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 <u>normal</u> 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:

- <u>do not</u> use in the presence of coronary artery disease,[4-6,10] heart failure, [6,10] or left ventricular hypertrophy[10]
- <u>do</u> 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]

Dose Comparison between Propafenone and Flecainide		
	Propafenone	**Flecainide**
Chronic Use[4,5,7]		
	Usual:150 mg q8h PO Max: 300 mg q8h PO	50 mg Q12H PO then ↑ by 50 mg increments based on QRS intervals. ↓dose if QRS increases more than 20% from baseline. Usual: 150 mg q12h PO Max: 200 mg q12h PO
Pill in Pocket[4,5,7]		
Weight less than 70kg	450 mg × 1 PO	200 mg x 1PO
Weight 70kg or more	600 mg × 1 PO	300 mg x 1 PO

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:

Antiarrhythmics to be Used as Alternatives to Propafenone and Flecainide According to Indication	
Arrhythmia Type	*Alternative to propafenone and flecainide*[4]
AVRT	beta blocker, diltiazem, verapamil, sotalol
AVNRT*	sotalol
Focal AT with frequent symptoms	beta blocker, diltiazem, verapamil
Sinus rhythm control AF with normal LVF	dronedarone (careful in combination with digoxin), sotalol; if ineffective → amiodarone
Paroxysmal AF	-
*unresponsive to beta blocker or calcium channel blocker in those not desiring radiofrequency ablation	

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