

Sotalol Shortage

Key Points

- Indication for sotalol must be confirmed
- Ensure cardiology/electrophysiology (EP) has been consulted (minimum GP phone consultation) regardless of indication
- Other cardiovascular factors need to be identified (e.g. presence of heart failure, left ventricular dysfunction, coronary artery disease, ejection fraction, etc.)
- Leave management of patients on sotalol for ventricular arrhythmias to cardiology/EP
- Patients must be monitored

Approved indications of sotalol¹:

- Ventricular arrhythmias

Off-label uses of sotalol^{1,2}:

- Atrial arrhythmias

Therapeutic alternatives:

All attempts should be made to consult a cardiologist for each patient as clinical considerations may be complex and will include arrhythmia type, comorbidities (especially cardiovascular), potential drug-drug and drug-disease interactions, past agent use and effect of those agents. As always cost and patient preference need to be considered if possible; however, options may be limited for some patients.

Atrial arrhythmias

Atrial Fibrillation (AF)/ Atrial Flutter (AFL)^{2,3}

Rate Control versus Rhythm Control (See Figure 3 from [2014 CCS AF Update](#))

- There is no difference in mortality between rhythm and rate control strategies⁴

A **rhythm-control** strategy is useful in patients with AF or AFL who remain symptomatic with rate-control therapy or in whom rate-control therapy is unlikely to control symptoms.² (See Figures 4 and 5 from [2012 CCS AF Update](#))

- Sotalol is used as a means of rhythm control in patients with an ejection fraction above 35%^{3,5}
 - Other antiarrhythmics used in atrial arrhythmias: amiodarone, dronedarone, flecainide and propafenone.²
 - Patients not eligible for available rhythm control agents will need to be switched to rate control.

*Antiarrhythmic Choices by Comorbidity*²

- If **NO structural heart disease** (no evidence of cardiomyopathy – dilated, ischemic, infiltrative or hypertrophic) and/or CAD -> consider propafenone or flecainide. Note: use concurrently with an AV nodal blocking agent (beta-blocker or calcium channel blocker).
- Patients with **structural heart disease and/or CAD** -> amiodarone if patient able to tolerate. If unable to tolerate amiodarone, in patients with NO heart failure and AF is NOT permanent, consider dronedarone
- Patients with **structural heart disease and/or CAD who do not tolerate amiodarone** -> consider a switch to a rate control with dose-equivalent beta blocker. (See Making the Switch below)

Table 1: Agents for Rhythm Control in Atrial Fibrillation^{2,5,6}

Antiarrhythmic/ Usual Dose in AF	AF Indication	Comments
Class Ic		
Flecainide 50-150 mg PO BID P-I-P: 200-300 mg PO x1 ↓dose if renal dysfunction	Normal LVF	<ul style="list-style-type: none"> • AVOID if structural heart disease • AVOID in patients who are post-MI or have asymptomatic ventricular arrhythmias - AVOID in CAD or LVD
Propafenone 150 mg PO TID P-I-P: 450-600 mg PO x1 ↓dose if renal or liver dysfunction		<ul style="list-style-type: none"> • ↓ dose if QRS ↑ >20% from baseline • should be combined with AV-nodal blocking agent (βB, diltiazem or verapamil) • Pill-in-Pocket (P-I-P): for infrequent recurrences; can be used on its own intermittently or added to low-dose chronic therapy
Class III		
Amiodarone 200-400 mg/d in 1 or 2 doses.	Abnormal LVF (regardless of EF) Normal LVF (2 nd line)	<ul style="list-style-type: none"> • Unless EF less than 35%, other agents preferred due to LT toxicity (hepatic, thyroid, pulmonary, ophthalmic) • d/c if serum aminotransferase ↑ more than 2-fold baseline • Many DIs
Dronedarone 400 mg PO BID	Normal LVF <u>Non-permanent AF only</u>	<ul style="list-style-type: none"> • ↑risk of CV death in permanent AF • Less efficacious than amiodarone but less serious adverse events • May be added to βB or CCB for rate control • Substrate of CYP3A4, prolongs QTc interval • Limited experience with this drug; expensive
AF= atrial fibrillation; AV = atrioventricular; βB=beta-blocker; CAD = coronary artery disease; CCB=calcium channel blocker; CV= cardiovascular; DI=drug interaction; EF= ejection fraction; LT=long term; LVD = left ventricular dysfunction; LVF= left ventricular function; MI= myocardial infarction; P-I-P=pill in the pocket (patients with infrequent recurrences keep the drug on hand to take only at times of symptoms)		

Rate control should be utilized to improve symptoms and clinical outcomes attributed to excessive ventricular rates.² (See Figure 3 from [2012 CCS AF Update](#)) Rate controlling agents include beta blockers (βB), non-dihydropyridine calcium channel blockers (CCB) (diltiazem, verapamil) and digoxin. βBs can be used regardless of heart failure or coronary artery disease (CAD) status. CCBs should not be used in patients with heart failure. Digoxin may be added to βB therapy in patients with heart failure; do not use as monotherapy in active patients, only those who are sedentary.

Table 2: Agents for Rate Control in Atrial Fibrillation^{2,7,8}

Drug	Dose	Use
1st Line: Beta-Blockers		
Bisoprolol	2.5-10 mg PO daily 2.5 mg bisoprolol ~ 80 mg sotalol	Any indication
Metoprolol	25 mg-200 mg PO BID 50-100 mg metoprolol ~ 80 mg sotalol	Preferred in CAD
1st Line: Non-Dihydropyridine Calcium Channel Blockers		
Diltiazem	120 – 480 mg PO daily 120-240 mg PO BID	CAD
Verapamil	120 – 480 mg PO daily 120-240 mg PO BID	Do not use in HF
2nd Line: Digoxin (if poor/no response or contraindication to 1st line)		
Digoxin	0.0625 – 0.25 mg PO daily	May be added to β B in HF Reserve for sedentary patients who have LVSD
β B = beta blockers; CAD= coronary artery disease; HF= heart failure; LVSD = left ventricular systolic dysfunction		

Making the switch^{1,9}

Because sotalol has beta-blockade properties, abrupt discontinuation may result in rebound tachycardia, headache, tremor, and chest pain; more rarely precipitation of ventricular tachyarrhythmias and/or, in those with CAD, precipitation of ischemic symptoms may occur.

Ideally, **sotalol should be tapered over 1-2 weeks**; this may not be possible in the face of a shortage. In the absence of evidence-based recommendations for this particular situation, sotalol should be temporarily replaced with another β B at a comparable dose to be tapered. [It makes sense to switch to a β B that is also used for AF/AFL though in a different capacity. These agents^{5,8} and their **approximate equivalent doses to sotalol 80 mg⁸**:

Bisoprolol: 2.5 (usual dose: 2.5-10 mg PO daily)

Metoprolol: 50-100 mg (usual dose: 25-200 mg PO BID) (choose dose based on frailty of patient, degree of symptoms, current heart rate, comorbidities)

Keep in mind patients being switched to propafenone or flecainide should be combined with an AV nodal blocking agent such as a β B in any case.

Monitoring:

- Monitor the patient for signs/symptoms of β B withdrawal: tachycardia, headache, tremor, chest pain, ventricular tachyarrhythmias, and ischemic symptoms.⁹
- Monitor patient for uncontrolled symptoms of arrhythmia (palpitations, lightheadedness/dizziness, shortness of breath [with heart failure])¹⁰
 - As these symptoms overlap, symptomatic patients will need to be evaluated

Ventricular arrhythmias

Consult cardiology, preferably electrophysiology.

Table 3: Suppliers of sotalol tablets in Canada¹¹:

Manufacturer	Strength	DIN	Status at McKesson* as of 21 Dec 2017 ¹²
APX	80 mg	02210428	29 Jan 2018 (100-count) Discontinued (500-count)
	160 mg	02167794	29 Jan 2018 (100- count) Indeterminate (500-count)
DOM	80 mg	02238634	No longer stocked
	160 mg	02238635	Discontinued
JPC	80 mg	02368617	25 Apr 2018 (100-count) Indeterminate (500-count)
	160 mg	02368625	26 Mar 2018
PMS	80 mg	02238326	24 Apr 2018 (100-count) Discontinued (500-count)
	160 mg	02238327	16 Aug 2018 (100-count)
PRO	80 mg	02316528	Not listed
	160 mg	02316536	Not listed
TEV	80 mg	02084228	Discontinued
	160 mg	02084236	Discontinued
SIV	80 mg	02385988	Not listed
	160 mg	02385996	Not listed
*medSask only has access to availability via McKesson. Certainly check with other suppliers to which you have access.			

Prepared by Carmen Bell BSP. Reviewed by Dr. William Semchuk, Manager, Clinical Pharmacy - Regina, Sk Health Authority
medSask | 22 Dec 2017

References:

- RxTx [Internet]. Ottawa (ON): Canadian Pharmacists Association; 2017. CPS online: Beta-adrenergic Blocking Agents; [revised 01 Feb 2014; cited 31 Mar 2017]. Available from: <http://www.e-therapeutics.ca>
- Skanes AJ, Healey J, Cairns J, et al. Focused 2012 update of the Canadian Cardiovascular society atrial fibrillation guidelines: recommendations for stroke prevention and rate/rhythm control. *Can J Cardiol* 2012; 28(2): 125-136
- Verma A, Cairns J, Mitchell B, et al. 2014 focused update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. *Can J Cardiol* 2014; 30(10): 1114-1130
- Wyse DG, Waldo AL, DiMarco JP et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;347(23):1825-33.
- Jin M, Kosar L. Atrial fibrillation (AF): treatment overview. RxFiles 01 Mar 2017
- RxTx[Internet]. Ottawa (ON): Canadian Pharmacists Association; 2017. Birnie D, Nery P. Supraventricular tachycardia; updated 01 Sep 2017; cited 31 Oct 2017]. Available from: <https://www.e-therapeutics.ca>
- Macle L, Cairns J, Leblank K, et al. The Canadian Cardiovascular Society's atrial fibrillation guidelines pocket guide. 2016. [cited 03 Nov 2017] Available at https://www.ccs.ca/images/Guidelines/PocketGuides_EN/AF_Gui_2016_PG_EN.pdf
- Atrial Fibrillation Clinic. General sotalol shortage plan. St. Paul's Hospital: Vancouver, BC. [cited 03 Dec 2017].
- Podrid P. Major side effects of beta blockers. In: UpToDate, Basow, DS (Ed), Waltham MA, 2017. Cited 03 Nov 2017. Available from www.uptodate.com. Subscription and login required.
- DynamedDynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2017. Record No. 115288, Atrial fibrillation; [updated 31 Oct 2017, cited 03 Nov 2017]; [about 61 screens]. Available from <http://www.dynamed.com/login.aspx?direct=true&site=DynaMed&id=115288> Registration and login required.
- Health Canada. Drug Product Database Online Query. Ottawa, ON: Health Canada; [cited 31 Oct 2017]. Available from <http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp>
- PharmaClik McKesson Canada; c2017 [cited 21 Dec 2017] PharmaClik; Available from <http://clients.mckesson.ca> Account required.