Oral Propafenone Drug Shortage

Important notes:

Ideally, the patient should see cardiologist for determination of the most appropriate alternative agent and how the agents should be switched. Failing that, a cardiology consult by the family physician is strongly encouraged.

Propafenone inhibits the metabolism of warfarin,$^{1,2}$ therefore, if propafenone is discontinued, INR will need to be monitored carefully, with the expectation a dose increase will be necessary. Dronedarone and verapamil may also potentiate warfarin’s effects, but if they do, it will not be to the same degree as propafenone.

Propafenone is indicated for treatment of documented life-threatening ventricular arrhythmias, such as sustained ventricular tachycardia prevention.$^3$

Specifically:

- Atrioventricular re-entry tachycardia (AVRT) with frequent symptoms$^4$
- Atrioventricular nodal re-entry tachycardia (AVNRT) unresponsive to a beta-blocker (BB) or calcium channel blocker (CCB) in a patient not desiring radiofrequency ablation$^4$
- Focal atrial tachycardia (AT) with frequent symptoms$^4$
- Maintenance of sinus rhythm in those with normal left ventricular function (LVF) and atrial fibrillation/flutter (AF)$^3,5,6$
- Paroxysmal AF (“pill-in-the-pocket”)$^5,7$

Flecainide is the only other Class 1C antiarrhythmic$^{8,9}$ and is an appropriate alternative to propafenone in all of the above conditions.$^4$

For both flecainide and propafenone:

- do not use in the presence of coronary artery disease,$^{4,6,10}$ heart failure,$^{6,10}$ or left ventricular hypertrophy$^{10}$
- do combine with AV nodal blocker (ex. metoprolol, diltiazem, verapamil, digoxin)$^{4,5,6}$
- pill-in-the-pocket strategy: co-administer with beta-blocker; i.e. metoprolol 50-100 mg x 1$^5,7$
- appear to have similar propensity to prolong QT interval$^{11,12}$

<table>
<thead>
<tr>
<th>Dose Comparison between Propafenone and Flecainide</th>
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<tbody>
<tr>
<td><strong>Propafenone</strong></td>
</tr>
<tr>
<td><strong>Chronic Use$^{4,5,7}$</strong></td>
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<tr>
<td>Usual: 150 mg q8h PO</td>
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<td>Max: 300 mg q8h PO</td>
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<tr>
<td><strong>Pill in Pocket$^{4,5,7}$</strong></td>
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<tr>
<td>Weight less than 70kg</td>
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<td>Weight 70kg or more</td>
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Switching to flecainide from propafenone:
It is advised to wait two to four half-lives after discontinuing the previous antiarrhythmic (propafenone) before initiating flecainide.\(^{13}\) Patients with atrial fibrillation and structural heart disease or conduction abnormalities should be observed in hospital during initiation of therapy for excessive PR prolongation or development of dangerous or worrisome arrhythmias.\(^{5}\) However, as neither flecainide nor propafenone should be used in patients with structural heart disease, this would be a complicated case that should be managed by a specialist.

The half-life of propafenone is affected by polymorphic variations of CYP 2D6.\(^{3}\) The t\(_{1/2}\) in extensive metabolizers is 2-10 hours; that in poor metabolizers is 10-32 hours.\(^{3,14,15}\) Micromedex indicates the t\(_{1/2}\) is 5-8 hours but that values ranging between 2-32 hours have been reported.\(^{14}\) Currently CYP 2D6 status remains unknown for most patients. Because of the large variation, ‘wash out’ time should be individualized to the patient based on risk of untreated arrhythmias versus adverse additive effects. As this will likely be a difficult assessment, inclusion of a cardiologist in the decision is key.

Other alternatives:

<table>
<thead>
<tr>
<th>Arrhythmia Type</th>
<th>Alternative to propafenone and flecainide(^^4)</th>
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<tbody>
<tr>
<td>AVRT</td>
<td>beta blocker, diltiazem, verapamil, sotalol</td>
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<tr>
<td>AVNRT*</td>
<td>sotalol</td>
</tr>
<tr>
<td>Focal AT with frequent symptoms</td>
<td>beta blocker, diltiazem, verapamil</td>
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<tr>
<td>Sinus rhythm control AF with normal LVF</td>
<td>dronedarone (careful in combination with digoxin), sotalol; if ineffective (\rightarrow) amiodarone</td>
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<td>Paroxysmal AF</td>
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</tbody>
</table>

*unresponsive to beta blocker or calcium channel blocker in those not desiring radiofrequency ablation

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References


