AHA/ACC/CDC Science Advisory

An Effective Approach to High Blood Pressure Control

A Science Advisory From the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention

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Cardiovascular diseases, including heart disease, hypertension and heart failure, along with stroke, continue to be leading causes of death in the United States.\textsuperscript{1,2} Hypertension currently affects nearly 78 million* adults in the United States and is also a major modifiable risk factor for other cardiovascular diseases and stroke.\textsuperscript{1} According to data from the National Health and Nutrition Evaluation Survey (NHANES) in 2007-2010, 81.5\% of those with hypertension are aware they have it, and 74.9\% are being treated but only 52.5\% are under control, with significant variation across different patient subgroups.\textsuperscript{1,3-6} Of those with uncontrolled hypertension, 89.4\% reported having a usual source of health care, and 85.2\% reported having health insurance.\textsuperscript{7} This is the current status, despite the fact that therapies to lower blood pressure and associated risks of cardiovascular events and death have been available for decades and various education and quality improvement efforts have been targeted at patients and healthcare providers.

The direct and indirect costs of hypertension are enormous, considering the number of patients and their families impacted as well as the healthcare dollars spent on treatment and blood pressure-related complications.\textsuperscript{8} Currently, hypertension affects 46\% of patients with known cardiovascular disease, 72\% of those who have suffered a stroke, and was listed as a primary or contributing cause in approximately 15\% of the 2.4 million deaths in 2009.\textsuperscript{1} In 2008, the total estimated direct and indirect cost of hypertension was estimated at $69.9 billion.\textsuperscript{8} Thus, it is imperative to identify, disseminate and implement more effective approaches to achieve optimal control of this condition.

\textsuperscript{*}The estimate is based on hypertension definition of blood pressure reading $\geq 140/90$ mm Hg, current use of antihypertensive medications, or being told of having hypertension on 2 occasions by a healthcare provider. When the third component of the definition is excluded, the estimated number of prevalence cases among US adults would be 67 million.\textsuperscript{7}
High-quality blood pressure management is multifactorial and requires engagement of patients, families, providers and healthcare delivery systems and communities. This includes expanding patient and healthcare provider awareness, appropriate lifestyle modifications, access to care, evidence-based treatment, a high level of medication adherence and adequate follow-up. Recognizing the urgent need to address inadequate control, the American Heart Association (AHA) has made hypertension a primary focus area of its 2014-2017 strategic plan as it seeks to improve the cardiovascular health of all Americans by 20% and reduce the death rate from cardiovascular disease and stroke by 20% by 2020. Similarly, Million Hearts, a US Department of Health and Human Services initiative spearheaded by the Centers for Disease Control (CDC) and Prevention and the Centers for Medicare & Medicaid Services (CMS) to prevent a million heart attacks and strokes by 2017, has focused its first 2 years on actions to improve and achieve control of hypertension.

We believe that identification of best practice, evidence-based management algorithms leading to standardization of treatment is a critical element in helping to achieve these ambitious national goals at a population level. In this paper, we describe the value of hypertension treatment algorithms, provide criteria for effective hypertension management algorithms, describe an AHA/American College of Cardiology (ACC)/CDC-recommended treatment algorithm based on current guidelines and describe examples of other specific algorithms that have been associated with improved blood pressure on a large scale.

The Value of Hypertension Treatment Algorithms As Part of a Multifactorial Approach to Improve Blood Pressure Control
As described previously, despite the strong evidence and consensus regarding the treatment and control of high blood pressure,\textsuperscript{9,12} as well as the availability of many different therapeutic options, achieving success in hypertension control at both the individual patient-level and even more importantly, the population-level, has remained a major challenge nationally.

Although there is no single explanation for the poor hypertension control seen in many patient subgroups, the fragmentation of health care for many patients and the lack of consistent implementation of system-level solutions in clinical practice and healthcare delivery systems appear to be important contributors. Efforts focused primarily on educating patients and providers about hypertension and the benefits of its treatment have not been sufficient in bringing hypertension under control. Similarly, interventions targeting only physicians have not led to consistent and meaningful improvements on a large scale.\textsuperscript{13} However, there are examples of substantial success that could be emulated and scaled with a high likelihood of important benefit.

To reduce the prevalence of hypertension in the United States,\textsuperscript{10,14} system-level approaches will be needed. Successful examples from other medical areas where a system-level approach has been taken include reducing medical errors and improving patient safety in the hospital setting\textsuperscript{15}; improving the inpatient treatment and outcomes of acute myocardial infarction, heart failure, stroke and cardiopulmonary resuscitation\textsuperscript{16}; reducing health disparities in the treatment of cardiovascular conditions\textsuperscript{16}; early detection and intervention in sepsis to lower case fatality\textsuperscript{17,18}, and reducing hospital-acquired infections.\textsuperscript{19,20} In the case of hypertension, system-level methods can address multiple factors in a coordinated manner:
• Identifying all patients eligible for management
• Monitoring at the practice/population level
• Increasing patient and provider awareness
• Providing an effective diagnosis and treatment guideline
• Systematic follow-up of patients for initiation and intensification of therapy
• Clarifying roles of healthcare providers to implement a team approach
• Reducing barriers for patients to receive and adhere to medications as well as to implementing lifestyle modifications
• Leveraging the electronic medical record systems being established throughout the US to support each of these steps

Several examples of success using a system-level paradigm have been recently reported. For example, within Kaiser Permanente Northern California, a large integrated healthcare delivery system caring for >3 million members, a regional hypertension program was implemented involving five major components: creation and maintenance of a health system-wide electronic hypertension registry, tracking hypertension control rates with regular feedback to providers at a facility- and provider-level, development and frequent updating of an evidence-based treatment guideline, promotion of single-pill combination therapies and using medical assistants for follow-up blood pressure checks to facilitate necessary treatment intensification. Between 2001 and 2009, the number of patients with hypertension increased from 349,937 to 652,763, but the proportion of hypertensive patients meeting target blood pressure goals improved substantially from 44% to >80%, and continued to improve to >87% in 2011. Favorable hypertension control was also achieved with single-pill combination therapies, which simplified treatment for both patients and providers. These successes demonstrate the potential of system-level approaches to improve hypertension control and provide insights for other healthcare systems aiming to enhance hypertension management.
control rates have been observed in other healthcare delivery systems\(^2\) as well as coordinated 
health systems such as the Veterans Affairs medical system.\(^{23-25}\)

Developing, disseminating and implementing an effective hypertension treatment algorithm is a 
critical part of a multipronged, systematic approach to controlling hypertension, as it facilitates 
clinical decision-making, provides a default approach with proven benefits, and engages multiple 
providers in a coordinated manner. We describe next the principles for developing such an 
algorithm.

**Principles for Algorithm Development**

The following is a summary of principles recommended by the AHA, ACC, and CDC for 
creating an effective hypertension management algorithm:

1. Base algorithm components and processes on the best available science.
2. Format to be simple to update as better information becomes available.
3. Create feasible, simple implementation strategy.
4. Include patient version at appropriate scientific and language literacy level.
6. Develop algorithm in format easily used within a team approach to health care.
7. Develop algorithm in a format able to be incorporated into electronic health records for 
   use as clinical decision support.
8. Include a disclaimer to ensure that the algorithm is not used to counter the treating 
   healthcare provider’s best clinical judgment.
The purpose of these principles is to establish a common platform for the development and implementation of hypertension management algorithms tailored to different practice settings and populations. We note the last principle supports the notion that treatment guidelines serve to facilitate a systematic approach to the management of hypertension, but provide appropriate modifications based on specific patient characteristics, preferences and other pragmatic factors (eg, cost, pill burden, risks of certain side effects) to optimize a personalized approach to the care of individual patients.9,12,26,27 In addition, ongoing randomized clinical trials (eg, SPRINT 28) are addressing optimal blood pressure targets for specific patient subgroups such as the elderly and patient with chronic kidney diseases to maximize net clinical benefit and avoid unnecessary complications.

AHA/ACC/CDC Hypertension Treatment Algorithm

In the Appendix is a template outlining a general approach for an effective treatment algorithm that incorporates the principles described previously and balances applicability the largest number of hypertensive patients with the flexibility and the level of detail to support individualization of therapy.

Several existing algorithms for hypertension treatment in large healthcare settings associated with improved blood pressure in populations21 have also been reviewed, which included a look at both private and public systems, systems with regional reach, as well as an algorithm used by the US Department of Veteran Affairs that are in support of the recommended principles. These algorithms are either attached in the online-only data supplement or are available for public use.
within the resources and tools section of the Million Hearts initiative Web site at

http://millionhearts.hhs.gov/resources.html.

Call-to-Action, Next Steps, and Conclusions

It is critical that the AHA, ACC and CDC, together with other organizations, continue to identify, define, and implement exemplary local, regional, and national programs that facilitate better blood pressure awareness, treatment, and control together with improving other cardiovascular health factors and behaviors. Arming healthcare providers, health systems, and communities with proven tools, algorithms, strategies, programs, and other best practices along with expertise and technical assistance for improving blood pressure awareness, treatment, and control is essential to reducing the tremendous burden of cardiovascular risk.

This advisory serves as a call to action for broad-based efforts to improve hypertension awareness, treatment, and the proportion of patients treated and controlled. There is a clear need to provide enhanced, evidence-based, blood pressure treatment systems for providers, including standardization of protocols and algorithms, incentives for improved performance based on achieving and maintaining patients at blood pressure goals, and technology-facilitated clinical decision support and feedback. As noted previously, health system wide implementation of focused evidence-based hypertension treatment algorithms together with regularly scheduled performance feedback within a coordinated multifactorial management program have been associated with substantially improved hypertension control in large populations and varied clinical practice settings. This approach can facilitate the ability to emphasize existing evidence-based recommendations and integrate new evidence as it becomes available. Successful
best practices or innovations can be further identified and then disseminated health system wide.21 Such an approach is scalable, sustainable, and of high value, especially as the use of electronic medical records becomes even more widespread nationally.21,33,34,40 This advisory has provided a number of examples of algorithms from successful programs that can be readily implemented in diverse healthcare settings. Greater participation in innovative programs such as the AHA’s Heart 360 personal health record,35 AHA/ASA’s Get With The Guidelines Program,36 the AHA/ADA/ACS Guideline Advantage Program,37 and the HHS Million Hearts initiative,11,15,30,31 as well as the ACC’s National Cardiovascular Data Registries (NCDR)38 and CDC Coverdell Stroke registry,39 should also be encouraged and incentivized.

Further engaging individuals in the hypertension control process, motivating more proactive management though shared accountability and incentives for blood pressure treatment and control are also essential.30 There are also opportunities for the increased role of pharmacists and other community-based providers in hypertension treatment and control.30,40,41 There is also great potential to apply an innovative mix of health information technology, peer support, feedback, and incentive programs designed to drive actionable, patient-centered blood pressure awareness, treatment and control programs. Workplace and community based wellness programs can also have significant impact.30

It is also vital that these programs are implemented among broader segments of the population. Disparities/inequities in hypertension awareness, treatment, and control continue to exist in a number of patient subgroups.6,42 Intervention programs for hypertension should be specifically targeted to groups with the greatest cardiovascular risk and disease burden based on clinical risk
factors and appropriate consideration of sex, race, ethnicity, socioeconomic status, disability, and geographic location. Additional research is needed to better define blood pressure treatment goals especially in specific populations including by age, sex, race, ethnicity, and comorbid conditions. It is essential that there be proportionate representation of these patient populations in the study of blood pressure goals as well as new hypertension treatment technologies such as catheter-based renal sympathetic denervation.

The AHA, ACC, CDC, and other organizations should continue to foster effective activities regarding hypertension which include surveillance, education and media, organizational partnerships, and environmental and policy changes. Building on such programs as the

- AHA’s Life’s Simple 7 program with a longitudinal cardiovascular health tracking system, patient-oriented clinical decision support tool, individual patient-oriented cardiovascular health performance measures, and data feedback, and
- ACC’s CardioSmart Patient Education Portal with a customized patient dashboard for blood pressure management, an interactive workbook to educate and motivate better health, and a patient text messaging program providing heart healthy tips aimed at primary prevention

should be considered within a comprehensive system-level management program. This approach may help to facilitate and incentivize improvement in blood pressure control, cardiovascular health, as well as enhance real-time surveillance of cardiovascular health. Further research efforts to enhance specific interventions for improving patient adherence and to identify optimal patient-centered, value oriented systems of care should continue to be supported.
This advisory is intended to complement and support clinical guidelines, providing clinicians and health systems tools to improve treatment and control of hypertension. The prevention of heart disease and stroke mandates a greater emphasis on the population-wide improvement of blood pressure awareness, treatment, and control together with other cardiovascular health factors.15,26,45
Controlling Hypertension in Adults

Systolic 140–159 or diastolic 90–99 (Stage 1 hypertension)
- Lifestyle modifications as a trial
- Consider adding thiazide

Recheck and review readings in 3 months*

Systolic >160 or diastolic >100 (Stage 2 hypertension)
Two drugs preferred:
- Lifestyle modifications and
- Thiazide and ACEI, ARB, or CCB
- Or consider ACEI and CCB

Recheck and review readings in 2–4 weeks*²

No

BP at goal?

Yes

Thiazide for most patients or ACEI, ARB, CCB, or combo
- If currently on BP med(s), titrate and/or add drug from different class

Recheck and review readings in 2–4 weeks*²

BP at goal?

No

Optimize dosage(s) or add medications
- Address adherence, advise on self-monitoring, and request readings from home and other settings
- Consider secondary causes

Yes

Encourage self-monitoring and adherence to meds
- Advise patient to alert office if he/she notes BP elevation or side effects
- Continue office visits as clinically appropriate

Consider referral to HTN specialist

*Recheck interval should be based on patient’s risk of adverse outcomes

This algorithm should not be used to counter the treating healthcare provider’s best clinical judgment.
The blood pressure (BP) goal for an individual is set by utilizing a combination of factors including scientific evidence, clinical judgment, and patient tolerance. For most people, the goal is $<140$ and $<90$; however, lower targets may be appropriate for some populations such as African-Americans, the elderly, or patients with LV hypertrophy, systolic or diastolic LV dysfunction, diabetes mellitus or chronic kidney disease. Lifestyle modifications (LM) should be initiated in all patients with hypertension (HTN) and they should be assessed for target organ damage and existing cardiovascular disease. Self-monitoring is encouraged for most patients throughout their care, and requesting and reviewing readings from home and community settings can help the provider assist the patient in achieving and maintaining good control. For patients with hypertension in combination with certain clinical conditions, specific medications should be considered first-line treatments.

### Suggested Medications for Treatment of Hypertension in Presence of Certain Medical Conditions

- Coronary artery disease/Post MI: BB, ACEI
- Systolic heart failure: ACEI or ARB, BB, ALDO ANTAG, thiazide
- Diastolic heart failure: ACEI or ARB, BB, thiazide
- Diabetes: ACEI or ARB, thiazide, BB, CCB
- Kidney disease: ACEI or ARB
- Stroke or TIA: thiazide, ACEI

### Lifestyle Modifications3 (LM)

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<th>Modification</th>
<th>Recommendation</th>
<th>Approximate SBP Reduction (Range)**</th>
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<tr>
<td>Reduce weight</td>
<td>Maintain normal body weight (body mass index 18.5–24.9 kg/m²)</td>
<td>5–20 mm Hg/10 kg</td>
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<tr>
<td>Adopt DASH*5 eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat</td>
<td>8–14 mm Hg</td>
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<td>Lower sodium intake*</td>
<td>a. Consume no more than 2,400 mg of sodium/day; b. Further reduction of sodium intake to 1,500 mg/day is desirable since it is associated with even greater reduction in BP; and c. Reduce intake by at least 1,000 mg/day since that will lower BP, even if the desired daily sodium intake is not achieved</td>
<td>2–8 mm Hg</td>
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<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 min per day, most days of the week)</td>
<td>4–9 mm Hg</td>
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<td>Moderation of alcohol consumption</td>
<td>Limit consumption to no more than 2 drinks (e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men, and to no more than 1 drink per day in women and lighter weight persons</td>
<td>2–4 mm Hg</td>
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* DASH, dietary approaches to stop hypertension  ** The effects of implementing these modifications are dose and time dependent, and could be greater for some individuals

### Abbreviations

ACEI, angiotensin-converting-enzyme inhibitor; ALDO ANTAG, aldosterone antagonist; ARB, angiotensin II receptor blocker; BB, β-blocker; BP, blood pressure; CCB, calcium channel blocker; HTN, hypertension; MI, myocardial infarction; SBP, systolic blood pressure; TIA, transient ischemic attack

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## Writing Group Disclosures

<table>
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*Modest.
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Add amlodipine 5 mg X ½ daily ➔ 5 mg X 1 daily ➔ 10 mg daily

SPIRONONACTONE OR BETA-BLOCKER
IF on thiazide AND eGFR ≥ 60 mL/min/1.73m² AND K < 4.5
Add spironolactone 12.5 mg daily ➔ 25 mg daily
OR
Add atenolol 25 mg daily ➔ 50 mg daily (Keep heart rate > 55)

• Consider medication non-adherence.
• Consider interfering agents (e.g., NSAIDs, excess alcohol).
• Consider white coat effect. Consider BP checks by medical assistant
(e.g., two checks with 2 readings each, 1 week apart).
• Consider discontinuing lisinopril / HCTZ and changing to chlorthalidone 25 mg plus lisinopril
40 mg daily. Consider additional agents (hydralazine, terazosin, reserpine, minoxidil).
• Consider stopping atenolol and adding diltiazem to amlodipine, keeping heart rate > 55.
• Avoid using clonidine, verapamil, or diltiazem together with a beta blocker.
  These heart-rate slowing drug combinations may cause symptomatic bradycardia over time.
• Consider secondary etiologies.
• Consider consultation with a hypertension specialist.

¹. ACE-Inhibitors are contraindicated in pregnancy and not recommended in most child-bearing age women.
2. NNT = number needed to treat to prevent one event, maintaining hypertension control for at least 5 years.
- Medication up-titrations are recommended at 2-4 week intervals (for most patients) until control is achieved. Consider follow-up labs when up-titrating or adding lisinopril/HCTZ, chlorthalidone, HCTZ, or spironolactone.
- Use lipid lowering therapy according to Dyslipidemia Management in Adults guideline: http://cl.kp.org/pkc/national/cmi/programs/dyslipidemia/guideline/index.html
- If pregnant, refer to OB/GYN for hypertension management. If on ACE-Is or ARBs, discontinue immediately.

**LIFESTYLE CHANGES ARE RECOMMENDED FOR ALL PATIENTS:**
- DASH diet.
- Sodium restriction (≤ 2.4 gm sodium daily).
- Weight reduction if BMI ≥ 25 kg/m².
- Exercise at a moderate pace to achieve 150 mins / week (i.e., 30 min / 5 days/wk).
- Limit daily alcohol to no more than 1 drink (women) or 2 drinks (men).
- Smoking cessation is strongly recommended; counsel tobacco users on the health risks of smoking, and the benefits of quitting.

**RECOMMENDATIONS FOR PATIENTS WITH ACE-I INTOLERANCE:**
1. HCTZ 25 mg, then 50 mg to achieve BP goal.
2. Add losartan 25 mg, then 50 mg, then 100 mg to achieve BP goal.
3. Add amlodopine 2.5 mg, then 5 mg, then 10 mg to achieve BP goal.

### Table 2: Dosage Range for Selected Antihypertensive Medications

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>GENERIC (OTHER NAMES)</th>
<th>USUAL DOSAGE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-I-THIAZIDE COMBINATION PILL</td>
<td>Lisinopril/HCTZ (Prinzide&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>10/12.5 mg daily 20/25 mg twice daily</td>
</tr>
<tr>
<td>THIAZIDE-TYPE DIURETICS</td>
<td>Hydrochlorothiazide [HCTZ], (Esidrix&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>25 - 50 mg daily</td>
</tr>
<tr>
<td>THIAZIDE-TYPE DIURETICS</td>
<td>Chlorthalidone (Hygroton&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>12.5 - 25 mg daily</td>
</tr>
<tr>
<td>THIAZIDE-TYPE DIURETICS</td>
<td>Indapamide (Lozol&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>1.25 - 2.5 mg daily</td>
</tr>
<tr>
<td>ACE INHIBITORS (ACE-I)</td>
<td>Lisinopril (Zestril, Prinvil&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>10 - 40 mg daily</td>
</tr>
<tr>
<td>ACE INHIBITORS (ACE-I)</td>
<td>Captopril (Capoten&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>25 - 50 mg twice daily</td>
</tr>
<tr>
<td>ACE INHIBITORS (ACE-I)</td>
<td>Benazepril (Lotensin&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>10 - 40 mg daily</td>
</tr>
<tr>
<td>ANGIOTENSIN II RECEPTOR BLOCKER (ARB)</td>
<td>Losartan (Cozaar&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>25 - 100 mg daily</td>
</tr>
<tr>
<td>LONG-ACTING DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS (CCB)</td>
<td>Amlodopine (Norvasc&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>2.5 - 10 mg daily</td>
</tr>
<tr>
<td>LONG-ACTING DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS (CCB)</td>
<td>Nifedipine ER (Procardia XL&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>30 - 90 mg daily</td>
</tr>
<tr>
<td>LONG-ACTING DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS (CCB)</td>
<td>Felodipine ER (Plendil&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>2.5 - 20 mg daily</td>
</tr>
<tr>
<td>ALDOSTERONE RECEPTOR BLOCKER</td>
<td>Spironolactone (Aldactone)</td>
<td>12.5 - 25 mg daily</td>
</tr>
<tr>
<td>BETTA-BLOCKERS (BB)</td>
<td>Atenolol (Tenormin&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>25 - 100 mg total, taken once or twice daily</td>
</tr>
<tr>
<td>BETTA-BLOCKERS (BB)</td>
<td>Metoprolol (Lopressor&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>25 - 100 mg BID</td>
</tr>
<tr>
<td>BETTA-BLOCKERS (BB)</td>
<td>Carvedilol (Coreg&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>3.125 - 25 mg BID</td>
</tr>
<tr>
<td>BETTA-BLOCKERS (BB)</td>
<td>Metoprolol ER (Toprol XL&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>50 - 100 mg daily</td>
</tr>
<tr>
<td>ACE-I-THIAZIDE COMBINATION PILL</td>
<td>Spironolactone/HCTZ (Aldactazide&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>25 / 25 mg daily</td>
</tr>
<tr>
<td>ALPHA BLOCKERS</td>
<td>Terazosin (Hytrin&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>1 - 20 mg daily</td>
</tr>
<tr>
<td>ALPHA BLOCKERS</td>
<td>Doxazosin (Cardura&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>1 - 16 mg daily</td>
</tr>
<tr>
<td>ALPHA BLOCKERS</td>
<td>Prazosin (Minipress&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>1 - 10 mg BID</td>
</tr>
<tr>
<td>DIRECT VASODILATORS</td>
<td>Hydralazine (Apresoline&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>25 - 100 mg BID</td>
</tr>
<tr>
<td>DIRECT VASODILATORS</td>
<td>Minoxidil (Loniten&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>2.5 mg daily - 20 mg BID</td>
</tr>
<tr>
<td>ALPHA-2 AGONISTS</td>
<td>Clonidine (Catapres&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>0.1 mg HS - 0.4 mg BID</td>
</tr>
<tr>
<td>PERIPHERAL ADRENERGIC INHIBITOR</td>
<td>Reserpine (Serpilan&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>0.05 - 0.1 mg daily</td>
</tr>
</tbody>
</table>

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1 Availability of medications may vary depending on regional formularies.