Ziprasidone Criteria for Use

VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel
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The following recommendations are dynamic and will be revised, as new clinical data become available. These guidelines are not intended to interfere with clinical judgment. Rather, they are intended to assist practitioners in providing cost effective, consistent, high quality care.

I. Ziprasidone may be considered in patients with significant intolerance (eg. weight gain, EPS) or poor response while taking another atypical. Before starting ziprasidone, obtain an ECG for any patient with suspected heart disease.

II. **Until more safety data is available, ziprasidone should not be used in patients with underlying risk factors for QT or QTc interval prolongation.**

A. Congenital long QT syndrome

B. Acquired prolongation of the QT interval

1. Receiving other drugs known to prolong QT interval

For example, ziprasidone should not be used in patients receiving the following agents:

- Antiarrhythmics - Class Ia quinidine, disopyramide, procainamide
  Class III dofetilide, sotolol, amiodarone, ibutilide
- Antipsychotics - thioridazine, mesoridazine, chlorpromazine
- Antidepressants - imipramine, amitriptyline, desipramine, nortriptyline, doxepin
- Fluoroquinolones - sparfloxacin, moxifloxacin, levofloxacin, gatifloxacin
- Macrolides - erythromycin, clarithromycin
- Antimalarials - halofantrine, mefloquine
- Pentamidine, droperidol, pimozide, arsenic trioxide, levomethadyl acetate, dolasetron mesylate, tacrolimus, carbamazepine*

*carbamazepine also is a CYP3A4 inducer, which can potentially decrease ziprasidone serum concentration

For more information, refer to http://www.torsades.org/druglist.cfm and the product package insert for ziprasidone

2. The azole antifungals (ketoconazole, itraconazole, fluconazole) inhibit CYP3A4. There is an increased risk of QT interval prolongation when the azoles are used concurrently with drugs having both the potential to prolong QT interval and which are metabolized by CYP3A4. One of the major metabolic pathways for ziprasidone is CYP3A4. In one small study, co-administration of ziprasidone and ketoconazole lead to no further prolongation of the QT interval despite a 39% increase in the serum concentration of ziprasidone. Until more safety data is available, it is best to avoid using ziprasidone with drugs that inhibit CYP3A4 (eg. nefazodone, protease inhibitors).

3. Cardiac factors:
   - Bradycardia - Sinus bradycardia, high-grade AV block
   - Myocardial diseases – Symptomatic and uncontrolled cardiac ischemia, cardiomyopathy, myocarditis, conduction delay
   - Electrolyte abnormalities - Hypokalemia, hypomagnesemia

III. **Dosage and administration:** The usual starting for ziprasidone is 20mg taken twice daily with food. The maximum dose is 80mg taken twice daily. Several weeks may be necessary before a response is noted.