

# Pharmacologic Management of Acute Agitation in the Adult Patient in the Emergency Department

## PURPOSE

The purpose of this document is to provide guidance to the healthcare professionals in the AUMC Emergency Department for the initiation of pharmacologic agents in adult patients displaying acute agitation.

## Background

Behavioral emergencies from acute psychotic disturbances, manic episodes, major depression, bipolar disorder, and substance abuse are responsible for approximately 6% of all emergency department (ED) visits in the United States.<sup>1</sup> Behavioral abnormalities and psychiatric illness can coexist with or be caused by medical disease.<sup>2-5</sup> The proper management of an agitated patient is essential to keep staff safe and ensure appropriate treatment for the patient. The goal of using medication is to calm the patient so that he or she can be more accurately assessed by clinicians. Medication used in this manner is consistent with current guidelines on medication administration, which state that the proper endpoint of medication administration is calming without inducing sleep.<sup>6</sup> There is no type of medication considered to be “best” in all cases of agitation but four general classes of medication have been studied and used most frequently for agitation, including first-generation antipsychotics, second-generation antipsychotics, NMDA receptor antagonist, and benzodiazepines. Treatment to correct the specific underlying medical disturbance is the definitive and preferred treatment of agitation in such cases, therefore, this guideline will discuss the best-practice pharmacologic approaches to use when agitation requires emergent management before stabilization of the underlying etiology.

## APPREVIATIONS & DEFINITIONS

- AC: Anticholinergic
- AP: Antipsychotic
- BP: Blood Pressure
- BHU: Behavior Health Unit
- BZD: Benzodiazepines
- ED: Emergency Department
- EtOH: Ethanol
- HR: Heart Rate
- NMDA: N-methyl-D-aspartate
- RASS: Richmond Agitation and Sedation Score

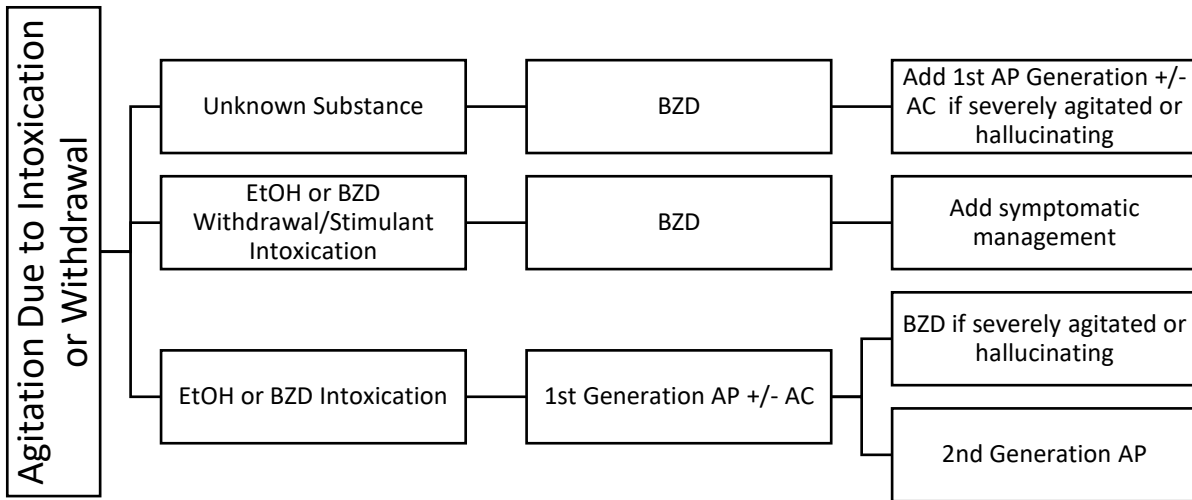
## Indications for Pharmacological Therapy

- Pharmacologic therapy is warranted in a patient that is displaying the extreme physical or vocal aggression that is an immediate threat to the patient and/or healthcare providers and has failed verbal calming and de-escalation techniques in adult patients.
  - For management of the patients that are  $\leq 18$  years of age, refer to the “Guideline for the Pharmacologic Management of Acute Agitation in the Pediatric Patient in the Emergency Department” for guidance.

## Goal of Pharmacologic Therapy <sup>7-8</sup>

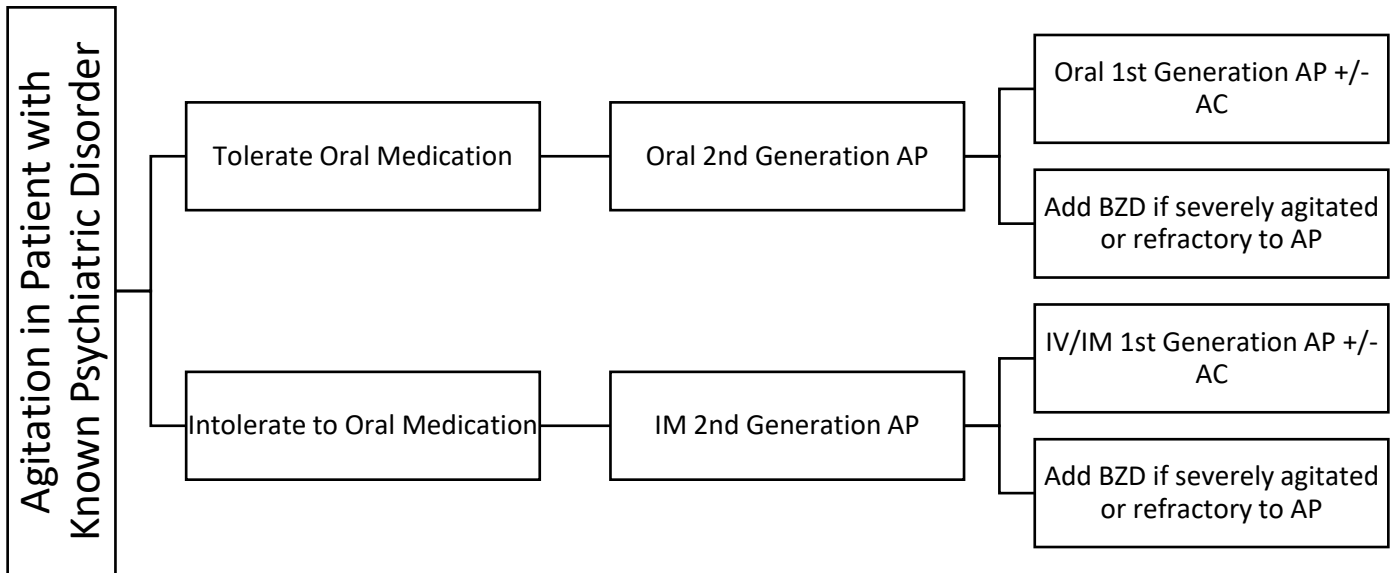
- The use of medications is intended at tranquilizing the patient as quickly as possible, reducing the risk of aggression, and the occurrence of adverse effects in order to allow the continuation of the diagnostic investigation and therapeutic intervention.
- The goal of rapid sedation is to produce a significant reduction in agitation and aggressiveness symptoms without the induction of deep or prolonged sedation, keeping the patient calm but fully or at least partially responsive.

**Table 1. Pharmacologic Treatment of Agitation Due to Intoxication or Withdrawal**



- Unknown Substance
  - Tolerate PO
    - 1<sup>st</sup> line: Lorazepam PO
      - Alternative: Diazepam PO
    - 2<sup>nd</sup> line: Haloperidol PO\*\*
  - Intolerate to PO
    - 1st line: Midazolam IM/IV
      - Alternative: Lorazepam IM/IV
    - 2nd line: Haloperidol IM/IV ± diphenhydramine IM/IV
      - Alternative: Droperidol IM/IV\*\*
- EtOH and Benzodiazepine withdrawal/ Stimulate Intoxication
  - Tolerate PO
    - 1<sup>st</sup> line: Lorazepam PO
      - Alternative: Diazepam PO
    - 2<sup>nd</sup> line: add Haloperidol PO ± diphenhydramine PO\*\*
      - Alternative: Droperidol IM/IV \*\*
  - Intolerate to PO
    - 1st line: Midazolam IM/IV
      - Alternative: Lorazepam IM/IV
    - 2nd line: Haloperidol IM/IV ± diphenhydramine IM/IV\*\*
      - Alternative: Droperidol IM/IV\*\*
- EtOH and Benzodiazepine Intoxication
  - Tolerate PO
    - 1<sup>st</sup> line: Haloperidol PO ± diphenhydramine PO
      - Alternative: Other 1<sup>st</sup> Gen. AP
    - 2nd line: Olanzapine PO
  - Intolerate to PO
    - 1st line: Haloperidol IM/IV ± diphenhydramine IM/IV
      - Alternative: Droperidol IM/IV
    - 2nd line: Olanzapine IM

**Table 2. Pharmacologic Treatment of Agitation in Patient with Known Psychiatric Disorder**

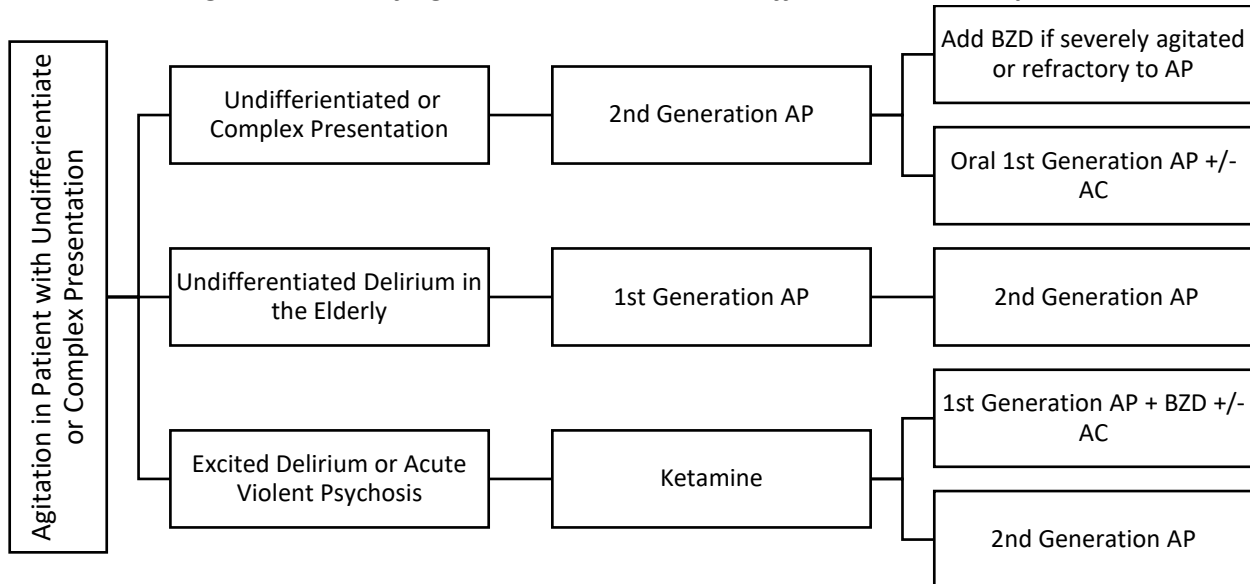


- Agitation in Patient with Known Psychiatric Disorder
  - Tolerate PO
    - 1st line: Olanzapine PO
      - Alternative: Quetiapine PO
    - 2<sup>nd</sup> line: Haloperidol PO ± diphenhydramine PO
      - Alternative: Other 1st/ 2nd Gen. AP
      - Alternative: Lorazepam PO\*\*
  - Intolerate to PO
    - 1st line: Olanzapine IM
      - Alternative: Ziprasidone IM or other 2<sup>nd</sup> generation AP
    - 2<sup>nd</sup> line: Haloperidol IM/IV ± diphenhydramine IM/IV or other 1st generation AP
      - Alternative: Midazolam IM/IV \*\*

\* Based on clinical judgement and product availability

\*\* Add to 1<sup>st</sup> line or trial as monotherapy after 1<sup>st</sup> line failure

**Table 3. Pharmacologic Treatment of Agitation in Patient with Undifferentiated or Complex Presentation**



- Undifferentiated or Complex Presentation
  - Tolerate PO
    - 1st line: Olanzapine PO
      - Alternative: Quetiapine PO
  - 2<sup>nd</sup> line: Haloperidol PO ± diphenhydramine PO
    - Alternative: Lorazepam PO\*\*
  - Intolerate to PO
    - 1st line: Olanzapine IM
      - Alternative: Ziprasidone IM or other 2<sup>nd</sup> generation AP
    - 2nd line: Haloperidol IM/IV ± diphenhydramine IM/IV
      - Alternative: Droperidol IM/IV or other 1st Generation AP
  
- Undifferentiated Delirium in the Elderly
  - Tolerate PO
    - 1<sup>st</sup> line: Haloperidol PO
    - 2nd line: Olanzapine PO
      - Alternative: Other 1<sup>st</sup>/2<sup>nd</sup> Gen AP.
  - Intolerate to PO
    - 1st line: Haloperidol IM/IV
      - Alternative: Droperidol IM/IV
    - 2nd line: Olanzapine IM
    - Alternative: 2<sup>nd</sup> Generation AP IM with low AC effects
  
- Excited Delirium and/or Acute Violent Psychosis
  - 1st line: IM Ketamine 2-5 mg/kg
  - 2nd line: Haloperidol IM/IV ± diphenhydramine IM/IV ± midazolam IM
    - Alternative: Droperidol IM/IV ± midazolam IM/IV

\* Based on clinical judgement and product availability  
 \*\* Add to 1<sup>st</sup> line or trial as monotherapy after 1<sup>st</sup> line failure

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## Appendix

### Appendix 1. Medications Recommended in the Treatment of Agitation

Medication	Route	Initial Dose (mg)	Max Daily Dose (mg)	Onset of Action (min)	Half-Life Elimination (hr)	Comment
Midazolam (benzodiazepine)	IM	5-10	UD	5-15	2-3	Rapid sedation compared to other benzodiazepines, monitor respiratory depression and hypotension
	IV	2-4		3-5		
Lorazepam (benzodiazepine)	PO	1-2	UD	20-30	12-14	IV/IM Formulated in Propylene glycol, monitor respiratory depression and hypotension
	IV	1-2		5-20		
	IM	1-2		20-35		
Diazepam (benzodiazepine)	PO	5-10	UD	30	44-72	IV/IM Formulated in Propylene glycol, monitor respiratory depression and hypotension
	IM	5-10		15-30		
Chlordiazepoxide (benzodiazepine)	PO	5-100	UD	30-60	24-48	Monitor respiratory depression and hypotension
<b>Second Generation Antipsychotics</b>						
Haloperidol (antipsychotic, 1 <sup>st</sup> Gen)	PO	0.5 to 5	20-30	30-60	10-37	Bioavailability with oral dosing is about 60%; dose adjustments between oral and parenteral administration should be made accordingly.  Intravenous use has not been approved by the US Food and Drug Administration and is associated with increased risk of QT prolongation
	IM	2-5		20-40		
Droperidol (antipsychotic, 1 <sup>st</sup> Gen.)	IM	5-10	20*	5-15	2	US Food and Drug Administration and is associated with increased risk of QT prolongation
	IV	2.5-5	10*	3-10		
Chlorpromazine (antipsychotic, 1 <sup>st</sup> Gen.)	PO	25 to 200	600	30-60	30	Oral absorption is variable and may require dose adjustment based on patient response.  Older adults and medically ill patients are unlikely to tolerate cardiovascular, sedating, and anticholinergic side effects.
	IM	25-50	200	15		
Fluphenazine (antipsychotic, 1 <sup>st</sup> Gen.)	PO	1-2.5	10-15	<60	6-28	Oral absorption is highly variable and dose must be individualized based on patient response.
	IM	1.25		< 60		
<b>Third Generation Antipsychotics</b>						
Aripiprazole (antipsychotic, 2 <sup>nd</sup> Gen.)	PO	10 to 15	30	45-60	75-94	Most common side effect of agitation, headache, and akathisia-like restlessness.
Olanzapine (antipsychotic, 2 <sup>nd</sup> Gen.)	PO	5-10	30	30-60	30-38	Smoking may decrease blood concentrations of antipsychotics primarily metabolized by CYP1A2.
	IM	5-10		15-45		
Risperidone (antipsychotic, 2 <sup>nd</sup> Gen.)	PO	1-2	6-8	30-120	20	May cause anticholinergic effects (confusion, agitation, constipation, xerostomia, blurred vision, urinary retention)

Quetiapine (antipsychotic, 2 <sup>nd</sup> Gen.)	PO	50-100	800	30-90	6-12	Titration most often limited by excessive sedation or orthostatic hypotension which should be monitored.
Ziprasidone (antipsychotic 2 <sup>nd</sup> Gen.)	PO	40 to 80	200	45-60	2-7	Oral preparation is not dependent on renal function for clearance but a component of the IM injection is cleared by the kidney.
	IM	10-40	40	15-45		
Ketamine (NDMA Antagonist)	IM	2-5 mg/kg	UD	3-10	2-3	Cautious in conditions in which an increase in blood pressure would be hazardous, emergence reactions, hypersalivation, and laryngospasm.
	IV	1-2 mg/kg		< 1		
Diphenhydramine (anticholinergic)	PO	25-50	300	15-60	7-9	Cautious in elderly patients
	IM/IV			IV < 2 IM: 20-30		
Benzotropine (anticholinergic)	PO	1-2	6	60-120	7-36	Cautious in elderly patients
	IM/IV	1-2		<2		

\*max for institution

UD= undefined in the literature

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