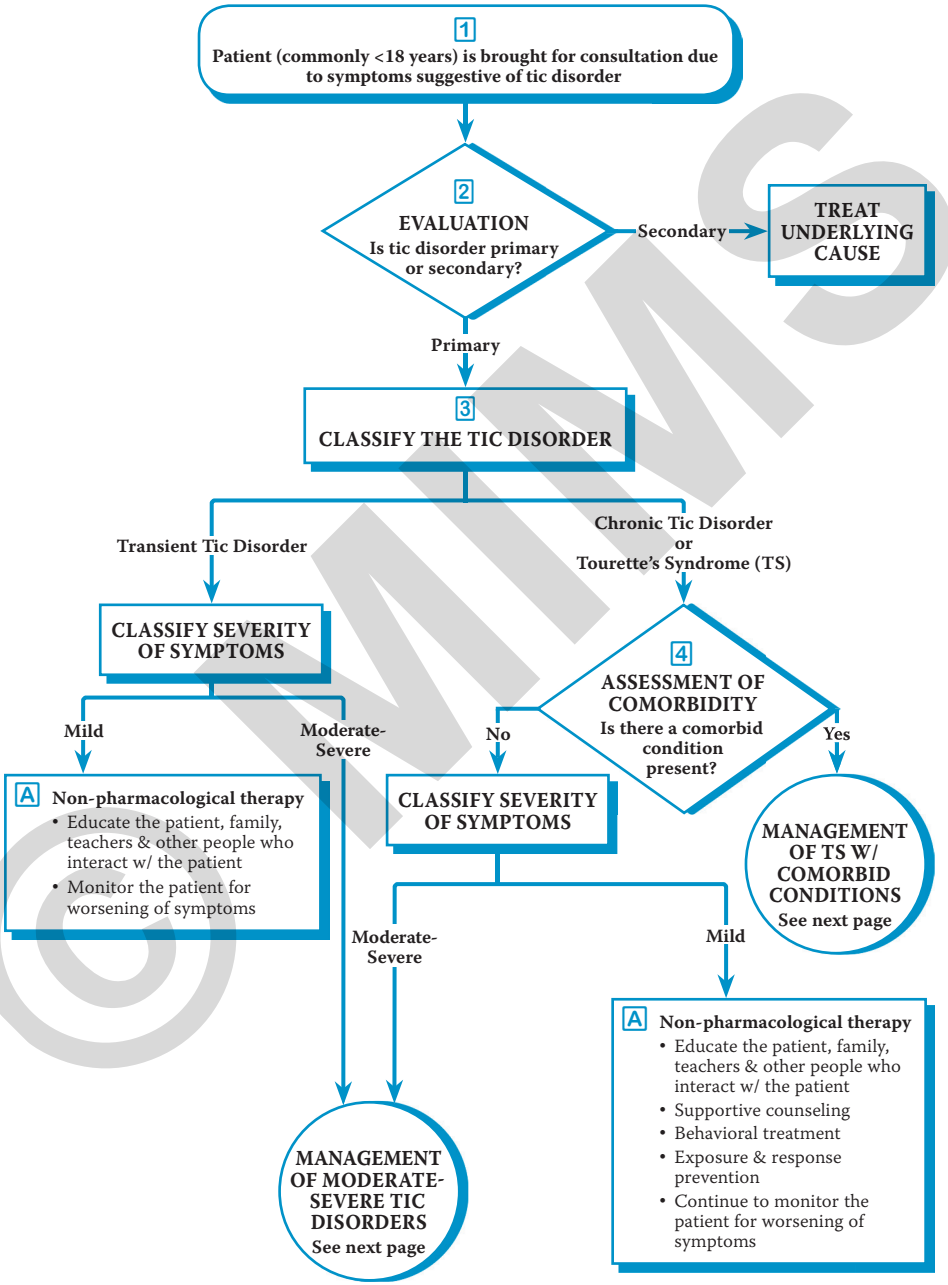
# Tourette's Syndrome & Other Tic Disorders (1 of 11)



**MANAGEMENT OF MODERATE-SEVERE TIC DISORDER**

**CONSIDER EXPERT REFERRAL**

**A** **Non-pharmacological therapy**
- Educate the patient, family, teachers & other people who interact w/ the patient
- Supportive counseling
- Behavioral treatment
- Deep brain stimulation

**B** **Pharmacological therapy**
- Clonidine
- Guanfacine
- Haloperidol
- Pimozide
- Sulpiride
- Tiapride
- Tetrabenazine
- Risperidone
- Botulinum toxin

**MANAGEMENT OF TOURETTE'S SYNDROME W/ COMORBID CONDITIONS**

**CONSIDER EXPERT REFERRAL**

**A** **Non-pharmacological therapy**
- Educate the patient, family, teachers & other people who interact w/ the patient
- Supportive counseling
- Behavioral treatment

**B** **Pharmacological therapy**

**Attention-Deficit/Hyperactive Disorder (ADHD)[1]**

**1st-line agent:**
- Stimulants

**Any *one* of the following:**
- Atomoxetine
- Clonidine + Methylphenidate (stimulant)
- Clonidine or Guanfacine

**Obsessive-Compulsive Disorder (OCD)[1]**

**1st-line agent:**
- SSRI

**Any *one* of the following:**
- Clomipramine
- Risperidone

[1]Please see ADHD & OCD management charts for detailed information concerning medications used for treatment.

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## 1 TIC DISORDER

**Tics**
- Sudden, rapid, non-rhythmic, repetitive, motor movements or vocalizations
- Mean age of onset is approximately 5 years old w/ peak severity occuring between 10-12 years of age & declining in many children during adolescence
- There is a strong genetic component showing a 10- to 100-fold increase in the rates of tics & Tourette syndrome among 1st-degree relatives of Tourette syndrome patients
- May be classified based on:
  - Type
    - Motor: Fragments of normal motor movements appearing out of context & arise in the voluntary musculature involving discrete muscles or group of muscles
    - Vocal or phonic: Noise produced by movement of air through the nose, mouth or pharynx
    - Sensory: These are premonitory sensations that precede tics characterized as unpleasant somatosensory sensations & often relieved by execution of the tic
    - Cognitive: These are repetitive thoughts that occur as a response to excessive urge to act upon provocative visual, auditory, tactile or inner stimuli, often called as impulsions
  - Complexity - simple or complex
  - Isolated (same anatomical location) or multiple locations
  - Location, number, frequency
  - Duration
    - Clonic: Tics are <100 milliseconds
    - Dystonic: Tics are >300 milliseconds, characterized by abnormal posture
    - Tonic: Tics are >300 milliseconds, characterized by isometric contraction

**Simple Tics**
- Simple motor tics are restricted to a single or a few muscle groups & last less than a fraction of a second
  - Eg eye blinking, nose wrinkling, neck jerking, shoulder shrugging, facial grimacing, abdominal tensing
- Simple vocal tics are elementary sounds
  - Eg throat clearing, grunting, sniffling, snorting

**Complex Tics**
- Complex motor tics involve larger muscle groups, usually last longer, & appear purposeful & goal-directed
  - Eg Copropraxia (repetitive obscene movements), echopraxia (mimicking others), self-injurious behavior, hand gestures, jumping, pressing, stomping, facial contortions, repeatedly smelling an object
- Complex vocal tics occur when sounds are elaborate or have a semantic content
  - Eg Palilalia (repeating one's own words), echolalia (repeating another's words or phrases), coprolalia (use of obscene words)

## 2 CAUSES OF TIC DISORDERS

**Primary Causes of Tic Disorders**

**Inherited Tic Disorders**
- Tourette syndrome (TS)
- Huntington's disease
- Primary dystonia
- Neuroacanthosis

**Sporadic Tics**
- Transient motor or phonic tics (<1 year duration)
- Chronic motor or phonic tics (>1 year duration)
- Adult-onset (recurrent tics)
- Tourette syndrome

**Secondary Causes of Tic Disorders**

**Primary Neurologic Disorders**
- Head trauma
- Stroke
- Encephalitis
- Carbon monoxide poisoning
- Neurosyphilis
- Sydenham's chorea
- Hypoglycemia
- Down syndrome
- Tuberous sclerosis
- Fragile X syndrome
- Klinefelter's syndrome
- Chromosomal disorders
- XYY karyotype
- Duchenne's disease
- Hallervorden-Spatz disease
- Creutzfeldt-Jakob disease

## 2 CAUSES OF TIC DISORDERS (CONT'D)

**Secondary Causes of Tic Disorders (Cont'd)**

**Primary Neuropsychiatric Disorders**

- Mental retardation
- Schizophrenia
- Asperger's syndrome/autism

**Drugs Which May Induce or Worsen Tics**

- Stimulants (eg Methylphenidate, Amphetamines, Pemoline)
- Cocaine
- Antipsychotics
- Antidepressants
- Anticonvulsants
- Antihistamines
- Lithium
- Opioids & opioid withdrawal
- Levodopa

**Other movement disorders that need to be ruled out:**

- Eg myoclonic movements, torsion dystonia, chorea, stereotypies

## 3 CLASSIFICATION OF TIC DISORDERS

- There are 3 types of tic disorders based on DSM-5 criteria

**Tourette's Disorder**

- Presence of both multiple motor tics & at least 1 vocal tic during the course of the illness, although they may not occur at the same time
- The tics may increase & decrease in frequency but have continued for >1 year since the first tic occurred
- Tics started before 18 years of age
- Symptoms are not due to effects of any substance (eg cocaine) or caused by any other medical condition (eg Hungtington's disease or postviral encephalitis)

**Persistent (Chronic) Motor or Vocal Tic Disorder**

- Presence of either one or more motor **or** vocal tics during the course of the illness
- The tics may increase & decrease in frequency but have continued for >1 year since the first tic occurred
- Tics started before 18 years of age
- Symptoms are not due to effects of any substance (eg cocaine) or caused by any other medical condition (eg Hungtington's disease or postviral encephalitis)
- The patient has not been diagnosed w/ Tourette's disorder
- Specify if the disorder has motor tics only **or** vocal tics only

**Provisional Tic Disorder**

- Presence of one or more motor &/or vocal tics
- The tics persisted for <1 year since the first tic occurred
- Tics started before 18 years of age
- Symptoms are not due to effects of any substance (eg cocaine) or caused by any other medical condition (eg Hungtington's disease or postviral encephalitis)
- The patient has not been diagnosed w/ Tourette's disorder or persistent (chronic) motor or vocal tic disorder

## 4 COMMON COMORBID CONDITIONS FOUND IN PATIENTS W/ TS

- Attention-deficit/hyperactivity disorder (ADHD)[1]
- Obsessive-compulsive disorder (OCD)[1]
- Learning, developmental & disruptive behavioral disorders

[1]Please see ADHD & OCD management charts for detailed information concerning medications used for treatment.

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## A NON-PHARMACOLOGICAL THERAPY

**Education**
- Educate the people who interact w/ the patient regarding variability of tics, natural history, treatment of the disorder, prognosis & possible coexisting problems
- Refer to local support groups, if available
- Physician, parents & teachers should work together to provide the best possible school environment for children w/ tic disorders

**Supportive Counseling**
- Attention to self-esteem, family issues, social coping & school adjustment may have ameliorative effects on anxiety & depression if present
  - May help decrease acute & chronic stress which can exacerbate tics
- Encourage parents to build on child's strengths

**Possible Preventive Factors**
- Good sleep & personal hygiene
- Informed & supportive school & home environment
- Regular physical exercise
- Encouragement of special talents (eg athletic skills, musical abilities, etc)

**Behavioral Treatment**
- Individualized, specifically based on the needs of the patient
- May be a treatment option for patients who prefer non-pharmacological treatment or patients intolerant or unresponsive to pharmacological therapy
- Most disabling symptoms should be targeted first
- Interventions which have been used in the treatment of tics:
  - Cognitive therapy
    - Recommended as 1st-line treatment for patients w/ tic disorders & OCD
  - Habit reversal training consists of tic-awareness training & competing-response training
    - May be effective in improving tics & controlling symptoms in Tourette syndrome based on findings from unblinded trials & a controlled trial w/ blinded outcome assessment
  - Massed negative practice
  - Assertiveness training
  - Relaxation therapy
  - Awareness training (including self-monitoring)
- Comprehensive Behavioral Intervention for Tics (CBIT) composed of habit reversal training, relaxation training & functional interventions addressing situations which sustain or worsen tics is a recommended treatment option for patients w/ tics

**Deep Brain Stimulation**
- An invasive neurosurgical procedure reserved for severe refractory cases of Tourette syndrome
- Considered to be an experimental option for intractable cases
- The largest published trial showed a mean reduction of 29% in the YGTSS

**Exposure & Response Prevention**
- Patients who have in a prolonged period of time w/ unpleasant premonitory sensations (exposure) & resisting the tic (response prevention), the patients may learn to tolerate the unpleasant sensation (habituation)
  - Habituation will lessen the urge or need to give into the tic, resulting in the reduction of tic behavior

## B PHARMACOLOGICAL THERAPY

- May be considered if symptoms interfere w/ normal functioning
- Successful treatment of comorbid disorder usually decreases tic severity
- There is no cure for Tourette syndrome; aim of pharmacological therapy is to reduce the frequency & severity of tics
- Goals should be to relieve tic-related discomfort/embarrassment & to allow the patient to function as normally as possible
- Choice of treatment depends on the following factors: severity of symptoms, address the most problematic symptom(s), patient's sense of urgency for treatment, & patient's aversion to risk of likely or unlikely adverse effects

**Alpha-Adrenergic Agents**

**Clonidine**
- May be preferred over antipsychotic medications because of decreased risk of acute & long-term side effects
- Useful for children who are hyperactive, impulsive & disinhibited
- Has been shown to improve tics & attention-deficit/hyperactivity disorder

**Guanfacine**
- Found to be less sedating & less hypotensive than Clonidine
- Has been shown to improve tics & attention-deficit/hyperactivity disorder
- Ensures more patient compliance as it can be given once at bedtime or 2x daily as compared w/ 3-4x daily doses of Clonidine

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## B PHARMACOLOGICAL THERAPY (CONT'D)

**Neuroleptics**
- Neuroleptics are considered the most effective drugs

**Conventional/Typical Antipsychotics**
- Haloperidol
  - Side effects tend to limit use & there are other agents that may be better tolerated
  - Many case reports & placebo-controlled studies have shown effectiveness
- Pimozide
  - Shown to be effective in Tourette syndrome
  - May be more effective than Haloperidol but studies comparing the 2 agents have been conflicting

**Selective Dopamine $D_2$ Receptor Antagonists**
- Sulpiride
  - A small number of uncontrolled studies have shown Sulpiride to be effective in treating tics in 59% of patients
  - Improves aggressive obsessive-compulsive behavior & mood
- Tiapride
  - Small number of studies have shown that it reduces tics without affecting cognitive impairment
- Tetrabenazine
  - Depletes dopamine by inhibiting vesicular monoamine transporter type 2
  - As effective as the typical neuroleptics but does not cause tardive dyskinesia
  - Studies have shown to be effective in hyperkinetic movement disorders

**Atypical Antipsychotic**
- Aripiprazole
  - Indicated for treatment of Tourette's disorder in pediatric patients 6-18 years
  - Acts as antagonist at D2 receptors under hyperdopaminergic conditions & displays agonist properties under hypodopaminergic conditions
- Risperidone
  - Extrapyramidal syndrome side effects are usually less compared w/ conventional antipsychotics
  - Most extensively studied of the atypical antipsychotics in the treatment of Tourette syndrome
  - Several studies show Risperidone is effective for Tourette syndrome
  - Has been advocated as 1st-line agent in patients w/ tics & obsessive-compulsive disorder symptoms
  - Based on a retrospective chart review, it has been shown to decrease aggressive behavior in patients w/ Tourette syndrome

**Selective Serotonin Reuptake Inhibitors (SSRIs)**[1]
- Considered 1st-line agents in patients w/ significant depression or obsessive-compulsive disorder symptoms
- May improve tics in some patients, may worsen them, or may have no effect on tics in others
- Eg Fluoxetine

**Selective Noradrenaline Reuptake Inhibitor (SNRI)**
- Atomoxetine
  - A nonstimulant found to be modestly effective in the treatment of Tourette syndrome-related ADHD

**Tricyclic Antidepressant**[1]
- Clomipramine
  - Has nonselective reuptake blocking properties that relieve symptoms of obsessive-compulsive disorder

**Stimulants**[2]
- Considered 1st-line agents in patients w/ attention-deficit/hyperactivity disorder
- Methylphenidate may be better tolerated than Dextroamphetamine in patients w/ Tourette syndrome
- Methylphenidate & Clonidine have additive benefits in Tourette syndrome & attention-deficit/hyperactivity disorder

**Botulinum Toxin**
- Involves local IM inj of the toxin to the affected muscle site
- Most useful for persistent, focal motor (eg eye blinking, neck & shoulder tics), & sometimes vocal tics by temporarily weakening the affected muscles
- Tic & tic urges have been shown to improve
- Effects can be seen in the absence of gross weakness
- Lasts for only 12-16 weeks

**Other Agents Reported to Improve Tics**
- Topiramate
  - Alternative agent in patients w/ mild but troublesome tics who are intolerant or unresponsive to other treatment agents
  - More studies are needed to confirm safety & efficacy
- Baclofen, Clonazepam, Fluphenazine, Levetiracetam, Lithium, Naloxone, Nicotine, Olanzapine, Quetiapine, Talipexole, Ziprasidone

[1]Please refer to Obsessive-Compulsive Disorder Management Chart for detailed discussion on treatment.
[2]Please refer to Attention Deficit/Hyperactivity Disorder Management Chart for detailed discussion on treatment.

# Dosage Guidelines

## ALPHA-ADRENERGIC AGONISTS

| Drug | Dosage | Remarks |
|---|---|---|
| Clonidine | **Childn ≥7 yr & Adolescents:**<br>**Initial dose:** 0.025-0.05 mg/day PO, increase by 0.025 mg/day to a 3-4 times daily schedule<br>**Usual daily dose:** 0.1-0.4 mg/day PO in 3-4 divided doses<br>**Max dose:** 0.4 mg/day | **Adverse Reactions**<br>• CV effects (hypotension, Raynaud's phenomenon, bradycardia or tachycardia, palpitations, impaired AV conduction); CNS effects (sedation, dizziness, headache, irritability, insomnia); GI effects (dry mouth, constipation, anorexia); Other effects (fluid retention, parotid pain)<br>• Guanfacine tends to be less sedating & hypotensive than Clonidine<br>**Special Instructions**<br>• Start w/ a low dose & increase slowly based on patient response<br>• Taper the dose slowly upon discontinuation to avoid tic flare-ups or rebound hypertension<br>• Contraindicated in patients receiving anticoagulation therapy<br>• Use w/ caution in patients w/ cerebrovascular disease, coronary insufficiency, recent MI, conduction disturbances, peripheral vascular disorders, renal or hepatic impairment<br>• Thorough CV assessment, especially in childn, prior to initiation of therapy<br>• Monitor BP, heart rate<br>• Monitor patients for signs of depression, chest pain, or signs of cardiac disease |
| Guanfacine | **Childn 6-16 yr:**<br>**Initial dose:** 0.5 mg PO at bedtime x 3 days, then 0.5 mg PO 12 hrly x 4 days, then 0.5 mg PO 8 hrly x 7 days<br>**Dose range:** 1.5-3 mg/day PO in 3 divided doses<br>**Max dose:** 4 mg/day | |

## ATYPICAL ANTIPSYCHOTIC

| Drug | Dosage | Remarks |
|---|---|---|
| **Other Antipsychotic** | | |
| Aripiprazole | **Childn ≥6 yr & Adolescents:**<br>***<50 kg:***<br>**Initial dose:** 2 mg PO 24 hrly x 2 days<br>Increase to target dose of 5 mg PO 24 hrly<br>Dose may further be titrated to 10 mg PO 24 hrly at wkly intervals in patients not achieving optimal control<br>**Max dose:** 10 mg/day<br>***≥50 kg:***<br>**Initial dose:** 2 mg PO 24 hrly x 2 days<br>Then increase to 5 mg PO 24 hrly x 5 days<br>Increase to target dose of 10 mg PO 24 hrly on day 8 of therapy<br>Dose may further be titrated at wkly intervals in 5 mg/day increments up to 20 mg PO 24 hrly in patients not achieving optimal control<br>**Max dose:** 20 mg/day | **Adverse Reactions**<br>• CNS effects (headache, anxiety, somnolence or insomnia); rare reports of tardive dyskinesia & neuroleptic malignant syndrome<br>• May cause salivary hypersecretion, orthostatic hypotension, seizure, dysphagia, or suicidal ideation<br>• Hyperglycemia may occur & in some cases be extreme, resulting in ketoacidosis, hyperosmolar coma, or death<br>**Special Instructions**<br>• Use w/ caution in patients w/ seizure disorders, in suicidal patients, & those w/ concomitant illness<br>• Monitor growth, including wt, ht & BMI in pediatric patients to check for metabolic effects of Aripiprazole |

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# Dosage Guidelines

| ATYPICAL ANTIPSYCHOTIC (CONT'D) | | |
|---|---|---|
| **Drug** | **Dosage** | **Remarks** |
| **Other Antipsychotic (cont'd)** | | |
| Risperidone | **Childn & Adolescents 7-17 yr:**<br>**Initial dose:** 0.25-0.5 mg PO 24 hrly at night<br>Titrate gradually every 4-5 days in 0.25-0.5 mg increments to<br>**Usual dose range:** 0.25-6 mg PO in 2 divided doses<br>**Adult:**<br>**Initial dose:** 0.25 mg PO 24 hrly<br>Increase gradually based on response & tolerability up to<br>**Usual dose:** 0.25-6 mg PO 24 hrly<br>**Max dose:** 6 mg/day | **Adverse Reactions**<br>• CNS effects (somnolence, dizziness, depression, insomnia, pseudoparkinsonism, EPS symptoms, acute dystonic reaction, akathisia, agitation, anxiety, aggressive behavior, fatigue, headache); GI effects (inc appetite, N/V, abdominal pain, constipation); Other effects (galactorrhea, weakness, sexual dysfunction, hyperglycemia)<br>• Use may be associated w/ neuroleptic malignant syndrome (NMS)<br>**Special Instructions**<br>• Start w/ a low dose & increase slowly based on patient response<br>• Taper the dose slowly upon discontinuation to avoid tic flare-ups<br>• Use w/ caution in patients w/ CV disease, recent MI, Parkinson's disease, renal or hepatic impairment, epilepsy<br>• Watch out for suicidal ideation, changes in mental status, orthostatic hypotension<br>• Monitor for FBS, $HbA_{1c}$ (especially in patients w/ or at risk of DM), lipid profile |



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# Dosage Guidelines

| CONVENTIONAL ANTIPSYCHOTICS | | |
|---|---|---|
| **Drug** | **Dosage** | **Remarks** |
| **Benzamides** | | |
| Sulpiride | **Childn:**<br>**2-12 yr:** 50-400 mg PO 12 hrly<br>**12-18 yr:** 100-400 mg PO 12 hrly<br>**Adult:**<br>200-400 mg PO 12 hrly | **Adverse Reactions**<br>• CNS effects (sleep disturbances, agitation, over stimulation, impaired cognition); Other effects (GI disturbances, nasal congestion, wt gain)<br>• EPS including tardive dyskinesia occur but may be milder<br>• Less likely to cause sedation & hypotension<br>• Antimuscarinic effects are minimal<br>• Use may be associated w/ NMS<br>**Special Instructions**<br>• Start w/ a low dose & increase slowly based on patient response<br>• Taper the dose slowly upon discontinuation to avoid tic flare-ups<br>• Contraindicated in patients w/ Parkinson's disease, pheochromocytoma, CNS depression, porphyria, prolactin-dependent tumors<br>• Use w/ caution in patients w/ CV disease, epilepsy, myasthenia gravis, severe resp disease, urinary retention, history of jaundice, w/ blood dyscrasias, DM, prostatic hypertrophy, angle closure glaucoma, renal or hepatic impairment. May potentiate mania |
| Tiapride | **Dose range:**<br>100-400 mg/day PO | **Adverse Reactions**<br>• CNS effects (sedation, depression, agitation, parkinsonism, dystonia); GI effects (increase in appetite, wt gain); Endocrine & metabolic effects (hyperprolactinemia & resulting menstrual disorders, rarely galactorrhea)<br>• Use may be associated w/ NMS, blood dyscrasias<br>**Special Instructions**<br>• See Sulpiride above |





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# Dosage Guidelines

| CONVENTIONAL ANTIPSYCHOTICS (CONT'D) | | |
|---|---|---|
| **Drug** | **Dosage** | **Remarks** |
| **Butyrophenone** | | |
| Haloperidol | **Childn 3-12 yr & weighing 15-40 kg:**<br>**Initial dose:** 0.25-0.5 mg/day PO in 2-3 divided doses<br>Increase by 0.25-0.5 mg every 5-7 days<br>**Usual maintenance dose:** 0.05-0.075 mg/kg/day in 2-3 divided doses<br>**Max dose:** 15 mg/day<br>**Childn weighing >40 kg & Adolescents:**<br>**Initial dose:** 0.25-0.5 mg/day PO in 2-3 divided doses<br>Increase gradually by 0.25-0.5 mg increments at 5-7 day intervals<br>**Usual dose:** 1-4 mg/day PO<br>**Adult:**<br>**Initial dose:** 0.5-5 mg PO 8-12 hrly<br>Adjust dose based on response & tolerability<br>**Max dose:** 100 mg/day PO | **Adverse Reactions**<br>• Less likely to cause sedation, hypotension & antimuscarinic effects but extrapyramidal movements are more common<br>• Wt gain, impaired cognition<br>• Use may be associated w/ NMS<br>**Special Instructions**<br>• Start w/ low dose & increase slowly based on patient response<br>• Taper the dose slowly upon discontinuation to avoid tic flare-ups<br>• Avoid in patients w/ thyrotoxicosis<br>• Contraindicated in patients w/ CNS depression, severe liver or CV disease, conduction abnormality, narrow-angle glaucoma, bone marrow suppression, parkinsonism, electrolyte imbalance, hypothyroidism<br>• Use w/ caution in patients w/ renal or hepatic dysfunction, resp disease, history of seizures |



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# Dosage Guidelines

| CONVENTIONAL ANTIPSYCHOTICS (CONT'D) | | |
|---|---|---|
| **Drug** | **Dosage** | **Remarks** |
| **Diphenylbutylpiperidine** | | |
| Pimozide | **Childn ≥2 yr & Adolescents:**<br>***Weight-directed dosing:***<br>**Initial dose:** 0.05 mg/kg PO at bedtime<br>**Max initial dose:** 1 mg/dose<br>May increase dose every 3 days, if needed<br>**Max dose:** 10 mg/day or 0.2 mg/kg/day, whichever is less<br>***Fixed dosing:*** 0.5-1 mg PO 24 hrly<br>**Usual dose:** 2-8 mg/day PO<br>**Adult:**<br>**Initial dose:** 1-2 mg/day PO in divided doses<br>Increase dosage every other day<br>**Max dose:** 10 mg/day or 0.2 mg/kg/day, whichever is less | **Adverse Reactions**<br>• CV effects [ventricular arrhythmias, ECG abnormalities (eg prolongation of QT interval & T-wave changes)]; Other effects (drowsiness, behavior changes, impaired motivation, impaired cognition, dysphoria, irritability, depression, wt gain, parkinsonism)<br>• Less likely to cause sedation, hypotension & antimuscarinic effects<br>• Rarely gynecomastia, amenorrhea, impotence, hostility, aggression<br>• More likely to cause EPS (eg akathisia, acute dystonic reactions)<br>• Use may be associated w/ NMS<br>**Special Instructions**<br>• ECG should be performed prior to therapy & periodically thereafter, especially during dose adjustment<br>• Start w/ a low dose & increase slowly based on patient response<br>• Taper the dose slowly upon discontinuation to avoid tic flare-ups<br>• Contraindicated in patients w/ CNS depression, cardiac arrhythmias, conduction abnormality, electrolyte imbalance<br>• Use w/ caution in patients w/ CV disease, narrow-angle glaucoma, myasthenia gravis, Parkinson's disease, renal or hepatic impairment, seizure disorder |



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*Please see the end of this section for the reference list.*