TRIHEXYPHENIDYL

THERAPEUTICS

**Brands**
- Artane
see index for additional brand names

**Generic?** Yes

**Class**
- Antiparkinson agent; anticholinergic

**Commonly Prescribed for**
(bold for FDA approved)
- Extrapyramidal disorders
- Parkinsonism
- Idiopathic generalized dystonia
- Focal dystonias
- Dopa-responsive dystonia

**How the Drug Works**
- Diminishes the excess acetylcholine activity caused by removal of dopamine inhibition when dopamine receptors are blocked
- May also inhibit the reuptake and storage of dopamine at central dopamine receptors, prolonging dopamine action

**How Long Until It Works**
- For extrapyramidal disorders and parkinsonism, onset of action can be within minutes or hours

**If It Works**
- Reduces motor side effects
- Does not lessen the ability of antipsychotics to cause tardive dyskinesia

**If It Doesn’t Work**
- For extrapyramidal disorders, increase to highest tolerated dose
- Consider switching to benztropine, diphenhydramine, or a benzodiazepine
- Disorders that develop after prolonged antipsychotic use may not respond to treatment
- Consider discontinuing the agent that precipitated the EPS

**Best Augmenting Combos**
- If ineffective, switch to another agent rather than augment

**Tests**
- None for healthy individuals

**SIDE EFFECTS**

**How Drug Causes Side Effects**
- Prevents the action of acetylcholine on muscarinic receptors

**Notable Side Effects**
- Dry mouth, blurred vision, diplopia
- Confusion, hallucinations
- Constipation, nausea, vomiting
- Dilation of colon
- Erectile dysfunction

**Life-Threatening or Dangerous Side Effects**
- Angle-closure glaucoma
- Heat stroke, especially in elderly patients
- Tachycardia, cardiac arrhythmias, hypotension
- Urinary retention
- Anticholinergic agents such as trihexyphenidyl can exacerbate or unmask tardive dyskinesia

**Weight Gain**
- Reported but not expected

**Sedation**
- Many experience and/or can be significant in amount

**What to Do About Side Effects**
- For confusion or hallucinations, discontinue use
- For sedation, lower the dose and/or take the entire dose at night
- For dry mouth, chew gum or drink water
- For urinary retention, obtain a urological evaluation; may need to discontinue use
Best Augmenting Agents for Side Effects
• Many side effects cannot be improved with an augmenting agent

DOSING AND USE

Usual Dosage Range
• Extrapyramidal disorders: 5–15 mg/day
• Parkinsonism: 6–15 mg/day

Dosage Forms
• Tablet 2 mg, 5 mg
• Injection 2 mg/5 mL

How to Dose
• Extrapyramidal disorders: 5–15 mg/day; assess effect and increase dose empirically as tolerated; total daily dose varies from patient to patient
• Parkinsonism (oral): initial 1 mg/day; after 3 days can increase the dose in 2 mg increments every 3–5 days as tolerated until clinical effect is reached; total daily dose should be divided into 3 doses and given with meals

Dosing Tips
• If drug-induced EPS occur soon after initiation of a neuroleptic drug, they are likely to be transient; thus, attempt to withdraw trihexyphenidyl after 1–2 weeks to determine if still needed
• To achieve more rapid relief, temporarily lower the dose of the offending agent (phenothiazine, thioxanthene, or butyrophenone) when starting trihexyphenidyl
• Taking trihexyphenidyl with meals can reduce side effects
• In Parkinson’s disease, the usual dose is 6–10 mg/day (divided into 3 doses) for idiopathic Parkinson’s disease and 12–15 mg/day (divided into 3 or 4 doses) for post-encephalitic Parkinson’s disease

Overdose
• Circulatory collapse, cardiac arrest, respiratory depression or arrest, CNS depression or stimulation, psychosis, shock, coma, seizure, ataxia, combativeness, anhidrosis and hyperthermia, fever, dysphagia, decreased bowel sounds, sluggish pupils

Long-Term Use
• Safe
• Effectiveness may decrease over time (years) and side effects such as sedation and cognitive impairment may worsen

Habit Forming
• No

How to Stop
• Taper not necessary

Pharmacokinetics
• Half-life 6–10 hours; time to peak effect is 1–1.3 hours
• Metabolism is not well understood

Drug Interactions
• Use with amantadine may increase side effects
• Trihexyphenidyl and all other anticholinergic agents may increase serum levels and effects of digoxin
• Can lower concentration of haloperidol and other phenothiazines, causing worsening of schizophrenia symptoms
• Can decrease gastric motility, resulting in increased gastric deactivation of levodopa and reduction in efficacy

Other Warnings/Precautions
• Use with caution in hot weather, as trihexyphenidyl may increase susceptibility to heat stroke
• Anticholinergic agents have additive effects when used with drugs of abuse such as cannabinoids, barbiturates, opioids, and alcohol

Do Not Use
• In patients with glaucoma, particularly angle-closure glaucoma
• In patients with pyloric or duodenal obstruction, stenosing peptic ulcers, prostate hypertrophy or bladder neck obstructions, achalasia, or megacolon
• If there is a proven allergy to trihexyphenidyl
TRIHEXYPHENIDYL

THE ART OF PSYCHOPHARMACOLOGY

Potential Advantages
- Extrapyramidal disorders related to antipsychotic use
- Generalized dystonias (well tolerated in younger age groups)

Potential Disadvantages
- Patients with long-standing extrapyramidal disorders may not respond to treatment
- Multiple dose-dependent side effects may limit use

Primary Target Symptoms
- Tremor, akinesia, rigidity, drooling, dystonia

Pearls
- Often abused in correctional settings for its euphoric and sedative/hypnotic action, especially at high doses
- Although any anticholinergic agent is potentially abusable, especially in a correctional setting, trihexyphenidyl may be more abusable than others, presumably due to its dopamine-enhancing actions
- Useful adjunct in younger Parkinson’s patients with tremor
- Useful in the treatment of post-encephalitic Parkinson’s disease and for extrapyramidal reactions, other than tardive dyskinesias
- Post-encephalitic Parkinson’s patients usually tolerate higher doses better than idiopathic Parkinson’s patients
- Generalized dystonias are more likely to benefit from anticholinergic therapy than focal dystonias; trihexyphenidyl is used more commonly than benztropine
- Sedation limits use, especially in older patients
- Patients with mental impairment do poorly
- Dystonias related to cerebral palsy, head injuries, and stroke may improve with trihexyphenidyl, especially in younger, cognitively normal patients
- Schizophrenia patients may abuse trihexyphenidyl and other anticholinergic medications to relieve negative symptoms, for a stimulant effect or to improve symptoms of drug-induced parkinsonism
- Can cause cognitive side effects with chronic use, so periodic trials of discontinuation may be useful to justify continuous use, especially in institutional settings as adjunct to antipsychotics

SPECIAL POPULATIONS

Renal Impairment
- No known effects, but use with caution

Hepatic Impairment
- No known effects, but use with caution

Cardiac Impairment
- Use with caution in patients with known arrhythmias, especially tachycardia

Elderly
- Use with caution
- Elderly patients may be more susceptible to side effects

Children and Adolescents
- Do not use in children ages 3 and younger
- Generalized dystonias may respond to anticholinergic treatment and young patients usually tolerate the medication better than the elderly
- Usual dose is 0.05 mg/kg once or twice daily

Pregnancy
- Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule (PLLR or final rule) applies only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001
- Controlled studies have not been conducted in pregnant women

Breast Feeding
- Unknown if trihexyphenidyl is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- Recommended either to discontinue drug or bottle feed unless the potential benefit to the mother justifies the potential risk to the child
- Infants of women who choose to breast feed while on trihexyphenidyl should be monitored for possible adverse effects

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Suggested Reading


