the list of the condemned drugs.
3. Thou shalt first try behavioral management.
4. Thou shalt document clinical indications and target symptoms.
5. Thou shalt honor the dose limits unless documented in the medical record.
6. Thou shalt honor the time limits on prescriptions unless documented in the chart.
7. Thou shalt monitor for side effects.
8. Thou shalt reduce or discontinue medications for adverse events.
9. Thou shalt comply with periodic dose reductions unless documented in thine record.
10. Thou shalt not seek to smite the surveyor. They are simply carrying the tablets.

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Decision Tree 2-6. Prescription of Antipsychotic Medications

Does the patient have appropriate diagnosis and target symptoms?

Yes ↓ No → Avoid antipsychotics

Will the patient comply with oral medications?

Yes ↓ No → Consider:
- Zydys or Risperdal M-tabs
- Liquid forms
- Injectable forms for emergencies
- Depot typical neuroleptics, e.g., Risperdal Consta

(See Table 2-4)

Does the patient manifest symptoms of Parkinsonism or DLBD?

Consider: ← Yes ↓ No → Consider any new antipsychotic
- Quetiapine

Is the patient diabetic?

Consider aripiprazole ← Yes ↓ No → Consider any new antipsychotic

Carefully monitor blood sugars

Is sedation a benefit or problem?

Consider risperidone ← Problem ↓ Benefit → Consider quetiapine

Is there significant concern about abnormal QTc?

Avoid ziprasidone, thioridazine ← Yes ↓ No → Consider any medication

Did the medication improve symptoms? → **NO.** Switch to next best choice or discontinue

↓

YES. Re-evaluate every 6 months for dose reduction

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