ANTIPSYCHOTICS AGENTS – CONVENTIONAL

A. FDA approved indications (Documentation Required)

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, Chlorpromazine)
9. Acute agitation associated with schizophrenia or Bipolar I disorder in adults (Inhaled Loxapine (Adasuve®))

B. Non-FDA approved, commonly used indications (Documentation Required)

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 (Documentation Required)

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 (Documentation Required)

1. When considering addition of more than one agent within a class, it is recommended to first titrate the initial agent to maximum tolerated dose; then provide clear supportive rationale for the additional agent(s).
2. When changing medications, a process of cross-tapering is recommended and may require up to 90 days to accomplish. If polypharmacy is necessary beyond the maximum period of 90 days to complete the cross-tapering, clear documentation of the rationale for continuation of the polypharmacy is necessary.

G. Standard laboratory and examination requirements (Documentation Required)

1. No FGA is entirely free of weight gain and related metabolic effects. The potential morbidity of these symptoms has led to recommendations for baseline and routine monitoring of weight, waist circumference, blood pressure, fasting glucose and lipid profile.

   Low potency FGAs such as: Chlorpromazine, Thoridazine, 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.

2. Basic laboratory studies on admission (inpatient only)

3. Document the Extrapyramidal Syndrome:
   Monitoring via an appropriate scale is required AT MINIMUM AT BASELINE AND ANNUALLY. Depending on the symptoms presented; AIMS, BARS OR SIMSON-ANGUS SCALE (SAS) MAY BE USED WHEN ANTICHOLINERGICS ARE USED.

4. ALL patients on Thoridazine, Mesoridazine or Pimozide are required to have Electrocardiogram.

5. All patients on Thoridazine and Mesoridazine are required to have electrolytes panel

6. 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.

7. There is an increased risk of Leukopenia/neutropenia/agranulocytosis with all antipsychotic agents especially in patients who are concomitantly on other myelosuppressive drugs i.e. CBZ and VPA. It is recommended to monitor more closely by ordering more frequent CBC with differentials.

H. Black Box Warning:

1. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death

2. Inhaled Loxapine can cause bronchospasm which may lead to respiratory distress and arrest. There is must be administered in an enrolled facility that can manage acute bronchospasm.
I. Warnings and Precautions (Documentation Required):

1. History of QT Interval prolongation and sudden death. Increased risk of sudden death likely due to QT interval prolongation is associated with exposure to any antipsychotic drug. Among FGAs, Thioridazine, and IV Haloperidol are known to be more likely to prolong the QT interval, with Pimozide posing an intermediate level of risk. 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. History of 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 any time (increased risk in hot weather). Other risk factors include polypharmacy, organic brain syndromes, mood disorders, dehydration, low serum sodium, exhaustion, and agitation.

3. History of Tardive dyskinesia: Anticholinergics worsen TD; therefore, they should be avoided and discontinued if TD develops.

   Extrapyramidal syndrome: When EPS presents:
   A. Reduce the dose if clinically indicated.
   B. Switch to another agent with lower liability to cause EPS.
   C. If 1 &2 above failed or clinically inappropriate, then management with anticholinergics may be initiated at the lowest effective dose for a short duration i.e. three months. It is recommended to taper to discontinuation after the management of acute EPS. This is intended to minimize, polypharmacy, risk of side effects including cognitive impairment and the risk of abuse.

4. History of allergy to this class of drugs
5. Myocardial infarction within 6 weeks
6. Age less than 5 years (age 3 for haloperidol, age 2 for thioridazine)
7. Convulsion
8. Syncope
9. Marked sedation or lethargy
10. Intentional overdose
11. Significant laboratory abnormalities during treatment
12. Use with caution in the elderly, in the presence of cardiovascular disease, chronic respiratory disorder, hypoglycemia, and convulsive disorders
13. Use with caution in patients with known or suspected liver disease. In such patients, monitor transaminases more frequently
14. Should be used very cautiously in patients with narrow angle glaucoma or prostatic hypertrophy. May lead to urinary retention
15. Cigarette smoking is reported to induce the metabolism and decrease the plasm level of certain antipsychotics i.e. Olanzapine and Clozapine
16. 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.

17. 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.

18. May cause confusion, poor concentration and disorientation at high dose or in the elderly.

19. 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.

20. Lower seizure threshold

21. Tardive dyskinesia

22. Constipation, urinary retention

23. Hypotension

24. EKG changes (T wave inversion, ST segment depression, QTc lengthening) may increase risk for arrhythmias. Electrolyte abnormalities including hypokalemia

25. Hypomagnesemia and hypocalcemia can contribute to the development of torsade’s de pointes

26. Sudden deaths of patients on antipsychotics is probably due to arrhythmias (rare)

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

28. Inhaled Loxapine is contraindicated in patients with current DX or h/o asthma, COPD, or other lung disease associated with bronchospasm, patients with acute respiratory sings/symptoms i.e. wheezing or currently using medications to treat airways disease, such as asthma or COPD.

**J. Adverse Effects: (See PI for each drug for a complete list of Adverse Effects)**

**Serious Adverse Effects:**
- Anaphylaxis
- Extrapyramidal symptoms
- Tardive dyskinesia
- Hyperpyrexia
- Heat stroke
- Neuroleptic Malignant syndrome
- Metabolic syndrome
- Hypotension (orthostatic)
- Arrhythmias (QTC prolongation, Torsade’s de pointes, Sudden death)
- Hyponatremia
- Seizure
- Hepatic impairment
- Leukopenia
- Neutropenia
- Agranulocytosis
- Cataracts
- Retinopathy
- Withdrawal symptoms (with high dose long-term use)

Common Adverse Effects:
- Drowsiness
- Dizziness
- Constipation
- Urinary retention
- Blurred vision
- Confusion
- Lethargy
- Xerostomia
- Hyperprolactinemia (Gynecomastia, galactorrhea)
- Sexual adverse effects
- Akathisia
- Tachycardia
- Insomnia
- Photosensitivity

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

References:
- UpToDate 2018: First-generation antipsychotic medications: Pharmacology, administration, and comparative side effects
- 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</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
### 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</td>
<td>Sln: 30mg/ml, 100 mg/ml</td>
<td>25, 100</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T: 10, 25, 50, 100, 200</td>
<td>Syr: 10mg/5ml</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ER: 30, 75, 150, 200</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>T: 1, 2.5, 5, 10</td>
<td>Elix: 2.5mg/5ml, 5mg/ml</td>
<td></td>
<td></td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>Fluphenazine dec</td>
<td></td>
<td></td>
<td>25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Haloperidol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T: .5, 1, 2, 5, 10, 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol dec</td>
<td></td>
<td></td>
<td></td>
<td>50, 100</td>
<td></td>
</tr>
<tr>
<td>Loxapine</td>
<td>C: 5, 10, 25, 50</td>
<td>25 mg/ml</td>
<td></td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>Mesoridazine</td>
<td>T: 10, 25, 50, 100</td>
<td>25 mg/ml</td>
<td></td>
<td></td>
<td>25</td>
</tr>
<tr>
<td>Molindone</td>
<td>T: 5, 10, 25, 50, 100</td>
<td>20 mg/ml</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perphenazine</td>
<td>T: 2, 4, 8, 16</td>
<td>16 mg/5ml</td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Pimozide</td>
<td>T: 1, 2</td>
<td></td>
<td></td>
<td></td>
<td></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></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiothixene</td>
<td>C: 1, 2, 5, 10, 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>T: 1, 2, 5, 10</td>
<td>10 mg/ml</td>
<td></td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>

Reference: Micromedex
Psychiatric Pharmacy Essentials: Antipsychotic Dose Equivalents

It is not uncommon that patients may need to be switched from one antipsychotic to another. Chlorpromazine equivalents help guide clinicians in estimating an apprx 1:1 mg dose when switching from one antipsychotic to another.

- How should I convert doses between different antipsychotics? 7

Antipsychotic Dose Equivalents (based on chlorpromazine)

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Dose Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Generation Antipsychotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>&quot;Thorazine&quot;</td>
<td>100 mg</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>Prolin</td>
<td>2 mg</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Haloperidol</td>
<td>2 mg</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>Levomepromazine</td>
<td>10 mg</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>Trilast</td>
<td>8 mg</td>
</tr>
<tr>
<td>Pimozide</td>
<td>Oep</td>
<td>2 mg</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Geotropil</td>
<td>15 mg</td>
</tr>
<tr>
<td>Trizol o p erazine ne</td>
<td>Sela ine</td>
<td>2 mg</td>
</tr>
<tr>
<td>Trilondazine</td>
<td>M ellard</td>
<td>10 mg</td>
</tr>
<tr>
<td>Thiothixone</td>
<td>Navane</td>
<td>4 mg</td>
</tr>
<tr>
<td>Second Generation on Antipsychotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 1969</td>
<td>11B</td>
<td></td>
</tr>
<tr>
<td>Asemapine</td>
<td>Saptrol</td>
<td>4 mg</td>
</tr>
<tr>
<td>, (TRK02bpr azole)</td>
<td>Resperil</td>
<td>NA</td>
</tr>
<tr>
<td>Cariprazine</td>
<td>Vorty</td>
<td>NA</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozaril</td>
<td>10 mg</td>
</tr>
<tr>
<td>Iloperidone</td>
<td>Fallaplic</td>
<td>3g mg'</td>
</tr>
<tr>
<td>Luras idooe</td>
<td>1a toid</td>
<td>16 mg'</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Zyproxa</td>
<td>1 mg</td>
</tr>
<tr>
<td>Palip e tio deve</td>
<td>2g mg'</td>
<td>2 mg</td>
</tr>
<tr>
<td>Ouatapline</td>
<td>5g mg'</td>
<td>75 mg</td>
</tr>
<tr>
<td>Rl par j done</td>
<td>Respendol</td>
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</tr>
<tr>
<td>Ziprasidone</td>
<td>Goodon</td>
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References
