

Taking the Pressure Off Hypertension Management

A VA Clinician's Guide



Contents

Hypertension in primary care	1
A step-by-step approach to identifying and managing hypertension	
Make the diagnosis	3
Set blood pressure goals	3
Encourage lifestyle modifications	6
Initiate treatment	ε
Resistant hypertension	9
Individualizing treatment in select populations	11
Hypertensive emergency and urgency	19
References	20



These materials were developed by:

VA PBM Academic Detailing Services

Your Partner in Enhancing Veteran Health Outcomes

VA PBM Academic Detailing Services Email Group:

PharmacyAcademicDetailingProgram@va.gov

VA PBM Academic Detailing Services SharePoint Site:

https://dvagov.sharepoint.com/sites/vhaacademicdetailing

VA PBM Academic Detailing Services Public Website:

http://www.pbm.va.gov/PBM/academicdetailingservicehome.asp



This document aims to provide clarity in selecting optimal blood pressure goals and evidence-based treatments for hypertension in primary care.

ACRONYMS:

ACEI: angiotensin-converting enzyme inhibitor

Afib: atrial fibrillation

ARB: angiotensin receptor blocker

ARNI: angiotensin receptorneprilysin inhibitor

ASCVD: atherosclerotic cardiovascular disease

BB: beta blocker **BP:** blood pressure

CAD: coronary artery disease

CBC: complete blood count

CCB: long-acting calcium channel blocker

CKD: chronic kidney disease

CVD: cardiovascular disease

DBP: diastolic blood pressure

DM: diabetes mellitus

HF: heart failure

HTN: hypertension

LFTs: liver function tests

mmHg: millimeters of mercury

MRA: mineralocorticoid receptor antagonist

RASI: renin-angiotensin system

inhibitor

SBP: systolic blood pressure

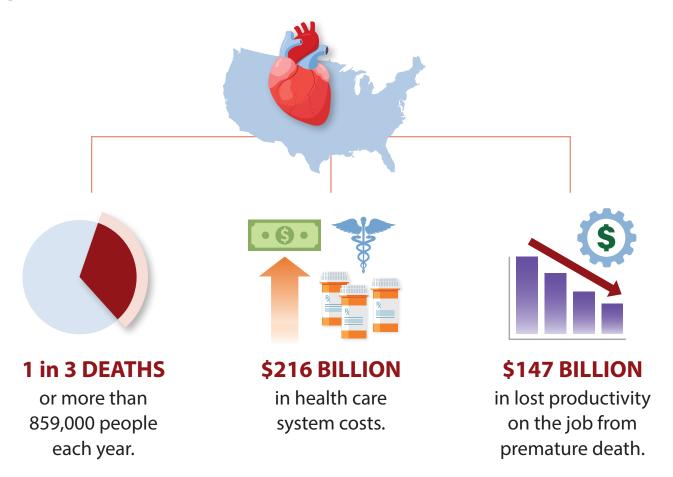
SGLT-2: sodium-glucose

co-transporter 2

Hypertension in primary care

In the Department of Veterans Affairs (VA) healthcare system, hypertension is the **most common chronic condition** with a prevalence of 37% (> 1 million Veterans). Hypertension is a modifiable risk factor for heart failure, kidney disease, and coronary artery disease. ²⁻⁴

Figure 1. In the United States, cardiovascular diseases cause:²



There are multiple hypertension guidelines in addition to disease-specific guidelines (e.g., chronic kidney disease, heart failure, etc.) that provide differing recommendations regarding treatment goals. The conflicting recommendations from expert opinion often provide uncertainty surrounding optimal blood pressure targets as well as the best pharmacotherapy options.

This document aims to provide clarity in selecting optimal blood pressure goals and evidence-based treatments for hypertension in primary care.

A step-by-step approach to identifying and managing hypertension³



Make the diagnosis

- Obtain two systolic blood pressure readings above 130 mmHg on separate office visits
- Ensure correct blood pressure measurement (see VA/DoD video)
- Rule out other causes



Set blood pressure goals

 Patient-specific factors will guide selection (e.g., age, diabetes, chronic kidney disease, cardiovascular disease, pregnancy)



Encourage lifestyle modifications

- Diet modifications (DASH diet, sodium reduction, potassium-rich diet)
- Physical activity/weight loss
- Smoking cessation

- Limited alcohol consumption
- Drug/disease interactions should be considered



Initiate treatment

- Select medication regimen based on patient-specific factors, comorbidities, and drug interactions
- Stage 1 hypertension = 1 medication regimen
- Stage 2 hypertension = consider combination therapy



Follow up and monitor

- If systolic blood pressure is 120-129 mmHg, follow up in 3 months
- If Stage 1 or 2 hypertension and medication is added, follow up in 1 month
- Confirm adherence with treatment plan

Make the diagnosis

Optimal management of hypertension starts with a proper diagnosis. Accurate measurement and documentation of blood pressure is key.



- Measure blood pressure with a validated device (automated office blood pressure measurement preferred when available) after the patient has been resting in a chair for at least 5 minutes.^{3,4}
- Counsel the patient to avoid caffeine, nicotine, and exercise for at least 30 minutes prior to the appointment.^{3,4}

A diagnosis of hypertension is based on the average of two or more readings obtained on two or more separate office visits. Please note: patients with diabetes and cardiovascular disease may be diagnosed with hypertension at a single visit if blood pressure > 180/110 mmHg.³⁻⁵

Table 1. Staging and diagnosing hypertension: guideline comparison (mmHg)^{3,4,6}

VA/DOD	STAGE	ACC/AHA (2017)	ISH
Diagnosis ≥130/90 No staging recommended	Stage 1	SBP 130-139	SBP 140-159
		DBP 80-89	DBP 90-99
	Stage 2	SBP ≥ 140	SBP ≥160
		DBP ≥ 90	DBP ≥ 100

ACC: American College of Cardiology; AHA: American Heart Association; DOD: Department of Defense; ISH: International Society of Hypertension; VA: Department of Veterans Affairs

For more detail on how staging affects treatment options, see Figure 7 on page 7.

Set blood pressure goals

Use shared decision-making to establish individualized blood pressure goals with Veterans.

- Consider age, renal function, and comorbidities (to include frailty and life expectancy).
- Select blood pressure goal based on risks and tolerance.

Choosing the most stringent blood pressure goal could provide the most benefit. However, if fluctuations in blood pressure results in adverse effects such as dizziness or falls, the blood pressure goal should be adjusted.^{3,7}



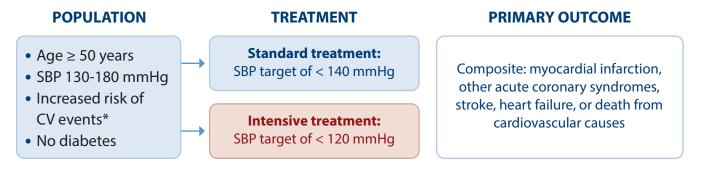
Table 2. Blood pressure goals from various clinical practice guidelines^{3-5,7-10}

General population blood pressure goals (mmHg)			
	VA/DOD (2020) ^a	ACC/AHA (2017) ^b	
Adults < 60 years old	< 130/90	< 130/80	
Older adults ≥ 60 years old	< 150/90		

Special populations blood pressure goals (mmHg)				
Diabetes	< 130/80 ^{b,c} < 140/90 ^{a,c} < 150/90 if limited life expectancy ^c	HF, stroke, or ASCVD with ≥ 10% 10-year risk	< 130/80 ^b	
CKD	< 120/80 if non-dialysis d,e < 130/80 if kidney transplant d,e	Pregnancy with chronic HTN	< 120-159/80-109 ^f < 110-35/85 if DM ^a	

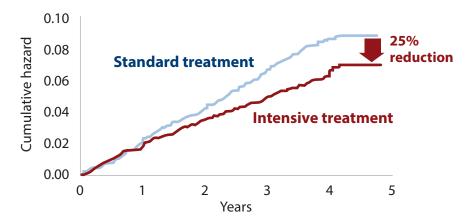
^a VA/DOD; ^bACC/AHA; ^cAmerican Diabetes Association (ADA); ^d The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI); ^eKidney Disease Improving Global Outcomes (KDIGO); ^fAmerican Congress of Obstetricians and Gynecologists (ACOG).

Figure 2. SPRINT Trial: What evidence supports current blood pressure goal recommendations?^{11,12}



^{*}Increased risk of CV events = One or more of the following: clinical or subclinical cardiovascular disease other than stroke; chronic kidney disease, excluding polycystic kidney disease, with an eGFR of 20 to less than 60 mL/min/1.73m²; 10-year risk of cardiovascular disease of 15% or greater on the basis of the Framingham risk score; or \geq 75 years old.

Figure 3. Intensive blood pressure control reduced CV outcomes and death¹¹



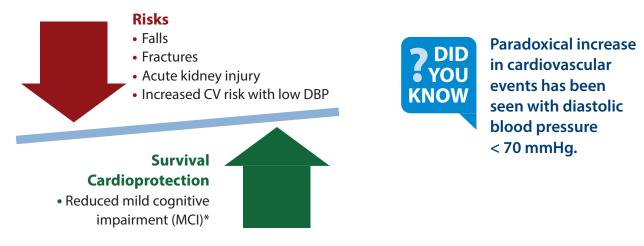
Hazard ratio with intensive treatment, 0.75 (95% CI, 0.64-0.89), p < 0.001

Based on the SPRINT trial results, the 2017 ACC/AHA ERC Systematic Review recommended that BP lowering to a SBP goal of < 130 mmHg reduces potential for major cardiovascular events.

The number needed to treat for intensive blood pressure control to prevent one primary outcome event was 61 (follow up period was a median of 3.26 years).¹¹⁻¹³

How low should you go?

Figure 4. Individual factors to consider when establishing blood pressure goals14,15



^{*}The SPRINT-MIND trial evaluated the effect of intensive BP control on dementia risk and MCI. It selected a target SBP of < 120 mmHg or < 140 mmHg. There was no statistical difference in the primary outcome of occurrence of dementia; however, in patients with an SBP < 120 mmHg, there was a statistically significant decrease in both MCI and the composite outcome of dementia and MCI. The impact of more intensive BP goals on dementia in older adults remains uncertain, emphasizing the need to individualize BP goals in this population. 16

Establish and document target blood pressure goal based on comorbidities and shared decision-making.

Figure 5. Patient case example

- 65-year-old with Afib, CKD, DJD of knee, OSA, TBI, severe COPD on long-term oxygen therapy, recent ED visit for fall 3 months ago
- Taking 3 anti-hypertensives (ACEI, CCB, BB)
- BP in office with medications: 158/91
- After review of labs, initiated chlorthalidone 12.5 mg and referred to registered dietician to assess sodium intake

BP target range < 150/90

New BP in clinic was 143/84

- Current medications:
 - Lisinopril 40 mg daily
 - Amlodipine 10 mg daily
 - Metoprolol succinate 100 mg daily
 - Chlorthalidone 12.5 mg daily
- Stopped adding extra salt to food
- Started mindfulness with Whole Health coach
- Cut back on alcohol intake
- Patient concerned about getting confused with medications since he lives alone

- Considered BP measurement technique in clinic
- Assessed medication adherence and timing of last dose
- Veteran made positive lifestyle changes and BP improved significantly

Not changing therapy and targeting less stringent BP goal is an acceptable approach given fall risk/frailty and patient preference

Consider combination therapy when possible. COPD: chronic obstructive pulmonary disease; DJD: degenerative joint disease; ED: emergency department; OSA: obstructive sleep apnea; TBI: traumatic brain injury

Encourage lifestyle modifications

Talk with the Veteran about lifestyle changes that may improve their blood pressure.



Figure 6. Lifestyle modifications that can result in a reduction of blood pressure^{3,17-43}

4 mmHg reduction 4-8 mmHg reduction 10 mmHg reduction Limit daily alcohol to Reduce sedentary time and Consider 10% weight loss ≤ 1 drink for women increase physical activity • Implement DASH diet and ≤ 2 drinks for men to 150 minutes/week • Keep sodium intake to -10% < 1 teaspoon (~2,300 mg) of table salt per day44 A potassium-rich diet may help reduce blood pressure



A reduction in blood pressure of just 20/10 mmHg is associated with a 50% decrease in cardiovascular risk.¹³

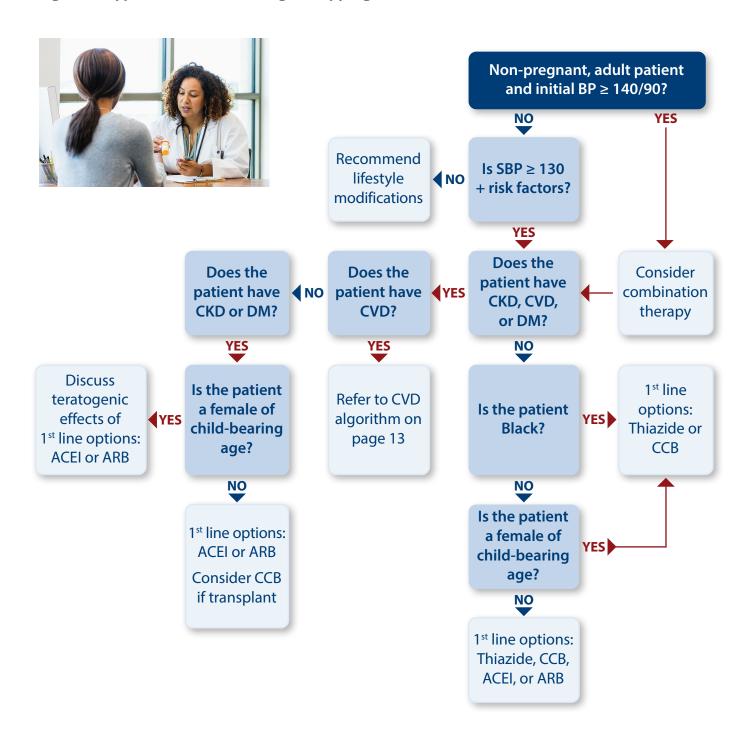
Initiate treatment

After setting individualized blood pressure goals, recommending lifestyle modifications, and assessing for secondary hypertension causes (see page 8), pharmacotherapy may be indicated. The following treatment algorithm is a general overview of initial treatment options for hypertension management.



It is important to individualize pharmacotherapy after considering patient-specific factors such as age, comorbidities, and lifestyle. When patients require multiple agents to lower their blood pressure, combination agents may lower pill burden and improve adherence.

Figure 7. Hypertension: initial drug therapy algorithm^{3,4,6}



CCBs, thiazide diuretics, and ACEIs or ARBs are first-line treatment for most patients. If additional BP lowering is needed, maximize first-line agents then consider a mineralocorticoid receptor antagonist.

If blood pressure is not at goal after initial medications:3,45,46

Assess adherence to medication regimen and optimize dose.

Screen for secondary causes of hypertension (e.g., primary aldosteronism, chronic kidney disease, hormonal imbalances in the renin-angiotensin system, pheochromocytoma, obstructive sleep apnea, substance use disorder).

Add/optimize calcium channel blocker, thiazide, ACE inhibitor, or angiotensin receptor blocker.

Re-evaluate diuretic:

Change from loop to thiazide.

Change from hydrochlorothiazide to chlorthalidone (♣ by 6-7 mmHg).

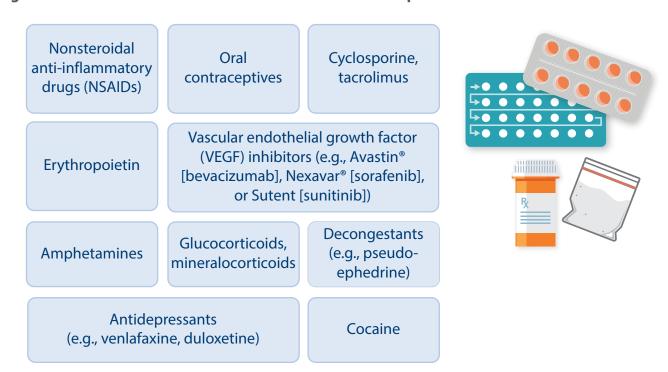
Re-evaluate beta blocker:

 If on a beta blocker for other indication, consider changing to carvedilol for enhanced blood pressure lowering.

Evaluate for medication-related secondary hypertension

Screening for secondary causes of hypertension is necessary for new onset or uncontrolled hypertension in adults, including drug-resistant (three or more drugs), abrupt onset, age < 30 years, or excessive target organ damage.⁴⁵

Figure 8. Medications and substances that increase blood pressure^{3,45}



Resistant hypertension

Resistant hypertension is high blood pressure that remains above patient-specific goal on three or more antihypertensive medications (one of which should be a diuretic) prescribed at optimal doses.³

If no cause of secondary hypertension is identified or modifiable:

- Consider adding a mineralocorticoid receptor antagonist.^{3,47}
- If blood pressure is still not at goal after initiation of a fourth-line medication, add medications with different mechanisms of action.³
- If heart failure or ischemic heart disease is present and heart rate is above 70 beats per minute, a beta blocker is an appropriate option for improved blood pressure control.⁴⁵
- Additional agents to consider include clonidine, hydralazine, or minoxidil.⁴⁵

Specialty care may be needed for management of resistant hypertension.3

Figure 9. Management of resistant hypertension without modifiable cause of secondary hypertension^{3,45}

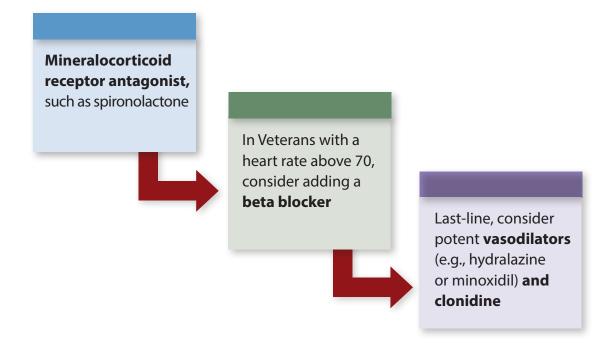


Figure 10. Last-line options for resistant hypertension⁴⁵



HYDRALAZINE

- Safe in pregnancy
- Three times daily dosing
- Side effects: headache, dose-related systemic lupus erythematosus



MINOXIDIL

- Once daily dosing
- Side effects: hypertrichosis/hirsutism, pericardial effusion



CLONIDINE

- Weekly patch available
- Avoid in elderly due to central nervous system side effects
- Side effects: somnolence, bradycardia, dry mouth, bone marrow suppression (rare), hemolytic anemia (rare), liver disorders (rare)





Consider using with a diuretic and BB to reduce edema and reflex tachycardia if present

Figure 11. Patient case example

- 45-year-old white male with HTN, DM, hyperlipidemia, chronic low back pain, OSA, and PTSD
- Taking 3 anti-hypertensives (ACEL, CCB, thiazide)
- BP in office with medications: 153/92
- After review of labs, increased chlorthalidone to 25 mg and reinforced lifestyle modifications

BP target range < 130/90

New BP in clinic was 147/85

- Current medications:
 - Lisinopril 40 mg daily
 - Amlodipine 10 mg daily
 - Chlorthalidone 25 mg daily
- Decreased eating out from 3 days/ week to 2 days/week and stopped adding extra salt to food
- Started mindfulness with Whole Health coach
- Cut back on alcohol intake

- Considered BP measurement technique in clinic
- Assessed medication adherence and timing of last dose
- Discussed adjusting regimen to include a combination therapy to reduce pill burden
- Assessed for secondary causes of HTN

Add spironolactone
12.5 mg daily

OSA: obstructive sleep apnea; PTSD: post traumatic stress disorder

10

Individualizing treatment in select populations

Consider patient-specific factors when creating a hypertension management plan. Use a shared decision-making approach to individualize the treatment plan and establish a clinically appropriate blood pressure goal based on risks and benefits given the patient's comorbidities.











Hypertension management in chronic kidney disease (CKD)

There is variability among hypertension guidelines on the ideal blood pressure goal for patients with chronic kidney disease (Table 2). The Kidney Disease Improving Global Outcomes (KDIGO) guideline has the most stringent goals for systolic blood pressure control in patients with CKD who are not on dialysis.⁸



A post-hoc analysis in the SPRINT CKD cohort demonstrated:12

- Intensive blood pressure management (SBP <120) significantly reduced adverse cardiovascular events* and all-cause mortality in patients with mild-to-moderate CKD (baseline eGFR 47.9 ml/min).
- This benefit was also seen in patients with lower baseline diastolic blood pressure.

There is insufficient high quality clinical evidence to recommend a specific blood pressure target that applies to *all* patients with CKD.⁴⁸ More intensive blood pressure goals may reduce cardiovascular risk, but evidence is lacking regarding prevention of kidney disease progression in patients with CKD.³

In patients with CKD, consider intensive blood pressure management along with individualized risk versus benefit and patient preference.^{4,8,48} For kidney transplant patients, use a goal of < 130/80.⁸

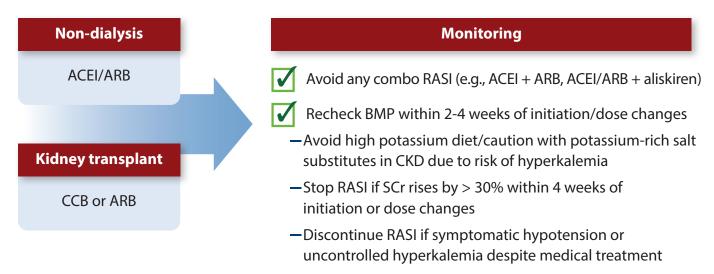
What about my patients on dialysis?

Due to the lack of quality evidence to inform recommendations for the management of many of the blood pressure and volume complications in patients on dialysis, few strong recommendations exist. An individualized approach to blood pressure management should be considered.⁴⁹

^{*}SPRINT trial primary cardiovascular outcome: composite of nonfatal myocardial infarction, other acute coronary syndromes, nonfatal stroke, nonfatal acute decompensated congestive heart failure, and cardiovascular death.

Pharmacotherapy considerations in CKD^{3,8,48}

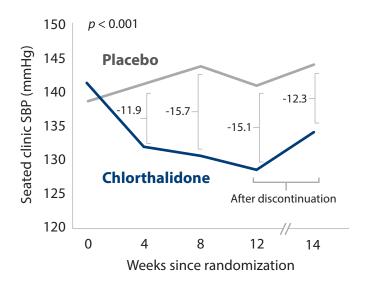
The evidence for benefit of using RASI to slow the progression of kidney disease is limited to patients with moderately or severely elevated urine albumin excretion (urine albumin-to-creatinine ratio > 30 mg/g).³



BMP: basic metabolic panel; SCr: serum creatinine

In patients with CKD + albuminuria, initiate ACEI or ARB as preferred first-line treatment for hypertension.

Figure 12. Chlorthalidone reduces blood pressure and albuminuria in advanced CKD (eGFR < 30 mL/min)⁵⁰



It was previously hypothesized that thiazide diuretics would be ineffective for BP management in patients with an eGFR of < 30 mL/min; however, this has been dispelled by a recent study. **Consider chlorthalidone in patients with CKD who are not optimized on first-line pharmacotherapy.**⁵⁰

To minimize risk of side effects,⁵¹ monitor BMP and start with a low dose of chlorthalidone (12.5 mg) daily; consider three times a week dosing if on a concomitant loop diuretic.

Chlorthalidone reduced the urinary albumin-to-creatinine ratio compared to placebo (-52% and -4%, respectively at 12 weeks, between group difference of -50%; 95% CI, -60 to -37). Incidence of electrolyte disturbances and increases in serum creatinine level were higher with chlorthalidone versus placebo.

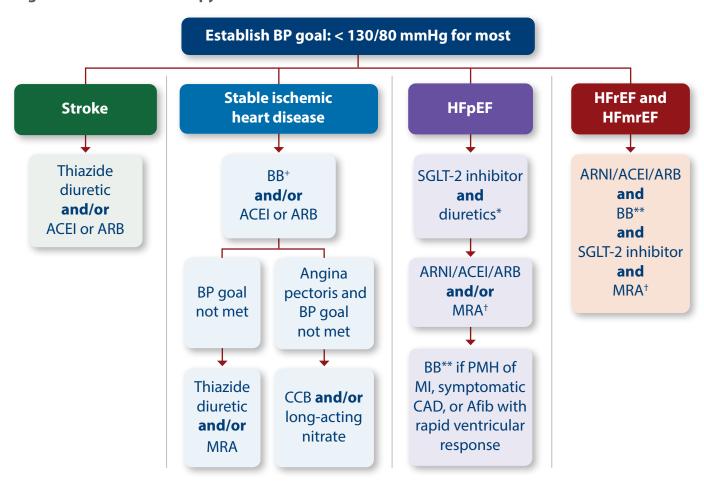
Hypertension management in cardiovascular disease

 Controlling blood pressure can reduce cardiovascular disease complications by 25% and all-cause mortality by 27%.³



- Considerations for specific cardiovascular conditions:
 - -History of stroke: Achieving blood pressure targets is more important than class of medication.⁵²
 - —Stable ischemic heart disease (SIHD): Use beta blockers to prevent angina pectoris, increase exercise time, and prevent coronary events.⁵³
 - -Heart failure: Optimize pharmacotherapy for both heart failure and hypertension.^{3,54}

Figure 13. Pharmacotherapy considerations in cardiovascular disease^{3,52-55}



 $^+$ BB: carvedilol, metoprolol tartrate/succinate, bisoprolol, nadolol, propranolol, timolol; $^+$ Diuretics are utilized for volume overload not HTN management; ** GDMT BB include bisoprolol, carvedilol, and metoprolol succinate; $^+$ MRA indicated for HFrEF NYHA class II-IV with CrCl >30 mL/min or SCR < 2.5 mg/dL in males or < 2 mg/dL in females and potassium <5 mEq/L; In HFpEF may be considered to decrease hospitalization for patients with EF >45%, elevated BNP levels or HF admission within 1 year, eGFR >30 mL/min, creatinine <2.5 mg/dL, potassium <5.0 mEq/L.

GDMT: guideline-directed medication therapy; HFmrEF: heart failure with mildy reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; PMH: past medical history

In patients with CVD, a BP target of < 130/80 is recommended.

In patients with HF, follow GDMT.

Hypertension management in diabetes

Diabetes is a major cause of morbidity and mortality in the United States due to increased risk for atherosclerotic cardiovascular disease and progression to chronic kidney disease.



- A 10 mmHg reduction in systolic blood pressure can result in a 12% relative risk reduction of cardiovascular events.⁵⁶
- Utilization of ACEI or ARB has been shown to reduce chronic kidney disease progression.
- For patients with urine albumin-to-creatinine ratio 30-299 mg/g creatinine, the addition of ACEI or ARB has demonstrated reduction in the progression of albuminuria.⁵⁷

Pharmacotherapy considerations in diabetes: preferred first-line therapy^{3,5,56}

Diabetes alone)	ACEI or ARB, CCB, or thiazide diuretic
Diabetes	CAD	ACEI or ARB
Diabetes	albuminuria (UACR ≥ 30mg/g)	ACEI or ARB

UACR: urine albumin-to-creatinine ratio

Target a systolic blood pressure goal of < 130 in patients with diabetes and utilize an ACEI or ARB with the presence of albuminuria.

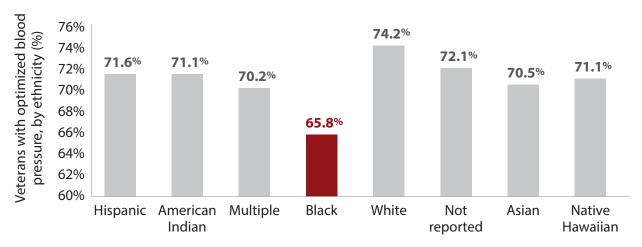


Hypertension management in Black patients

In addition to other disease states, patient ethnicity can impact drug selection. Healthcare disparities continue to prevail within the VA population.^{58,59}

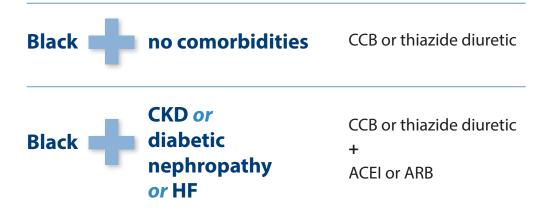


Figure 14. The Black Veteran population has fewer individuals with optimized blood pressure compared to other ethnicities



Data extracted from the VA Corporate Data Warehouse on 3/17/2022. Numerator patients with hypertension were identified by using ICD-10 & ICD-9 codes in visits and problem lists. Denominator patients were active users of VA healthcare benefits in the last 2 years.

Pharmacotherapy considerations in Black patients: preferred first-line therapy^{3,4}



CLINICAL PEARLS

Recommended first-line antihypertensives in Black patients are dihydropyridine CCBs and thiazide diuretics. ACEIs and ARBs should be avoided as initial therapy unless a compelling indication exists (e.g., heart failure, diabetes, chronic kidney disease).^{3,4} If ACEI or ARB therapy is desired for comorbidity management, ARBs are preferred given that incidence of angioedema is lower than that of ACEIs.^{3,4} ACEIs are used preferentially in black patients with HFrEF.⁵⁵

Hypertension management in female Veterans

Managing hypertension in females of childbearing age can be complicated, as many of our first-line pharmacotherapy options are contraindicated in pregnancy, and hypertension is defined differently in pregnancy. Individualizing therapy to the patient's age and conception desires/plans is important when defining goals of care.



Figure 15. Key considerations when starting antihypertensives in women of childbearing age^{60,61,*}

Key things to assess in females of childbearing age*



Ask about pregnancy prior to prescribing new antihypertensive medications. Ask:

- "Do you have a known or suspected pregnancy?"
- "Are you considering pregnancy in the near future?"
- "When was your last menstrual period?"



Medications to avoid if potential for pregnancy is noted

- ACEIs
- ARBs
- aliskerin
- MRAs

Definitions of hypertension in pregnancy⁹

Hypertension in pregnancy

 SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg measured on 2 occasions at least 4 hours apart



Severe-range hypertension

 SBP ≥ 160 mmHg and/or DBP ≥ 110 mmHg measured on 2 occasions at least 4 hours apart

Chronic hypertension

- Hypertension diagnosed/present before pregnancy or before 20 weeks of gestation
- Hypertension diagnosed for the first time during pregnancy that does not resolve in the postpartum period

Chronic hypertension with superimposed preeclampsia

 Preeclampsia in a patient with a history of hypertension before pregnancy or before 20 weeks of gestation

^{*}Childbearing age = commonly defined as 18-52 years old. It is important to take into consideration menstrual stage.

Blood pressure targets in pregnant women with hypertension^{5,9}



^aAmerican Diabetes Association (ADA); ^bAmerican Congress of Obstetricians and Gynecologists (ACOG)

Figure 16. Managing blood pressure during pregnancy^{5,9,62-68}

Treat chronic hypertension if SBP > 160 mmHg and/or > 110 mmHg after individual risks versus benefit analysis.*

If a patient with chronic hypertension becomes pregnant, consider changing medications based on individualized maternal and fetal risks.



FIRST-LINE OPTIONS

labetalol

100-2,400 mg/day in 2-3 divided doses

nifedipine ER

30-120 mg/day once daily

OTHER OPTIONS

methyldopa

500-3,000 mg/day in 2-4 divided doses

hydrochlorothiazide

12.5-50 mg/day once daily

AVOID due to teratogenic potential

- ACEIs
- ARBs
- Renin inhibitors
- MRAs



MONITORING

Blood pressure:

- Maintain SBP 120-160 mmHg
- Maintain DBP 80-110 mmHg

MONITORING

Labs:

- CBC
- Creatinine
- LFTs

Additional vigilance:

- Ultrasound for fetal development
- Proteinuria
- Preeclampsia

Assess potential for pregnancy at every visit in females of childbearing age. Avoid use of ACEIs, ARBs, and MRAs in patients who are pregnant or may become pregnant.

^{*}ACOG has one of the higher thresholds for initiation of treatment in pregnancy. Many guidelines recommend treatment with BPs as low as 140/90 mmHg. There is an ongoing trial in the US comparing intensive treatment to traditional treatment, which may impact future decisions. In the meantime, consider lower BP thresholds in patients with risk factors.⁶⁹

SGLT-2 inhibitors and benefits in select populations

While SGLT-2 inhibitors are not utilized as antihypertensive agents, there are many benefits of SGLT-2 inhibitors across the special populations discussed in this document. In addition to blood glucose lowering and prevention of cardiovascular and renal complications in patients with diabetes and heart failure, SGLT-2 inhibitors may also have some impact on blood pressure.⁷⁰⁻⁷²

When adding an SGLT-2 inhibitor, blood pressure may decrease over time and other antihypertensive agents may require adjustment.

Figure 17. Comorbidities that may improve with the addition of SGLT-2 inhibitors⁷⁰⁻⁷²



HEART FAILURE

Associated with a reduction in cardiovascular death and heart failure hospitalization in patients with heart failure regardless of ejection fraction



DIABETES AND ASCVD

Associated with prevention of cardiovascular events and a reduction in cardiovascular mortality



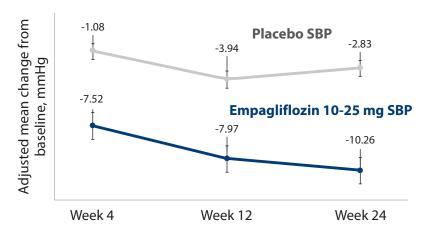
CHRONIC KIDNEY DISEASE

Associated with slower progression of kidney disease and lower rates of clinically relevant renal events

Empagliflozin can reduce blood pressure in Black patients⁷³

Figure 18. Empagliflozin reduces blood pressure in Black patients—maximum effects may take up to 6 months⁷³

- A recent study revealed that Black patients with diabetes had a reduction in A1c, body weight, and blood pressure when treated with empagliflozin.⁷³
- This study also noted that it may take ≥ 6 months for the full antihypertensive effect to be fully realized.⁷³



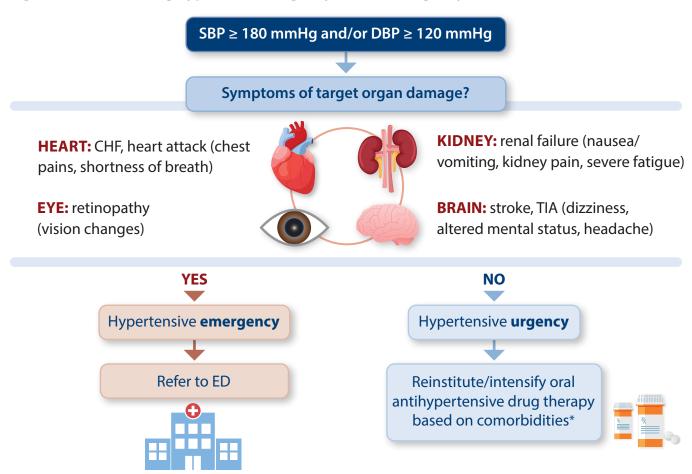
Hypertensive emergency and urgency

Approximately 1-2% of American adults will suffer from a hypertensive crisis, indicated by a markedly elevated blood pressure (≥ 180/120 mmHg).^{3,74} Hypertensive crisis is an umbrella term that encompasses hypertensive urgencies and emergencies.¹

Key points to lowering blood pressure in a hypertensive emergency/urgency:^{3,74}

- Avoid lowering BP by more than 25% in the first hour (e.g., SBP 184 mmHg by 25% = 138 mmHg).
- Excessive reduction of BP may cause or contribute to renal, cerebral, or coronary ischemia.

Figure 19: Determining hypertensive urgency versus emergency^{3,74}



^{*}See Figure 13 page 13 for recommended antihypertensive drug therapy based on comorbidities.

Recommendations for management of hypertensive urgency is limited. Hypertensive urgency is typically triggered by non-adherence to antihypertensive therapies and anxiety—thus, it is better to focus on therapy adherence. There is no indication for referral to the ED.

Counsel all patients with hypertension to recognize the symptoms of target organ damage and seek emergency treatment immediately if noticed.

References

- 1. Borzecki AM, et al. Hypertension control: how well are we doing? Arch Intern Med. 2003;163(22):2705-2711.
- 2. National Center of Chronic Disease Prevention. Heart Disease and Stroke. March 7, 2022. https://www.cdc.gov/chronicdisease/resources/publications/factsheets/heart-disease-stroke.htm.
- Whelton PK, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71(6):e13-e115.
- Tschanz CMP, et al. Synopsis of the 2020 U.S. Department of Veterans Affairs/U.S. Department of Defense Clinical Practice Guideline: The Diagnosis and Management of Hypertension in the Primary Care Setting. Ann Intern Med. 2020;173(11):904-913.
- 5. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022;45(Suppl 1):S144-S174.
- 6. Unger T, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020;75(6):1334-1357.
- 7. Dasgupta I, Zoccali C. Is the KDIGO Systolic Blood Pressure Target <120 mm Hg for Chronic Kidney Disease Appropriate in Routine Clinical Practice? *Hypertension*. 2022;79(1):4-11.
- 8. Cheung AK, et al. Executive summary of the KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney Int.* 2021;99(3):559-569.
- 9. ACOG Practice Bulletin No. 203: Chronic Hypertension in Pregnancy. Obstet Gynecol. 2019;133(1):e26-e50.
- 10. Kramer HJ, et al. KDOQI US Commentary on the 2017 ACC/AHA Hypertension Guideline. Am J Kidney Dis. 2019;73(4):437-458.
- 11. SPRINT Research Group. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015 Nov 26;373(22):2103-16.
- 12. Hu AH, Chang TI. SPRINT-A Kidney-Centric Narrative Review: Recent Advances in Hypertension. Hypertension. 2021;78(4):946-954.
- 13. Reboussin DM, et al. Systematic review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *Hypertension*. 2018;71(6):e116-e135.
- 14. Tringali S, et al. Low Diastolic Blood Pressure as a Risk for All-Cause Mortality in VA Patients. Int J Hypertens. 2013;2013:178780.
- 15. Lewington S, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360(9349):1903-1913.
- The SPRINT MIND Investigators for the SPRINT Research Group. Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia: A Randomized Clinical Trial. JAMA. 2019;321(6):553-561.
- 17. National High Blood Pressure Education Program Working Group report on primary prevention of hypertension. Arch Intern Med. 1993;153(2):186-208.
- 18. Whelton PK, et al. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. JAMA. 1997;277(20):1624-1632.
- 19. Aburto NJ, et al. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. BMJ. 2013;346:f1378.
- 20. Geleijnse JM, et al. Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomised trials. J Hum Hypertens. 2003;17(7):471-480.
- 21. Mozaffarian D, et al. Global sodium consumption and death from cardiovascular causes. N Engl J Med. 2014;371(7):624-634.
- 22. He FJ, et al. Plasma sodium and blood pressure in individuals on haemodialysis. J Hum Hypertens. 2013;27(2):85-89.
- 23. Graudal NA, et al. Effects of low-sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). *Am J Hypertens*. 2012;25(1):1-15.
- 24. Sacks FM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med. 2001;344(1):3-10.
- 25. Kumanyika SK, et al. Sodium reduction for hypertension prevention in overweight adults: further results from the Trials of Hypertension Prevention Phase II. *J Hum Hypertens*. 2005;19(1):33-45.
- 26. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels. Results of the Trials of Hypertension Prevention, Phase I. *JAMA*. 1992;267(9):1213-1220.
- 27. Cook NR, et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ.* 2007;334(7599):885-888.
- 28. Xin X, et al. Effects of alcohol reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension. 2001;38(5):1112-1117.
- 29. Stewart SH, et al. Blood pressure reduction during treatment for alcohol dependence: results from the Combining Medications and Behavioral Interventions for Alcoholism (COMBINE) study. Addiction. 2008;103(10):1622-1628.
- 30. Dickinson HO, et al. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. J Hypertens. 2006;24(2):215-233.
- 31. Wallace P, et al. Randomised controlled trial of general practitioner intervention in patients with excessive alcohol consumption. BMJ. 1988;297(6649):663-668.
- 32. Lang T, et al. Improving hypertension control among excessive alcohol drinkers: a randomised controlled trial in France. The WALPA Group. *J Epidemiol Community Health*. 1995;49(6):610-616.
- 33. Roerecke M, et al. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. Lancet Public Health. 2017;2(2):e108-e120.
- 34. Whelton SP, et al. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med. 2002;136(7):493-503.
- 35. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013;2(1):e004473.
- 36. Rossi AM, et al. The evolution of a Canadian Hypertension Education Program recommendation: the impact of resistance training on resting blood pressure in adults as an example. Can J Cardiol. 2013;29(5):622-627.

20

- 37. García-Hermoso A, et al. Effects of exercise on resting blood pressure in obese children: a meta-analysis of randomized controlled trials. Obes Rev. 2013;14(11):919-928.
- 38. Carlson DJ, et al. Isometric exercise training for blood pressure management: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(3):327-334.
- 39. Neter JE, et al. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension. 2003;42(5):878-884.
- 40. Ho M, et al. Effectiveness of lifestyle interventions in child obesity: systematic review with meta-analysis. Pediatrics. 2012;130(6):e1647-1671.
- 41. Cai L, et al. Effect of childhood obesity prevention programs on blood pressure: a systematic review and meta-analysis. Circulation. 2014;129(18):1832-1839.
- 42. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, phase II. The Trials of Hypertension Prevention Collaborative Research Group. Arch Intern Med. 1997;157(6):657-667.
- 43. Whelton PK, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA*. 1998;279(11):839-846.
- 44. Mayo Clinic Staff. Nutrition and healthy eating: Nutrition basics. https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/sodium/art-20045479. Accessed October 2022.
- 45. Carey RM, et al. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. *Hypertension*. 2018;72(5):e53-e90.
- 46. Stafylas PC, Sarafidis PA. Carvedilol in hypertension treatment. Vasc Health Risk Manag. 2008;4(1):23-30.
- 47. Williams B, et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. *Lancet*. 2015;386(10008):2059-2068.
- 48. *U.S. Department of Veterans Affairs/U.S. Department of Defense Clinical Practice Guideline: The Management of Chronic Kidney Disease.* Version 4.0;2019. https://www.healthquality.va.gov/quidelines/CD/ckd/VADoDCKDCPGProviderSummaryFinal5082142020.pdf.
- 49. Flythe JE, et al. Blood pressure and volume management in dialysis: Conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2020 Mar;97(5):861-876.
- 50. Agarwal R, et al. Chlorthalidone for Hypertension in Advanced Chronic Kidney Disease. N Engl J Med. 2021;385(27):2507-2519.
- 51. Agarwal R. Spironolactone and chlorthalidone—old drugs, new uses—but approach with caution. Nephrol Dial Transplant. 2022;37(3):407-408.
- 52. Kleindorfer DO, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021;52(7):e364-e467.
- 53. Fihn SD, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAl/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation*. 2012;126(25):e354-471.
- 54. Yancy CW, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136(6):e137-e161.
- 55. Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(18):e895-e1032.
- 56. Ettehad D, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016;387(10022):957-967.
- 57. Draznin B, et al. 11. Chronic Kidney Disease and Risk Management: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022;45(Suppl 1):S175-S184.
- 58. Trivedi AN, et al. Despite improved quality of care in the Veterans Affairs health system, racial disparity persists for important clinical outcomes. *Health Aff (Millwood)*. 2011;30(4):707-715.
- 59. Williams SK, et al. Hypertension Treatment in Blacks: Discussion of the U.S. Clinical Practice Guidelines. Prog Cardiovasc Dis. 2016;59(3):282-288.
- 60. VHA Directive 1330.01(4), Health Care Services for Women Veterans, February 15, 2017, amended January 8, 2021.
- 61. VHA Directive 1330.03, Maternity Health Care and Coordination, November 3, 2020.
- 62. Lisinopril. Agent. Reprotox. Last Modified September 2021. Accessed April 2022.
- 63. Labetalol. Agent. Reprotox. Last modified June 2021. Accessed April 2022.
- 64. Nifedipine. Agent. Reprotox. Last modified August 2021. Accessed April 2022.
- 65. Methyldopa. Agent. Reprotox. Last modified August 2021. Accessed April 2022.
- 66. Hydrochlorothiazide. Agent. Reprotox. Last modified August 2021. Accessed April 2022.
- 67. Losartan. Agent. Reprotox. Last modified May 2021. Accessed April 2022.
- 68. Spironolactone. Agent. Reprotox. Last modified June 2021. Accessed April 2022.
- 69. Garovic V, et al. Hypertension in Pregnancy: Diagnosis, Blood Pressure Goals, and Pharmacotherapy: A Scientific Statement From the American Heart Association. *Hypertension*. 2022;79:e21–e41.
- 70. Packer M, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med. 2020;383 (15):1413-1424.
- 71. McMurray JJV, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med. 2019;381(21):1995-2008.
- 72. Wanner C, et al. Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes. N Engl J Med. 2016;375(4):323-334.
- 73. Ferdinand KC, et al. Antihyperglycemic and Blood Pressure Effects of Empagliflozin in Black Patients With Type 2 Diabetes Mellitus and Hypertension. *Circulation*. 2019;139(18):2098-2109.
- 74. Alley WD, Copelin IE. Hypertensive Urgency. In: StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2022.

Acknowledgments

THIS GUIDE WAS WRITTEN BY:

Jennifer Bolduc, PharmD

Steffanie Danley, PharmD, BCACP, BCPS

Mindy Guerra, PharmD, BCGP

Amanda Holloway, PharmD

Cain Eric Kirk, PharmD, BCACP

Morgan Moulton, PharmD, BCPS

Alivia Price, PharmD

K. Alexis Pruitt, PharmD, BCPS

Bridget Roop, PharmD

Amee Shah, PharmD

Heather Tanner, PharmD

Raymond Tidwell, PharmD

ACADEMIC DETAILING SERVICE SUPPORT:

Sarah Popish, PharmD, BCPP

WE THANK OUR EXPERT REVIEWERS:

Elaine Furmaga, PharmD

Linda Hemann, MD

Mary Julius, RD

Paul Palevksy, MD

David Parra, PharmD, FCCP, PAHA

Leigh Vasko, PharmD, BCAP



This reference guide was created to be used as a tool for VA providers and is available from the Academic Detailing SharePoint.

These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

VA PBM Academic Detailing Services Email Group:

PharmacyAcademicDetailingProgram@va.gov

VA PBM Academic Detailing Services SharePoint Site:

https://dvagov.sharepoint.com/sites/vhaacademicdetailing

VA PBM Academic Detailing Services Public Website:

http://www.pbm.va.gov/PBM/academicdetailingservicehome.asp

October 2022 IB 10-1685 P97122