TETRABENAZINE

THERAPEUTICS

Brands
• Nitoman, Xenazine

Generic?
Yes

Class
• Antiadrenergic, antidopaminergic, synaptic vesicle blocker, antimonoaminergic

Commonly Prescribed for
(FDA approved in bold)
• Chorea in Huntington’s disease (HD)
• Dyskinesias in HD
• Psychosis
• Hemiballism
• Dystonia (especially tardive)
• Myoclonus
• Gilles de la Tourette syndrome (GTS) or tics
• Hypertension

How the Drug Works
• Depleting agent that reversibly depletes stores of monoamines (dopamine, norepinephrine, serotonin, and histamine) from nerve terminals and blocks postsynaptic dopamine receptors. Effectiveness is likely related to dopamine depletion

How Long Until It Works
• Usually less than 1 week

If It Works
• In neurologic conditions, continue to assess effect of the medication, determine if still needed and adjust to optimal dose

If It Doesn’t Work
• Chorea: Consider benzodiazepines and anticonvulsants (valproate). Neuroleptics are usually effective. Reserpine is an alternative depleting agent
• Generalized dystonia: Anticholinergics, baclofen, or benzodiazepines may be effective. Surgical treatments (including pallidotomy, thalamotomy, deep brain stimulation, myotomy, rhizotomy, or peripheral denervation) are reserved for refractory cases
• GTS/tics – Neuroleptics and alpha-2 adrenergic agonists are often effective

Best Augmenting Combos for Partial Response or Treatment-Resistance
• Chorea – combine with anticonvulsants, neuroleptics, or benzodiazepines
• Dystonia – combine with anticholinergics or benzodiazepines
• GTS/tics – Combine with neuroleptics for refractory cases

Tests
• At doses of 50 mg or greater, test patients for the CYP-450 2D6 gene to determine if they are poor, intermediate, or extensive metabolizers

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
• Related to monoamine depletion

Notable AEs
• Drowsiness, fatigue, dizziness, depression, anxiety, insomnia
• Parkinsonism, akathisia, orthostatic hypotension, nausea
• Upper respiratory tract infection, dyspnea, dysuria

Life-Threatening or Dangerous AEs
• Falls and resulting trauma
• Neuroleptic malignant syndrome
• Parkinsonism and extrapyramidal tract dysfunction (less common than neuroleptics)
• QTc prolongation (usually mild)
• Dysphagia

Weight Gain
• Common

Sedation
• Common

What to Do About AEs
• Reducing doses improves most AEs

Best Augmenting Agents for AEs
• Most AEs cannot be improved by an augmenting agent
TETRABENAZINE (continued)

**DOSING AND USE**

**Usual Dosage Range**
- 50–200 mg/day

**Dosage Forms**
- Tablets: 12.5 mg, 25 mg

**How to Dose**
- Start at 12.5 mg daily in the AM and increase to 12.5 mg twice a day in 1 week. Increase as needed by 12.5 mg/week and dose 3–4 times daily. Avoid single doses over 50 mg. Most patients require doses of 100 mg or less

**Dosing Tips**
- Food has no effect on absorption

**Overdose**
- Reported symptoms include acute dystonia, oculogyric crisis, nausea and vomiting, sweating, sedation, hypotension, confusion, diarrhea, hallucinations, and tremor

**Long-Term Use**
- Safe, but monitor for long-term AEs

**Habit Forming**
- No

**How to Stop**
- No need to taper but symptoms usually reappear

**Pharmacokinetics**
- Rapidly metabolized to metabolites, predominantly by CYP-450 2D6 isoenzymes and mostly excreted in urine. Half-life about 10 hours

**Drug Interactions**
- Do not use with monoamine oxidase (MAO) inhibitors
- Do not use within 20 days of reserpine
- Strong CYP2D6 inhibitors (fluoxetine, paroxetine, quinidine) approximately double levels requiring reduction in dose. Weaker 2D6 inhibitors (duloxetine, amiodarone, or sertraline) may also increase levels

**Other Warnings/Precautions**
- Sedation increases with the use of CNS depressants, such as alcohol
- May elevate prolactin levels
- May cause severe depression that may lead to suicide
- Proven hypersensitivity, active depression or history of suicidal tendencies, or hepatic disease

**SPECIAL POPULATIONS**

**Renal Impairment**
- Patients with renal insufficiency may adjust poorly to lowered blood pressure

**Hepatic Impairment**
- Concentrations of drug and metabolites and elimination half-life are dramatically increased. Do not use

**Cardiac Impairment**
- May increase QTc interval. Avoid in patients with congenital long QT syndrome or in patients on QT-prolonging medications. Patients with recent myocardial infarction or unstable disease were excluded from clinical trials

**Elderly**
- No known effects

**Children and Adolescents**
- Not well studied but occasionally used for the treatment of generalized dystonias. Monitor for parkinsonism and hypotension. A trial of levodopa should be considered to rule out dopa-responsive dystonia

**Pregnancy**
- Category C. Use only if there is a clear need

**Breast Feeding**
- Unknown if excreted in breast milk. Use only if clearly needed
TETRABENAZINE

Potential Advantages
• Useful for the treatment of hyperkinetic movement disorders, with fewer AEs than reserpine

Potential Disadvantages
• Not available in many countries. Drowsiness and parkinsonism limit titration. Multiple doses per day needed

Primary Target Symptoms
• Reduction in severity of chorea, dystonia, myoclonus, or tics

Pearls
• Most effective in the treatment of tardive dyskinesias, tardive dystonia, HD, and myoclonus
• Somewhat effective in idiopathic dystonia and GTS

• Dyskinesia related to Parkinson’s disease should be treated with lowering levodopa medication doses and using extended-release forms, amantadine, or clozapine. Tetrabenazine may worsen orthostatic hypotension
• In refractory dystonia, tetrabenazine with trihexyphenidyl and pimozide may be effective
• For the treatment of chorea in HD, aripiprazole often has fewer AEs and is more likely to improve depression rather than worsen symptoms
• Parkinsonism is more common at higher doses (100 mg or greater)
• Although common, weight gain is less common than with neuroleptics in the treatment of GTS
• Compared to reserpine, has a shorter half-life and has fewer peripheral effects (lower incidence of GI AEs and hypotension)

Suggested Reading

