

GENERAL PRINCIPLES FOR THE PHARMACOLOGIC MANAGEMENT OF CHRONIC HEART FAILURE (HF)

- Treatment of HF is based upon classification into four stages:

ACC/AHA Staging (Classification based on disease progression)
Stage A: Patients who are high risk for developing HF, but do not have structural heart disease
Stage B: Patients who have structural damage to the heart, but have not developed symptoms
Stage C: Patients with past or current HF symptoms and evidence of structural heart damage
Stage D: Patients with end-stage disease, requiring special interventions

Adapted from Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). 2001. American College of Cardiology Web site. Available at: http://www.acc.org/clinical/guidelines/failure/hf_index.htm

NYHA Functional Classification (Estimates severity of disease based on patient symptoms)
Class I: No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or angina.
Class II: Slight limitation of physical activity. Ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
Class III: Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
Class IV: Unable to carry on any physical activity without discomfort. Symptoms are present at rest. With any physical activity, symptoms increase.

Adapted from the Criteria Committee of the American Heart Association. 1994 revisions to the classification of functional capacity and objective assessment of patients with disease of the heart. *Circulation* 1994;90:644-5.

- Stage A, B, or C: Implement non-pharmacologic interventions, manage concomitant cardiac conditions and risk factors, and address underlying causes; Stage D: Consider referral to a cardiologist or other specialist
- Stage B: **Initiate angiotensin-converting enzyme inhibitor (ACEI) or β -blocker** as indicated; once stable, add other agent if warranted

- Stage C:
 - A **diuretic** should be used in the treatment of patients with signs of fluid overload
 - An **ACEI** should be initiated and titrated to target dose as tolerated, unless contraindicated or not tolerated
 - A **β -blocker** should be used in conjunction with an ACEI in all patients with stable HF
 - Digoxin** should be used in patients with HF whose symptoms persist despite treatment with an ACEI, a β -blocker, and a diuretic
 - An **angiotensin II receptor antagonist (AIIRA)** may be considered as an alternative for patients who cannot tolerate an ACEI due to cough
 - Hydralazine and isosorbide dinitrate (HYD/ISDN)** may be considered in patients with contraindications to or who cannot tolerate an ACEI due to hypotension, renal insufficiency, or possibly, angioedema
 - Low dose **spironolactone** should be considered in patients with recent NYHA class IV HF and current class III or IV symptoms and LVEF \leq 35%, unless contraindications exist

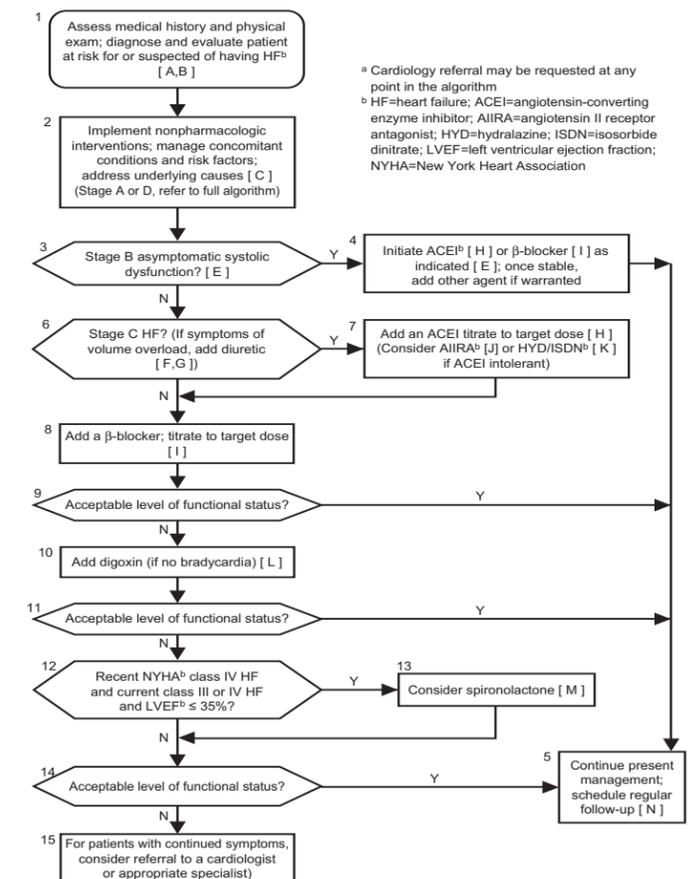
PATIENT EDUCATION AND FOLLOW-UP

- Patients should be scheduled for regular follow-up and assessed for change in functional status
- Proper education of patients and their family is imperative so that they may have an understanding of the cause of HF, prognosis, therapy, dietary restrictions, risk factor modification, activity, adherence, and the signs and symptoms of recurrent HF
- Instruct patient and/or caregiver on daily weight measurements to assess for fluid retention
- Nonpharmacologic therapy including abstaining from alcohol and tobacco, limiting dietary sodium, reducing weight if appropriate, and participating in exercise training programs should be discussed with the patient
- Inquiry should be made as to the patient's adherence to the medication regimen and nonpharmacologic measures, and adverse effects to therapy
- Some facilities may have interdisciplinary HF disease management clinics to provide continuity of care for patients with HF

Symptoms of HF	Signs of HF
Shortness of breath (SOB)	Tachycardia
Cough	Increasing weight
Orthopnea	Jugular venous distention (JVD) or hepatojugular reflux
Paroxysmal nocturnal dyspnea (PND)	Presence of S ₃ (third heart sound)
Dyspnea on exertion (DOE)	Laterally displaced apical impulse
Edema	Pulmonary crackles or wheezes
Fatigue	Hepatomegaly
Weight gain (anorexia may be seen in advanced HF)	Peripheral edema

The Pharmacologic Management of Chronic Heart Failure Pharmacy Benefits Management-Strategic Healthcare Group and Medical Advisory Panel (PBM-MAP) Pocket Guide

Update 2003



Specific Recommendations for Oral Medications Used in the Treatment of HF		
Diuretic	Dose Range	Comments/Cautions
Loop diuretic Furosemide Bumetanide Torsemide	Range = 20-400* mg/d Range = 0.5-10 mg/d Range = 10-200 mg/d	<ul style="list-style-type: none"> Loop diuretics are more effective than thiazide diuretics in patients with severe volume overload Usually administered once daily unless higher doses (e.g., furosemide > 160 mg/d) are needed, then more frequent daily dosing should be considered Effective in patients with CrCl < 30 mL/min
Thiazide diuretic^b Hydrochlorothiazide (HCTZ) Chlorthalidone	Range= 12.5-50 mg/d Range = 12.5-50 mg/d	<ul style="list-style-type: none"> Loss effectiveness in patients with CrCl < 30 mL/min; change to loop diuretic Monitor serum K⁺ at 1 to 2 weeks after initiating therapy or changing dose, then every few months; more frequently if patient is also on digoxin or has demonstrated hypokalemia Add potassium supplement or low dose potassium-sparing diuretic^c if the patient becomes hypokalemic (serum K⁺ < 4.0 mEq/L) Use cautiously in poorly controlled DM, symptomatic benign prostatic hyperplasia, or in patients with increased risk of volume depletion
Thiazide-related Indapamide Metolazone ^d Zaroxolyn ^e Mykrox ^f	Range = 2.5-5 mg/d Range = 5-20* mg/d ^g Range = 0.5-1 mg/d ^g	<ul style="list-style-type: none"> Reserve indapamide for patients with CrCl < 25 mL/min Reserve metolazone for intermittent use as an adjunct to loop diuretics for diuresis in patients with HF or in patients with CrCl < 25 mL/min; thiazide/loop combinations are also effective and are less expensive
ACEI (Annotation H)	Initial dose (Target doses ^e)	Comments/Cautions
Captopril ^h	6.25-12.5 mg tid (50 mg tid)	<ul style="list-style-type: none"> Start with lower or less frequent doses in patients with renal insufficiency
Enalapril	2.5 mg bid (10-20 mg bid)	<ul style="list-style-type: none"> CrCl < 30 mL/min, initial dose 2.5 mg qd
Fosinopril	5-10 mg qd (20-40 mg qd)	<ul style="list-style-type: none"> Start with 5 mg qd if moderate to severe renal failure
Lisinopril	2.5-5 mg qd (20-40 mg qd)	<ul style="list-style-type: none"> CrCl < 30 mL/min, initial dose 2.5 mg qd
Also refer to PBM-MAP Criteria for use of ramipril, available at www.vapbm.org or http://vaww.pbm.med.va.gov		<p align="center">Contraindications to all ACEI</p> <ul style="list-style-type: none"> History of angioedema or other documented hypersensitivity to an ACEI; Bilateral renal artery stenosis or renal artery stenosis in a solitary kidney; Symptomatic hypotension; Pregnancy; Serum potassium > 5.5 mEq/L that cannot be reduced
β-Blocker (Annotation I)	Dose Range	Comments/Cautions
Cardioselective Metoprolol XL ^g Bisoprolol	Initial 12.5-25 mg qd; double dose every 2 wks to target dose 200 mg qd (or as tolerated) Initial 1.25 mg qd; increase by 1.25 mg q wk until 5 mg qd, then increase by 2.5 mg q 4 wks to target 10 mg qd	<ul style="list-style-type: none"> Agents listed are those with positive outcomes in systolic dysfunction Cardioselectivity is dose related Caution should be used when using β-adrenergic blockers in patients with systolic dysfunction Low initial doses should be implemented Use slow gradual increases in the dosage Effects are generally seen in 3-12 months Do not use in patients with bronchospastic disease, symptomatic bradycardia, or advanced heart block without a pacemaker Should not be abruptly discontinued Carvedilol should be given with food to reduce the incidence of orthostatic hypotension; consider separating the ACEI, adjusting dose of diuretic, or temporary ACEI dose reduction if dizziness occurs Refer to PBM-MAP Recommendations for use of β-adrenergic blockers in VA patients with HF, available at www.vapbm.org or http://vaww.pbm.med.va.gov
α & β antagonist Carvedilol ^h	Initial 3.125 mg bid, (patients ≥ 85 kg may be titrated to 50 mg bid); titrate at minimum of q 2 wks to target 25-50 mg bid	<ul style="list-style-type: none"> Refer to PBM-MAP Recommendations for use of β-adrenergic blockers in VA patients with HF, available at www.vapbm.org or http://vaww.pbm.med.va.gov

Specific Recommendations for Oral Medications Used in the Treatment of HF (con't)		
AIIRA (Annotation J)	Dose Range	Comments/Cautions
Candesartan	4-32 mg divided qd-bid	<ul style="list-style-type: none"> All AIIRAs are contraindicated in 2nd and 3rd trimesters pregnancy due to potential neonatal/fetal morbidity and death Use AIIRAs with caution in patients with renal artery stenosis Initiate losartan at 25 mg and use telmisartan with caution in patients with hepatic impairment Consider lower doses in patients with intravascular volume depletion An AIIRA should be used with caution, if at all, in patients who have previously experienced angioedema with an ACEI
Eprosartan	400-800 mg divided qd-bid	
Irbesartan	75-300 mg qd	
Losartan	25-100 mg divided qd-bid	
Olmesartan	5-40 mg qd	
Telmisartan	20-80 mg qd	
Valsartan	80-320 mg qd (divided bid in Val-HeFT)	
Drug (Annotation K)	Dose Range	Comments/Cautions
Hydralazine	Initial = 75 mg/d (3-4 divided doses); Range = 75-300 mg/d (3-4 divided doses); (ave. dose V-HeFT II 200 mg/d)	<ul style="list-style-type: none"> Monitor adverse effects: dizziness, headache, lupus-like syndrome, nausea, tachycardia, postural hypotension Advise patient to take with food
Isosorbide dinitrate	Initial= 30 mg/d (3 divided doses); Range=30-160 mg/d (3 divided doses); (ave. dose V-HeFT II 100 mg/d)	<ul style="list-style-type: none"> Monitor adverse effects: flushing, headache, postural hypotension, rash May cause an increase in ocular pressure; caution with presence of glaucoma
Drug	Dose Range	Comments/Cautions
Digoxin (Annotation L)	Initial = 0.125 mg qd-qod Usual maintenance 0.125 - 0.25 mg/d	<p>Trough serum digoxin levels should be monitored if:</p> <ul style="list-style-type: none"> HF worsens or renal function deteriorates Signs of toxicity develop (e.g., confusion, nausea, vomiting, abdominal pain, diarrhea, anorexia, fatigue, arrhythmias, visual disturbances) Dose adjustments are made Medications added that affect digoxin concentration (e.g., quinidine, verapamil, amiodarone, antibiotics, anticholinergics)
Spirolactone (Annotation M)	Initial = 25 mg qd Range = 25 mg qod - 50 mg qd	<ul style="list-style-type: none"> Potential side effects include gastrointestinal, gynecomastia, hyperkalemia, menstrual irregularities Hyperkalemia occurs more frequently in patients on K⁺ supplements and patients with renal insufficiency K⁺ supplements should be avoided with spironolactone unless hypokalemia develops Use with caution in patients with renal insufficiency Schedule follow-up electrolytes (check K⁺ q 4 wks for first 3 months, then q 3 months for first yr and then q 6 months) and renal function after initiation and dose adjustments Use with caution in patients receiving ACEIs due to the potential for hyperkalemia

Bold = National Formulary item
 Adapted from Hebel SK, ed. *Drug Facts and Comparisons*, St. Louis, Missouri: Facts and Comparisons Inc., 2000; *Heart failure: Management of patients with left ventricular systolic dysfunction. Clinical Practice Guideline*, No. 11. Rockville, MD. U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research. AHCPR Publication No. 94-0613; McEvoy GK, ed. *American Hospital Formulary Service Drug Information*, Bethesda, MD: American Society of Health-System Pharmacists, Inc., 2002.

^a Higher doses have been effective and tolerated
^b Unless patients have persistent hypokalemia or are being treated with low dose spironolactone for severe HF (Annotation M), potassium-sparing diuretics should not be used in combination with ACEI (Appendix 1)
^c The brand names of metolazone are not bioequivalent, therefore doses vary
^d Intermittent use recommended once the response of the patient is stabilized
^e Target doses for HF were derived from major trials and AHCPR guidelines. Excluding captopril and enalapril, doses for HF reflect doses used to increase exercise tolerance in HF patients
^f One hour before meals, on an empty stomach
^g FDA approved for the treatment of stable, NYHA class II or III HF
^h Carvedilol is FDA approved for the treatment of mild-moderate HF stabilized on standard therapy