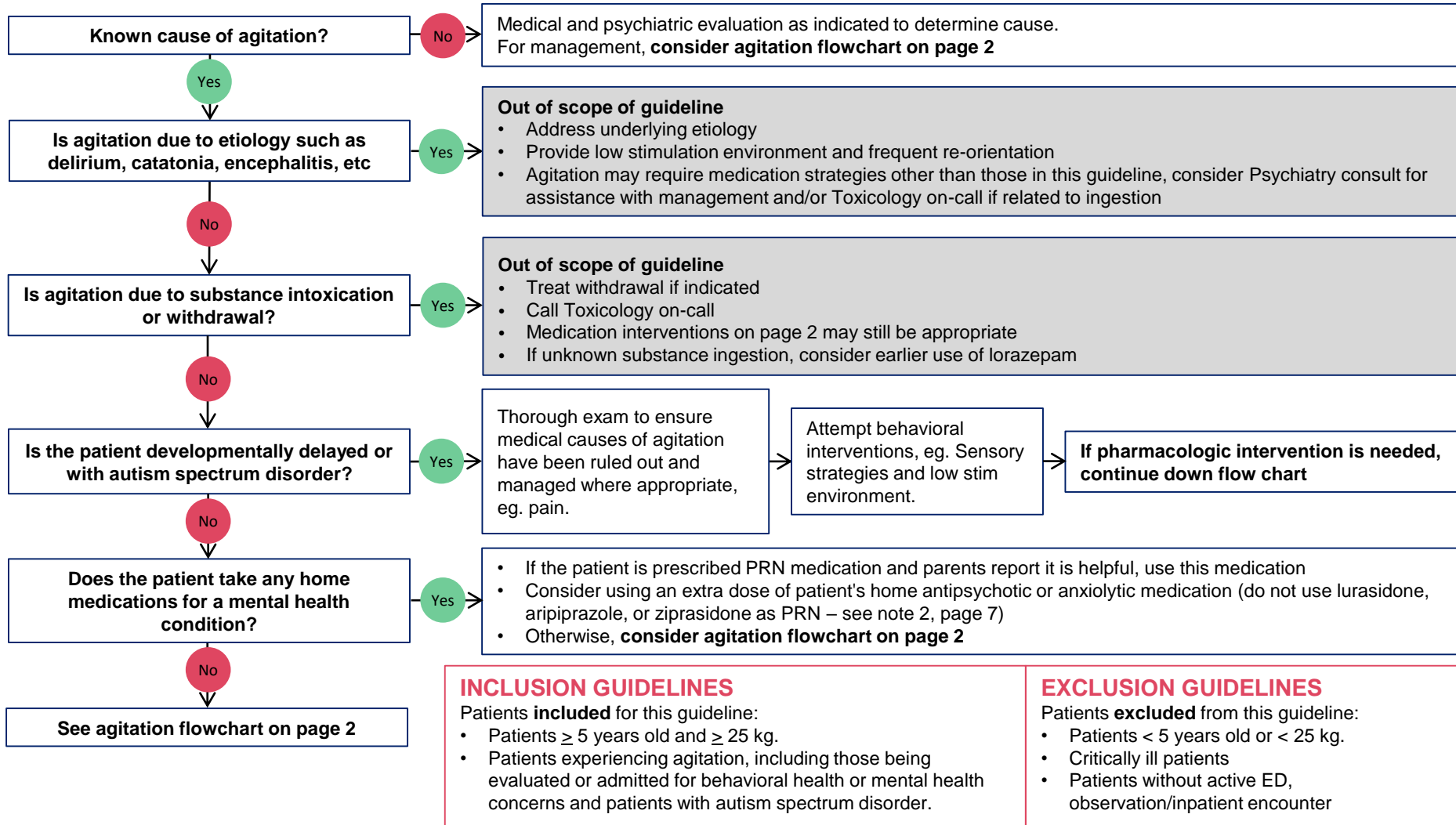


Aim: To standardize pharmacological management of agitation in the hospital setting.

For all patients, treat any underlying medical concerns and attempt nonpharmacologic interventions first whenever safe to do so. Refer to [SOP ED Inpatient - Response to Patients Exhibiting Red Scale Behaviors](#)



Aim: To standardize pharmacological management of agitation in the hospital setting.

Assess level of current agitation

Agitated (Mild Agitation)	Disruptive (Moderate Agitation)	Destructive (Severe Agitation)	Dangerous (Severe Agitation)
<ul style="list-style-type: none"> • Not engaging with others • Pacing • Fidgeting • Rocking 	<ul style="list-style-type: none"> • Engaging others • Yelling • Inappropriate language • Gesturing 	<ul style="list-style-type: none"> • Destroying property • Kicking objects • Throwing objects away from people 	<ul style="list-style-type: none"> • Harmful to oneself and others • Spitting, biting, hitting • Forceful head banging • Scratching that breaks skin • Throwing objects at people • Attempted elopement by a person with imminent risk of danger

Behavioral interventions and offer hydroxyzine*

- Assess and mitigate triggers (e.g., hunger, pain)
- Consider additional de-escalation strategies (note 1, page 7)
- Reassess in <60 minutes, and continue to follow algorithm if not de-escalating
- **See page 3, Note B**

Escalate if not responding to interventions

Offer olanzapine*

- Activate staff duress system if indicated to activate code green (note 3, page 7)
- Continue de-escalation strategies (note 1, page 7)
- Reassess <30 minutes and continue to follow algorithm if not de-escalating.
- **See page 3, Note B**

Escalate if not responding to interventions

Offer olanzapine*

- Activate staff duress system if indicated to activate code green (note 3, page 7)
- Continue de-escalation strategies (note 1, page 7)
- Give IM medication if unable or unwilling to take PO AND behavior is dangerous**
- Reassess <10 minutes and continue to follow algorithm if not de-escalating.
- If possible, give medication >30 minutes for effect before giving additional medication
- **See page 3, Note B**

*These are the recommended first line medications for agitation unless:

- there is a contraindication, such as anticholinergic toxidrome, QTc prolongation, etc
 - see details on page 3, Note A
- the underlying etiology requires a different treatment, such as catatonia, withdrawal etc
 - out of scope of guideline

In these cases, consider Psychiatry consultation for help managing agitation.

See medication table on pages 4-5 for dosing and other considerations

If still escalating or no longer has olanzapine available (page 3, Note C):

- Consider **lorazepam**, especially if concerned for agitated catatonia or if antipsychotics seem to be worsening agitation. *Monitor closely if olanzapine IM and lorazepam IM are given w/in 1 hour due to risk of sedation and respiratory suppression*
- Consider **haloperidol**. Give with diphenhydramine to minimize risk of EPSE/dystonia, though *be mindful of anticholinergic burden*
- **Consider use of **restraints** per Children's policy if needed for safety. This may need to occur before or concurrently with IM medication administration.

Per Children's policy, do NOT use restraints or force IM medication unless patient is at Dangerous level of agitation

Aim: To standardize pharmacological management of agitation in the hospital setting.

Note A: When to consider alternative medication strategies:

- Agitation management in **diagnoses out of scope of this guideline** may require other strategies. Eg. in cases of agitated delirium, encephalitis, substance intoxication or withdrawal, catatonia, etc.
- **If QTc is prolonged**, consider use of benzodiazepines over antipsychotic medication.
- **If patient is prone to EPSE (Extrapyramidal Side Effects)**, use recommended medications, avoid haloperidol or make sure to give with diphenhydramine (note 5, page 7)
- **If patient has anticholinergic side effects** (note 8, page 7), avoid olanzapine, chlorpromazine and antihistamines, favor haloperidol or lorazepam. In this case, do not give diphenhydramine with haloperidol.
- **If antipsychotics seem to be worsening presentation**, consider side effects such as akathisia (note 4, page 7) vs underlying etiologies such as catatonia, encephalitis, delirium and treat appropriately.

Note B: For all patients:

- When an episode of agitation occurs, alert primary provider as soon as able, and plan for next steps if behavioral escalation continues after first-line medications.
- Give time for PRN medication to have effect before re-dosing to avoid over sedation and other side effects. Dosing table has time to peak effect data, but most medications show some effect within 30-60 minutes.
- Typically recommend maximizing dose of one medication before adding another.
- Clearly document *specific* behaviors that indicated use of PRN medication and *response* to PRN medication including behavior and time to calm.
- Monitor for side effects to medications including:
 - Over sedation, respiratory suppression, EPSE (note 5)
 - Paradoxical reaction, disinhibition, and akathisia (note 4), which can all present as worsening agitation
 - Serotonin syndrome (note 6), neuroleptic malignant syndrome (NMS) (note 7) and anticholinergic toxidrome (note 8), which can be serious conditions caused or contributed to by medications used to manage agitation and other psychiatric medications.
- Suggest ordering EKG to assess QTc if taking multiple QT prolong medications at baseline and/or if requiring multiple behavioral PRNs in a 24 hours period
 - See Tables 4-6 on Page 6 for a list of medications that can prolong QT and increase risk for TdP

Note C: When to consider consulting Psychiatry for agitation:

- If this guideline is not adequately managing agitation, Psychiatry can help consider other medication and behavioral strategies.
- If there are concerns or questions about patient's scheduled medication regimen that may be affecting their presentation
- If there are concerns for psychiatric diagnoses such as psychosis, mania, or catatonia or medical etiology underlying agitation that may require other agitation management strategies (as indicated above)

Aim: To standardize pharmacological management of agitation in the hospital setting.

Table 1. Medication Information: Antihistamines and benzodiazepines

Medication & Class	Dosing	Time to peak effect	½ life	Max daily dosing	Side effects	Notes/monitoring
Diphenhydramine <i>Antihistamine</i>	PO/IM: by weight 12.5-50 mg (1 mg/kg/dose) May administer q6-8 hours. For EPSE, may repeat dose after 30 min if no response.	PO: 2 hours	4-8 hours	<50 kg: 50-100 mg ≥50 kg: 100-200 mg	<ul style="list-style-type: none"> - Drowsiness - May have paradoxical reaction - more common in younger and developmentally delayed children 	<p>Avoid in delirium.</p> <p>Can treat EPSE (note 5, page 7) with antipsychotics, especially haloperidol.</p> <p>Be mindful of anticholinergic burden (note 8, page 7).</p>
Hydroxyzine <i>Antihistamine</i>	PO: by age (note 9, page 7) 5-10 yo: 12.5 mg 11-15 yo: 25 mg 16+ yo: 50 mg May administer q6-8 hours.	PO: 2 hours	7 hours	5-10 yo: 50 mg 11-15 yo: 100 mg 16+ yo: 200 mg	<ul style="list-style-type: none"> - Drowsiness - Prolonged QT 	<p>Less anticholinergic than diphenhydramine, still may contribute to risk.</p> <p>Be mindful of co-administration of hydroxyzine and diphenhydramine, only use diphenhydramine after hydroxyzine if treating EPSE.</p>
Lorazepam <i>Benzodiazepine</i>	PO/IV/IM: by weight 0.5-2 mg (0.05 mg- 0.1mg /kg/dose) May administer q4-6 hours. May repeat dose after 1-2 hours not to exceed max daily dose.	PO/IM: 1-2 hours IV: 10 min	17 hours	≤40 kg: 4 mg >40 kg: 6-8 mg, dependent on weight, prior exposure	<ul style="list-style-type: none"> - Drowsiness - Poor coordination, - May cause disinhibition in younger or developmentally delayed youth. 	<p>First line for suspected catatonia.</p> <p>Can be given IM with haloperidol or chlorpromazine.</p> <p>Delayed clearance in hepatic insufficiency.</p> <p>Caution if olanzapine IM and a benzodiazepine IM are given within 1 hour due to risk of excess sedation and respiratory depression. Monitor closely if this occurs. Warning does not apply to PO administration.</p>

Aim: To standardize pharmacological management of agitation in the hospital setting.

Table 2. Medication Information: Antipsychotic agents

Medication & Class	Dosing	Time to peak effect	½ life	Max daily dosing	Side effects (short term)	Notes/monitoring
Olanzapine <i>2nd generation antipsychotic</i>	PO/ODT/IM: by age (note 9, page 7) <11 yo: 2.5mg 11-15 yo: 5mg 16+ yo: 10mg Typically ordered q6-8 hours, may repeat dose after 1-2 hours not to exceed max daily dose	PO: 5 hours (range from 1-8 hours) IM: 15-45 min	37 hours	≤40 kg: 20mg >40 kg: 30mg	<ul style="list-style-type: none"> - Sedation - Orthostatic hypotension - Prolonged QT - EPSE (note 5, page 7) - Anticholinergic side effects - NMS 	<p>Caution if olanzapine IM and a benzodiazepine IM are given within 1 hour due to risk of excess sedation and respiratory depression. Monitor closely if this occurs.</p> <p>Be mindful of anticholinergic burden, and assess for side effects (note 8, page 7).</p> <p>Consider EKG, especially if on multiple QT prolonging medications and no recent EKG is available</p>
Haloperidol <i>1st generation antipsychotic</i>	PO: by weight 0.025-0.075 mg/kg/dose Children: 0.5-2 mg/dose Adolescents: 2-5 mg/dose IM: Start with ½ PO dose May repeat q1-2 hours not to exceed max daily dose	PO: 2 hours IM: 20 min	10-37 hours	≤40 kg: 6 mg >40 kg: 15 mg	<ul style="list-style-type: none"> - Sedation - EPSE (high risk, note 5, page 7) - Sedation - Prolonged QT - Hypotension - NMS 	<p>Give with diphenhydramine to decrease the risk of dystonic reaction unless using d/t concern for anticholinergic toxidrome.</p> <p>Suggest EKG for QT prolongation, especially for parenteral administration.</p> <p>Get temps and assess stiffness twice daily for at least 48 hours after administration. Consider getting CK if giving IM, or if restraints have been utilized.</p>
Chlorpromazine <i>1st generation antipsychotic</i>	PO/IM: by weight 12.5-60 mg (0.55 mg/kg/dose) IM: start with ½ PO dose May administer q4-6 hours	PO: 30-60 mins IM: 15 min	6 hours	≤25 kgs: 40 mg >25 kgs: 75 mg	<ul style="list-style-type: none"> - Sedation - Prolonged QT - EPSE (note 4, page 7) - Hypotension - Anticholinergic side effects - NMS 	<p>Suggest EKG for QT prolongation, especially if on multiple QT prolonging medications.</p> <p>Be mindful of anticholinergic burden and assess for side effects (note 8, page 7).</p> <p>Vs olanzapine – shorter time to peak effect and half-life, may be more sedating, higher risk of cardiac and extrapyramidal side effects</p>

Aim: To standardize pharmacological management of agitation in the hospital setting.

Table 3. Medication Information: Droperidol

Medication & Class	Dosing	Time to effect	½ life	Max daily dosing	Side effects (short term)	Notes/monitoring
Droperidol <i>First generation antipsychotic; Antiemetic</i>	IM/IV in children >= 7yo Weight based: 0.1-0.2 mg/kg/dose Fixed dosing: <34kg: 0.625mg 34-57kg: 1.25mg 58-68kg: 1.875mg >68kg: 2.5mg Max 10 mg/dose May repeat dose in 15-30 mins if no response	Onset: 3-10mins Peak: ~30mins Duration: 2-4 hours, may extend to 12	~1.7 hours	20 mg	<ul style="list-style-type: none"> - Prolonged QT and/or torsades de pointes - Hypotension - Tachycardia - EPSE (note 5, page 7) - NMS 	<p>Due to risk for proarrhythmic effects, droperidol is not recommended in this guideline. It is included here as patients may have received prior to arrival. May consider use if patients fail to show adequate response to other treatments or other medications in this guideline are contraindicated.</p> <p>It is recommended to obtain an ECG prior to use of droperidol or for patients who received droperidol prior to arrival.</p> <p>Do NOT use in patients with prolonged QT.</p> <p>May use with benzodiazepine.</p>

Table 4. Conditional Risk of Torsades de Pointes (TdP)*

These medications are associated with TdP but only under certain circumstances
Diphenhydramine – Use with other QTc Meds, Excessive Dose
Hydroxyzine – Bradycardia, Low K+ or Mg+, Excessive Dose
Olanzapine – Use with other QTc Meds, Low K+ or Mg+
Quetiapine – Bradycardia, Low K+ or Mg+, Excessive Dose, Impaired Drug Elimination
Risperidone – Use with other QTc Meds, Bradycardia, Low K+ or Mg+, High Dose
Ziprasidone – Use with other QTc Meds, Bradycardia, Low K+ or Mg+, Excessive Dose

Table 5. Possible Risk of TdP*

Can cause QT Prolongation, but currently lack evidence for a risk of TdP when taken as recommended
Aripiprazole
Lurasidone
Paliperidone

Table 6. Known Risk of TdP*

Can cause QT Prolongation and are clearly associated with a known risk of TdP, even when taken as recommended
Chlorpromazine
Droperidol
Haloperidol

**This is not a complete list of medications that carry risk of QT prolongation and TDP, many psychiatric and other medications carry this risk. When ordering agitation PRNs, please be mindful of a patient's comorbidities and medication list. In the setting of polypharmacy, electrolyte abnormalities, bradycardia, etc., consider obtaining an EKG prior to ordering QT prolonging medications for agitation.*

Aim: To standardize pharmacological management of agitation in the hospital setting.

Notes:

1. **For de-escalation strategies see** [SOP ED Inpatient - Response to Patients Exhibiting Red Scale Behaviors](#)
2. **Considerations when giving additional doses of home medication.** Additional doses of aripiprazole and lurasidone are unlikely to be acutely helpful. Ziprasidone is also not likely to be acutely helpful and increases risk of prolonged QT. Be mindful of maximum daily dosing of antipsychotics, especially olanzapine.
3. **Staff duress system** is Pinpoint. This should be activated if patient is escalating and nonpharmacologic de-escalation attempts are not being effective, and/or there is a concern for greater resource need to maintain safety for staff and/or patient. This will result in a Code Green Team activation.
4. **Akathisia is a movement side effect that consists of intense restlessness.** It can manifest as an inability to stay seated, intense urge to pace, can also look like restless legs. It may also manifest as a busy mind or anxiety. It is commonly seen with aripiprazole and lurasidone, but all antipsychotics carry risk. If this is driving agitation, consider decreasing use of antipsychotics. Can be symptomatically managed with benzodiazepines or propranolol.
5. **EPSE = Extrapyrimal Side Effects:** Broad category of movement side effects often seen with antipsychotics. Can consist of Parkinsonism, rigidity, akathisia, and dystonia (involuntary contractions of major muscle groups) which can be painful. Diphenhydramine can be used to treat EPSE other than akathisia (see above).
6. **Serotonin Syndrome** also known as serotonin toxicity can range from mild to potentially life-threatening condition characterized by mental status changes, autonomic instability (most commonly fever, tachycardia, hypertension) and neuromuscular excitability (tremor, clonus, rigidity, and/or hyperreflexia). It typically develops quickly (w/in 24 hours) and resolves quickly when treated appropriately. If you suspect serotonin syndrome, discontinue serotonergic medications, provide supportive care, consider benzodiazepines for agitation if needed. Call Toxicology on-call for acute management and consider Psychiatry consult for alternative medication strategies.
7. **Neuroleptic Malignant Syndrome (NMS)** is a neurologic emergency associated with the use of antipsychotic medications and some antiemetics and is characterized by fever, rigidity w/ bradyreflexia, mental status changes, and autonomic instability. It can develop rapidly but typically develops over days to weeks. If you suspect NMS, remove the causative medication as well as other potentially contributing medications (lithium, anticholinergic and serotonergic medications), provide supportive therapy. Consider benzodiazepines for agitation if needed. Consider Toxicology and Psychiatry consults.
8. **Pay attention to anticholinergic burden.** Adding multiple anticholinergic medications increases risk of side effects like urinary retention, constipation/ileus, dry mouth/skin, confusion and delirium. If multiple anticholinergic medications are used, monitor for these and other anticholinergic side effects. If concerned about anticholinergic burden, use lorazepam and haloperidol as PRN alternatives (if using haloperidol due to anticholinergic burden, do not need to give with diphenhydramine). **If anticholinergic toxidrome or delirium,** recommend discussing with Toxicology on-call.
9. **Age cut-offs are strong suggestions.** If you have an exceptionally small or large patient for their age, consider bumping to lower or higher dosing bracket based on clinical judgement.

Aim: To standardize pharmacological management of agitation in the hospital setting.

References:

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Other clinical guidelines reviewed: UNC HealthCare, CHOP, Lurie Children's, Allina

Lalemond scale adapted from Welle Training (2023)

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