ANTIPSYCHOTICS AGENTS – CONVENTIONAL

A. FDA approved indications

1. Psychotic Disorder (Haloperidol, Thiothixene)
2. Schizophrenia
3. Bipolar Disorder, Manic (Chlorpromazine)
4. Severe Behavioral Problems in children 6mo-12yo (Chlorpromazine)
5. Severe Behavioral Problems (Chlorpromazine, Haloperidol)
6. Tourette’s Syndrome (Haloperidol, Pimozide)
7. Delirium (Haloperidol)
8. Hyperactive Behavior, Short-term Treatment (Haloperidol)

B. Non-FDA approved, commonly used indications

1. Agitation
2. Augmentation in refractory obsessive compulsive disorder
3. Pervasive developmental disorders
4. Impulse control disorder
5. Other neurological conditions (e.g. ALS, Huntington’s)

C. Minimal documentation

1. All standard outpatient & inpatient requirements
2. Document rationale for use of a conventional neuroleptic, in lieu of an atypical agent, given the increased risk of tardive dyskinesia
3. Document rationale for use of mesoridazine or thioridazine in lieu of another antipsychotic medication, given the increased risk for cardiac arrhythmia

D. Maximum Dosage – see Medication Summary for MDD

E. Duration

1. For Outpatient: Document rationale when making any drug switch.
2. For Inpatient: Document rational when making more than 3 changes in any 7-day period.
F. Polypharmacy & Drug Interactions

1. Adequate medication doses should be used over a sufficient period of time to obtain desired results before polypharmacy is introduced.
2. Use of more than one antipsychotic agent for any period greater than 90 days is discouraged.
3. If using >1 antipsychotic is necessary, provide clear supportive rationale for adding the second antipsychotic.

G. Serious adverse effects

1. **Black Box Warning for Mesoridazine and Thioridazine:**
   Mesoridazine Besylate and Thioridazine hydrochloride have been shown to prolong the QTc interval in a dose related manner, and drugs with this potential, including thioridazine hydrochloride, have been associated with torsades de pointes-type arrhythmias and sudden death. Due to its potential for significant, possibly life-threatening, proarrhythmic effects, thioridazine hydrochloride should be reserved for use in the treatment of schizophrenic patients who fail to show an acceptable response to adequate courses of treatment with other antipsychotic drugs, either because of insufficient effectiveness or the inability to achieve an effective dose due to intolerable adverse effects from those drugs.

2. Neuroleptic malignant syndrome (signs include fever, rigidity, diaphoresis, confusion, tremors, elevated CK)
3. Tardive dyskinesia
4. Acute dystonia
5. Cardiac arrhythmia or significant QTc prolongation on EKG
6. Convulsion
7. Syncope
8. Marked sedation or lethargy
9. Intentional overdose
10. Significant laboratory abnormalities during treatment
H. Standard laboratory and examination requirements

1. Weight and/or body mass index calculation (BMI)
2. Basic laboratory studies on admission (inpatient only)
3. Baseline fasting glucose
4. Lipid panel
5. Document the examination for abnormal movements with the AIMS scale every twelve months
6. ALL patients on Thioridazine, Mesoridazine or Pimozide are required to have Electrocardiogram.
7. All patients on Thioridazine and Mesoridazine are required to have electrolytes panel
8. More frequent and/or additional monitoring should be considered depending on the clinical situation and whenever there is a change in the patient’s status.
9. Low potency FGAs such as: Chlorpromazine, Thioridazine, and mesoridazine, may confer greater risk of metabolic abnormalities compared to mid and high potency agents. Therefore, more frequent monitoring of Fasting Blood Glucose and lipid panel recommended with such agents.
10. There is an increased risk of Luekopenia/neutropenia/agranulocytosis with all antipsychotic agents especially in patients who are concomitantly on other myelosuppresive drugs i.e. CBZ and VPA. It is recommended to monitor more closely by ordering more frequent CBC with differentials.

I. Relative contraindications (requires documentation of justification)

1. History of allergy to this class of drugs
2. Myocardial infarction within 6 weeks
3. History of tardive dyskinesia
4. History of cardiac arrhythmia or cardiac conduction disorder or congenital QTc prolongation (thioridazine or mesoridazine)
5. Age less than 5 years (age 3 for haloperidol, age 2 for thioridazine)
6. History of neuroleptic malignant syndrome

J. Precautions

1. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death (Black-Box Warning)
2. Use with caution in the elderly, in the presence of cardiovascular disease, chronic respiratory disorder, hypoglycemia, and convulsive disorders
3. Use with caution in patients with known or suspected liver disease. In such patients, monitor transaminases more frequently
4. Should be used very cautiously in patients with narrow angle glaucoma or prostatic hypertrophy. May lead to urinary retention
5. Cigarette smoking is reported to induce the metabolism and decrease the plasma level of certain antipsychotics i.e. Olanzapine and Clozapine
6. Concomitant use of Phenothiazine and Clozapine should be approached with caution because both are metabolized by cytochrome P450 2D6. Lower doses may be required than previously prescribed for either Clozapine or Phenothiazine.
7. Abrupt cessation of high doses may cause discontinuation syndrome with gastritis, nausea, vomiting, dizziness, tremors, feelings of warmth or cold, sweating, tachycardia, headache, and insomnia
8. May cause confusion, poor concentration and disorientation at high dose or in the elderly
9. Thioridazine taken at larger than recommended doses can cause pigmentary retinopathy, which is characterized by diminution of visual acuity, brownish coloring of vision, and impairment of night vision.
10. Lower seizure threshold
11. Increased risk of EPS (dystonias, dyskinesias, akathisia, pseudoparkinsonism, perioral tremor, “rabbit syndrome”) with the high potency antipsychotics agents.
12. Tardive dyskinesia
13. Constipation, urinary retention
14. Hypotension
15. EKG changes (T wave inversion, ST segment depression, QTc lengthening) may increase risk for arrhythmias. Electrolyte abnormalities including hypokalemia
16. Hypomagnesemia and hypocalcemia can contribute to the development of torsades de pointes
17. Sudden deaths of patients on antipsychotics is probably due to arrhythmias (rare)
18. Low potency agents confer greater risk of metabolic abnormality
19. Neuroleptic malignant syndrome – rare disorder characterized by muscular rigidity, tachycardia,
hyperthermia, altered consciousness, autonomic dysfunction, and increases in CPK—can occur with any class of antipsychotic agent, at any dose, and at anytime (increased risk in hot weather). Other risk factors include polypharmacy, organic brain syndromes, mood disorders, dehydration, low serum sodium, exhaustion, and agitation.

20. Pregnancy Category and Nursing mother: See Table 1: Adverse Drug Effects and Pregnancy Categories, Nursing Mother

Attachments:
Table 1: Adverse Drug Effects and Pregnancy Categories, Nursing Mother
Table 2: Drug Formulations
Table 3: Dosage Equivalency Table

References:

- APA 2004 Practice Guideline for the Treatment of Patients With Schizophrenia
- WWW.Epocrates.com
- WWW.MicroMedix.com
- Package Insert for involved medications
- J Clin Psychiatry 2003;64 (Suppl 12)
### Table 1: Adverse Effect Profile, Pregnancy Categories, and Nursing Mother

<table>
<thead>
<tr>
<th>Potency</th>
<th>Anticholinergic Effects</th>
<th>Sedation</th>
<th>Orthostatic Hypotension</th>
<th>EPS Es</th>
<th>Pregnancy Category (PC)/Nursing Mother (NM)</th>
</tr>
</thead>
</table>
| Chlorpromazine | Low | +++ | +++ | +++ | ++ | PC: Unknown  
| | | | | | | NM: Infant risk can not be ruled out |
| Fluphenazine | High | + | + | + | +++ | PC: Unknown  
| | | | | | | NM: Avoid breastfeeding |
| Haloperidol | High | + | + | + | +++ | PC: C  
| | | | | | | NM: Infant risk can not be ruled out |
| Loxapine | Moderate | ++ | ++ | + | +++ | PC: C  
| | | | | | | NM: Infant risk can not be ruled out |
| Mesoridazine | Low | ++++ | +++ | +++ | ++ | PC: C  
| | | | | | | NM: Infant risk can not be ruled out |
| Molindone | Moderate | ++ | ++ | + | +++ | PC: C  
| | | | | | | NM: Infant risk can not be ruled out |
| Perphenazine | Moderate | ++ | ++ | + | +++ | PC: Unknown  
| | | | | | | NM: Infant risk can not be ruled out |
| Pimozide | High | + | + | + | +++ | PC: C  
| | | | | | | NM: Infant risk can not be ruled out |
| Thioridazine | Low | ++++ | +++ | +++ | ++ | PC: Unknown  
| | | | | | | NM: Infant risk can not be ruled out |
| Thiothixene | High | ++ | ++ | + | +++ | PC: C  
| | | | | | | NM: Infant risk can not be ruled out |
| Trifluoperazine | High | ++ | ++ | + | +++ | PC: Unknown  
| | | | | | | NM: Infant risk can not be ruled out |

Key: (1) the more “+” a drug has, the more pronounced the adverse effect.  (2) PC: C means “Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.”

*Potency is defined as:*

**References:**


(2) Micromedex

Rev. 2/29/12 MT
# Table 2: Drug Formulations

<table>
<thead>
<tr>
<th>Drug</th>
<th>Tablets (T) or capsule (C)</th>
<th>Oral solution/syrup</th>
<th>Rectal Suppository</th>
<th>Depot (mg/ml)</th>
<th>IM (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>C: 30, 75, 150, 200 T: 10, 25, 50, 100, 200 ER: 30, 75, 150, 200</td>
<td>Sln: 30mg/ml, 100 mg/ml Syr: 10mg/5ml</td>
<td>25, 100</td>
<td>25, 100</td>
<td>25</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>T: 1, 2.5, 5, 10</td>
<td>Elix: 2.5mg/5ml, 5mg/ml</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>T: .5, 1, 2, 5, 10, 20</td>
<td></td>
<td>25, 100</td>
<td>25, 100</td>
<td>25</td>
</tr>
<tr>
<td>Haloperidol dec</td>
<td></td>
<td></td>
<td>50, 100</td>
<td>50, 100</td>
<td>50</td>
</tr>
<tr>
<td>Loxapine</td>
<td>C: 5, 10, 25, 50</td>
<td>25 mg/ml</td>
<td>50, 100</td>
<td>50, 100</td>
<td>50</td>
</tr>
<tr>
<td>Mesoridazine</td>
<td>T: 10, 25, 50, 100</td>
<td>25 mg/ml</td>
<td>50, 100</td>
<td>50, 100</td>
<td>25</td>
</tr>
<tr>
<td>Molindone</td>
<td>T: 5, 10, 25, 50, 100</td>
<td>20 mg/ml</td>
<td>50, 100</td>
<td>50, 100</td>
<td>50</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>T: 2, 4, 8, 16</td>
<td>16 mg/5ml</td>
<td>5, 10</td>
<td>5, 10</td>
<td>5</td>
</tr>
<tr>
<td>Pimozide</td>
<td>T: 1, 2</td>
<td></td>
<td>5, 10</td>
<td>5, 10</td>
<td>5</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>T: 10, 15, 25, 50, 100, 150, 200</td>
<td>30 mg/ml, 100 mg/ml</td>
<td>20, 100</td>
<td>20, 100</td>
<td>20</td>
</tr>
<tr>
<td>Thiothixene</td>
<td>C: 1, 2, 5, 10, 20</td>
<td></td>
<td></td>
<td>20, 100</td>
<td>20</td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>T: 1, 2, 5, 10</td>
<td>10 mg/ml</td>
<td>20, 100</td>
<td>20, 100</td>
<td>20</td>
</tr>
</tbody>
</table>

Reference: Micromedex
**Guideline 2: Adequate Dose of Antipsychotics**

We asked the experts to write-in doses of conventional and atypical antipsychotics that they would recommend in different treatment situations. We used the mean and standard deviations of their responses to generate real-world doses rounded to currently available pill strengths. The experts' dosing recommendations generally agree closely with recommended doses given in the package labeling. For olanzapine and quetiapine, their recommendations for highest acute dose are somewhat higher than the highest doses for which safety data from clinical trials are available (20 mg of olanzapine and 800 mg of quetiapine). The panel would generally use higher doses for a patient who had had multiple episodes of psychosis than for a first-episode patient. The recommended dose ranges for maintenance treatment are also slightly lower than for acute treatment.

<table>
<thead>
<tr>
<th>Medication</th>
<th>First-episode patient</th>
<th>Multi-episode patient</th>
<th>Highest final acute dose (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute treatment (mg/day)*</td>
<td>Maintenance treatment (mg/day)</td>
<td>Acute treatment (mg/day)*</td>
</tr>
<tr>
<td><strong>Atypicals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>300–500</td>
<td>250–500</td>
<td>400–600</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>10–20</td>
<td>10–20</td>
<td>15–25</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>350–700</td>
<td>300–600</td>
<td>500–800</td>
</tr>
<tr>
<td>Risperidone</td>
<td>2.5–5.0</td>
<td>2.0–4.5</td>
<td>4.0–6.5</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>100–160</td>
<td>80–160</td>
<td>140–180</td>
</tr>
<tr>
<td><strong>Conventional</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>200–650</td>
<td>150–600</td>
<td>400–800</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>2.5–15.0</td>
<td>2.5–12.5</td>
<td>5.0–22.5</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>3.0–13.5</td>
<td>1.5–10.5</td>
<td>7.0–18.5</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>8–38</td>
<td>6–36</td>
<td>16–48</td>
</tr>
<tr>
<td>Thiothixene‡</td>
<td>225–550</td>
<td>150–500</td>
<td>350–650</td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>5–30</td>
<td>2–30</td>
<td>10–40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluphenazine decanoate (mg/2–3 wk)</td>
<td>12.5–37.5</td>
<td>6.25–37.5</td>
<td>12.5–62.5</td>
</tr>
<tr>
<td>Haloperidol decanoate (mg/4 wk)</td>
<td>50–200</td>
<td>50–200</td>
<td>100–250</td>
</tr>
</tbody>
</table>

*In beginning treatment with an oral antipsychotic for which titration is not required or with a long-acting injectable antipsychotic, the experts recommend starting with a low dose and increasing the dose based on level of response and side effects, or starting with a moderate dose. The experts do not recommend starting with a relatively high dose and then decreasing it if possible.*

†Safety of doses of olanzapine > 20 mg/day and of quetiapine > 800 mg/day have not been evaluated in clinical trials.

‡The package labeling for thoridazine includes a black box warning stating that this agent "has been shown to prolong the QTc interval in a dose related manner, and drugs with this potential, including thoridazine, have been associated with torsades de pointes-type arrhythmias and sudden death. Due to its potential for significant, possibly life-threatening, proarrhythmic effects, thioridazine should be reserved for use in the treatment of schizophrenic patients who fail to show an acceptable response to adequate courses of treatment with other antipsychotic drugs."

**J Clin Psychiatry 2003;64 (suppl 12)**

Table 3: Dosage Equivalency Table