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Atrial Fibrillation – Diagnosis and Management

Effective Date: April 1, 2015

Scope

This guideline provides recommendations for the diagnosis and management of atrial fibrillation (AF) including the primary prevention of stroke and transient ischemic attack (TIA) in adults aged ≥19 years. This guideline focuses primarily on non-valvular AF.

This guideline is part of the BCGuidelines.ca – *Stroke and Atrial Fibrillation* series. The series includes three other guidelines: *Stroke and Transient Ischemic Attack – Acute and Long-Term Management*; *Use of Non-Vitamin K Antagonist Oral Anticoagulants (NOAC) in Non-Valvular Atrial Fibrillation;* and *Warfarin Therapy Management.*

Key Recommendations

- Determine the patient's cardiac stability and provide emergency stabilization if needed.
- Consider all patients with atrial fibrillation for antithrombotic therapy (short and long term).
- Establish the risk of stroke in patients with atrial fibrillation using age (≥ 65) and $CHADS_2$.
- Oral anticoagulants are recommended in patients with $CHADS_2 = 0$ and age ≥ 65 years.
- The goals of rate and/or rhythm control strategies are to improve patient symptoms, exercise tolerance, quality of life, prevent hospitalizations and improve left ventricular function.
- Manage co-morbidities that may raise atrial fibrillation risk, such as hypertension, diabetes and heart failure.

Definition

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with resulting deterioration of atrial mechanical function.[1] For practical purposes, because the management differs, AF can be divided into two main types, valvular or non-valvular AF (for definitions of AF subgroups see *Appendix A: Types of Atrial Fibrillation). Valvular AF* is caused by significant structural changes in the valves or congenital heart disease. Therefore, valvular AF occurs in the **presence** of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair. *Non-valvular AF* occurs in **absence** of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

Epidemiology and Risk Factors

Individuals with AF have a 3 to 5 times greater risk for ischemic stroke.[2] It is estimated that 20% of all strokes are caused by AF.[2] The majority (70 – 95%)[3,4] of AF cases are non-valvular.

Approximately 44,000, or 6%, of British Columbians aged > 65 years live with AF.[5,6] Key risk factors for the development of AF include increasing age, hypertension, myocardial infarction (MI), congestive heart failure, and valvular heart disease.[7] Lifetime risks for the development of AF, based on the Framingham Heart Study, are 1 in 4 for men and women 40 years of age and older.[8] The Rotterdam study showed that prevalence and incidence of AF increases with age.[9] After the age of 55, the risk of developing AF doubles with each decade of life.[5,10]

Established associations exist between AF and other cardiovascular disease processes, such as coronary heart disease, diabetes, hypertension, congestive heart failure and valvular heart disease.[7,11-13] Possible causes of AF are listed in *Appendix B: Possible Causes of Atrial Fibrillation.*

Diagnosis

Patients may present with or without symptoms such as palpitations, dyspnea, dizziness, presyncope, syncope, chest pain, weakness or fatigue. Ask about palpitations and check for irregular heart rhythm during a routine exam in patients at risk for stroke.[2,14,15]

For patients who present with the above symptoms, ascertain if any of these symptoms are present during AF. If so, they are likely caused by AF. Refer to *Appendix C: Assessing Atrial Fibrillation Symptom Severity with the CCS-SAF Scale.*

A pulse check that detects an irregularity can be confirmed by an electrocardiogram (ECG).[2] Ambulatory ECG monitoring (e.g., Holter) for intermittent AF can be considered after clinical evaluation, risk assessment, and baseline ECG have been completed. See BCGuidelines.ca – *Ambulatory ECG Monitoring – Holter Monitor and Other Devices.*

Standard tests used to evaluate cardiac function, identify precipitating factors and/or identify common co-morbidities, include:

- Complete blood count – To identify comorbid conditions (e.g., anemia, infection)
- Thyroid stimulating hormone – To identify hyperthyroidism
- Serum creatinine and electrolytes – To assess kidney function
- Fasting blood glucose OR hemoglobin A1c – To screen for diabetes
- Lipid profile – To identify hyperlipidemia
- Echocardiogram – To assess heart size and shape; chamber sizes and pressures; valve structure and function; presence of pericardial effusion; wall motion abnormalities; systolic and diastolic function.

Management

A. VALVULAR ATRIAL FIBRILLATION

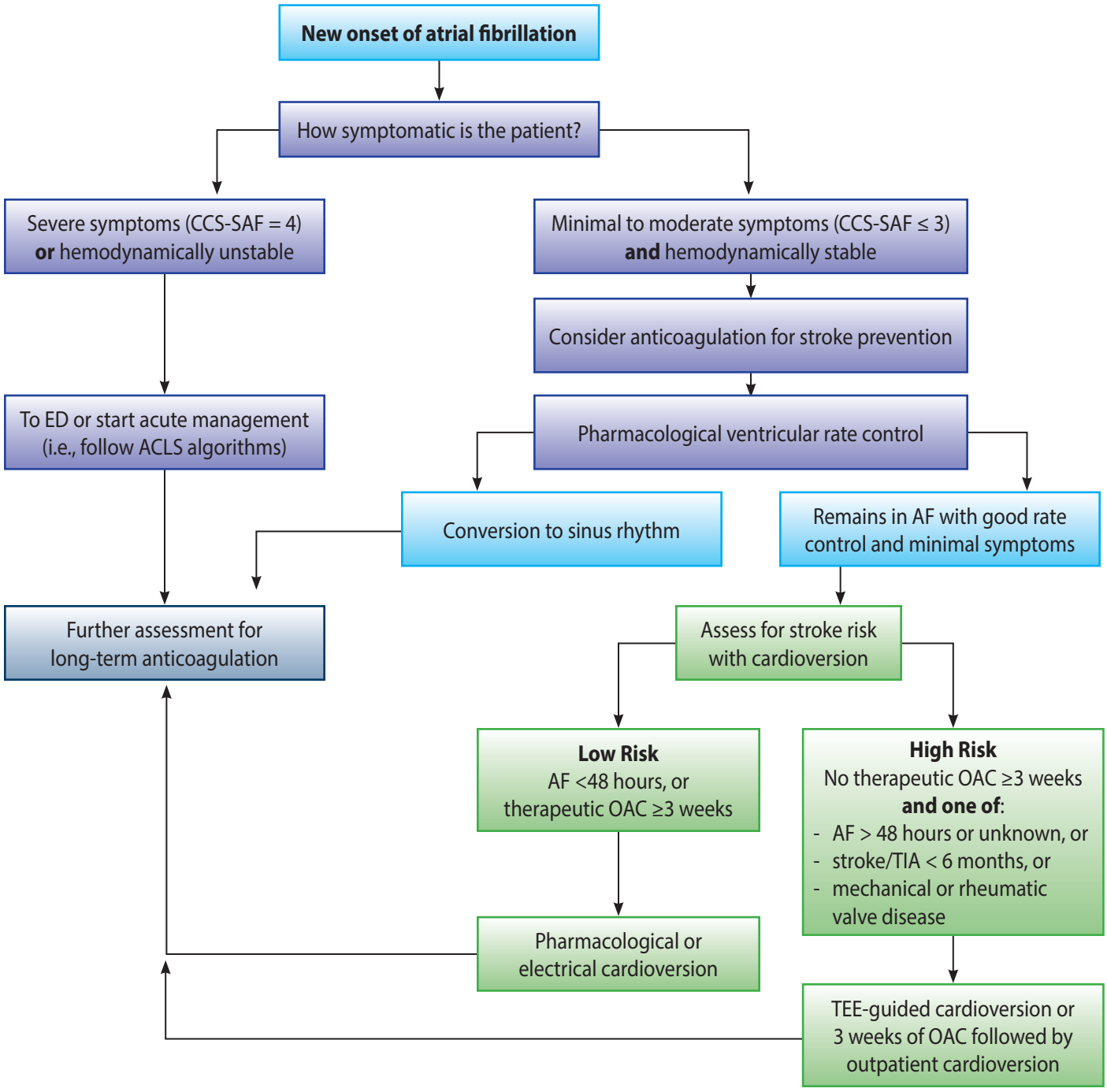
Patients with valvular AF (AF in the **presence** of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve or mitral valve repair) are at significantly increased risk for ischemic stroke, and warfarin is recommended. Treatment with a non-vitamin K antagonist oral anticoagulant (NOAC; e.g., dabigatran, rivaroxaban, apixaban) is not recommended in patients with valvular AF and these drugs are not approved for use in this patient group. This is because at this time, the clinical trials for NOACs were conducted in patients with non-valvular AF only. Rate and rhythm control recommendations are the same in valvular AF as in non-valvular AF (see below).[16]

B. NON-VALVULAR ATRIAL FIBRILLATION

Review the following 3 considerations for newly detected non-valvular AF (see Figure 1).

1. How symptomatic is the patient?
2. Should an anticoagulant be used for stroke prevention?
3. Is this a rate or rhythm control strategy?

Figure 1. Management of newly detected non-valvular atrial fibrillation[17]



Abbreviations: ACLS = advanced cardiovascular life support; AF = atrial fibrillation; CCS-SAF = Canadian Cardiovascular Society Severity of Atrial Fibrillation score; ED = emergency department; OAC = oral anticoagulants; TEE = transesophageal echocardiography; TIA = transient ischemic attack.

STEP 1: How symptomatic is the patient?

Determine the patient's cardiac stability and provide emergency stabilization if needed. Consider utilizing the Canadian Cardiovascular Society Severity of Atrial Fibrillation (CCS-SAF) scale to assess AF symptom severity and impact on quality of life. Details on classification can be found in *Appendix C: Assessing Atrial Fibrillation Symptom Severity with the CCS-SAF Scale.*

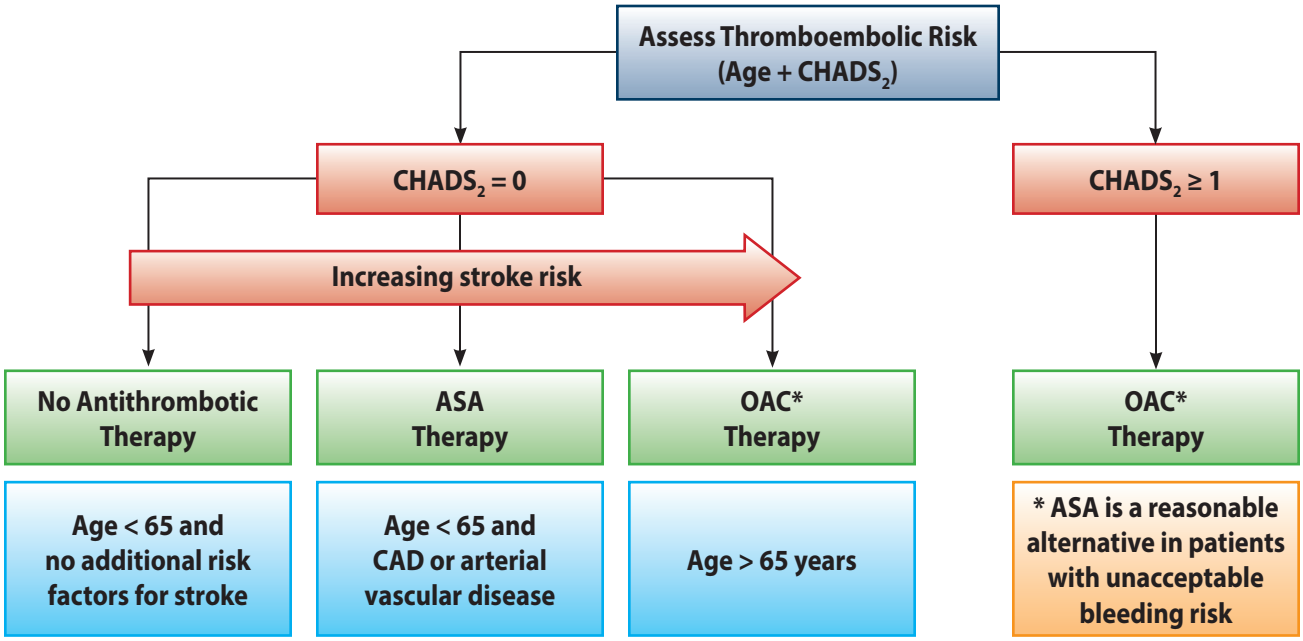
- Refer for or start acute management if hemodynamically unstable.
- Consider referral to the emergency department or start acute management if highly symptomatic (e.g., CCS-SAF = 4, severe effects on patient's quality of life).
- Start rate/rhythm control if not highly symptomatic (e.g., CCS-SAF ≤ 3, minimal to moderate effects on patient's quality of life) and hemodynamically stable (systolic blood pressure > 90 mmHg, a heart rate < 120 beats per minute (BPM) and without clinical signs of shock).

STEP 2: Should an anticoagulant be used for stroke prevention?

Consider all patients with AF, including those with paroxysmal AF or intermittent AF, for antithrombotic therapy (see Figure 2). The decision to place a patient on long-term anticoagulation must be based on an analysis of risk and benefit, with consideration of patient values and preferences.

A predisposition to falls, even when considering potential head trauma, is rarely a contraindication to the use of anticoagulants in elderly patients with AF.[18] Even when taking anticoagulants, the risk of subdural hematoma is so low that persons with an average risk of stroke from AF (5% per year in the absence of anticoagulation) must fall approximately 300 times in a year for the risks of anticoagulation to outweigh its benefits on a statistical basis.[19]

Figure 2. Recommendations for antithrombotic agent use based on age and $CHADS_2$ Score[20]



Abbreviations: ASA = acetyl-salicylic acid; CAD = coronary artery disease; OAC = oral anticoagulants.

Stratification of Stroke Risk

Risk stratification tools exist that use the overlapping characteristics that make up the major risk factors for ischemic stroke and systematic embolism in patients with non-valvular AF.[20] There is also similar factors that are associated with increased risk of bleeding.

Scoring Stroke Risk: $CHADS_2$

Establish the risk of stroke in patients with AF using the **C**ardiac failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke system ($CHADS_2$) Risk **S**coring System.[13]

Letter	Clinical Characteristic	Score (if present)
C	Congestive heart failure	1
H	Hypertension	1
A	Age 75+	1
D	Diabetes	1
S	Prior Stroke or TIA	2
	Total $CHADS_2$ Score	Maximum score = 6

Details can be found in *Appendix D: Stroke Risk Assessment in Atrial Fibrillation: $CHADS_2$ Score*. The score and the patient's age aids in determining best treatment recommendations (see Figure 2).

Scoring Bleeding Risk: HAS-BLED

The HAS-BLED score may aid decision making as it estimates major bleeding risk in patients with AF.[21] HAS-BLED is commonly used in trials but is only validated in AF patients treated with warfarin. It should be noted that ischemic stroke (and its consequences) is relatively frequent, so the competing risk of bleeding due to anticoagulant treatment may be acceptable. It is important to address and manage the causes of potential bleeding. Details can be found in *Appendix E: HAS-BLED Score for Major Bleeding*.

Antithrombotic Therapy

Patients for whom anticoagulation is recommended for stroke prevention, warfarin or NOACs are available options. Existing evidence does not provide a definitive ability to recommend one class of OAC over another (see Controversies in Care below). In addition to current evidence, both the clinician and patient are encouraged to carefully consider the advantages and disadvantages of warfarin compared to the NOACs. When making a decision, the patient's values and preferences should be taken into account.

For more information, refer to *Appendix F: Comparisons of Anticoagulants for Atrial Fibrillation*, *Appendix G: Prescription Medication Tables for Atrial Fibrillation*; and to BCGuidelines.ca – *Use of Non-Vitamin K Antagonist Oral Anticoagulants (NOAC) in Non-Valvular Atrial Fibrillation* and *Warfarin Therapy Management*.

There are no randomized controlled trial data for NOAC treatment for dialysis dependent patients with non-valvular AF (hemodialysis and peritoneal). Therefore, routine use of NOACs in this patient group cannot be recommended. Anticoagulation with warfarin can be considered in cases if the stroke risk is considered very high and bleeding risk low.

When any chronic anticoagulation is contraindicated and the patient is at high risk of a stroke, then alternative interventions can be considered (e.g., left atrial appendage occlusion/resection). Consider urgent consultation and/or referral to a specialist. Use of ASA might have some benefit while waiting for consultation. There is insufficient evidence to recommend an ASA dose in this setting; however, common practice is to use 81 mg/day.

Concomitant use of ASA along with anticoagulants is not recommended in most cases.[19] In cases where the patient is already on ASA, consider consulting with the patient's cardiologist first before stopping ASA when there is an indication for ASA use such as the presence of a stent.

Controversies in Care: Warfarin versus NOACs

Since the available evidence does not provide a definitive ability to recommend one class of OAC over another, international organizations provide different recommendations based on their interpretation of the same studies (see Table 1).

Table 1. Comparison of organizations' recommendations on oral anticoagulants

Organization	Recommendation	Conditions
Canadian Agency for Drugs and Technologies in Health (CADTH)[22]	Warfarin over NOACs	For patients doing well on warfarin there is no evidence to support switching therapies. NOACs are a 2nd-line option for some patients with non-valvular AF who are not doing well on warfarin. NOACs are as effective at preventing stroke as warfarin, but are more expensive and little is known about their long-term safety.
American Heart Association (AHA)/ American College of Cardiology (ACC) / Heart Rhythm Society (HRS)[23]	No recommendation of one over another	Selection individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including time in INR therapeutic range if the patient has been taking warfarin.
Canadian Cardiovascular Society (CCS)[24]	NOACs over warfarin for non-valvular AF	The preference for one of the NOACs over warfarin is less marked among patients already receiving warfarin with stable therapeutic INRs, no bleeding complications, and who are not requesting a change in OAC therapy.
European Cardiovascular Society's (ECS)[25]	NOACs over warfarin for non-valvular AF	NOACs so far tested in clinical trials have all shown non-inferiority compared with warfarin, with better safety, consistently limiting the number of intracranial hemorrhage.

Abbreviations: AF = atrial fibrillation; INR = International Normalized Ratio**;** NOAC = Non-Vitamin K Antagonist Oral Anticoagulants; OAC = oral anticoagulants.

STEP 3: Is this a rate or rhythm control strategy?

Table 2. Factors favouring rate versus rhythm control

Favours Rate Control	*Favours Rhythm Control*
• Persistent AF • Less symptomatic • Aged ≥ 65 years • Hypertension • No history of CHF • Previous antiarrhythmic drug failure • Patient preference • High stroke risk with cardioversion	• Paroxysmal AF • Newly detected AF • More symptomatic • Aged < 65 years • No hypertension • HF clearly exacerbated by AF • No previous antiarrhythmic drug failure • Patient preference • Low stroke risk with cardioversion

Abbreviations: AF = atrial fibrillation; CHF = congestive heart failure; HF = heart failure.
Adapted from: Gillis AM, et al. Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Rate and Rhythm Management, Canadian Journal of Cardiology 2011;27:47-59.

Rate Control

The goals of rate control are to improve patient symptoms, exercise tolerance and quality of life, prevent hospitalizations and, where possible, to improve left ventricular function. Substantial periods of excessively rapid ventricular rates during AF or atrial flutter can lead to deterioration of cardiac function.[19]

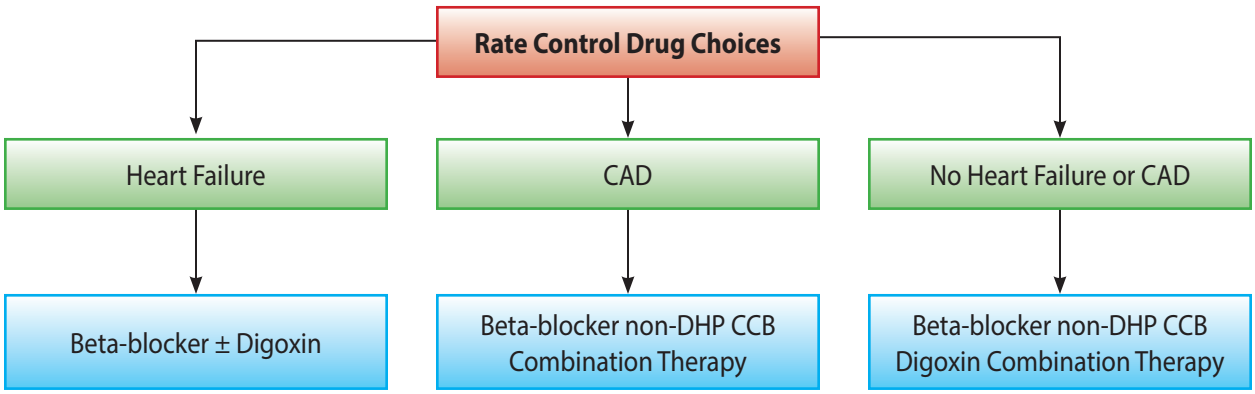
The optimal level of heart rate control is unknown. A lenient rate control strategy (resting heart rate < 110 BPM) is easier to achieve and is as effective for preventing cardiovascular morbidity and mortality as a strict rate control (resting heart ate < 80 BPM and heart rate during moderate exercise < 110 BPM).[26] At present, the consensus is that a resting heart rate of < 100 BPM is recommended, but the heart rate target may need modification based on patient symptoms, preferences and tolerance of rate controlling medications.[17]

Assess ventricular rate in all patients with persistent and permanent AF or atrial flutter. Patients with exertional symptoms may need titration according to their response to moderate exercise (e.g., brisk walking or climbing stairs).

Rate Control Drug Choices

Beta-blockers or non-dihydropyridine calcium channel blockers (non-DHP CCBs; i.e., verapamil or diltiazem) are recommended as initial treatment for rate control in most AF or atrial flutter patients without a history of MI or left ventricular dysfunction. Beta-blockers are preferred in patients with coronary artery disease.[27] Digoxin is not recommended as an initial therapy for active patients because during exercise vagal tone is withdrawn, so that digoxin controls the heart less effectively than beta-blockers or non-DHP CCBs. Digoxin may be considered for patients who are sedentary or who have left ventricular systolic dysfunction in combination with beta-blockers. Digoxin may be considered as monotherapy only in particularly sedentary individuals. Refer to *Appendix G: Prescription Medication Table for Atrial Fibrillation*.

Figure 3. Rate control drug therapy



Abbreviations: CAD = coronary artery disease; non-DHP CCB = non-dihydropyridine calcium channel blockers.

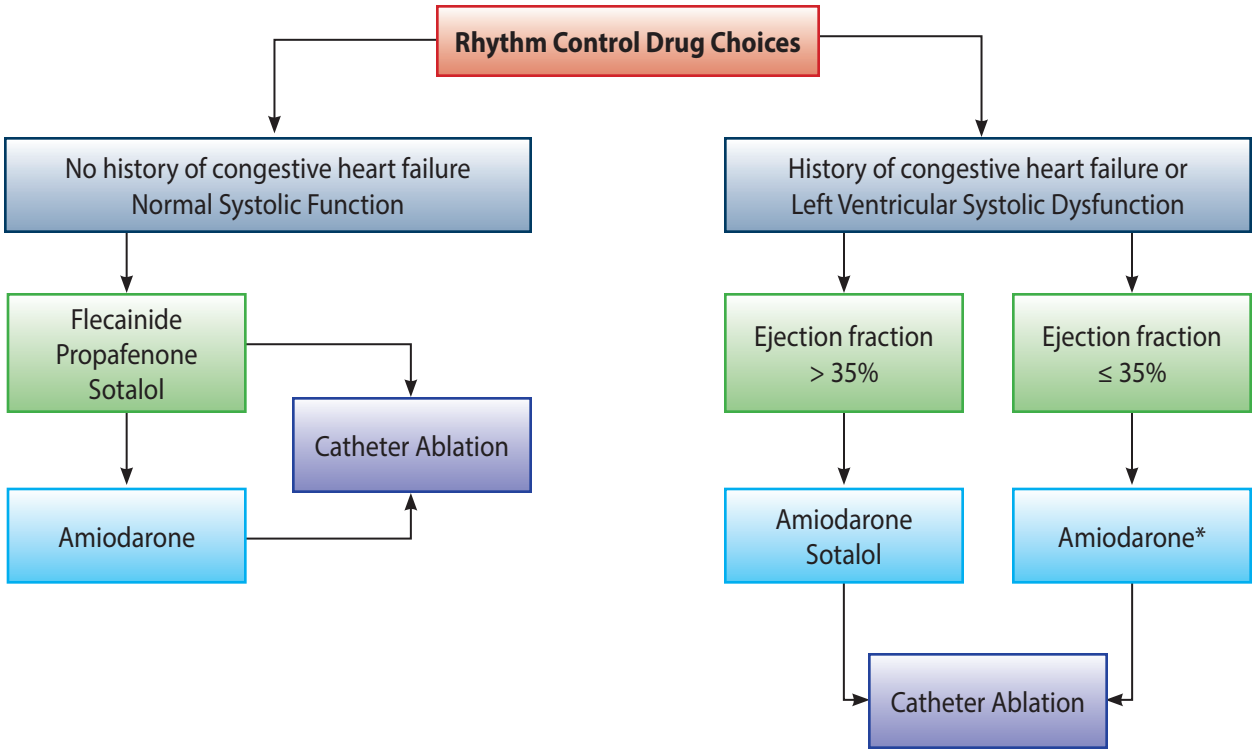
Rhythm Control

The goals of rhythm control therapy are to improve patient symptoms (e.g., palpitations, fatigue, exercise intolerance, or symptoms of heart failure), quality of life, as well as improve left ventricular function by restoring sinus rhythm.[17]

Randomized controlled trials have shown no improvement in major outcomes, including thromboembolism, of a rhythm control strategy versus rate control; however, individual patients may gain symptomatic benefit and even long-term freedom from AF after electrical or pharmacologic cardioversion. The strongest predictor of initial and persistent success with cardioversion is short (< 48 hours) duration of the AF before cardioversion.[17] Rhythm control can improve left ventricular function in patients with AF and left ventricular systolic dysfunction.

Rhythm Control Drug Choices

Figure 4. Antiarrhythmic drug therapy



Footnote: * In patients with left ventricular ejection fraction ≤ 35% amiodarone is the only drug recommended because of the low risk of proarrhythmia in heart failure.[28,29] Amiodarone or sotalol are recommended in those with ejection fraction > 35%.[17]

Consider referral for catheter ablation after failed antiarrhythmic drug therapy in patients with highly symptomatic or recurrent paroxysmal AF.[2,15,17,30] Prior to either electrical or pharmacological cardioversion patients should be adequately anticoagulated to prevent thromboembolic events.[1,31,32] Successful ablation does not alleviate the need for long-term anticoagulation. Long-term anticoagulation should be considered based on age and $CHADS_2$ score model (i.e., independent of current rhythm).

Potential Indications for Referral

Cardiology or Internal Medicine:

- A review by a specialist can be considered for patient eligibility for long-term OAC or for an alternative treatment if the patient has a contraindication to anticoagulants.
- Consider referral if poor or incomplete response, or ongoing symptoms.

Neurology or Internal Medicine:

- Recurrent TIA/minor stroke.

Specialty Clinics:

- AF clinics.
- Management of co-morbid conditions (e.g., diabetes clinics, heart failure clinics).

Management with Co-Morbid Conditions

Co-morbidities such as hypertension, diabetes[33] and congestive heart failure[34] raise AF risk and should be adequately managed to decrease morbidity and mortality. Bleeding risk can be reduced by managing hypertension. Hypertension control can also reduce the recurrence of AF and decrease ER visits and hospitalizations. For more recommendations on managing these conditions, refer to BCGuidelines.ca.

C. ATRIAL FIBRILLATION IN OTHER CIRCUMSTANCES

Transient AF

Episodes of transient AF as short as 5 – 6 minutes have been shown to be associated with a 2 – 2.5 fold increase in strokes in patients with implanted devices. Evidence is unclear on the risk of stroke with these transient AF events.[23] Until further information is available it is reasonable to consider OAC therapy for patients age ≥ 65 years or $CHADS_2$ score ≥ 1 who have episodes of AF lasting > 24 hours, or for shorter episodes in high-risk patients. AF is considered a marker of vascular ill health. Managing other risk factors such as hypertension and or diabetes may reduce the risk of recurring AF episodes.

Post-Operative AF

Transient AF in the post-operative setting may be a harbinger of future stroke risk. Closer monitoring of these patients for further episodes of AF may be warranted. At the present time there is no data to support use of OAC to prevent stroke or systemic emboli in patients with AF in the post-operative setting.[35] But, beta-blockers are recommended as prevention and treatment of post-operative AF unless contraindicated in patients that are undergoing cardiac or thoracic surgery.[16,36] Preoperative amiodarone reduces the incidence of AF with cardiac surgery and is reasonable as prophylactic therapy for patients at high risk of post-operative AF.[16]

Thyrotoxicosis

Beta-blockers are recommended to control ventricular rate with AF complicating thyrotoxicosis unless contraindicated. Non-DHP CCBs are recommended to control the ventricular rate with AF and thyrotoxicosis when beta-blockers cannot be used.[36]

Hypertrophic Cardiomyopathy (HCM)

Anticoagulation is indicated in HCM with AF independent of the stroke risk score. Antiarrhythmic drugs can be useful to prevent recurrent AF in HCM. Amiodarone, or disopyramide combined with beta-blockers or Non-DHP CCBs are reasonable.[37]

Ongoing Care

In most patients the burden of AF is a progressive condition where they spend longer in AF leading to permanent AF. Screen for other conditions that impact vascular health. Reassess age and $CHADS_2$ risk especially if previous score was 0. Patients require regular monitoring for possible adverse events from anticoagulants and assessment of renal function on a 6 monthly basis for those on NOACs. See BCGuidelines.ca – *Use of Non-Vitamin K Oral Anticoagulants in Non-Valvular Atrial Fibrillation.*

Resources

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Resources

- BC Guidelines, www.BCGuidelines.ca – *Ambulatory ECG Monitoring – Holter Monitor and Other Devices; Cardiovascular Disease – Primary Prevention; Diabetes Care, Heart Failure – Diagnosis and Management; Hypertension – Diagnosis and Management.*
- Heart and Stroke Foundation – British Columbia and Yukon, www.heartandstroke.bc.ca
- Canadian Stroke Network, www.canadianstrokenetwork.ca
- Stroke Services BC, www.phsa.ca/AgenciesAndServices/Services/stroke-services-bc.htm
- Rapid Access to Consultative Expertise (RACE), www.raceconnect.ca or by telephone 604-696-2131, toll free 1-877-696-2131, program designed to increase family physician access to specialist consultation.
- HealthLinkBC, www.healthlinkbc.ca or by telephone (toll free in BC) 8-1-1 or 7-1-1 (for the hearing impaired) for health information, translation services and dieticians.
- PharmaCare Special Authority, www.health.gov.bc.ca/pharmacare/sa/saindex.html#list, provides benefit status for medication coverage and specific medical circumstances of coverage depending on BC PharmaCare plan rules.

Diagnostic code: 427.3, I48

Appendices

- Appendix A: Types of Atrial Fibrillation
- Appendix B: Possible Causes of Atrial Fibrillation
- Appendix C: Assessing Atrial Fibrillation Symptom Severity with the CCS-SAF Scale
- Appendix D: Stroke Risk Assessment in Atrial Fibrillation: $CHADS_2$ Score
- Appendix E: HAS-BLED Score for Major Bleeding
- Appendix F: Comparisons of Anticoagulants for Atrial Fibrillation
- Appendix G: Prescription Medication Table for Atrial Fibrillation

Associated Documents

The following documents accompany this guideline:

- BCGuidelines.ca – *Stroke and Transient Ischemic Attack – Acute and Long-Term Management*
- BCGuidelines.ca – *Use of Non-Vitamin K Antagonist Oral Anticoagulants (NOAC) in Non-Valvular Atrial Fibrillation*
- BCGuidelines.ca – *Warfarin Therapy Management*
- BC Pharmacare – Special Authority Request Form 5391 – Apixaban /Dabigatran/ Rivaroxaban for Atrial Fibrillation

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

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- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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Disclaimer

Appendix A: Types of Atrial Fibrillation[1,2]

Abnormalities or damage to the heart's structure are the most common cause of atrial fibrillation (AF). Note these types are not exclusive of each other.

Valvular AF	Occurs in the presence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve or mitral valve repair.
Non-valvular AF	Occurs in absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.
New-onset AF	AF not previously documented.
Paroxysmal AF	AF which terminates spontaneously or with intervention within 7 days of onset. The duration of the paroxysmal AF is usually less than 24 – 48 hours but can last up to a week. Paroxysmal AF may occur only once or may be recurrent.
Persistent AF	Continuous AF that is sustained greater than 7 days.
Permanent AF	Permanent AF is when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm. Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF.
Chronic AF	Implies continuing AF and does not address the important clinical distinction between persistent and permanent AF.
Focal AF	Initiated or sometimes maintained by arrhythmogenic foci, often pulmonary veins. It could be paroxysmal or persistent.
Lone or idiopathic AF	Occurs in the absence of structural heart disease, hypertension, diabetes or other identifiable cause for the arrhythmia (e.g., hyperthyroidism or alcohol abuse).
Transient AF	An irregular heartbeat pattern presented in individuals who are otherwise healthy. A transient AF episode can be the result of stress, dehydration, alcohol or drug use as well as secondary to other conditions.

References:

1. Kaiser Permanente, Southern California. Clinical Practice Guidelines Handbook, 8th ed.,2008.
2. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the management of patients with atrial fibrillation: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2014 Apr 10.

Appendix B: Possible Causes of Atrial Fibrillation

Possible cardiac and non-cardiac causes of atrial fibrillation (AF) include: (not a complete list)

Cardiac causes of AF	Non-cardiac causes of AF
Common cardiac causes: • Hypertension (especially with associated left ventricular hypertrophy) • Ischemic heart disease • Rheumatic heart disease • Valvular heart disease (especially mitral valve stenosis) • Cardiac surgery • Myocarditis • Sick sinus syndrome • Pre-excitation syndromes with accessory conduction pathways (e.g., Wolff-Parkinson-White syndrome) Less common cardiac causes: • Dilated and hypertrophic cardiomyopathy • Pericardial disease (e.g., pericardial effusion, constrictive pericarditis) • Atrial septal defect • Atrial myxoma	• Hyperthyroidism • Acute infections, especially pneumonia in the elderly • Acute excess alcohol intake or chronic excess alcohol intake • Narcotic abuse • Obesity • Sleep apnea • Hemochromatosis • Sarcoidosis • Respiratory causes: - Lung cancer - Chronic obstructive pulmonary disease (COPD) - Pleural effusion - Pulmonary embolism - Pulmonary hypertension

Appendix C: Assessing Atrial Fibrillation Symptom Severity with the CCS-SAF Scale[1]

The 3 steps of the Canadian Cardiovascular Society (CCS) Severity of Atrial Fibrillation (SAF) Scale:

Step 1: Symptoms

Identify the presence of the following symptoms:

A. Palpitations
B. Dyspnea
C. Dizziness, presyncope, or syncope
D. Chest pain
E. Weakness or fatigue

Step 2: Association

Is atrial fibrillation (AF), when present, associated with the symptoms (A – E) listed above?
For example, ascertain if any of the above symptoms are present during AF and likely caused by AF.

Step 3: Functionality

Determine if the symptoms associated with AF (or the treatment of AF) affect the patient's functionality (subjective quality of life).

The CCS-SAF Scale:

Class	Definition
0	Asymptomatic with respect to AF.
1	Symptoms attributable to AF have **minimal** effect on patient's general quality of life: • minimal and/or infrequent symptoms; or • single episode of AF without syncope or heart failure.
2	Symptoms attributable to AF have **minor** effect on patient's general quality of life: • mild awareness of symptoms in patients with persistent/permanent AF; or • rare episodes (e.g., less than a few per year) in patients with paroxysmal or intermittent AF.
3	Symptoms attributable to AF have **moderate** effect on patient's general quality of life: • moderate awareness of symptoms on most days in patients with persistent/permanent AF; or • more frequent episodes (e.g., more than every few months) or more severe symptoms, or both, in patients with paroxysmal or intermittent AF.
4	Symptoms attributable to AF have **severe** effect on patient's general quality of life: • very unpleasant symptoms in patients with persistent/paroxysmal AF; and/or • frequent and highly symptomatic episodes in patients with paroxysmal or intermittent AF; and/or syncope thought to be due to AF; and/or • congestive heart failure secondary to AF.

Reference:

1. Dorian P, Cvitkovic SS, Kerr CR, et al. A novel, simple scale for assessing the symptom severity of atrial fibrillation at the bedside: The CCS-SAF Scale. Can J Cardiol. 2006;22:383-386.

Appendix D: Stroke Risk Assessment in Atrial Fibrillation: $CHADS_2$ Score

The following is provided to aid in the counselling of patients for or against anticoagulants usage in atrial fibrillation (AF) for the prevention of stroke.

Establish the risk of stroke in AF using the **C**ardiac failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke score ($CHADS_2$):[1]

Letter	Clinical Characteristic	Score (if present)
C	Congestive heart failure	1
H	Hypertension	1
A	Age 75+	1
D	Diabetes	1
S	Prior Stroke or TIA	2
	Total $CHADS_2$ Score	Maximum score = 6

These scores have been validated to be approximately equivalent to the following stroke risks (see below). In diabetic patients, the $CHADS_2$ score may underestimate the risk.[2] Generally speaking, the risks of being on anticoagulants are less than the risk of a stroke. The higher the baseline risks of stroke, the greater the benefit of anticoagulants.

Annual stroke risk with or without treatment based on $CHADS_2$ score[a]

$CHADS_2$ Score	Approximate annual stroke risk without treatment (%)	Annual stroke risk with treatment (%)	
		ASA	Anticoagulants[b]
0	1.9	1.3	1.0
1	2.8	2.0	1.4
2	4.0	2.8	2.0
3	5.9	4.1	3.0
4+	8.5 or more	6.0 or more	4.3 or more

Annual bleeding complications due to treatment based on $CHADS_2$ score[a]

$CHADS_2$ Score	Bleeding complication	Annual risk of bleeding complication (%)[c]	
		ASA	Anticoagulants
All scores	Major bleed (all types)	0.25	Up to 1.04[3]
	Intracranial bleed	< 0.1[4]	0.2 to 0.8[d]

Foonotes:

a. Throughout the table these point estimates are shown without respective confidence intervals and represent a range of results. Confidence intervals, if applied, are broad.

b. Based on an estimate of relative risk reduction (RRR) of 30% for ASA and 50% for anticoagulants. (Benavente, 1999) For elderly populations, RRR is estimated at 0.48 (Estimates range as high as 0.68 RRR) (Mant, 2007; Albers, 2001).

c. Increased absolute risk of hemorrhage associated with ASA alone compared to placebo ranges from < 0 (a reduction) to 0.5 % annually in 4 studies. Harms of warfarin are also taken from this same reference. Harms of warfarin may be more than this in the very old. A recent study of major hemorrhage among elderly patients found cumulative risk of major hemorrhage of 13.1 per 100 patient years for patients ≥80 years of age.

d. The higher rates of intracranial bleeds exist in those on warfarin compared to NOACs.

References:

1. Gage BF. Waterman AD, Shannon W. et al. Validation of clinical classification of schemes for predicting stroke: Results from the National Registry of Atrial Fibrillation. JAMA. 2001;285:2864-2870.
2. Stevens RJ, Kotahri V, Adler A, et al. The UKPDS risk engine: A model for the risk of coronary heart disease in type 2 diabetes (UKPDS 56). Clin Sci. 2001; 101(6):671-9.
3. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883-91.
4. Diener H, Eikelboom J, Connolly SJ, et al. Apixaban versus aspirin in patients with atrial fi brillation and previous stroke or transient ischaemic attack: A predefined subgroup analysis from AVERROES, a randomised trial. Lancet Neurol, 2012;11:225–31.

Appendix E: HAS-BLED Score for Major Bleeding[1]

Establish stratified risk score of bleeding for those on oral anticoagulation treatment for atrial fibrillation (AF).

HAS-BLED score for bleeding risk on oral anticoagulation in atrial fibrillation

Letter	Clinical Characteristic	Score (if present)
H	Hypertension (systolic ≥ 160 mmHg) – on treatment	1
A	Abnormal renal function (Dialysis, transplant, Cr > 2.6 mg/dL or > 200 µmol/L)	1
A	Abnormal liver function (Cirrhosis or bilirubin >2xNormal or AST/ALT/AP >3xNormal)	1
S	Stroke in past	1
B	Prior major bleeding or predisposition to bleeding	1
L	Labile INRs (Unstable/high INRs, time in therapeutic range <60%)	1
E	Elderly – age ≥ 65 years	1
D	Drugs: Medication usage predisposing to bleeding (antiplatelet agents, NSAIDs)	1
D	Drugs: Concomitant alcohol intake (≥8 drinks/week)	1
	Total HAS-BLED Score	Maximum score = 9

The risk of major bleeding within 1 year in patients with AF enrolled in the Euro Heart Study

Risk	Score Range	Annual risk of bleeding (%)
Low	0	1.13
Moderate	1 – 2	1 – 2
High	3+	2 – 12

A score of 3 or more indicates increased one year bleed risk on anticoagulation sufficient to justify caution or more regular review. The risk is for intracranial bleed, bleed requiring hospitalization or a hemoglobin drop > 2 g/L or that needs transfusion.

Reference:

1. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess one-year risk of major bleeding in atrial fibrillation patients: The Euro Heart Survey. Chest. 2010; 138(5):1093-100.

Appendix F: Comparisons of Anticoagulants for Atrial Fibrillation

Non-Vitamin K Antagonist Oral Anticoagulants (NOACs) versus warfarin for prevention of stroke or systemic embolism in non-valvular atrial fibrillation

Outcomes	Dabig atran 110 mg twice daily	Dabigatran 150 mg twice daily	Rivaroxaban 20 mg once daily	Apixaban 5 mg twice daily
Stroke or systemic embolism prevention	↔	↓*	↔	↓*
Major bleeding	↓*	↔	↔	↓*
Intracranial hemorrhage	↓*	↓*	↓*	↓*
Mortality	↔	↔	↔	↓

Footnotes: ↔ no worse than warfarin; ↓ lower risk than warfarin; * result is statistically significant.

Advantages and disadvantages of warfarin versus NOACs

Favours Warfarin	Favours NOAC
• Inexpensive • Prone to skipping doses (e.g., dementia) • Drug interaction with P-gp/CYP3A4 • Renal impairment (CrCl < 30 mL/min) • History of GI bleed • Also needs ASA or other antiplatelet therapy • Extremes of body weight (< 40 kg or > 120 kg) • Lack of long-term toxicity data for NOAC • Reversal agents available	• Convenience • Prone to skipping laboratory testing • Poor venous access or lab access • Variable diet or frequent alcohol use • History of intracranial bleed

Abbreviations: ASA = acetyl-salicylic acid; CrCl = creatinine clearance; CYP3A4 = cytochrome P450 3A4 isoenzymes; GI = gastrointestinal; kg = kilogram; mL/min = milliliter per minute; NOAC = non-vitamin K antagonist oral anticoagulants; P-gp = P-glycoprotein.

For more information, refer to BCGuidelines.ca – *Use of Non-Vitamin K Antagonist Oral Anticoagulants (NOAC) in Non-Valvular Atrial Fibrillation.*

Appendix G: Prescription Medication Tables for Atrial Fibrillation[1, 2, 3]

Generic Name	Trade name (dosage form and strength)	Adult dose	Cost per 30 days[a]	PharmaCare coverage[b]	Common and/or serious side effects	Therapeutic considerations
Drugs for heart rate control						
Beta-blockers						
atenolol	Tenormin®, G (IR tablet: 25, 50, 100 mg)	**IR tablet**: 50-150 mg PO once daily. Reduce dose by 25-50% if used concurrently with digoxin, calcium channel blockers, or amiodarone.	$5-13 (G)	Regular Coverage	Bradycardia, hypotension, dyspnea, fatigue, and depression	Use with caution in patients with diabetes, heart failure, or bronchospastic lung disease. $Beta_1$-selective. Less likely to cause depression.
bisoprolol	G (IR tablet: 5, 10 mg)	**IR tablet**: 5-20 mg PO once daily. Reduce dose by 25-50% if used concurrently with digoxin, calcium channel blockers, or amiodarone.	$1-17 (G)	Regular Coverage	Bradycardia, hypotension, dyspnea, fatigue, and depression	Use with caution in patients with diabetes, heart failure, or bronchospastic lung disease. $Beta_1$-selective.
metoprolol	Betaloc®, Lopresor®, G (IV injection: 1 mg/mL; IR tablet: 25, 50, 100 mg; SR tablet: 100, 200 mg)	**IV injection**: 5-10 mg q5 min x 3 doses. **IR tablet**: 50-200 mg PO BID. **SR tablet**: 100-400 mg PO once daily. Reduce dose by 25-50% if used concurrently with digoxin, calcium channel blockers, or amiodarone.	IR tablet: $4-17 (G) SR tablet: $4-17 (G)	Regular Coverage	Bradycardia, hypotension, dyspnea, fatigue, and depression	Use with caution in patients with diabetes, heart failure, or bronchospastic lung disease. $Beta_1$-selective.
nadolol	Nadolol, G (IR tablet: 40, 80, 160 mg)	20-160 mg PO once daily. Reduce dose by 25-50% if used concurrently with digoxin, calcium channel blockers, or amiodarone.	$8-39 (G)	Regular Coverage	Bradycardia, hypotension, dyspnea, fatigue, and depression	Use with caution in patients with diabetes, heart failure, or bronchospastic lung disease. Less likely to cause depression.
propranolol	Inderal®, G (IV injection: 1 mg/mL; IR tablet: 10, 20, 40, 80, 120 mg; SR capsule: 60, 80, 120, 160 mg)	**IV injection**: 1-3 mg q2 minutes x 2 doses. May repeat in 4 hours. **IR tablet**: 20-80 mg PO TID. **SR capsule:** 80-240 mg PO once daily. Reduce dose by 25-50% if used concurrently with digoxin, calcium channel blockers, or amiodarone.	IR tablet: $9-14 (G) SR tablet: $21-64	Regular Coverage (IR tablet: 10, 20, 40, 80 mg; SR capsule: 60, 80, 120, 160 mg No Coverage (IR tablet: 120 mg)	Bradycardia, hypotension, dyspnea, fatigue, and depression	Use with caution in patients with diabetes, heart failure, or bronchospastic lung disease. SR dosage forms preferred to prolong the dosing interval and improve patient compliance.

Generic Name	Trade name (dosage form and strength)	Adult dose	Cost per 30 days[a]	PharmaCare coverage[b]	Common and/or serious side effects	Therapeutic considerations
Calcium channel blockers: Non-Dihydropyridine						
verapamil	Isoptin®, G (IV injection: 2.5 mg/mL; IR tablet: 80, 120 mg; SR tablet: 120, 180, 240 mg)	**IV injection**: 5-10 mg. May give an extra 10 mg in 30 minutes. **Starting dose**: 120 mg/day PO. **Maximum dose**: 480 mg/day PO. **IR tablet** given in divided doses TID – QID. **SR tablet** given once daily or in divided doses BID.	IR tablet: $14-55 (G) SR tablet: $17-33 (G)	Regular Coverage	Bradycardia, hypotension, constipation, and flushing	Use with caution in patients with heart failure. SR dosage generally preferred to prolong the dosing interval and improve patient compliance.
diltiazem	Cardizem®, G (IV injection: 5 mg/mL; IR tablet: 30, 60 mg; ER capsule: 120, 180, 240, 300 mg) Tiazac®, G (ER capsule: 120, 180, 240, 300, 360 mg)	0.25 mg/kg. May give another 0.25 mg/kg after 15 minutes if needed. 180-540 mg/day PO. **IR tablet** given in divided doses TID – QID. **ER capsule**: 120-540 mg PO once daily.	IR tablet: $32-99 (G) ER capsule: $7-46 (G)	Regular Coverage	Bradycardia, hypotension, and ankle swelling	Use with caution in patients with heart failure. SR dosage generally preferred to prolong the dosing interval and improve patient compliance.
Digoxin						
digoxin	Toloxin®, G (IV injection: 50, 250 µg/mL; IR tablet: 0.0625, 0.125, 0.25)	**Loading**: 1-1.5 mg in divided doses PO or IV. **Maintenance**: 0.125-0.375 mg PO daily. Reduce dose by 25-50% if used concurrently with beta-blockers, calcium channel blockers, or quinidine.	IR tablet: $8-16	Regular Coverage	Bradycardia, nausea, vomiting, visual disturbances, and proarrhthmogenic	Only in patients with AF due to heart failure. Check serum and potassium levels. Correct hypokalemia if present.
Drugs for rhythm control						
Class IC Antiarrhythmics						
flecainide	Tambocor®, G (IR tablet: 50, 100 mg)	**Starting dose**: 50 mg PO q12h. Reduce by 50% in patients with renal dysfunction. **Titration**: increase by 50 mg increments based on QRS intervals. Reduce dose if QRS increases >20% from baseline. **Maximum dose**: 200 mg q12h PO.	$26-104 (G)	Regular Coverage	Ventricular proarrhythmia, tremor, blurred vision, and heart failure	Should be used concurrently with a beta-blocker or nondihyropyridine calcium channel blocker. Do not use in patients with coronary artery or structural heart disease. Metabolized by CYP2D6, resulting in many potential drug interactions.

Generic Name	Trade name (dosage form and strength)	Adult dose	Cost per 30 days[a]	PharmaCare coverage[b]	Common and/or serious side effects	Therapeutic considerations
propafenone	Rythmol®, G (IR tablet: 150, 300 mg)	150 – 300 mg PO q8h. Reduce initial dose by 50% and increase dosing interval to q12h in patients with renal or hepatic dysfunction.	$29-51 (G)	Regular Coverage	Constipation, headache, metallic taste, and ventricular proarrhythmia	Should be used concurrently with a beta-blocker or nondihyropyridine calcium channel blocker. Do not use in patients with coronary artery or structural heart disease. Reduce dose of concurrently administered digoxin by 25-50%. Metabolized by CYP2D6, resulting in many potential drug interactions. Monitor QRS duration carefully as active metabolites accumulate in rapid metabolizers.
Class III Antiarrhythmics						
amiodarone	Cardarone®, G (IV: 50 mg/ml; IR tablet: 100, 200 mg)	200 mg PO TID x 2 weeks, then 200-400 mg once daily PO. **IV loading**: 150 mg IV over 10 minutes, followed by 1.2-1.8 g/day to a total of 10 g Loading doses may vary.	$17-33 (G)	Regular Coverage	Various GI, dermatologic, neurologic, ophthalmologic, ventricular proarrhythmia and thyroid abnormalities Rare, but potentially life-threatening pulmonary fibrosis, hepatic dysfunction, and aggravation of arrhythmias	Monitor transaminases and thyroid function every 6 months. Reduce dose of concurrently used beta-blockers, procainamide, quinidine, and warfarin by 50%.
dronedarone	Multaq® (IR tablet: 400 mg)	400 mg PO BID.	$139	Limited Coverage Special Authority	Diarrhea, dyspepsia, nausea, and hepatic dysfunction (rare) Slight increase in plasma creatinine related to inhibition of secretion	Contraindicated in patients with severe heart failure (NYHA class IV). Contraindicated in patients using strong CYP3A4 inhibitors. Use with caution with drugs metabolized by CYP3A4. Not recommended in patients with permanent AF.
sotalol	Sotalol, G (IR tablet: 80, 160, 240 mg)	**Starting dose**: 80 mg PO q12h. **Titration**: increase by 80 mg increments if QTc <460 ms. Reduce dose if QTc ≥500 ms. **Maximum**: 240 mg PO q12h. **Elderly**: reduce initial dose to 40 mg PO q12h. **Renal dysfunction**: reduce initial dose in renal failure.	$19-30 (G)	Regular Coverage (IR tablet: 80, 160 mg) No Coverage (IR tablet: 240 mg)	Hypotension, bradycardia, wheezing, ventricular proarrhythmia Torsades de pointes, especially at higher doses or with renal dysfunction	Concurrent use with digoxin, diltiazem, verapamil, or other beta-blockers may cause AV block and bradycardia. Use with caution in patients with risk for QT prolongation or torsades de pointes.

Generic Name	Trade name (dosage form and strength)	Adult dose	Cost per 30 days[a]	PharmaCare coverage[b]	Common and/or serious side effects	Therapeutic considerations
Oral anticoagulants						
Vitamin K Antagonists						
warfarin	Coumadin®, G (IR tablet: 1, 2, 2.5, 3, 4, 5, 6, 7.5, 10 mg	Initial: 2.5-10 mg PO daily, then individualize to maintain an INR of 2-3.	$2-10	Regular Coverage	Bleeding and skin necrosis	Contraindicated in pregnancy. Many potential interactions.
Direct Factor Xa Inhibitors						
dabigatran	Pradaxa® (IR capsule: 110, 150 mg)	150 mg PO BID or 110 mg PO BID for patients with ≥ 1 of the following: - age ≥ 75 years - CrCl 30-50 mL/min - concurrent use of strong P-gp inhibitor or antiplatelet agent - previous GI bleed	$104	Limited Coverage[c] Special Authority	Bleeding and GI intolerance	Contraindicated in combination with strong inhibitors of P-gp. Use cautiously with other drugs acting on P-gp. No reversal agents available.
Direct Thrombin Inhibitors						
rivaroxaban	Xarelto® (IR tablet: 10, 15, 20 mg)	20 mg PO daily with food or 15 mg PO daily with food for patients with CrCl 30-49 mL/min	$92	Limited Coverage[c] Special Authority	Bleeding	Contraindicated in combination with strong inhibitors of both CYP3A4 and P-gp. No reversal agents available.
apixaban	Eliquis® (IR tablet: 2.5, 5 mg)	5 mg PO BID or 2.5 mg PO BID for patients with ≥ 2 of the following: - age ≥ 80 years - body weight ≤ 60 kg - serum creatinine ≥ 133 µmol/L	$104	Limited Coverage[c] Special Authority	Bleeding	Contraindicated in combination with strong inhibitors of both CYP3A4 and P-gp. No reversal agents available.

Abbreviations: AF = atrial fibrillation; BID = twice daily; CrCl = creatinine clearance; CYP3A4 = cytochrome P450 3A4 isoenzymes; ER = extended-release; GI = gastrointestinal; G = generic version(s) available; h = hour(s); IR = immediate-release; IV = intravenous; kg = kilogram; µmol/L = micromolar per litre; mg = milligram; mL/min = milliliter per minute; P-gp = P-glycoprotein; PO = taken orally; QID = four times daily; q = every; QTc = corrected QT; SR = sustained-release; TID = three times daily.

Note: Please review product monographs at hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

Footnotes:

a Pricing is approximate as per PharmaNet 2014/08/20 and does not include dispensing fee

b PharmaCare Coverage Definitions: **G:** generic(s) are available; **Regular Coverage:** also known as regular benefit; does not require Special Authority. Regular benefits may be fully or partially covered.*; **Limited Coverage:** requires Special Authority for coverage. Limited Coverage benefits approved by Special Authority may be fully or partially covered.*; **RDP**: Reference Drug Program. Drugs included in the RDP are comparable agents of the same therapeutic class. Patients receive full coverage of drugs designated as the Reference Drug(s) of the therapeutic class. Other drugs in the same RDP category are covered up to the price of the Reference Drug; **No coverage:** also known as non-benefit; does not fit the above categories.

* Note: Information on which products PharmaCare covers can be obtained using the B.C. PharmaCare Formulary Search (www.health.gov.bc.ca/pharmacare/benefitslookup/). In all cases, coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

c PharmaCare coverage is currently limited to patients with non-valvular atrial fibrillation for the prevention of stroke and systemic embolism **AND** in whom anticoagulation is inadequate following at least a 2-month trial of warfarin **OR** for whom anticoagulation using warfarin is contraindicated or not possible due to inability to regularly monitor the patient via International Normalized Ratio (INR) testing (i.e., not access to INR testing services at a laboratory, clinic pharmacy, and at home).

References:

1. e-CPS [Internet]. Ottawa, ON: Canadian Pharmacists Association; 2014 [cited 2014/08/20].
2. Health Canada Drug Product Database Product Monographs. Ottawa, ON: Health Canada; 2014 [cited 2014/08/20].
3. e-Therapeutics [Internet]. Ottawa, ON: Canadian Pharmacists Association; 2014 [cited 2014/08/20].