# The Pharmacologic Management of Hypertension

## Supplement to the VHA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting

VHA's Pharmacy Benefits Management (PBM) Strategic Healthcare Group (SHG) has been directed by the Under Secretary for Health to coordinate the development of guidelines for the pharmacologic management of common diseases treated within the VA, to establish a national level VA formulary, to manage pharmaceutical costs and utilization, and to measure outcomes as they apply to patient care. The Medical Advisory Panel (MAP) provides support and direction to the PBM staff, located in Hines, Illinois.

The Department of Defense (DoD) Pharmacoeconomics Center (PEC) supports the DoD Pharmacy and Therapeutics Committee in managing the DoD Basic Core Formulary (BCF) and National Mail Order Pharmacy (NMOP), participates in the development of joint guidelines with the VA, helps manage pharmaceutical costs and utilization, and measures outcomes as they apply to patient care.

This document is a supplement to the treatment guideline on the management of hypertension developed as a joint venture with experts practicing at Veterans Affairs Medical Centers and Department of Defense Treatment Facilities. The VHA/DoD Guidelines for the Diagnosis and Management of Hypertension in the Primary Care Setting can be found at http://vaww.va.gov/quality/quality/cpg/hypertension.cfm. The supplement summarizes relevant aspects of the VHA/DoD treatment guideline and focuses on recommendations for the pharmacologic management of the veteran or DoD beneficiary with hypertension.

This document should not be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgement regarding the propriety of any course of conduct must be made by the clinician in light of individual patient situations.

# THE PHARMACOLOGIC TREATMENT OF HYPERTENSION: RECOMMENDATIONS FOR DISEASE MANAGEMENT

The information herein is presented according to the various elements of disease management (i.e., screening, prevention, management, education, and outcomes) and their relation to the participants (i.e., patient, provider, system). This document focuses on the pharmacologic management of hypertension (HTN). For a comprehensive guideline on the management of hypertension, please refer to the VHA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting at http://vaww.va.gov/quality/quality/cpg/hypertension.cfm, www.vapbm.org or http://vaww.pbm.med.va.gov

## SCREENING

Screening of a population without the diagnosis is the first element.

Recommendations include screening the ***patient*** for:

- Blood pressure (BP) elevation (discuss additional screening opportunities with the patient e.g., drug stores, health fairs, and other community settings)
- Smoking
- Dyslipidemia
- Diabetes mellitus (DM)

The ***provider*** can make the diagnosis of HTN based upon the following criteria:

**Blood Pressure Classification**[a]

| STAGE[b,c] | SBP[c] (mm Hg) | DBP[c] (mm Hg) |
|---|---|---|
| Normal | <130 | <85 |
| High-normal | 130 to 135 | 85 to 89 |
| Stage 1 HTN | 140 to 159 | 90 to 99 |
| Stage 2 HTN | 160 to 179 | 100 to 109 |
| Stage 3 HTN | ≥180 | ≥110 |

[a] Adapted from the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). Arch Intern Med 1997;157:2413-46.

[b] Based on the average of 2 or more readings taken at each of 2 or more visits after an initial screening in patients not currently on antihypertensive drugs or who are not acutely ill. Risk classification also depends on presence or absence of target organ damage or clinical cardiovascular disease (CVD) and additional risk factors.

[c] When systolic BP (SBP) and diastolic BP (DBP) fall into different categories, the higher category should be selected to classify the individual's blood pressure status. Isolated systolic hypertension (ISH) is defined as SBP of ≥ 140 mm Hg and DBP <90 mm Hg.

The ***system*** attempts to provide:

- Computer reminders or provider's lists of patients who need screening
- Established programs for screening and prevention

## PREVENTION

Prevention and risk reduction for those with an established diagnosis is the next element.

Target values for the ***patient*** are:

- Weight reduction to within 10% of ideal body weight
- Alcohol intake limited to no more than 1 oz (24 oz of beer or 10 oz of wine; or 2 oz of 100-proof whiskey) per day for men, or 0.5 oz of alcohol per day for women and smaller individuals
- Sodium intake limited to no more than 2.4g/day
- Moderate aerobic exercise for 30-45 minutes, 3-5 times per week
- Diet modified as recommended in the Dietary Approaches to Stop Hypertension (DASH) clinical study, to be rich in fruits, vegetables, and low-fat dairy foods; low in saturated and total fat and cholesterol; high in dietary fiber, potassium, calcium, and magnesium; and moderately high in protein.
- Smoking cessation

It is recommended that the ***provider*****:**

- Assess patient for target organ damage and clinical cardiovascular disease

| |
|---|
| **Heart diseases**<br>• Left ventricular (LV) hypertrophy<br>• Angina or prior myocardial infarction (MI)<br>• Prior coronary revascularization<br>• Heart failure<br>**History of transient ischemic attack or stroke**<br>**Peripheral arterial disease**<br>**Renal disease**<br>**Retinopathy** |

Adapted from JNC VI

- Assess patient for major risk factors for cardiovascular disease and treat as indicated

| |
|---|
| **Smoking**<br>**Dyslipidemia**<br>**DM**<br>**Age >60 yr**<br>**Gender**<br>• Men<br>• Postmenopausal women<br>**Family history of CVD**<br>• Men <55 yr<br>• Women <65 yr |

Adapted from JNC VI

- Perform a medical history, physical exam, laboratory and other diagnostic procedures to determine causative factors and degree of HTN (recommended tests include urinalysis, complete blood count, chemistries including serum creatinine and blood urea nitrogen, lipid profile, and electrocardiogram; for optional tests refer to VHA/DoD Clinical Practice Guideline for the Diagnosis and Management of

Hypertension in the Primary Care Setting at
http://vaww.va.gov/quality/quality/cpg/hypertension.cfm or www.vapbm.org

The ***system*** attempts to provide:

- Computer reminders to the provider
- Mailed patient reminders
- Smoking cessation program
- Dietary consult
- Cardiac education classes
- Exercise programs

## MANAGEMENT

The ***patient*** makes an effort to:

- Implement diet and lifestyle modifications
- Minimize cardiac risk factors
- Adhere to treatment regimen

It is recommended that the ***provider*** consider the following when managing patients with HTN:

- Pharmacotherapy for the treatment of HTN is predicated on monotherapy whenever possible.
- Preferred agents for patients with uncomplicated HTN are thiazide diuretics and β-blockers as these have been shown to lower morbidity and mortality associated with HTN. Multi-drug regimens should include a thiazide diuretic for synergy, except when contraindicated.
- Patients with compelling indications for selected antihypertensive drug therapy should be initiated on these agents, unless contraindicated. Other agents may have favorable effects on comorbid conditions and should be considered in selected patients (refer to table on Special Populations, Comorbidities, and Preferred Agents, page 7). The goal of therapy is to reduce BP to less than 140/90 mm Hg, without orthostatic hypotension. Further reduction is reasonable in patients with diabetes (to 140/85 mm Hg [as per the VHA Clinical Guidelines for Management of Diabetes Mellitus] or lower, if tolerated) or with renal disease and protein excretion greater than or equal to 1g/day (to 125/75 mm Hg). For patients with ISH, often found in older patients, the initial goal of therapy includes a reduction of SBP to less than 160 mm Hg for patients with SBP greater than 180 mm Hg, and a reduction by at least 20 mm Hg if the SBP is between 160-179 mm Hg.
- In the management of HTN, patients are classified into risk groups based on presence or absence of clinical CVD or target organ damage and other risk factors. Therefore, it is important to ascertain the patient's risk group to determine optimal BP management and to modify risk factors.
- Nonpharmacologic therapy should be instituted in all patients. Lifestyle modifications include diet restrictions, exercise, weight reduction, and reduction of

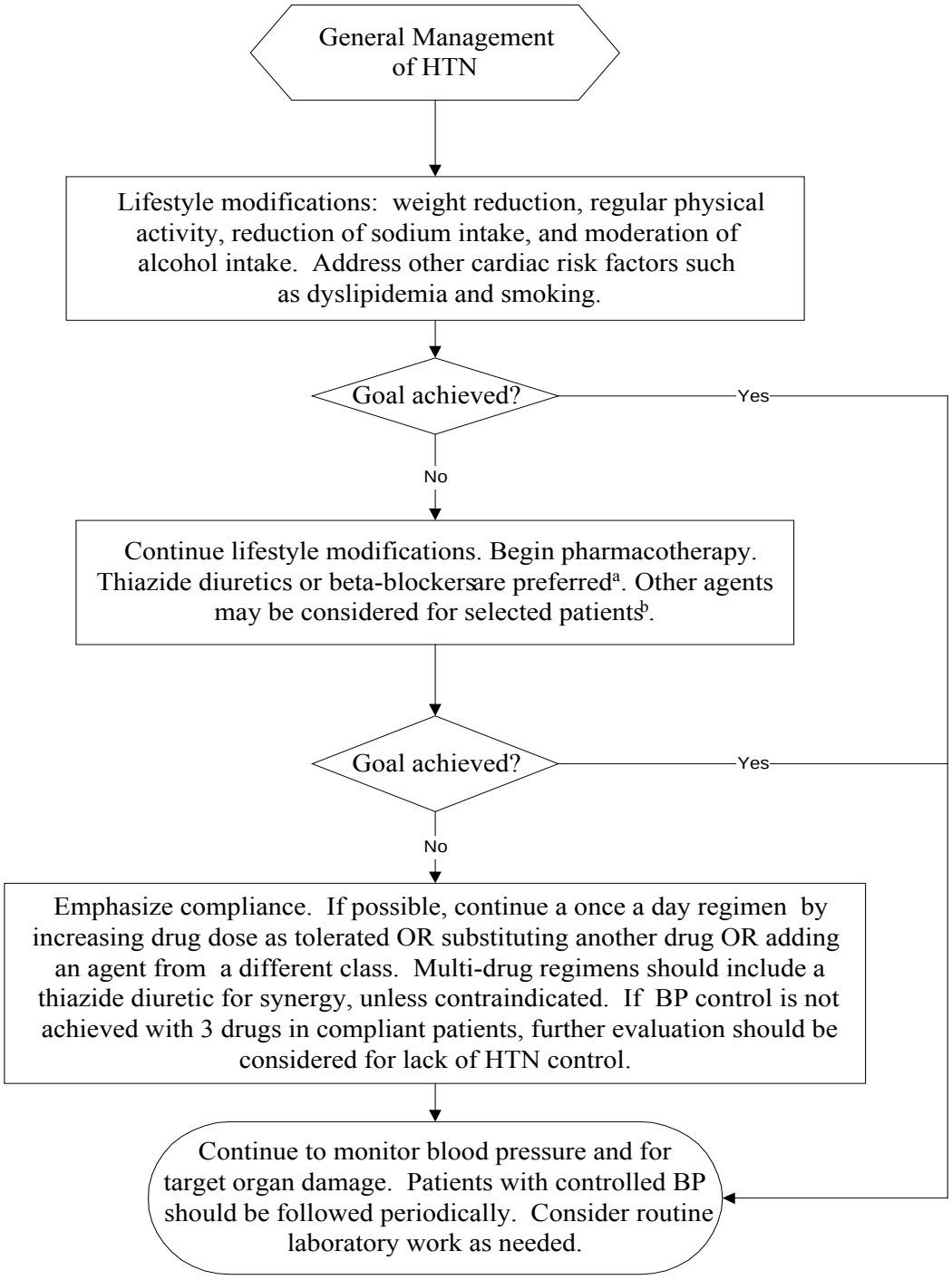
excessive ethanol use. Smoking and other cardiac risk factors should be addressed, when appropriate.

**General Guidelines for Management[a-c]**

| BP STAGE | RISK GROUP A[d] | RISK GROUP B[e] | RISK GROUP C[f] |
|---|---|---|---|
| High-normal | Advise about lifestyle modifications for reducing BP | Advise about lifestyle modifications for reducing BP | Consider drug therapy for patients with heart failure, renal insufficiency, or DM |
| Stage 1 | Advise about lifestyle modifications for controlling BP (up to 12 mo) | Advise about lifestyle modifications for controlling BP (up to 6 mo) | Begin drug therapy and advise about lifestyle modifications |
| Stages 2 & 3 | Begin drug therapy and advise about lifestyle modifications[g] | Begin drug therapy and advise about lifestyle modifications | Begin drug therapy and advise about lifestyle modifications |

[a]Adapted from JNC VI
[b]For patients with known HTN and for selection of drug therapy, refer to the table on Special Populations, Comorbidities, and Preferred Agents (page 7)
[c]Acute target organ damage (e.g., papilledema) associated with HTN requires immediate management
[d]Risk Group A=no CVD risk factors; no target organ damage or clinical CVD
[e]Risk Group B=at least 1 risk factor for CVD (not including DM); no evidence of target organ disease or clinical CVD
[f]Risk Group C=evidence of target organ disease or clinical CVD and/or DM with or without other CVD risk factors
[g]Consider aggressive lifestyle modification alone in selected patients with Stage 2 HTN in Risk Group A

## Algorithm




[a] Due to reduction in morbidity and mortality

[b] Refer to the table on Special Populations, Comorbidities, and Preferred Agents (page 7)

## Special Populations, Comorbidities, and Preferred Agents [a,b]

| | PREFERRED AGENTS | ALTERNATE AGENTS | OTHER SELECTED AGENTS | COMMENTS |
|---|---|---|---|---|
| **Uncomplicated** | thiazide diuretic, β-blocker | ACEI, CCB | α-blocker, clonidine, reserpine | Short-acting nifedipine should not be used for long-term management of HTN |
| **African-American Race** | thiazide diuretic | CCB, β-blocker, ACEI | α-β-blocker, clonidine, α-blocker | Differences in efficacy among patient populations are not as apparent when diuretics are added to ACEIs and β-blockers |
| **Asthma/COPD** | thiazide diuretic | ACEI, CCB | clonidine, α-blocker | β-blockers relatively contraindicated in patients with bronchospastic disease |
| **BPH – Symptomatic** | *α-blocker*[c] | β-blocker, ACEI, thiazide diuretic (low dose), CCB | clonidine | Diuretics may influence symptoms of polyuria and frequency |
| **Coronary artery disease** | ***β-blocker*** (non-ISA post-MI) | *verapamil, diltiazem* | DHP SR, ACEI, thiazide diuretic | Non-ISA β-blockers are the drugs of choice post-MI; ACEIs are also indicated post-MI in patients with systolic dysfunction |
| **LVD - Diastolic** | β-blocker, diuretic | verapamil, diltiazem | ACEI, α-blocker | Diuretics are first-line agents if symptoms of volume overload exist |
| **LVD - Systolic** | **ACEI[d], diuretic[d]** | angiotensin II antagonist, hydralazine/nitrate | amlodipine, felodipine | ACEIs are preferred for their potential improvement in morbidity and mortality in this patient population; diuretics should be used if symptoms of volume overload exist; angiotensin II antagonists may be used where an ACEI is not tolerated; other selected agents may be used in conjunction with an ACEI in stable CHF patients; β-blockers[d] and CCBs should be used with caution |
| **CRI (CrCl < 25ml/min or $S_{cr}$ >2.5 mg/dL)** | furosemide, ACEI | β-blocker, CCB, α-blocker, indapamide, metolazone | clonidine, minoxidil, hydralazine | Potassium ($K^+$)-sparing diuretics, $K^+$ supplements, and/or ACEI may cause ↑ $K^+$; use ACEI with caution in patients with $S_{cr}$ >3.0 mg/dL; metoprolol is the preferred β-blocker due to hepatic excretion |
| **Depression** | thiazide diuretic | ACEI, CCB, α-blocker | | Clonidine, reserpine, methyldopa, β-blockers may exacerbate depression |
| **DM** | ***ACEI***[e](types 1 & 2 DM with proteinuria) | *thiazide diuretic* (low dose), CCB, β-blocker, α-blocker | angiotensin II antagonist | High-dose thiazide diuretics and β-blockers may worsen glucose control; β-blockers may mask hypoglycemia; use of DHP SR in patients with HTN and type 2 DM remains controversial |
| **Elderly (age >65 yrs)** | thiazide diuretic | β-blocker, CCB, ACEI | α-blocker | Use caution with α-blockers in elderly due to first-dose syncope or dizziness |
| **Gout** | β-blocker | ACEI, CCB, thiazide diuretic (low dose) | α-blocker | Diuretic-induced hyperuricemia does not require treatment in the absence of gout or kidney stones |
| **Dyslipidemia** | thiazide diuretic (low dose), β-blocker | ACEI, CCB, *α-blocker* | | Thiazide diuretics may↑ TC and ↑ TG and non-ISA β-blockers may ↓ HDL and ↑ TG, although these effects may be transient |
| **Isolated systolic hypertension** | **thiazide diuretic** | DHP SR, β-blocker, ACEI | α-blocker | The use of DHP SR as first-line therapy remains controversial, although studies are available to indicate benefit |
| **Left ventricular hypertrophy** | ACEI, thiazide diuretic, β-blocker | CCB | α-blocker, clonidine | Direct-acting vasodilators do not reduce left ventricular hypertrophy |
| **Peripheral vascular disease** | thiazide diuretic, ACEI | CCB, β-blocker | α-blocker | Nonselective β-blockers without α-blockade may worsen resting ischemia or severe claudication symptoms |
| **Pilots** | thiazide diuretic, lisinopril | | | |
| **Pregnancy (chronic HTN)** | methyldopa | labetalol | hydralazine (generally used for preeclampsia) | Except for ACEI and angiotensin II antagonists that are contraindicated during pregnancy, any antihypertensive drug may be continued if taken prior to pregnancy; β-blockers may cause growth retardation in 1st trimester |

[a]Adapted from JNC VI; **Bold**=compelling indication per outcome data (unless contraindicated); *Italics*=may have favorable effect on comorbid conditions

[b]ACEI =angiotensin-converting enzyme inhibitor; BUN=blood urea nitrogen; CCB=calcium channel blocker; DHP SR=long-acting dihydropyridine; COPD=chronic obstructive pulmonary disease; BPH=benign prostatic hyperplasia; ISA=intrinsic sympathomimetic activity; MI=myocardial infarction; LVD=left ventricular dysfunction; CHF=chronic heart failure; CRI=chronic renal insufficiency; DM=diabetes mellitus; TC=total cholesterol; TG=triglycerides; HDL=high-density-lipoprotein cholesterol

[c]Generally recommended for use as adjunct therapy to other antihypertensive agents; refer to text

[d]There is compelling evidence to use β-blockers as adjunct therapy in patients with NYHA II to III CHF who are stable on an ACEI with or without a diuretic; refer to PBM-MAP The Pharmacologic Management of Chronic Heart Failure at www.vapbm.org or http://vaww.pbm.med.va.gov

[e]Compelling indication in type 1 DM with proteinuria; preferred agent in types 1 and 2 DM with proteinuria

## Pharmacotherapy

### *Diuretics*

- Thiazides are proven to reduce cardiovascular morbidity and mortality from HTN and are the preferred agents to reduce BP. Hydrochlorothiazide (HCTZ) is inexpensive and efficacious at low doses, and is generally the thiazide of choice.
- Loop diuretics, metolazone, and indapamide should generally be reserved for patients with CRI.
    - Hypokalemia occurs in 10-15% of patients on low-dose thiazides, and therefore potassium ($K^+$) supplements are needed in only selected cases. Combination thiazide/triamterene diuretics are not usually necessary, but may be prudent when thiazide doses are high (e.g., HCTZ >25 mg) or $K^+$ <3.5 mEq/L on a thiazide diuretic or when a low $K^+$ may potentiate drug toxicity such as with digoxin. Combination therapy may not prevent hypokalemia.

| **THIAZIDES**[a-c] | **DOSE**[d] | **COMMENTS/CAUTIONS** |
|---|---|---|
| Hydrochlorothiazide (HCTZ)[e] | 12.5-25 mg/day<br>max = 50 mg/day | • Monitor serum $K^+$ 2-4 wk after initiating therapy or changing dose, then q 12 mo<br>• Hypokalemia may potentiate digitalis toxicity<br>• Monitor for hypotension, especially in the elderly<br>• Thiazides may have diminished effects in patients with Cr Cl <40-50 mL/min (or $S_{cr}$ >2.5 mg/dL)<br>• Use diuretics cautiously in poorly controlled DM, symptomatic BPH, or in patients with increased risk of volume depletion<br>• $K^+$-sparing combination may be preferred at higher thiazide doses<br>• Use HCTZ/triamterene with caution with ACEI and other $K^+$-retaining drugs or supplement |
| HCTZ/Triamterene [e] | Initial/max =<br>25/37.5 - 50/75 mg/day | |

[a] Adapted from Diuretics. In: Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons, Inc., 1998.
[b] Semla TP, Beizer JL, Higbee MD, eds. APhA Geriatric Dosage Handbook. 2nd ed. Hudson: Lexi-Comp Inc.,1995-96.
[c] Partial list
[d] Once-daily dosing unless specified otherwise
[e] DoD BCF item; all BCF items are available through the DoD NMOP

## *β-Blockers*

- β-blockers have been proven to reduce cardiovascular morbidity and mortality from HTN, although these effects have not been proven with β-blockers with intrinsic sympathomimetic activity (ISA).
- Non-ISA β-blockers are the preferred agents for coexisting coronary artery disease, especially post-MI.
- Use cautiously in patients with resting ischemia or severe claudication secondary to peripheral vascular disease (PVD), COPD with bronchospasm, systolic congestive heart failure, DM, or depression. β-blockers are contraindicated in asthma patients.
- α- and β-blocking agents are also available (e.g., labetolol, carvedilol). Carvedilol is FDA-approved for the treatment of CHF due to systolic dysfunction. Metoprolol and bisoprolol have also demonstrated positive outcomes in patients with New York Heart Association class II or III CHF. The decision to treat CHF patients with a β-blocker should be made with the expertise of a cardiologist if clinicians do not feel comfortable or do not have experience with these agents in patients with CHF. Caution should be exercised (refer to PBM-MAP The Pharmacologic Management of CHF at www.vapbm.org or http://vaww.pbm.med.va.gov).

| β-BLOCKERS[a-d] | DOSE[e] | COMMENTS/CAUTIONS |
|---|---|---|
| **Noncardioselective** | | • As doses increase, cardioselectivity decreases<br>• Monitor for bradycardia, CHF, fatigue, insomnia, cold extremities, impotence, and nightmares<br>• Monitor pulse rate<br>• May mask the symptoms of hypoglycemia in DM<br>• Discontinue with slow taper for 1 week |
| Propranolol IR[f] | 40-480 mg/day (in divided doses) | |
| Propranolol SR[f] | 80-160 mg/day | |
| **Cardioselective** | | |
| Atenolol[f] | 25-100 mg/day (dose adjustments are needed in CRI) | |
| Metoprolol IR | 50-300 mg/day (single or divided doses) | |

[a] Adapted from Beta-adrenergic blocking agents. In: Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons, Inc., 1998.
[b] Semla TP, Beizer JL, Higbee MD, eds. APhA Geriatric Dosage Handbook. 2nd ed. Hudson: Lexi-Comp Inc.,1995-96.
[c] Partial list
[d] IR = immediate release; SR = sustained release
[e] Once-daily dosing unless specified otherwise
[f] DoD BCF item; all BCF items are available through the DoD NMOP

### *Calcium Channel Blockers (CCBs)*

- When CCBs are chosen for HTN therapy, verapamil or diltiazem should be considered for patients with Stage 1 HTN (BP <160/100 mm Hg) due to the lower price of these agents. Verapamil should be avoided in patients with AV node dysfunction (2nd or 3rd degree heart block), and/or left ventricular (systolic) dysfunction when ejection fraction is <45%.
- When a CCB is indicated and a patient cannot tolerate verapamil or diltiazem OR for patients with Stage 2 and Stage 3 HTN, long-acting dihydropyridines (DHPs) can be considered. **Short-acting nifedipine should not be used for the treatment of essential hypertension.** Patients on this agent should be switched to a long-acting DHP or to another class of drugs.
- Felodipine and sustained-release nifedipine (Adalat® CC) are listed on the VA National Formulary to be prescribed when a long-acting DHP is considered the treatment of choice. Sustained-release nifedipine (Adalat® CC) is listed on the DoD Basic Core Formulary as the long-acting DHP of choice. Refer to the criteria for use of long-acting DHP calcium antagonists at www.vapbm.org or http://vaww.pbm.med.va.gov. Amlodipine is listed on the VA National Formulary but is restricted to the following criteria:
  1. when a long-acting DHP is considered the most appropriate treatment for angina AND the patient has a documented adverse reaction to felodipine AND long-acting nifedipine
  2. for the treatment of HTN and/or angina in patients with advanced heart failure who are already receiving appropriate therapy for CHF
- A long-acting DHP may be considered in patients with ISH when a thiazide diuretic is contraindicated. This recommendation is based on a 42% reduction in fatal and nonfatal stroke in patients with ISH found in a European study using nitrendipine (not available in the U. S.).
- The use of a long-acting DHP in patients with HTN and type 2 DM remains controversial. Two studies in patients with HTN and type 2 DM showed an increased risk of major vascular events (FACET with amlodipine) and a higher incidence of fatal and nonfatal myocardial infarctions (ABCD with nisoldipine) when a long-acting DHP was compared to treatment with an ACEI. In another trial (MIDAS with isradipine) in patients with HTN, there was an increased incidence of vascular events in patients treated with isradipine compared to those receiving a thiazide diuretic. It should be noted that these outcome measures were secondary endpoints of these three trials. In a post hoc analysis of MIDAS, it was found that patients with HTN and prediabetes treated with isradipine experienced more adverse cardiovascular events than patients treated with a thiazide diuretic. However, patients with diabetes receiving nitrendipine in the Syst-Eur study experienced a decrease in cardiovascular events and mortality. An improvement in cardiovascular outcomes was also seen in patients with diabetes treated with felodipine in the HOT trial. Until these issues can be resolved, long-acting DHPs should be used cautiously in patients with HTN and type 2 DM.

| CCBs[a-d] | DOSE [e,f] | COMMENTS/CAUTIONS |
|---|---|---|
| **Verapamil IR[g]**<br>**Verapamil SR**<br>Covera-HS®<br>Verapamil SR[g,h]<br><br>Verelan®<br>Verelan® PM | 120-360 mg/day (in 2-3 divided doses)<br>180-240 mg/day at hs<br>120-480 mg/day<br>(once daily or 2 divided doses)<br>120-480 mg/day<br>100-400 mg/day at hs | • Monitor for bradycardia and heart block<br>• Contraindicated in AV node dysfunction (2nd or 3rd degree heart block), systolic CHF and decreased LV function<br>• Doses >360 mg/d tend to increase side effects with minimal added benefit |
| **Dihydropyridines**<br>Amlodipine<br><br><br>Felodipine<br><br>Nifedipine CC[g] | <br>5-10 mg/day<br>elderly initial = 2.5 mg/day<br><br>2.5-10 mg/day<br><br>30-90/120 mg/day | • Monitor adverse effects: potent vasodilators can cause ankle edema, dizziness, flushing, headache<br>• CCBs should, in general, be used with caution in patients with CHF. Felodipine and amlodipine have been shown to be safe in long-term studies in patients with CHF on standard therapy (i.e., diuretics, ACEI, digoxin) |
| **Diltiazem IR[g]**<br><br>**Diltiazem SR**<br>Tiazac®[g] | 90-360 mg/day (in 3-4 divided doses)<br><br>120-540 mg/day | • Long-acting preparations may be used for patients with any of the following: atrial arrhythmia, sinus tachycardia, and/or angina or asymptomatic ischemia<br>• Monitor heart rate; may decrease sinus rate and cause heart block |

[a] Adapted from Calcium channel blocking agents. In: Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons, Inc., 1998.
[b] Semla TP, Beizer JL, Higbee MD, eds. APhA Geriatric Dosage Handbook. 2nd ed. Hudson: Lexi-Comp Inc.,1995-96.
[c] IR= immediate release formulation; SR=sustained release formulation; CR =controlled release; CC=Adalat ® CC
[d] Partial list
[e] Once-daily dosing unless otherwise specified
[f] For all CCBs, use caution in patients with liver and renal dysfunction; monitor effect and adjust dose when appropriate
[g] DoD BCF item; all BCF items are available through the DoD NMOP
[h] Available as Calan® SR, Isoptin® SR, and generic

### *Angiotensin-Converting Enzyme Inhibitors (ACEIs)*

- ACEIs should be considered preferred therapy in patients with HTN and one or more of the following compelling indications: heart failure, post-MI with systolic dysfunction, or type 1 DM with proteinuria. These agents may also be preferred in patients with renal insufficiency or who have type 2 DM with proteinuria, due to their potential favorable effects.
- ACEIs should be used very cautiously in patients with bilateral renal artery stenosis and in patients with renal artery stenosis in a solitary kidney.
- If the patient's BP has not adequately responded after titration to a standard maintenance dose, a low-dose thiazide diuretic should be added (unless contraindicated) for synergy. Otherwise, another medication should be added, or the ACEI should be discontinued and an agent in another drug class substituted.
- If adding an ACEI to a diuretic, consider starting at lower doses of ACEI or holding the diuretic for 1-2 days to avoid hypotension, especially in patients at risk for orthostatic hypotension or postural changes.

| ACEIs[a-c] | DOSE[d] | COMMENTS/CAUTIONS |
|---|---|---|
| Captopril[e] | 50-150[f,g] mg/day (in 2-3 divided doses); elderly initial = 12.5 mg/day | • Monitor for hyperkalemia<br>• Obtain baseline serum potassium, creatinine, and BUN, repeat labs within 2 wk after initiating; Discontinue ACEI if significant elevations occur<br>• Avoid other $K^+$-sparing medications<br>• Avoid in 2nd and 3rd trimesters of pregnancy due to possible fetal and neonatal morbidity and death |
| Fosinopril | 10-40[h] mg/day | |
| Lisinopril[e] | 10-40 mg/day<br>If CrCl 10-30 mL/min, initial = 5 mg/d | |

[a] Adapted from Angiotensin Converting Enzyme Inhibitors. In: Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons, Inc., 1998.
[b] Semla TP, Beizer JL, Higbee MD, eds. APhA Geriatric Dosage Handbook. 2nd ed. Hudson: Lexi-Comp Inc.,1995-96.
[c] Partial list
[d] For most ACEIs (except captopril) once-daily dosing is usually adequate. In selected instances the manufacturer recommends dividing doses when the trough effect is inadequate. Note that the manufacturer of lisinopril does not mention dividing doses.
[e] DoD BCF item; all BCF items are available through the DoD NMOP
[f] In general, higher doses than 150 mg/d of captopril are not used for HTN
[g] Patients should take 1 hr prior to food ingestion (empty stomach)
[h] Doses >40 mg/day potentially increase side effects with minimal additional BP control

### *α-Adrenergic Blockers*

- Results of The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) comparing doxazosin with chlorthalidone in the treatment of patients with HTN and at least one other coronary heart disease (CHD) risk factor were recently published. The doxazosin treatment arm of the study was discontinued by the National Heart, Lung, and Blood Institute based on comparisons with chlorthalidone. In response to the results, the American College of Cardiology (ACC) released a statement that patients treated with an α-adrenergic blocker (doxazosin) for HTN should be reevaluated to determine the most appropriate antihypertensive therapy. The PBM-MAP issued recommendations that patients on doxazosin as monotherapy for the treatment of HTN should have their therapy adjusted in light of the ALLHAT results that patients on a thiazide diuretic had better outcomes than patients receiving an α-adrenergic blocker as initial therapy for HTN. It is unclear if the results also apply to patients receiving treatment with prazosin or terazosin for HTN, however it is prudent to consider this a class effect until information to the contrary becomes available. An α-adrenergic blocker may be used as adjunct therapy for patients with HTN and BPH, or if HTN is not controlled by other therapies, although clinicians may still wish to reevaluate patients receiving an α-adrenergic blocker as adjunct therapy for HTN (i.e., taking into consideration concomitant diseases, patient response, clinical outcomes, drug interactions, adverse effects, adherence, and cost). It is unknown how the ALLHAT results translate into recommendations for patients who are being treated with an α-adrenergic blocker for the management of BPH. However, patients receiving monotherapy with an α-adrenergic blocker for the treatment of BPH and HTN should have their therapy reevaluated for potential modifications. Refer to the PBM-MAP Statement on the Use of α-Adrenergic Blockers in the Management of Patients with Hypertension, June 2000 at www.vapbm.org or http://vaww.pbm.med.va.gov
- Initiate α-blockers at low doses (1 mg) and titrate to avoid side effects: dizziness (10-20%), postural hypotension (1%), headache, flushing, and occasional reflex tachycardia. The first dose should be given at bedtime to avoid syncope.
- α-blockers may be beneficial in patients with symptomatic BPH (refer to the PBM-MAP The Pharmacologic Management of Benign Prostatic Hyperplasia at www.vapbm.org or http://vaww.pbm.med.va.gov).

| **α-BLOCKERS**[a-c] | **DOSE**[d] | **COMMENTS/CAUTIONS** |
|---|---|---|
| Prazosin[e] | 1-15 mg/day (in 2-3 divided doses) max = 20 mg/day | • Monitor BP for orthostatic hypotension<br>• Use cautiously in elderly due to first-dose syncope or dizziness<br>• Avoid in volume-depleted patients due to orthostasis<br>• Decrease in low-density-lipoprotein cholesterol and increases in HDL cholesterol have been seen, but clinical significance is unknown |
| Terazosin[e] | 1-5 mg/day max = 20 mg/day | |

[a] Adapted from Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons, Inc., 1998.
[b] Semla TP, Beizer JL, Higbee MD, eds. APhA Geriatric Dosage Handbook. 2nd ed. Hudson:Lexi-Comp, Inc., 1995-96.
[c] Partial list
[d] Once-daily dosing unless specified otherwise
[e] DoD BCF item; all BCF items are available through the DoD NMOP

### *Angiotensin II Antagonists*

- Due to the limited data on clinical outcomes and the high cost, these agents should be reserved for patients with an indication for an ACEI (e.g., patients with CHF due to systolic dysfunction) and a documented adverse drug reaction (e.g., cough) to at least one ACEI.

| **ANGIOTENSIN II ANTAGONISTs**[a,b] | **DOSE**[c] | **COMMENTS/CAUTIONS** |
|---|---|---|
| Candesartan | 8-32 mg/day (once daily or 2 divided doses) | • Initiate dose of losartan 25 mg in patients with possible depletion of intravascular volume (e.g., diuretics) and in hepatic impairment<br>• Contraindicated in 2nd and 3rd trimesters of pregnancy due to potential for fetal and neonatal morbidity and death |
| Irbesartan | 150-300 mg/day | |
| Losartan | 50-100 mg/day (once daily or 2 divided doses) | |
| Telmisartan | 20-80 mg/day | |
| Valsartan | 80-320 mg/day | |

[a] Adapted from Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons, Inc., 1998.
[b] Semla TP, Beizer JL, Higbee MD, eds. APhA Geriatric Dosage Handbook. 2nd ed. Hudson:Lexi-Comp, Inc., 1995-96.
[c] Once-daily dosing unless specified otherwise

## Other Agents

- *Clonidine:* Although some patients benefit from this medication, side effects (sedation, postural dizziness, and dry mouth) may limit its usefulness. The clonidine patch may be useful in patients who have difficulty adhering to a daily medication regimen.
- *Reserpine:* Due to its long half-life, this drug may be beneficial in low doses for patients who are intermittently compliant (e.g., take medication, but not on a daily basis). Because of proven efficacy in clinical trials, this agent may be helpful as an alternative agent for physicians familiar with its use.
- *Minoxidil:* Should be reserved for refractory HTN. Treatment with minoxidil may also be considered in patients with severe HTN, especially those with renal impairment. Minoxidil should be used in conjunction with β-blockers (or other adrenergic inhibitors) and loop diuretics to alleviate reflex tachycardia and edema.
- *Hydralazine:* As with minoxidil, hydralazine should be used in conjunction with β-blockers (or other adrenergic inhibitors) and diuretics to alleviate reflex tachycardia and edema.

| AGENT[a,b] | DOSE[c] | COMMENTS/CAUTIONS |
|---|---|---|
| **CENTRALLY ACTING** | | • Taper dose to discontinue; do not discontinue suddenly<br>• Antihypertensive effects of the patch are not seen until 2-3 days after initiation; when switching from oral clonidine to a patch the oral dose should be gradually tapered down over 2-3 days when the patch is first given<br>• Clonidine patches are costly, but may be useful in selected patients<br>• Monitor for sedation (usually transient) during initial therapy with methyldopa or whenever the dose is increased |
| Clonidine tablet[d] | 0.1-0.8 mg/d (max can be up to 2.4 mg/d) | |
| Clonidine patch | (in 2-3 divided doses)<br>0.1-0.6 mg patch weekly | |
| Methyldopa | 500 mg-3g/d<br>(in 2-4 divided doses)<br>Initial dose usually 250 mg bid-tid in the first 48 hr; maintenance usually bid | |
| **PERIPHERALLY ACTING** | | • Monitor for sedation, nightmares, tremors, nasal congestion, activation of peptic ulcer; higher doses than listed are associated with increased incidence of depression |
| Reserpine | 0.05-0.25 mg/d | |
| **VASODILATORS** | | • Monitor for edema and for reflex tachycardia with worsening angina<br>• Monitor for headache and systemic lupus erythematosus (dose-related) with hydralazine<br>• Monitor for hypertrichosis, pericardial effusions with minoxidil<br>• Minoxidil or hydralazine should be used with a diuretic and β-blocker to reduce reflex tachycardia and edema<br>• Due to potential for serious adverse effects, minoxidil should be reserved for HTN not responding to maximum doses of a diuretic with 2 other antihypertensive agents |
| Minoxidil | 5-40 mg/d (once daily or 2 divided doses)<br>max = 100 mg/day | |
| Hydralazine[d] | 40-200 mg/d<br>(in 2-3 divided doses)<br>initial dose = 10 mg tid<br>elderly initial = 10 mg bid-tid | |

[a] Adapted from Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons, Inc., 1998.
[b] Semla TP, Beizer JL, Higbee MD, eds. APhA Geriatric Dosage Handbook. 2nd ed. Hudson:Lexi-Comp, Inc., 1995-96.
[c] Once-daily dosing unless specified otherwise
[d] DoD BCF item; all BCF items are available through the DoD NMOP

## Drug Interactions with Antihypertensive Agents[a-e]

| DRUG CLASS | INTERACTING DRUG | DESCRIPTION |
|---|---|---|
| **DIURETICS** | | |
| | *ACEI* | ↑ hypotensive effect in the presence of intensive diuretic therapy due to sodium depletion and hypovolemia; at low doses this combination may be used synergistically |
| | Bile Acid Resins | ↓ absorption of all diuretics; take diuretics 1 hr prior or 4 hr after bile acid resin |
| | *Digoxin* | All diuretics may induce hypokalemia which may ↑ risk of digitalis toxicity |
| | **Lithium** | With thiazides, a compensatory ↑ in proximal tubule reabsorption of sodium occurs, which results in ↑ lithium reabsorption (reduce lithium dose by 50%); furosemide appears to have little effect in most people |
| | NSAIDs | NSAIDs ↓ antihypertensive effect when used with thiazides due to inhibition of PG synthesis resulting in ↓ GFR, ↓ sodium and water excretion, and vasoconstriction |
| | *Oral hypoglycemics* | Thiazides may ↓ hypoglycemic effects of sulfonylureas possibly due to ↓ insulin sensitivity, ↓ insulin secretion or ↑ in $K^+$; clinical significance unclear |
| | $K^+$ preparations, ACEIs, NSAIDs | $K^+$-sparing diuretics used concomitantly may ↑ $K^+$ serum levels |
| **β-BLOCKERS** | | |
| | *Cimetidine* | Hypotension and bradycardia have been reported with propranolol and metoprolol when used with cimetidine due to ↑ serum levels of β-blockers that undergo hepatic metabolism |
| | *Diltiazem Verapamil* | Combination may potentiate the pharmacologic effects of β-blockers; additive effects on cardiac conduction |
| | **Epinephrine** | Noncardioselective agents may ↑ the pressor response resulting in ↑ in HTN/ bradycardia |
| | *Lidocaine* | ↑ toxicity due to reduced hepatic metabolism of lidocaine |
| | *NSAIDs* | NSAIDs ↓ antihypertensive effect due to inhibition of PG synthesis resulting in ↓ GFR, ↓ sodium and water excretion, and vasoconstriction |
| | *Neuroleptics* | Some β-blockers and neuroleptics (chlorpromazine/thioridazine) may ↑ the plasma concentrations of one another; monitor for enhanced effects of both drugs |
| | *Oral hypoglycemics* | With noncardioselective agents, ↓ hypoglycemic action may occur due to possible inhibition of insulin secretion and also mask symptoms of hypoglycemia; clinical significance unclear |
| | *Prazosin* | ↑ postural hypotension due to ↓ compensatory cardiovascular response |
| | *Propafenone* | ↑ hypotensive effect has been seen with propranolol and metoprolol due to inhibition of metabolic clearance; heart failure and nightmares have been reported |
| | *Rifampin* | May enhance the hepatic metabolism of propranolol and metoprolol; enzyme induction effect may resolve after a 3-4 wk washout period |
| | *Theophylline* | ↑ serum concentration in a dose-dependent manner has been seen with propranolol |

## Drug Interactions with Antihypertensive Agents[a-e] (Continued)

| DRUG CLASS | INTERACTING DRUG | DESCRIPTION |
|---|---|---|
| **CCBs** | | |
| | *Carbamazepine* | ↑ toxicity has been noted with verapamil and diltiazem use due to reduced metabolism of carbamazepine; interaction more significant with verapamil. Felodipine bioavailability may be reduced, making it difficult to achieve therapeutic felodipine concentrations |
| | *Cimetidine* | Metabolism has been ↓ especially with verapamil, diltiazem, nifedipine |
| | *Cyclosporine* | Blood concentrations have increased with verapamil, diltiazem and nicardipine; renal toxicity has been reported |
| | *Digoxin* | Verapamil, diltiazem, bepridil, nisoldipine have ↑ digoxin levels by 20-70% |
| | *Lithium* | Combination use with verapamil or diltiazem may result in neurotoxicity which may occur without attendant increase in serum level |
| | **Lovastatin** | Diltiazem produces marked ↑ lovastatin concentrations through inhibition of CYP3A4, therefore potential for ↑ toxicity; verapamil likely to produce similar changes; simvastatin also likely to be affected; atorvastatin and cerivastatin also significantly metabolized by CYP3A4 enzymes |
| | *Quinidine* | Verapamil inhibits metabolism of quinidine leading to ↑ toxicity; nifedipine appears to reduce blood concentrations although mechanism unknown |
| | *Theophylline* | Inhibition of hepatic metabolism with verapamil may lead to increase serum levels |
| **ACEIs** | | |
| | **Allopurinol** | Isolated case reports with allopurinol and captopril or enalapril may have caused predisposition to hypersensitivity reactions (e.g., Stevens Johnson Syndrome, anaphylaxis, skin eruptions, fever, and arthralgias) |
| | *Lithium* | ↑ toxicity; suggested mechanism is ACEI-induced sodium depletion resulting in ↑ reabsorption |
| | *NSAIDs* | NSAIDs ↓ antihypertensive effects due to inhibition of PG synthesis resulting in ↓ GFR, ↓ sodium and water excretion, and vasoconstriction |
| | $K^+$ preparations $K^+$-sparing diuretics | Concomitant therapy may ↑ $K^+$ serum levels |
| **α-BLOCKERS** | | |
| | *β-blockers* | Prazosin may ↑ postural hypotension due to ↓ compensatory cardiovascular response |
| | Indomethacin | May ↓ antihypertensive action with prazosin due to inhibition of PG synthesis |
| | Verapamil | May cause greater hypotensive effect with prazosin or terazosin than with either drug alone |

## Drug Interactions with Antihypertensive Agents[a-e] (Continued)

| | | |
|---|---|---|
| **ANGIOTENSIN II ANTAGONIST** | | |
| | Cimetidine | Coadministration led to an ↑ of about 18% in the area under the curve (AUC) of losartan, but did not affect the pharmacokinetics of its active metabolite |
| | Fluconazole | Inhibits CYP2C9 resulting in reduced concentration of losartan's active metabolite |
| | Phenobarbital | Coadministration led to a reduction of about 20% in the AUC of losartan and that of its active metabolite |
| **CENTRALLY ACTING** | | |
| | *β-blockers* | The severity of withdrawal HTN caused by abrupt discontinuation of clonidine may be greater in patients taking β-blockers possibly due to unopposed α-adrenergic stimulation; methyldopa and β-blockers may rarely cause paradoxical HTN |
| | Levodopa | Methyldopa may enhance the therapeutic response to levodopa |
| | *Lithium* | ↑ lithium toxicity has been reported with methyldopa use in a few patients |
| | **MAOIs** | Reserpine may cause a hypertensive reaction when initiated in patients receiving MAOIs |
| | Sympathomimetics | Methyldopa may potentiate the pressor effects and lead to HTN |
| | *TCA* | May inhibit the antihypertensive response of clonidine; mechanism not established |
| **PERIPHERALLY ACTING** | | |
| | Sympathomimetics | Concurrent use with reserpine may prolong effects of direct-acting sympathomimetics (epinephrine); concurrent use with indirect-acting sympathomimetics (ephedrine) may inhibit effects |
| | TCA | Concurrent use with reserpine may ↓ antihypertensive effects |
| **VASODILATORS** | | |
| | *Indomethacin* | ↓ antihypertensive effect of hydralazine due to PG synthesis inhibition |
| | Propranolol Metoprolol | Serum levels of propranolol or metoprolol may be ↑ with hydralazine use; clinical significance unknown |

[a] Adapted from JNC VI
[b] Hebel SK, ed. Drug Facts and Comparisons, St. Louis: Facts and Comparisons, Inc., 1998.
[c] Mignat C, Unger T. ACE inhibitors. Drug interactions of clinical significance. Drug Safety 1995 May 12(5):334-47.
[d] Hansten PD, Horn JR eds. Drug Interactions Analysis and Management, Vancouver: Applied Therapeutics, Inc., 1998.
[e] **Bold =** serious drug interaction; *Italics* = moderate; Regular = minor**;** ACEI = angiotensin-converting enzyme inhibitor; NSAID = nonsteroidal anti-inflammatory drug; GFR = glomerular filtration rate; CCB = calcium channel blocker; $K^+$ = potassium; PG = prostaglandin; CYP=cytochrome P-450 enzyme system; MAOI = Monoamine oxidase inhibitor; TCA= tricyclic antidepressants

**Adherence to Therapy**

- Every effort should be made to incorporate the medication regimen and lifestyle modifications into the patient's daily routine. Measures should be taken to determine the reason for difficulty in adhering to the medication regimen (e.g., side effects, social issues, cost).
- HTN should be managed with monotherapy and/or with a once-daily regimen whenever possible.
- Patients should be educated regarding the importance of adherence to the medication regimen and changes in lifestyle in order to achieve BP control and reduce risk of long-term complications.

**Resistant Hypertension**

- Resistant HTN is failure of three properly dosed agents (one of which should be a diuretic) to reduce BP to target levels.
- Failure to adhere to the medication regimen is a common cause of resistant HTN. If BP control is not achieved with three medications in patients adhering to the medication regimen, further evaluation should be considered for lack of HTN control (e.g., volume overload, drug-related causes, associated conditions, identifiable causes).
- Even though the goal BP may not be achieved, any BP reduction is important in contributing to a decrease in morbidity and mortality. An initial 10 mm Hg decrease from pretreatment levels is desirable.

**Step-Down Therapy**

- Refers to reducing antihypertensive therapy after good control is achieved for an extended period of time (usually after follow-up for >1 year and at least 4 visits). Step-down therapy is most useful for patients who have adopted lifestyle modifications.
- Step-down therapy should be a deliberate, gradual approach in patients willing to undergo regular follow-up, as BP tends to rise over time (especially if lifestyle changes cease).

The ***system*** attempts to provide:

- Disease-specific computer prompts for provider
- Computerized progress notes

## EDUCATION

The ***patient*** should understand:

- Diet and lifestyle modifications
- Medication use and potential side effects
- Importance of adherence to therapy
- Necessity of reporting chest pain, shortness of breath, or signs of stroke to provider
- When to contact the provider regarding possible adverse effects of the medication

The ***provider*** should understand:

- Screening guidelines
- Risk factor modification
- Medication management

The ***system*** attempts to provide:

- Patient handouts on HTN and CVD risk factors
- Medication information sheets
- Cardiac education classes
- Links to:
  VHA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting at http://vaww.va.gov/quality/quality/cpg/hypertension.cfm or www.vapbm.org,
  PBM-MAP The Pharmacologic Management of Hyperlipidemia at www.vapbm.org
  PBM-MAP The Pharmacologic Management of Chronic Heart Failure at www.vapbm.org
  VHA Clinical Guidelines for Management of Diabetes Mellitus at www.va.gov/health/diabetes
  VHA CARE-GUIDE for Ischemic Heart Disease at www.med.va.gov/health/clinical.htm
  VHA/DoD Clinical Practice Guideline to Promote Tobacco Use Cessation in the Primary Care Setting at http://vaww.va.gov/quality/quality/qi_VHA_guidelines.cfm

## OUTCOME

Outcome monitoring is the last element.

The ***patient*** can be queried for:
- Satisfaction with care
- Quality of life
- Comprehension of disease
- Adherence to treatment regimen

The ***provider*** can be queried for:
- Achieving BP goal <140/90 (may be lower in patients with DM or renal disease with proteinuria)
- Providing patient education on diet and lifestyle modifications
- Treating risk factors for CVD
- Selecting appropriate drug therapy and dose
- Identifying and managing side effects
- Evaluating adherence to treatment regimen
- Performing follow-up laboratory parameters as indicated by drug therapy and to assess target organ damage
- Evaluating BP control:
    1. Depending on the type of medication, severity of BP, and presence or absence of target organ damage, patients need to be monitored shortly after initiating antihypertensive therapy and frequently during titration.
    2. Routine follow-up every 3-12 months for patients with stabilized BP is generally appropriate.

The ***system*** attempts to provide:
- Timely feedback on performance measures
- Cost data stratified by disease severity
- Clinical pathway variation analysis and reporting

**Costs for Selected Hypertension Drug Therapy**

| DRUG[a] | DOSE[b] | FSS[c] COST/MONTH | DAPA[d] COST/MONTH |
|---|---|---|---|
| **THIAZIDE DIURETICS** | | | |
| Hydrochlorothiazide[e] | 25 mg qd | $ 0.32 | $ 0.20 |
| HCTZ/Triamterene[e] | 50 mg/75 mg qd | $ 0.60 | $ 0.67 |
| **β-BLOCKERS** | | | |
| ***Noncardioselective*** | | | |
| Propranolol[e] | IR: 40 mg bid | $ 0.49 | $ 0.00[g] |
| | SR: 80 mg qd | $ 2.39 | $ 0.00[g] |
| ***Cardioselective*** | | | |
| Atenolol[e] | 50 mg qd | $ 0.37 | $ 0.37 |
| Metoprolol | IR: 50 mg bid | $ 0.91 | $ 0.90 |
| **CCBs** | | | |
| Verapamil IR[e] | 120 mg bid | $ 2.08 | $ 1.99 |
| Verapamil SR[f] | 240 mg qd | $ 1.74 | $ 1.74 |
| Diltiazem IR[e] | 60 mg tid | $ 2.59 | $ 2.52 |
| Diltiazem SR (Tiazac®[e]) | 240 mg qd | $ 8.10 | $ 8.10 |
| ***Dihydropyridines*** | | | |
| Amlodipine | 5 mg qd | $20.06 | $19.95 |
| Felodipine | 5 mg qd | $13.87 | $14.61 |
| Nifedipine SR (Adalat®CC[e]) | 60 mg qd | $12.31 | $12.31 |
| **ACEIs** | | | |
| Captopril[e] | 25 mg bid | $ 0.64 | $ 0.64 |
| Fosinopril | 20 mg qd | $ 4.50 | $ 4.50 |
| Lisinopril[e] | 20 mg qd | $ 4.20 | $ 4.20 |
| **α-BLOCKERS** | | | |
| Prazosin[e] | 2 mg bid | $ 1.18 | $ 1.14 |
| Terazosin[e] | 5 mg qd | $ 1.71 | $ 1.71 |
| **ANGIOTENSIN II ANTAGONIST** | | | |
| Candesartan | 16 mg qd | $ 19.19 | $ 19.09 |
| Irbesartan | 150 mg qd | $ 22.30 | $ 22.19 |
| Losartan | 50 mg qd | $ 21.65 | $ 21.41 |
| Telmisartan | 40 mg qd | $ 15.08 | $ 15.00 |
| Valsartan | 160 mg qd | $ 19.70 | $ 19.60 |
| **CENTRALLY ACTING** | | | |
| Clonidine Tablet[e] | 0.2 mg bid | $ 0.64 | $ 0.73 |
| Clonidine Patch | 0.2mg/24hr q wk | $ 32.73 | $ 32.72 |
| Methyldopa | 500 mg tid | $ 6.22 | $ 6.22 |
| **PERIPHERALLY ACTING** | | | |
| Reserpine | 0.1 mg qd | $ 0.60 | $ 1.17 |
| **VASODILATING AGENTS** | | | |
| Minoxidil | 10 mg qd | $ 1.48 | $ 1.53 |
| Hydralazine[e] | 25 mg tid | $ 1.17 | $ 1.16 |

[a] Partial list
[b] Usual doses; does not reflect equivalent doses
[c] Federal Supply Schedule; for current VA prices refer to www.vapbm.org
[d] Distribution and pricing agreement; updated prices may be obtained from the Defense Supply Center Philadelphia (DSCP) on a monthly basis (215) 737-7013
[e] DoD BCF item; all BCF items are available through the DoD NMOP
[f] Calan® SR, Isoptin® SR, and generic equivalents are on the DoD BCF
[g] $0.01 per bottle of 1000

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