Pimozide (pi-mo-zide)

**Classification**: Antipsychotic (conventional)

**Pregnancy Category**: C

**Indications**

Suppression of motor and vocal tics in Tourette's Disorder with severe, compromising symptoms in patients with an unfavorable response to haloperidol. Second line treatment after failure with atypical antipsychotics.

**Unlabeled Use**: Psychotic disorders that fail to respond to standard treatment.

**Action**

Blocks dopamine receptors in the CNS. Increases brain turnover of dopamine, blocks calcium channels, and may antagonize opiate receptors. 

**Therapeutic Effects**: Decreased tics in patients with Tourette's disorder.

**Pharmacokinetics**

**Absorption**: 50% absorbed following oral administration.

**Distribution**: Unknown.

**Metabolism and Excretion**: Undergoes extensive first-pass hepatic metabolism, primarily by CYP3A4 and to a lesser extent by CYP1A2 and CYP2D6 enzyme systems; the CYP2D6 enzyme system exhibits genetic polymorphism (7% of population may be poor metabolizers and may have significantly lower pimozide concentrations and at an increased risk of adverse effects). Some metabolites have CNS activity.

**Half-life**: 29–111 hr.

**TIME/ACTION PROFILE (blood levels)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
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<tr>
<td>PO</td>
<td>unknown</td>
<td>6–8 hr</td>
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**Contraindications/Precautions**

**Contraindicated in**: Hypersensitivity (cross-sensitivity with other antipsychotics may occur). Concurrent use of agents that may be causing the motor and vocal tics, Congenital long QT syndrome (increases risk of serious arrhythmias).

Recent MI, heart failure. Concurrent use of agents that prolong the QT interval, including dofetilide, citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, olanzapine, dihydroergotamine, mirtazapine, propranolol, pimozide, prazosin, quinidine, azilsartan, amlodipine, esmolol, ranolazine, thioridazine, chlorpromazine, clozapine, droperidol, metergoline, mesoridazine, moricizine, pipamperone, protriptyline, sotalol, terazosin, tolvaptan, ziprasidone, trimethoprim-sulfamethoxazole, treprostinil, azithromycin, citalopram, escitalopram, paroxetine, nefazodone, zileuton, ketoconazole, and ergot alkaloids.

**Use Cautiously in**: History of breast cancer; Congenital long QT syndrome; Congenital long QT syndrome; Angle-closure glaucoma; History of paralytic ileus; Hepatic or renal impairment; Prostatic hyperplasia; History of seizures (threshold may be lowered); Hypokalemia (increases risk of serious arrhythmias).

**Adverse Reactions/Side Effects**


**Interactions**

**Drug-Drug**: Concurrent use of macrolide anti-infectives (erythromycin, clarithromycin, azithromycin), dofetilide, sotalol, quinidine, other Class IA or III antiarrhythmics, thioridazine, chlorpromazine, droperidol, gemifloxacin, moxifloxacin, nefazodone, pimozide, terazosin, doxepin, and cyclosporine (increases risk of serious ventricular arrhythmias and should be avoided; similar effects may occur with Class IA and III antiarrhythmics, methadone, nefazodone, and fluoxetine).
tricyclic antidepressants, disopyramide, or procainamide. Blood levels and risk of cardiac arrhythmias are...Continued use of ritonavir, disopyramide, or other CYP2D6 inhibitors; concurrent use may...Blood levels and effectiveness; avoid concurrent use.

**Drug-Food:** Grapefruit juice may affect pimozide levels and effectiveness; avoid concurrent use.

**Drug-Natural Products:** St. John’s wort, kava, valerian, or chamomile can...Increased bulk and fluids in the diet help minimize constipating effects.

**Assess:** For onset of akathisia (restlessness or desire to keep moving), which may appear within 6 hr of 1st dose and may be difficult to distinguish from psychotic agitation. Benzodiazepines may alleviate akathisia.

**Assess:** For tics during therapy. Increased bulk and fluids in the diet help minimize constipating effects.

**Assess:** Positive (hallucinations, delusions, agitation) and negative (social withdrawal) symptoms of psychotic disorder.

**Assess:** Weight and BMI initially and throughout therapy.

**Monitor:** BP (sitting, standing, lying) and ECG prior to and periodically during therapy, especially during period of dosage adjustment. May cause QT interval changes, flattening, notching, and inverting of T-wave, and the appearance of U-waves on ECG.

**Monitor:** Tardive dyskinesia (uncontrolled rhythmic movements of mouth, face, difficulty speaking or swallowing, loss of balance control, pill rolling of hands, mask-like face, shuffling gait, rigidity, tremor, and dysphoria—muscle spasm, resting tremor, swallowing, incoordination, weakness of arm or leg) shortness of breath, pallor, tiredness, severe muscle stiffness, loss of balance control, pill rolling of hands, mask-like face, shuffling gait, rigidity, tremor, and dysphoria—muscle spasm, resting tremor, swallowing, incoordination, weakness of arm or leg)

**Monitor:** Fasting blood glucose and cholesterol levels initially and throughout therapy.

**Obtain:** Serum potassium levels initially and throughout therapy.

**Obtain:** Serum pregnancy levels initially and throughout therapy.

**Obtain:** Urinalysis.

**Lab Test Considerations:** May cause false-positive pregnancy tests with immunoassays.

**Lab Test Considerations:** Obtain serum prothrombin levels initially and throughout therapy.

**Lab Test Considerations:** Obtain fasting blood glucose and cholesterol levels initially and throughout therapy.

**Potential Nursing Diagnoses:** Impaired social interactions (hallucinations) Bulimia nervosa (Side Effects)

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pimozide

Implementation

- Dose should be reduced periodically to determine whether tics persist. Increase in tics may be due to withdrawal phenomenon rather than the persistence of tics. Allow 1–2 wk to elapse before concluding that an increase in symptoms is due to an increase in tics instead of withdrawal symptoms.

- Tourette’s Disorder: When dosing exceeds 0.05 mg/kg/day in children or 4 mg in adults CYP 2D6 genotyping should be obtained. In poor CYP 2D6 metabolizers, doses should not exceed 0.05 mg/kg/day, and should not be increased earlier than 14 days.

- PO: May be administered as a single daily dose.

- Do not administer with grapefruit juice.

Patient/Family Teaching

- Advise patient to take medication exactly as directed and to avoid grapefruit juice during therapy. Skipping doses and returning to regular schedule, do not double doses. May require several weeks to obtain desired effects. Do not increase dose or discontinue medication without consulting health care professional. Abrupt withdrawal may cause dizziness, nausea, vomiting, GI upset, trembling, or uncontrollable movements of mouth, tongue, or jaw. Dosage should be gradually decreased over several weeks to minimize withdrawal symptoms.

- Instruct patient to report symptoms immediately.

- Advise patient to change positions slowly to minimize orthostatic hypotension.

- May cause drowsiness. Caution patient to avoid driving or other activities requiring alertness until response to medication is known.

- Care patient to avoid taking alcohol or other CNS depressants concurrently with this medication.

- Advise patient to use sunscreen and protective clothing when exposed to the sun to prevent photosensitivity reactions. Extremes of temperature should also be avoided, because this drug impairs body temperature regulation.

- Instruct patient to report symptoms immediately.

- Advise patient to notify health care professional promptly if weakness, tremors, visual disturbances, dark-colored urine or clay-colored stools, sore throat, fever, or symptoms of acute hepatic dysfunction occur.

- Emphasize the importance of routine follow-up exams to monitor response to medication and detect side effects.

- Why was this drug prescribed for your patient?

- Decrease in the frequency and severity of tics in patients with Tourette’s Disorder.

- Decrease in positive (hallucinations, delusions, agitation) symptoms of psychotic disorders.

- Decrease in negative (apathy, flattening of emotions, withdrawal) symptoms of psychotic disorders.

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