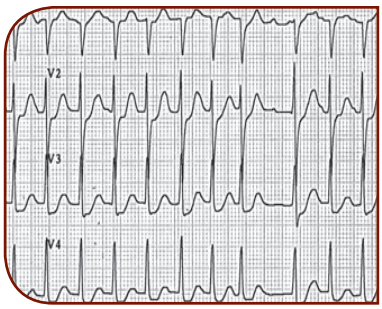


GUIDE TO OUTPATIENT MANAGEMENT OF

Atrial fibrillation

This care process model (CPM) was developed by an interdisciplinary team formed by SelectHealth and Intermountain that included primary care providers and Intermountain experts in heart rhythm treatment, cardiology, and anticoagulation. It is based on current guidelines[1-3] and provides practical guidance for atrial fibrillation treatment. **Please note that while this document presents an evidence-based approach that is appropriate for most patients, it should be adapted to meet the needs of individual patients and situations, and should not replace clinical judgment.**

Key points

- **Atrial fibrillation (AF) can be managed through rhythm control or rate control.** For most patients, it's helpful to begin by attempting rhythm control; this typically involves a cardiologist referral.
- **Most AF patients should have long-term anticoagulation, even if restored to sinus rhythm, depending on their stroke risk.** While CHADS2 has often been used to decide which patients need chronic anticoagulation, the newer **CHA_2DS_2VASc** score represents the optimal risk stratification tool. *See page 7.*
- **The best anticoagulation strategies are based on factors specific to each patient.** Assessment of bleeding risk is appropriate to plan risk reduction and monitoring. However, it should not influence decision making on whether to apply anticoagulation therapy. *See pages 7 to 10* for guidance on choosing an anticoagulant, monitoring, and other practical issues.
- **A working knowledge of AF and its types can help with treatment decisions.** See the definitions below, adapted from American College of Cardiology guidelines.[2]

ATRIAL FIBRILLATION (AF): DEFINITION AND TYPES

- **Basic definition:** Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of atrial mechanical function — documented continually on an ECG or **for at least 30 seconds on monitoring.** (For signs and symptoms, *see page 3.*)
- **ECG:** On an electrocardiogram (ECG), AF is characterized by the replacement of consistent P waves by rapid oscillations or fibrillatory waves that vary in amplitude, shape, and timing, associated with an irregular, frequently rapid ventricular response when atrioventricular (AV) conduction is intact.
- **Valve involvement:** Patients may have valvular AF (caused by rheumatic disease of the mitral valve or with a history of valve replacement) or nonvalvular AF. This distinction can affect treatment choices.
- **Duration and/or recurrence:** The duration of AF and/or potential recurrence of resolved AF can affect treatment decisions.
  - **Paroxysmal AF:** AF that ends in fewer than 7 days and can be recurrent. (This includes episodes that end spontaneously or are resolved with cardioversion.)
  - **Persistent AF:** Continuous AF (present on every ECG test) that is sustained longer than 7 days.
  - **Longstanding persistent AF:** Continuous AF that lasts longer than 12 months' duration, with continued efforts to restore to sinus rhythm.
  - **Permanent AF:** Continuous AF of longer than 12 months' duration, when no further interventions to restore to sinus rhythm are planned.

Why Focus ON AF?

- **AF prevalence is high in the elderly.** It increases with age and is estimated at 17.8% in adults age 85 and older.[4]
- **Mortality and morbidity in AF are significant.** AF-associated strokes are more severe, with 30-day mortality of 25% compared to 14% in non-AF strokes.[5]
- **AF has a tendency to recur,** even if patients are restored to normal sinus rhythm. This tendency increases the importance of appropriate oral anticoagulation.
- **Emerging models for stroke risk and bleeding risk** can make the choice of anticoagulation safer and more effective.

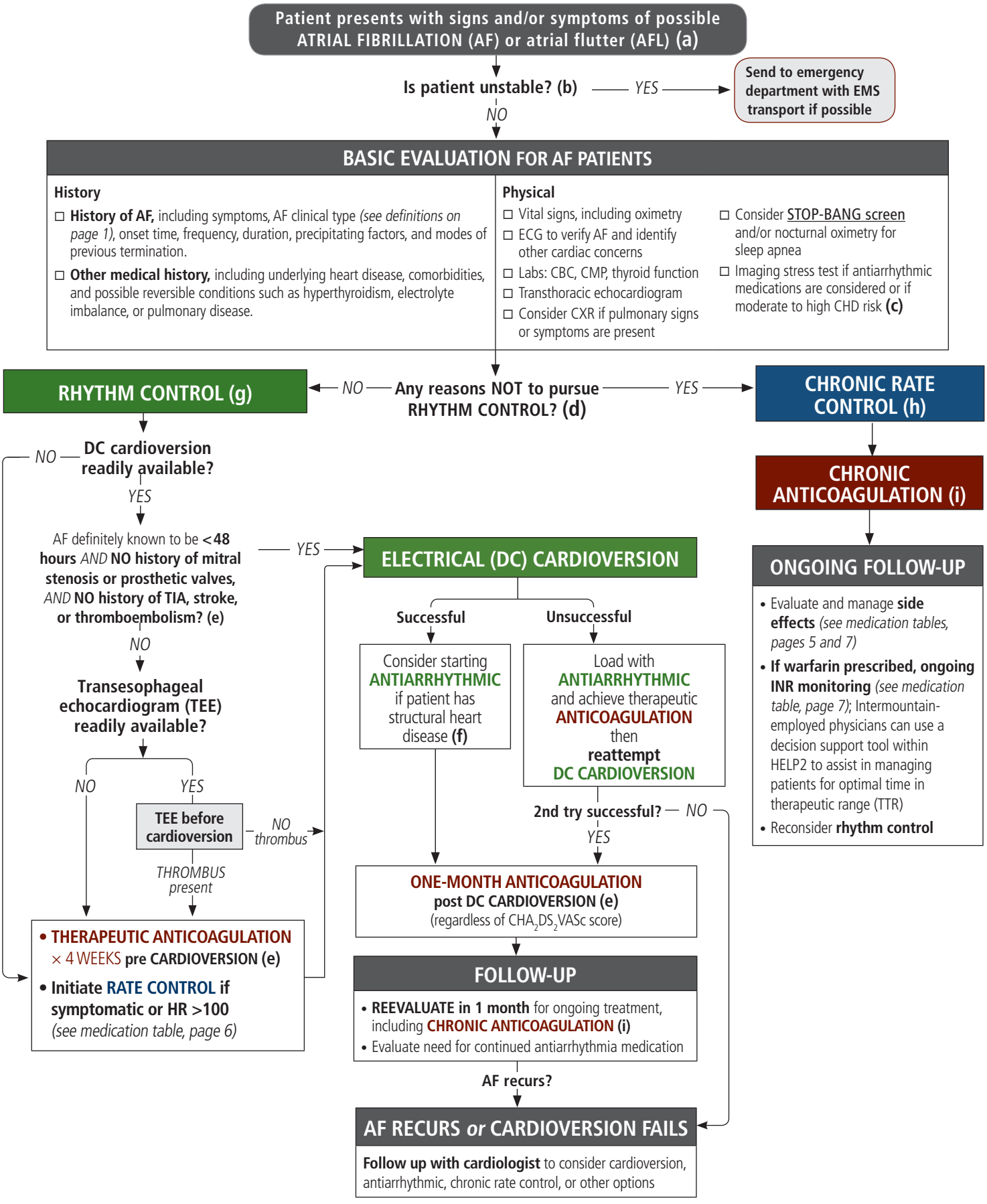
Goals OF THIS CPM

- Enhance quality of life for AF patients
- Facilitate evidence-based care for AF
- Guide and standardize appropriate AF workup and rhythm control
- Limit the duration of AF by converting patients to sinus rhythm as quickly as possible
- Optimize the use of appropriate anticoagulation

What's Inside

Intermountain® Healthcare

ALGORITHM



ALGORITHM NOTES

(a) SYMPTOMS associated with AF or AFL

- Fatigue/tiredness
- Dyspnea
- Chest pain
- Palpitations
- Dizziness
- Weakness

(b) Signs of INSTABILITY

- Unstable vital signs
- Ongoing chest pain with AF
- Decompensated heart failure
- Myocardial ischemia
- Hypotension

(c) Coronary heart disease (CHD) risk

Mild: 1 to 2 risk factors; **Moderate:** 3 risk factors; **High:** ≥4 risk factors

- ☐ Age (men >45, women >55 years)
- ☐ Cigarette smoking
- ☐ BP >140/90 or on antihypertensive medication
- ☐ Low HDL cholesterol (men <40, women <50)
- ☐ Impaired fasting glucose (101–125)
- ☐ Family history of premature CHD (male 1st-degree relative <60 years or female 1st-degree relative <70 years)
- ☐ Non-HDL cholesterol >160

(d) Reasons NOT to pursue RHYTHM CONTROL

The following are reasons to pursue chronic rate control rather than attempting rhythm control:

- Elderly asymptomatic patient with relatively normal heart function
- Risks of cardioversion may outweigh benefits (e.g., multiple comorbidities or overall poor prognosis)
- History of ≥2 previous DC cardioversions while on antiarrhythmic
- Low chance of success (AF duration >1 year; moderate to severe mitral stenosis)

(e) PRE- AND POST-CARDIOVERSION ANTICOAGULATION

PRE-cardioversion — 3 options:

- If 4 weeks therapeutic anticoagulation with apixaban, rivaroxaban, dabigatran, or warfarin (INR range 2–3 or if patient has mechanical valve, INR 2.5–3.5), then elective DC cardioversion is acceptable.
- If AF <48 hours *AND* NO history of mitral stenosis/prosthetic valves, TIA, stroke, or thromboembolism, then DC cardioversion without TEE is acceptable. If patient is not fully anticoagulated, give enoxaparin (30 mg IV and 1 mg/kg subcut) before cardioversion.
- If AF ≥48 hours (or duration unknown) *OR* there are any of the thrombosis risk factors above, then TEE-guided cardioversion is warranted. If patient is not fully anticoagulated, give enoxaparin (30 mg IV and 1 mg/kg SCQ) before cardioversion.

POST-cardioversion:

- **One (1) month therapeutic anticoagulation for all patients, *regardless* of CHA_2DS_2VASc score** (see note **i**). Anticoagulation is important due to risk of AF recurrence during this time window. Warfarin, apixaban, rivaroxaban, or dabigatran may be used; if warfarin is used, bridge with enoxaparin until therapeutic INR has been achieved for 2 days.
- **Evaluate need for CHRONIC ANTICOAGULATION,** based on CHA_2DS_2VASc score (see note **i**). (Note: After DC or spontaneous cardioversion, AF should be considered paroxysmal and chronic anticoagulation is appropriate; *see page 7.*)

(f) Risk of AF recurrence after cardioversion

The AF recurrence rate after cardioversion is high. Studies have shown AF recurrence of up to 70% in patients not taking antiarrhythmics.[6-8] Structural heart disease (moderate mitral regurgitation, moderate left ventricular hypertrophy, LAA enlargement, stenotic valve disease) increases the risk of recurrence after cardioversion. Antiarrhythmic medications reduce the risk of AF recurrence and persistent AF.

(g) RHYTHM CONTROL *(see page 4 for details)*

Why it's important	The longer a patient is in AF, the more likely it is to become permanent. Rhythm control is recommended for most patients, and should be achieved ASAP if possible.
DC cardioversion	DC cardioversion should be pursued in most patients unless the risks outweigh the benefits or there is a low chance of success *(see factors listed in **d** at left).*
Antiarrhythmic medications	**Post cardioversion:** Consider antiarrhythmic medication unless it is the 1st episode *and* there is no structural heart disease. **Chronic:** Consider cardiologist referral to evaluate the need for chronic antiarrhythmic medication.

(h) CHRONIC RATE CONTROL *(see page 6 for details)*

When to consider	Patients with the factors listed in note **(d)** and patients for whom rhythm control has failed
Treatment goal	60 to 100 bpm
Strategy	Use diltiazem or verapamil and/or beta blocker, unless EF <35%; options include digoxin and amiodarone

(i) CHRONIC ANTICOAGULATION *(see pages 7–10 for details)*

CHA_2DS_2VASc scoring:

Factor	Points
☐ **C**ongestive heart failure	1 pt
☐ **H**ypertension	1 pt
☐ **A**ge ≥75 years	2 pts
☐ **A**ge 65 to 74 years	1 pt
☐ **D**iabetes mellitus	1 pt
☐ **S**troke/TIA/VTE	2 pts
☐ **S**ex = female	1 pt
☐ **Vasc**ular disease (MI, PAD, or aortic plaque)	1 pt

***Examples* of AF patients with score ≥2, who will need chronic anticoagulation:**

- A woman with *any* of these: hypertension, CHF, age 65, diabetes, or vascular disease
- A 65-year-old with *any* of these: female sex, CHF, diabetes, or vascular disease
- Any patient 75 years old

Using the score:

Score = 0	**No therapy**
Score = 1	Decision determined by bleeding risk *(see page 7)*: • **Aspirin alone** (75 mg to 325 mg daily) ***OR*** • **Aspirin plus clopidogrel**
Score ≥ 2	**Chronic anticoagulation:** • **DOACs (direct oral anticoagulants: apixaban, dabigatran, rivaroxaban):** – Recommended for most AF patients, unless contraindicated or warfarin is strongly preferred – Contraindicated in valvular heart disease (mitral stenosis or valve surgery) or renal impairment (eGFR <30) • **Warfarin:** – Mandatory choice in patients with valvular heart disease – Recommended if TTR (time in therapeutic INR range) is ≥65% • **Aspirin and clopidogrel as last alternative** if anticoagulation is contraindicated or patient will not take an anticoagulant (for reasons other than concerns about bleeding) **Relative contraindications** to anticoagulation include history of transfusion-dependent bleed (≥2 units) or intracranial bleed; *see page 7* for information on the HAS-BLED score

☑ *RHYTHM CONTROL: KEY PRINCIPLES*

- Cardiovascular factors help determine the best medication choice. Choose therapy based on the patient's most serious condition.
- Pharmacological cardioversion conversion is discouraged *(see note below).*

PHARMACOLOGICAL CARDIOVERSION

Pharmacological cardioversion is discouraged due to low efficacy, the dosage required, and the need for inpatient initiation with most patients.

WHEN TO CONSIDER AF ABLATION

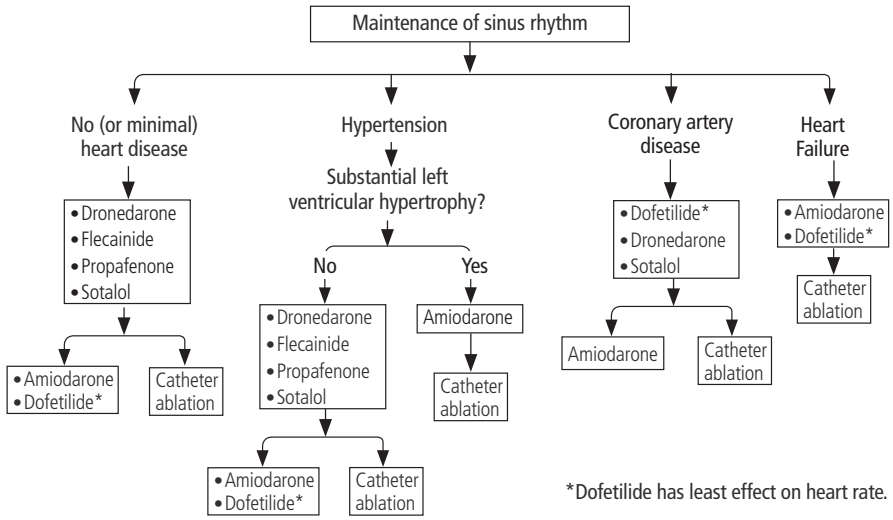
Consult a cardiologist to consider catheter ablation for symptomatic patients who have failed one or more trials of antiarrhythmic medication. See Heart Rhythm Society guidelines for more information.[1]

RHYTHM CONTROL

Consult a cardiologist to evaluate the need for antiarrhythmic medication after DC cardioversion, especially if the patient has structural heart disease.

1 Choose the desired medication.

The algorithm below is based on ACCF/AHA guidelines[2] for maintaining sinus rhythm in patients with recurrent/persistent AF after cardioversion; choose therapy based on the patient's most serious condition.



*Dofetilide has least effect on heart rate.

TABLE 1. Rhythm control medications

RHYTHM CONTROL MEDICATION OPTIONS				
Medication	**Dosage**	**Contraindications and potential adverse drug reactions (ADRs)**	**Drug-drug interactions**	**SH tier, cost***
amiodarone (Cordarone, Pacerone)	100 mg to 400 mg, once daily	ADRs: photosensitivity, pulmonary fibrosis/toxicity, GI upset, bradycardia, hepatic toxicity, thyroid dysfunction, eye complications, skin discoloration	Use caution with drugs that prolong QT interval; CYP3A4 inhibitors may increase concentrations of amiodarone.	Tier 1, $
dofetilide (Tikosyn)	125 mcg to 500 mcg, twice daily	ADRs: torsades de pointes, heart block, and arrhythmias (ventricular arrhythmias, fibrillation, or tachycardia)	Use caution with drugs that prolong QT interval. Avoid meds that inhibit renal tubular secretion (cimetidine, trimethoprim).	Tier 2, $$$$
dronedarone (Multaq)	400 mg, twice daily	Contraindications: persistent/chronic AF, bradycardia (< 50 bpm), recently decompensated or Class IV HF, second- or third-degree heart block ADRs: liver failure, CVA, prolonged QT interval, new or worsening heart failure, diarrhea, nausea, abdominal pain, pulmonary toxicity	May interact with CYP3A inhibitors and drugs that prolong QT interval. Reduce concurrent calcium channel blocker/ beta blocker dose to reduce bradycardia risk. Hypokalemia and hypomagnesemia with diuretics that deplete K+.	Tier 2, $$$$
flecainide (Tambocor)	50 mg to 150 mg, twice daily	Contraindications: ischemic heart disease, second- or third-degree AV block, right bundle branch block, left ventricular hypertrophy that is more than mild, renal failure ADRs: cardiac arrest, other dysrhythmias, heart failure	Use caution with drugs that prolong QT interval. Beta blockers carry the potential to increase negative inotropic effects.	Tier 1, $
propafenone (Rythmol) *Immediate-release (IR) or sustained-release (SR)*	IR: 150 to 225 mg, every 8 hours SR: 225 mg to 425 mg, every 12 hours	Contraindications: ischemic heart disease, heart failure, left ventricular hypertrophy that is more than mild, renal failure ADRs: ventricular tachycardia, heart failure, first-degree AV block, bradyarrhythmia, chest pain	Use caution with drugs that prolong QT interval. Avoid potent CYP2D6 inhibitors (e.g., bupropion, some SSRIs, terbinafine).	Generic (IR): Tier 1, $ Brand (SR): Tier 3, $$$$$
sotalol (Betapace AF)	80 mg to 160 mg, twice daily	Contraindications: renal failure, QTc > 500 ms in the absence of bundle branch block, QTc > 550 ms in the presence of bunch branch block ADRs: QT prolongation, bradycardia, dyspnea, fatigue	CCBs, digoxin, use caution with drugs that prolong QT interval and catecholamine-depleting drugs (reserpine and guanethidine).	Tier 1, $

***Tier and cost:** Tier 1 = $5 to $10 copay; Tier 2 = $30 to 50% coinsurance; Tier 3 = $50 to 50% coinsurance (based on SelectMed 2013 benefit design; benefit designs may differ). Cost is 30-day actual cost (not copay) and based on generic unless otherwise noted: $ = $1 to $25; $$ = $26 to $75; $$$ = $76 to $150; $$$$ = $151 to $300, $$$$$ = over $300

2 Initiate and monitor therapy appropriately.

See the table below for guidance on initiating and monitoring antiarrhythmic therapy.

Stop medication if any contraindication develops; *see the list of contraindications for each medication in Table 1, page 4.* (Note that severe sinus bradycardia of HR < 50 is a relative contraindication to initiating any antiarrhythmic medication.)

MEDICATION	INITIATION DOSE	SHORT-TERM MONITORING	LONG-TERM MONITORING
amiodarone (Cordarone, Pacerone)	200 mg twice daily, then reduce to 200 mg daily after 8 grams have been administered.	• Basic laboratory testing to include liver function tests, pulmonary function tests, and thyroid function tests. • Patients should use adequate UVA/UVB sun block. If skin discoloration (bluish tint) occurs, reduce dose or discontinue.	• Biannual liver function testing • Annual or symptom-driven thyroid function testing • Annual pulmonary physical exam; additional testing (PFT and consider DLCO) if signs/symptoms of amiodarone-associated pulmonary toxicity • Periodic eye exams; monitor for visual acuity changes
dofetilide (Tikosyn)	Dofetilide can only be prescribed by qualified individuals. If you are interested in prescribing this medication you must become certified *(see tikosynrems.com)*. Initiation of dofetilide requires 3 days in the hospital to assess the impact of the drug on the QT interval.		• Every 3 months: ECG to assess QT interval • Every 3 months: basic metabolic profile to determine kidney function
dronedarone (Multaq)	400 mg twice daily.	• Liver function tests • ECG to determine if sinus rhythm is present; if not, the patient needs to be cardioverted before drug initiation or < 1 week after initiation	• Biannual liver function testing
flecainide (Tambocor)	100 mg twice daily (typical starting dose). (Also start beta blocker or calcium channel blocker.)	• Inpatient initiation if started in the presence of atrial fibrillation. • Outpatient initiation if started in sinus rhythm with a normal QRS. Follow-up ECG after 4–6 doses to measure the QRS change.	• Biannual ECG to assess QRS duration. • Annual assessment of metabolic profile to assess renal and liver function.
propafenone (Rythmol) *Immediate-release (IR) or sustained-release (SR)*	IR: 150 mg, 3 times daily (typical starting dose). SR: 225 mg, twice daily (typical starting dose). (Also start beta blocker or calcium channel blocker.)	• Inpatient initiation if started in the presence of atrial fibrillation. • Outpatient initiation if started in sinus rhythm with a normal QRS. Follow-up ECG after 4–6 doses to measure the QRS change.	• Biannual ECG to assess QRS duration. • Annual assessment of metabolic profile to assess renal and liver function.
sotalol (Betapace AF)	80 mg, twice daily (typical starting dose).	• Inpatient initiation is recommended with serial assessment of the QT interval for 3–4 doses.	• Biannual ECG to measure QT interval. • Biannual basic metabolic profile to assess renal function.

☑ *ANTIARRHYTHMIC INITIATION AND MONITORING: KEY PRINCIPLES*

- Careful initiation and monitoring can prevent complications.
- Severe sinus bradycardia (heart rate < 50 BPM) is a relative contraindication to initiating any antiarrhythmic medication.
- Stop the medication if any contraindication develops during antiarrhythmic therapy. The monitoring described in the table at left assists in checking for contraindications.

☑ *RATE CONTROL: KEY PRINCIPLES*

- Aim for a heart rate of 60 to 100 BPM.
- In some circumstances (reduced ejection fraction, etc.), add digoxin, a beta blocker, or a calcium channel blocker *(details appear at right).*

CHRONIC RATE CONTROL

Medications to meet the goal of 60 to 100 BPM include diltiazem, metoprolol, propranolol, and verapamil. *See the table below* for details on preferred rate control medications.

Consider additional medications based on patient's circumstances:

- If the patient's ejection fraction is less than 35% (chronic), add digoxin or a beta blocker.
- If the patient's heart rate is high at rest and the patient is already taking a calcium channel blocker or beta blocker, add digoxin.
- If the patient's elevated heart rate is exertion-induced, add a beta blocker or calcium channel blocker.

TABLE 3. Preferred rate control medications

RATE CONTROL MEDICATIONS			
Medication	**Dosing**	**Special considerations:**	**SH tier, cost***
carvedilol (Coreg, Coreg CR) *Immediate-release (IR) or extended-release (ER)*	IR: 3.125 mg to 25 mg, twice daily ER: 10 mg to 80 mg, once daily	Major potential ADRs: Bradyarrhythmia, hypotension, hyperglycemia, fatigue, dizziness, headache Preferred for patients with heart failure or diabetes, due to increases in insulin sensitivity	**IR:** Tier 1, $ **ER:** Tier 3, $$$ *(generic not available)*
diltiazem (Cardizem CD, Dilacor CD, Tiazac)	120 mg to 480 mg, once daily	Major potential ADRs: bradyarrhythmia, dizziness, headache, cough, fatigue, heart block, heart failure Causes less constipation or edema	Tier 1, $
metoprolol succinate (Toprol XL) **metoprolol tartrate (Lopressor)**	Toprol XL: 25 mg to 300 mg, once daily Lopressor: 25 mg to 100 mg, twice daily	Major potential ADRs: bradyarrhythmia, dizziness, dyspnea, fatigue, heart block, heart failure Succinate (Toprol XL) preferred for patients with heart failure	Tier 1, $
verapamil (Calan, Isoptin, Verelan, Covera-HS) *Immediate-release (IR) or extended-release (ER)*	IR: 60 mg to 80 mg, 3 to 4 times daily SR: 120 mg to 360 mg, once daily	Major potential ADRs: AV block, edema, constipation, dizziness, headache Consider for AF driven by hypertension and patients with PVCs	Tier 1, $

***Tier and cost:** Tier 1 = $5 to $10 copay; Tier 2 = $30 to 50% coinsurance; Tier 3 = $50 to 50% coinsurance (based on SelectMed 2013 benefit design; benefit designs may differ). Cost is 30-day actual cost (not copay) and based on generic unless otherwise noted: $ = $1 to $25; $$ = $26 to $75; $$$ = $76 to $150; $$$$ = $151 to $300

CHRONIC ANTICOAGULATION

Chronic oral anticoagulation (OAC) — lifelong therapy with close follow-up — is recommended for most AF patients, due to the high rate of AF recurrence (often subclinical) and the devastating outcomes from strokes. Patients with paroxysmal AF (which includes AF that spontaneously cardioverts) should have chronic OAC according to their stroke risk score. (Note: If AF is *definitely* known to be secondary to surgery or other illness, OAC can be stopped after 6 months if there are no clinical symptoms or recurrence of AF, the secondary cause has been addressed, and an ambulatory telemetry test at 6 months is negative.)

1 Assess stroke risk

The CHA_2DS_2VASc score, based on the widely used $CHADS_2$ score, adds 3 factors (age 65 to 74, female sex, and vascular disease) that are validated for predicting stroke risk.[8]

CHA_2DS_2VASc SCORING		USING THE SCORE
Factors:	**Points:**	**Strategy based on total score:**
☐ **C**ongestive heart failure	1 pt	**Score = 0:** No antithrombotic therapy needed
☐ **H**ypertension	1 pt	**Score = 1:** Aspirin (75 to 325 mg daily) *and/or* clopidogrel
☐ **A**ge > 75	2 pts	**Score ≥ 2:** Anticoagulation unless contraindicated
☐ **A**ge 65 to 74	1 pt	*See below and pages 7 to 9 for information on bleeding risk stratification and management, medication choices, and medication management.*
☐ **D**iabetes mellitus	1 pt	
☐ **S**ex-female	1 pt	
☐ **S**troke/TIA/TE	2 pts	
☐ **Vasc**ular disease (MI, PAD, aortic plaque)	1 pt	

2 Assess and manage bleeding risk

Because many stroke risk factors can also increase bleeding risk on oral anticoagulants, it's important to assess and manage the patient's risk. Bleeding risk is not a reason to withhold anticoagulation. However, management of modifiable bleeding risk factors enhances care. The HAS-BLED score has been validated for accuracy in multiple studies.[10] *See below.*

HAS-BLED SCORING	USING THE SCORE
Each checkmark = 1 point:	**Score = 0–1:** Low risk
☐ **H**ypertension (SBP >160 mm Hg)	**Score = 2:** Moderate risk
Abnormal: ☐ Kidney function: serum creatinine >2.26	**Score = 3:** High risk
☐ Liver function: Bili > 2X ULN *and* LFTs > 3X LN	**For patients at high bleeding risk, consider:**
☐ **S**troke history	☐ Optimizing blood pressure control
☐ **B**leeding history or predisposition	☐ More frequent INRs in first 3 months of warfarin
☐ **L**abile INRs: TTR 60%	☐ Anticoagulation clinic management
☐ **E**lderly: > 65 years	☐ Fall prevention interventions, if needed
Drugs: ☐ ETOH abuse	☐ Use of NOAC (*see next page*)
☐ ASA or NSAID use	

Notes:

- Regardless of bleeding risk magnitude, concurrent aspirin/clopidogrel with oral anticoagulation should be used ONLY for patients with a recent history (12 months) of stent placement, high-risk mechanical heart valve placement, or acute coronary syndrome.
- Patients with stable CAD may be managed with oral anticoagulants alone; adding aspirin increases bleeding risk and does not reduce MI/stroke risk.
- Even after significant GI bleed or intracranial hemorrhage, consider restarting chronic anticoagulation in patients at risk for thrombotic events.

☑ *CHRONIC ANTICOAGULATION: KEY PRINCIPLES*

- Most AF patients should have lifelong OAC, based on stroke risk.
- Assess bleeding risk to plan monitoring but not to withhold anticoagulation.

CHA_2DS_2VASc SCORE AND STROKE RATES

The CHA_2DS_2VASc score is effective in predicting future stroke in patients who do not receive anticoagulation,[9] as shown below:

CHA_2DS_2VASc Total Score	Stroke Rate (% per year)
0	0%
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	6.7%
9	15.2%

☑ *ANTICOAGULANT CHOICE: KEY PRINCIPLES*

- The best medication choice is based on a range of factors *(see the tables at right)*. These include time in therapeutic INR range (TTR) on warfarin, access to INR monitoring, cost, medication interactions, and kidney function.
- Shared decision-making in choosing an oral anticoagulant can improve patient safety and compliance. A shared decision-making conversation includes a brief discussion of the pros and cons of the medications being considered, including convenience and cost. It's helpful to explain the reasons behind your recommendations. Also, consider asking patients to explain key information about their new prescription back to you in their own words.

3 Choose the desired anticoagulant

The choice of **warfarin versus DOAC (direct oral anticoagulant: apixaban, rivaroxaban, or dabigatran)** is based on certain medical conditions, medication interactions, and the **TTR (time in therapeutic INR range)** that can be achieved with warfarin. *See below* for information on choosing between warfarin or DOAC. Table 3 below provides dosage and management guidance for individual medications.

WARFARIN MANDATORY	WARFARIN PREFERRED	DOAC PREFERRED	UNCERTAIN
• Valvular heart disease • Renal failure (see CrCl and eGFR notes below)	• If patient is taking meds that interact with NOAC • If patient prefers warfarin and TTR is at least 65% to 70% • NOAC is cost prohibitive • Chronic kidney disease (see CrCl and eGFR notes below)	• For most patients with nonvalvular AF, unless warfarin preferred • If TTR on warfarin is less than 65% to 70%, not due to noncompliance • If patient has limited access to INR monitoring • If frequent procedures interrupt anticoagulation • If patient is taking meds that interact with warfarin • If it is necessary to achieve therapeutic effect quickly	• Stable coronary artery disease (guidelines vary) • High GI bleed risk (some NOACs may increase GI bleeding) • Frail elderly patients: age ≥ 75, weight < 60 kg, eGFR 30–49, and/or polypharmacy (many bleeds on NOACs occur when one or more of these are present)

TABLE 3. Anticoagulants

ANTICOAGULANT MEDICATIONS					
Medication	**Dosage**	**Contraindications, ADRs, and drug-drug interactions**	**Other special considerations and monitoring**	**Antidote**	**SH tier, cost***
apixaban (Eliquis) *Factor Xa inhibitor*	5 mg, twice daily (2.5 mg twice daily if 2 of these factors: age > 80, weight < 60 kg, or sCr > 1.5 mg/dL)	Contraindications: DO NOT use in severe liver disease; DO NOT use in patients on dialysis or if CrCl < 15 Drug-drug interactions: azoles, HIV protease inhibitors, macrolide antibiotics, carbamazepine, phenytoin, rifampin	Only DOAC with proven survival benefit against warfarin; lower bleeding risk than aspirin. Activated charcoal may be useful in managing overdose or accidental ingestion (by leading to a more rapid fall in apixaban blood levels).	None	Tier 2, $$$
dabigatran (Pradaxa) *Direct thrombin inhibitor*	150 mg, twice daily (Do not use 75 mg dose)	Contraindication: DO NOT use if CrCl < 30 mL/min ADRs: dyspepsia, other GI side effects, increased GI bleeds Drug-drug interactions: antacids, verapamil, amiodarone, clarithromycin, rifampin, SJW, carbamazepine	DO NOT use 75 mg dose in renal impairment, as this dose has never been studied. Must remain in original packaging.	None	Tier 3, $$$
rivaroxaban (Xarelto) *Factor Xa inhibitor*	20 mg, once daily (15 mg daily if CrCl is 15–50)	Contraindication: DO NOT use in liver disease or if CrCl < 15 Drug-drug interactions: azoles, carbamazepine, HIV protease inhibitors, macrolide antibiotics, phenytoin, primidone, rifampin, phenobarbital	Once daily dosing and fewer GI effects may make this the preferred NOAC for some patients.	None	Tier 2, $$$
warfarin (Coumadin) *Vitamin K antagonist*	Dose based on current and previous INR (No dose change for renal dysfunction)	Interactions: Many drug-drug and food-drug interactions	Monitoring: INR tests at least every 4 weeks with frequency based on INR level. Intermountain's decision support tool: the chronic anticoagulation module in HELP2 helps optimize TTR and provides a longitudinal anticoagulation record *(see page 12)*.	Vitamin K, fresh frozen plasma	Tier 1, $

***Tier and cost:** Tier 1 = $5 to $10 copay; Tier 2 = $30 to 50% coinsurance; Tier 3 = $50 to 50% coinsurance (based on SelectMed 2013 benefit design; benefit designs may differ). Cost is 30-day actual cost (not copay) and based on generic unless otherwise noted: $ = $1 to $25; $$ = $26 to $75; $$$ = $76 to $150

4 Switch between anticoagulants wisely

See below for the recommended procedure for switching between anticoagulants.

SWITCH	PROCEDURE
Warfarin → NOAC	Stop warfarin. Start apixaban, dabigatran, or rivaroxaban as soon as INR is less than 2.5. (Note: Do not use DOAC in patients with valvular disease.)
Apixaban* → warfarin†	Start warfarin while patient is still taking apixaban. Check INR‡ on day 4 of overlap. • If the INR is ≥ 2.0, stop apixaban and repeat INR after 1 to 2 days of warfarin alone. • If the INR is < 2.0, consider continuing apixaban along with warfarin; repeat INR 1 to 2 days later.
Dabigatran† → warfarin[2,3]	Start warfarin while patient is still taking dabigatran. Stop dabigatran 1 to 4 days later, with timing based on patient's creatinine clearance (CrCl) and INR level:‡ • **If CrCl > 50:** Check INR on day 4 of overlap. – If INR is ≥ 2.0, stop dabigatran; repeat INR after 1 to 2 days of warfarin alone. – If INR is < 2.0, consider continuing dabigatran along with warfarin; repeat INR 1 to 2 days later. • **If CrCl = 31–50:** Stop dabigatran 2 days later and check INR after 2 days of warfarin alone. • **If CrCl < 30:** Stop dabigatran 1 day later and check INR after 3 days of warfarin alone.
Rivaroxaban† → warfarin	Start warfarin while patient is still taking rivaroxaban. Stop rivaroxaban 2 to 4 days later, with timing based on patient's creatinine clearance (CrCl) and INR level:‡ • **If CrCl >50:** Check INR on day 4 of overlap. – If INR is ≥ 2.0, stop rivaroxaban; repeat INR after 1 to 2 days on warfarin alone. – If INR is < 2.0, consider continuing rivaroxaban along with warfarin; repeat INR 1 to 2 days later. • **CrCl = 31–50:** Stop rivaroxaban 3 days later; check INR after patient has received 1 to 2 days of warfarin only. • **If CrCl < 30:** Stop rivaroxaban 2 days later; check INR after patient has received 2 days of warfarin only.
Enoxaparin → NOAC	• Start dabigatran, rivaroxaban, or apixaban 10 to 12 hours after last enoxaparin dose.
NOAC → IV UH or LMWH	• **Apixaban:** Start unfractionated heparin or low molecular-weight heparin 12 hours after last apixaban dose. • **Dabigatran:** – **If CrCl > 30,** start unfractionated heparin or low molecular-weight heparin 12 hours after last dabigatran dose. – **If CrCl ≤ 30,** consider starting LMWH 24 hours after last dabigatran dose, based on clinical interpretation of the patient's risk of bleeding and thrombosis. • **Rivaroxaban:** Start unfractionated heparin or low molecular-weight heparin 12 hours after last rivaroxaban dose if patient is within first 21 days of treatment for VTE, or 24 hours after last rivaroxaban dose for other indications.

Notes:

* This recommendation differs from the apixaban package insert, which suggests use of an injectable anticoagulant during the transition from apixaban to warfarin. This CPM suggests the above course for pragmatic patient management to avoid introducing an injectable agent while assuring adequate overlap of anticoagulation. The apixaban recommendation differs from those for rivaroxaban and dabigatran because apixaban has a different renal clearance than the other two DOACs.

† All DOACs may prolong the INR in an unpredictable fashion when coadministered with warfarin. These recommendations place value on avoiding interruption of therapeutic anticoagulation when transitioning from an DOAC to warfarin, as interruption has been associated with an increase in thromboembolic events.[11]

‡ Point-of-care INR monitors should not be used to assess INR during transitions between the DOACs and warfarin, due to unreliability.[14,15]

☑ *ANTICOAGULATION SWITCHING: KEY PRINCIPLES*

- When switching medications, an important goal is to avoid interrupting therapeutic anticoagulation during the transition.
- The protocols for switching at left are based on a range of factors and are designed to meet this goal.

☑ *ANTICOAGULATION INITIATION AND BRIDGING: KEY PRINCIPLES*

- The initiation dose of warfarin should take into account warfarin sensitivity; checking INR frequently during titration is the key to effective initiation.
- Periprocedural bridging of warfarin and direct OACs should be based on the patient's thromboembolism risk and the bleeding risk of the procedure.

5 Initiate warfarin wisely

For patients starting on warfarin, follow Intermountain's Warfarin Initiation Guidelines available from the Anticoagulation Task Force.

- **Consider warfarin sensitivity.** The Initiation Guidelines specify a lower initiation dose for patients in the following situations: age greater than 75 years, congestive heart failure, diarrhea, drug interactions, elevated baseline INR, fever, hyperthyroidism, malignancy, and malnutrition or NPO greater than 3 days.
- **Check INR frequently during titration.** Obtain an INR 3 days after the first starting dose, then every 2 to 3 days until in-range INR is achieved on two measurements. Then check INR one week after the second in-range INR. See the Initiation Guidelines for details.

6 Manage bleeding or supratherapeutic INR

- **Severe or life-threatening bleeding, on any anticoagulant:** Send the patient to the ED with EMS transport.
- **Minor bleeding on apixaban, rivaroxaban, or dabigatran:** Assess the patient individually. If necessary, hold 1 to 2 doses to achieve homeostasis, then restart the medication.
- **Supratherapeutic INR on warfarin:**
  - **If INR is 4.5 to 10:** Hold 1 to 2 doses; check INR more frequently (1 to 3 days). Resume warfarin at adjusted dose when INR returns to therapeutic range.
  - **If INR is over 10:** Hold warfarin and give vitamin K 2.5 to 5 mg orally. Check INR more frequently (e.g. every 1 to 3 days); give additional vitamin K if needed. Resume warfarin at adjusted dose when INR returns to therapeutic range.

7 Manage periprocedural bridging

For bridging patients on warfarin, see these Intermountain materials:

- **For Providers:** Anticoagulation Bridging Guidance and Decision Tree
- **For Patients:** Bridging handouts based on thromboembolism (TE) risk and the bleeding risk of the procedure:
  - A pre-procedure handout (customizable by TE and bleeding risk)
  - A post-procedure handout for moderate TE risk, moderate bleeding risk
  - A post-procedure handout for moderate TE risk, high bleeding risk
  - A post-procedure handout for high TE risk, moderate bleeding risk
  - A post-procedure handout for high TE risk, high bleeding risk

For bridging patients on NOACs, see information provided in these Intermountain resources:

- Provider information sheet for dabigatran
- Provider information sheet for rivaroxaban
- Provider information sheet for apixaban

REFERENCES

1. Calkins H, Kuck KH, Cappato R, et al; Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. *Heart Rhythm.* 2012;9(4):632-696.
2. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (Updating the 2006 Guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Heart Rhythm.* 2011;8(1):157-176.
3. You JJ, Singer DE, Howard PA, et al; American College of Chest Physicians. Antithrombotic therapy for atrial fibrillation: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012;141(2 Suppl):e531S-e575S.
4. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J.* 2006;27(8):949-953.
5. Lin HJ, Wolf PA, Kelly-Hayes M, Beiser AS, Kase CS, Benjamin EJ, D'Agostino RB. Stroke severity in atrial fibrillation. The Framingham Study. *Stroke.* 1996;27(10):1760-1764.
6. Singh BN, Singh SN, Reda DJ, et al; Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T) Investigators. Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med.* 2005;352(18):1861-1872.
7. Fetsch T, Bauer P, Engberding R, et al; Prevention of Atrial Fibrillation after Cardioversion Investigators. Prevention of atrial fibrillation after cardioversion: results of the PAFAC trial. *Eur Heart J.* 2004;25(16):1385-1394.
8. Kirchhof P, Andresen D, Bosch R, et al. Short-term versus long-term antiarrhythmic drug treatment after cardioversion of atrial fibrillation (Flec-SL): a prospective, randomised, open-label, blinded endpoint assessment trial. *Lancet.* 2012;380(9838):238-246.
9. Lip GY, Frison L, Halperin JL, Lane DA. Identifying patients at high risk for stroke despite anticoagulation: a comparison of contemporary stroke risk stratification schemes in an anticoagulated atrial fibrillation cohort. *Stroke.* 2010;41(12):2731-2738.
10. Lane DA, Lip GY. Use of the CHA_2DS_2-VASc and HAS-BLED scores to aid decision making for thromboprophylaxis in nonvalvular atrial fibrillation. *Circulation.* 2012;126(7):860-865.
11. Patel MR, Mahaffey KW, Garg J, et al; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med.* 2011;365(10):883-891.
12. Schulman S, Crowther MA. How I treat with anticoagulants in 2012: new and old anticoagulants, and when and how to switch. *Blood.* 2012;119(13):3016-3023.
13. Turpie AG, Kreutz R, Llau J, Norrving B, Haas S. Management consensus guidance for the use of rivaroxaban — an oral, direct factor Xa inhibitor. *Thromb Haemost.* 2012;108(5):876-886.
14. Kubitza D, Becka M, Wensing G, Voith B, Zuehlsdorf M. Safety, pharmacodynamics, and pharmacokinetics of BAY 59-7939 — an oral, direct Factor Xa inhibitor — after multiple dosing in healthy male subjects. *Eur J Clin Pharmacol.* 2005;61(12):873-880.
15. Samama MM, Martinoli JL, LeFlem L, et al. Assessment of laboratory assays to measure rivaroxaban — an oral, direct factor Xa inhibitor. *Thromb Haemost.* 2010;103(4):815-825.