Quick Reference for the Treatment of Acute Agitation

**Goals of pharmacologic therapy of acute agitation:**
- Produce calming effect quickly without excessive sedation
- Provide early treatment of underlying psychosis
- Minimize treatment-related adverse events
- Assure patient and staff safety

**Options for Management of Acute Agitation with Intramuscular Therapy**

**Acute Agitation Requiring Intramuscular Therapy**

- **Psychotic agitation**
  - Acute substance intoxication (alcohol or stimulant)
    - LRZ
    - HLD ± LRZ
    - ZIP

- **Undifferentiated agitation**
  - No concomitant substance intoxication
    - LRZ (DOC)
    - HLD ± LRZ
    - ZIP
    - OLZ

- **Schizophrenia**
  - OLZ
  - ZIP
  - HLD ± LRZ

- **Psychotic depression**
  - OLZ

- **Mania**
  - OLZ
  - ZIP
  - HLD ± LRZ

**Should initial treatment fail to produce an adequate response after 2-4 hours (see table opposite side for dosing frequency), options include:**
- Give another dose of same medication if partially effective, or a different medication if first medication ineffective
- Give a dose of lorazepam if first medication was an antipsychotic
- Give a combination of the same antipsychotic and lorazepam (except olanzapine)

**Table of Options**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Medication Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute substance intoxication (alcohol or stimulant)</td>
<td>LRZ, HLD ± LRZ, ZIP</td>
</tr>
<tr>
<td>No concomitant substance intoxication</td>
<td>LRZ (DOC), HLD ± LRZ, ZIP, OLZ</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>OLZ, ZIP, HLD ± LRZ</td>
</tr>
<tr>
<td>Psychotic depression</td>
<td>OLZ</td>
</tr>
<tr>
<td>Mania</td>
<td>OLZ, ZIP, HLD ± LRZ</td>
</tr>
</tbody>
</table>

**Abbreviations**

- HLD: haloperidol
- LRZ: lorazepam
- OLZ: olanzapine
- ZIP: Ziprasidone
- ARP: Aripiprazole
- DOC: drug of choice
## Comparison of IM Treatment Options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dose</th>
<th>Max Single Dose</th>
<th>Repeat Dosing</th>
<th>Max Adult Dose / 24hrs</th>
<th>Time to Onset (minutes)</th>
<th>Time to Peak Cp (hours)</th>
<th>Half-life (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>1-2mg</td>
<td>4mg</td>
<td>0.5-1 hour</td>
<td>10mg</td>
<td>15</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>5-10mg</td>
<td>10mg</td>
<td>0.5-1 hour</td>
<td>30mg</td>
<td>20-40</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Chlorpromazine*</td>
<td>25-50mg</td>
<td>100mg</td>
<td>1 hour</td>
<td>400mg</td>
<td>15</td>
<td>1-4</td>
<td>6</td>
</tr>
<tr>
<td>Ziprasidone**</td>
<td>10mg</td>
<td>20mg</td>
<td>2 hours</td>
<td>40mg</td>
<td>15-30</td>
<td>30-45</td>
<td>2-5</td>
</tr>
<tr>
<td>Olanzapine**</td>
<td>10mg</td>
<td>10mg</td>
<td>2-4 hours</td>
<td>30mg</td>
<td>20-60</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>9.75mg</td>
<td>15mg</td>
<td>2 hours</td>
<td>30mg</td>
<td>45-60</td>
<td>60-180</td>
<td>75</td>
</tr>
</tbody>
</table>

* IM chlorpromazine is not recommended as an option for the management of acute agitation due to significant risk of QTc prolongation and hypotension in doses required for acute agitation, slow onset of effect, and local irritation at the injection site (NICE guidelines)
** Reconstitution required before administration

## Comparison of Oral Agents for Acute Agitation

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dose</th>
<th>Max Single Dose</th>
<th>Max Adult Dose / 24hrs</th>
<th>Time to Onset (minutes)</th>
<th>Time to Peak Cp (hours)</th>
<th>Half-life (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>1-2mg</td>
<td>4mg</td>
<td>10mg</td>
<td>30-60</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>5-10mg</td>
<td>10mg</td>
<td>40mg</td>
<td>60-120</td>
<td>2-6</td>
<td>20</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>25-50mg</td>
<td>100mg</td>
<td>2000mg</td>
<td>30-60</td>
<td>2.8</td>
<td>30</td>
</tr>
<tr>
<td>Ziprasidone**</td>
<td>20-40mg</td>
<td>40mg</td>
<td>240mg</td>
<td>*</td>
<td>6-8</td>
<td>2-5</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>5-10mg</td>
<td>10mg</td>
<td>30mg</td>
<td>≤ 60</td>
<td>5-8</td>
<td>30</td>
</tr>
<tr>
<td>Olanzapine Zyd</td>
<td>5-10mg</td>
<td>10mg</td>
<td>30mg</td>
<td>*</td>
<td>3-5</td>
<td>75</td>
</tr>
<tr>
<td>Risperidone***</td>
<td>1-2mg</td>
<td>2mg</td>
<td>8mg</td>
<td>*</td>
<td>1-2</td>
<td>1-2</td>
</tr>
</tbody>
</table>

* Not studied as a treatment for acute agitation and aggression
** The absorption of oral ziprasidone is significantly decreased in the absence of a meal (250-500 calories)
*** When given in combination with IM lorazepam
**Acute Agitation Clinical Pearls**

- If appropriate, offer oral medication first. This may help the patient restore some feeling of control and ease escalating agitation.
- Rule-out medical complications as a potential cause of agitation (hyper- or hypoglycemia, electrolyte disturbance, renal or hepatic failure, thyroid or adrenal disorders, Wernicke’s encephalopathy, hypotension, heart failure, neurologic disorders (stroke), meningitis infection (especially in elderly), and dementia).
- Rule-out substance intoxication or withdrawal.
- Rule-out medication causes of acute agitation (steroids, anticholinergics, barbiturates, amphetamines, antipsychotic-induced akathisia).
- Lorazepam is preferred for undifferentiated agitation (provides muscle relaxation, anxiolytic, anticonvulsant effects, and generalized sedation).
- Haloperidol has a relatively low propensity for sedation and hypotension compared with other IM agents; however, it does have a higher incidence of EPS.
- The combination of a benzodiazepine and a typical antipsychotic (i.e., haloperidol) has been shown to be superior to monotherapy with either agent, and may allow for decreased doses of the antipsychotic medication. The combination can cause excessive sedation.
- After treatment with IM agents: monitor vitals and clinical status at regular intervals.
- Allow adequate time for clinical response between doses.
- Use lower starting and maximum doses in the elderly and child and adolescent population.