

Drug Treatment for Hypertension

Agent	Mechanism of Action	Dosage	Benefits	Side Effects	Notes
<p>Thiazide Diuretics:</p> <ol style="list-style-type: none"> 1. Chlorthalidone (Clorpres[®], Tenoretic[®], Thalitone[®]) 2. Hydrochlorothiazide (eg, Microzide[®], HydroDIURIL[®], Aldactazide[®]) 3. Indapamide (Lozol[®]) 4. Metolazone (MyKrox[®], Zaroxolyn[®]) 	<p>Inhibits the reabsorption of sodium and chloride in the distal renal tubule, thus promoting water loss.</p>	<p>Chlorthalidone: 12.5–100 mg qd; dosage above 100 mg qd usually does not increase effectiveness.</p> <p>Hydrochlorothiazide: 12.5–50 mg qd</p> <p>Indapamide: 1.25–2.5 mg qd</p> <p>Metolazone: 0.5–5 mg qd</p>	<p>In ALLHAT, chlorthalidone (12.5–25 mg qd) lowered systolic blood pressure (SBP) by approximately 12 mm Hg; lowered diastolic blood pressure (DBP) by approximately 9 mm Hg, depending on dose.¹</p> <p>In a study involving hydrochlorothiazide (12.5 mg qd in the first month and 25 mg qd in the second month), basal mean BP was decreased nearly 13 mm Hg.²</p> <p>In a study involving indapamide (2.5 mg qd) SBP/DBP were decreased by 5/2 mm Hg (PATS).³</p>	<p>Hypokalemia, hyperuricemia, and rise in blood lipids. Occasional urticaria and skin rash; postural hypotension; gastrointestinal (GI) distress; loss of appetite; impotence; vertigo.</p>	<p>Thiazide diuretics are indicated in the management of hypertension either as the sole therapeutic agent or to enhance the effect of other antihypertensive drugs in the more severe forms of hypertension. They should be used with caution in severe renal disease, which may precipitate azotemia, and in patients with impaired hepatic function or progressive liver disease. They are contraindicated in patients with anuria, hepatic coma, or precoma; or known allergy or hypersensitivity to these products or other sulfonamide-derived drugs.</p>
<p>Loop Diuretics:</p> <ol style="list-style-type: none"> 1. Bumetanide (Bumex[®]) 2. Furosemide (Lasix[®]) 3. Torsemide (Demadex Oral[®]) 	<p>Prevents the kidneys from retaining fluid by blocking the reabsorption of sodium.</p>	<p>Bumetanide: 0.5–2 mg bid</p> <p>Furosemide: 20–80 mg bid</p> <p>Torsemide: 2.5–10 mg qd</p>	<p>In a study involving bumetanide (1 mg qd) and furosemide (40 mg qd), overall SBP/DBP were 12/4 mm Hg lower during therapy with either loop diuretic therapy than with placebo treatment (BUFUL).⁴</p> <p>In a study involving torasemide (10–20 mg qd) SBP/DBP were decreased by 21/18 mm Hg.⁵</p>	<p>Hypokalemia, hyponatremia, low magnesium plus calcium, dehydration, postural hypotension, tinnitus, hyperuricemia, leading to gout. Increased sensitivity to sunlight.</p>	<p>Loop diuretics are indicated for the treatment of mild-to-moderate hypertension and in the management of edema associated with congestive heart failure, and hepatic and renal disease, including the nephritic syndrome. Hypertensive patients who cannot be adequately controlled with thiazides will probably also not be adequately controlled with furosemide alone.</p>

					The antihypertensive effects of torsemide are, like those of other diuretics, on the average greater in African-American patients (a low-renin population) than in non-African-American patients.
<p>Potassium-Sparing Diuretics:</p> <ol style="list-style-type: none"> 1. Amiloride hydrochloride (Midamor[®]) 2. Amiloride hydrochlorothiazide (Moduretic[®]) 3. Spironolactone (Aldactone[®]) 4. Triamterene (Dyrenium[®]) 5. Eplerenone (Inspra[®]) 	Acts on the kidneys to increase urine output without excreting potassium.	<p>Amiloride hydrochloride: 5–10 mg qd or bid</p> <p>Amiloride hydrochlorothiazide: 5 mg qd of anhydrous amiloride HCl and 50 mg qd of hydrochlorothiazide</p> <p>Spironolactone: 25–50 mg qd</p> <p>Triamterene: 50–100 mg qd or bid</p> <p>Eplerenone: 50–100 mg qd</p>	<p>In ASCOT, spironolactone reduced mean SBP/DBP by 21.9/9.5 mm Hg depending on dose.⁶</p> <p>In a study using eplerenone, SBP/DBP were reduced by 16.5/13.3 mm Hg.⁷</p>	Nervousness, skin rash, increased sensitivity to sunlight, confusion, irregular heart rhythm, shortness of breath, lethargy, and weakness.	Potassium-sparing diuretics are indicated for the treatment of hypertension or edema in patients who develop hypokalemia on hydrochlorothiazide alone. The use of potassium-sparing agents is often unnecessary in patients receiving diuretics for uncomplicated essential hypertension when such patients have a normal diet.
<p>Peripheral Adrenergic Inhibitor:</p> <ol style="list-style-type: none"> 1. Reserpine (Serpasil[®], Serpalan[®]) 	Depletes stores of serotonin and norepinephrine and reduces the re-uptake of catecholamines by adrenergic nerve terminals.	0.1–0.25 mg qd	Not widely used today as other more effective antihypertensive agents are available and tendency to cause depression. Do not use in patients receiving monoamine oxidase inhibitor therapy.	Increased respirations, increased GI motility and gastric secretion, miosis, decreased large-volume Ringer's lactate (LVRL), sexual dysfunction in men, depression.	Indicated for mild essential hypertension; also useful as adjunctive therapy with other antihypertensive agents in the more severe forms of hypertension. Extreme caution should be exercised in treating patients with a history of mental depression.
<p>Central Adrenergic Inhibitors:</p> <ol style="list-style-type: none"> 1. Clonidine hydrochloride (Catapres[®], Catapres-TTS[®], Clorpres[®], Duraclon[®]) 	Depletes stores of serotonin and norepinephrine and reduces the re-uptake of catecholamines by adrenergic nerve terminals.	<p>Clonidine hydrochloride: 0.1–0.8 mg bid</p> <p>Guanabenz acetate: 4–8 mg qd</p> <p>Guanfacine</p>	In a study using guanfacine hydrochloride, sitting SBP/DBP was reduced by 6–18/8–16 mm Hg in Caucasians and 0–19/2–15 mm Hg in African-	Increased respirations, increased GI motility and gastric secretion, miosis, decreased LVRL, sexual dysfunction in men.	Central adrenergic inhibitors are indicated in the treatment of hypertension. They may be employed alone or concomitantly with other

<ol style="list-style-type: none"> 2. Guanabenz acetate (Wytensin[®]) 3. Guanfacine hydrochloride (Tenex[®]) 4. Methyldopa (Aldomet[®], Aldochlor[®], Aldoril[®]) 		<p>hydrochloride: 0.5–2 mg qd</p> <p>Methyldopa: 250–1000 mg qd</p>	<p>Americans, depending on the dose.⁸</p>		<p>antihypertensive agents, especially thiazide-type diuretics.</p>
<p>Alpha-Adrenergic Blockers:</p> <ol style="list-style-type: none"> 1. Doxazosin mesylate (Cardura[®], Cardura[®] XL) 2. Prazosin hydrochloride (Minipress[®]) 3. Terazosin hydrochloride (Hytrin[®]) 	<p>Peripheral vasodilatation by selective, competitive inhibition of alpha-adrenergic receptors, thereby reducing peripheral resistance and BP.</p>	<p>Doxazosin mesylate: 1–16 mg qd</p> <p>Prazosin hydrochloride: 2–20 mg bid or tid</p> <p>Terazosin hydrochloride: 1–20 mg qd or bid</p>	<p>In a study of doxazosin mesylate versus placebo, sitting SBP/DBP was reduced by approximately 4.9/2.4 mm Hg and standing SBP/DBP by approximately 5.3/2.6 mm Hg.⁹</p>	<p>Alters lipid metabolism by decreasing LDL-C and VLDL-C, mild sexual dysfunction, dizziness, lightheadedness, headache, drowsiness, fatigue, nausea, vomiting, peripheral edema, nasal congestion, palpitations.</p>	<p>Alpha-adrenergic blockers are indicated for the treatment of hypertension and may be used alone or in combination with diuretics, beta-adrenergic blocking agents, calcium channel blockers or angiotensin-converting enzyme inhibitors (ACEIs).</p>
<p>Beta-Adrenergic Blockers (beta-blockers):</p> <ol style="list-style-type: none"> 1. Acebutolol (Sectral[®]) 2. Atenolol (Tenormin[®]) 3. Betaxolol hydrochloride (Betoptic[®], Betoptic S[®], Kerlone[®]) 4. Bisoprolol fumarate (Zebeta[®]) 5. Metoprolol tartrate (Lopressor[®]) 6. Metoprolol succinate (Toprol XL[®]) 7. Nadolol (Corgard[®]) 8. Penbutolol sulfate (Levitol[®]) 9. Pindolol (Visken[®]) 10. Propranolol hydrochloride (Inderal[®], Inderal[®] LA, Inderide[®], Innopran[®] XL) 	<p>Selectively blocks beta-adrenergic receptors in the heart and vascular smooth muscle causing decreased heart rate and cardiac output, decreased SBP and DBP, and suppression of renin release from the kidneys.</p>	<p>Acebutolol: 200–800 mg bid</p> <p>Atenolol: 25–100 mg qd</p> <p>Betaxolol hydrochloride: 5–20 mg qd</p> <p>Bisoprolol fumarate: 2.5–10 mg qd</p> <p>Metoprolol tartrate: 50–100 mg qd or bid</p> <p>Metoprolol succinate: 50–100 mg qd</p> <p>Nadolol: 40–120 mg qd</p> <p>Penbutolol sulfate: 10–40 mg qd</p> <p>Pindolol: 10–40 mg bid</p> <p>Propranolol</p>	<p>Studies showed that:</p> <p>Atenolol reduced mean SBP/DBP by 29/17 mm Hg, depending on dose (LIFE)¹⁰</p> <p>Bisoprolol fumarate decreased sitting SBP/DBP by 10.4–12.8/8.0–11.9 mm Hg, depending on dose¹¹</p> <p>Metoprolol succinate decreased sitting SBP/DBP by 6–8/4–7 mm Hg (placebo-corrected change from baseline) at 24 hrs post-dose, depending on dose¹²</p> <p>Penbutolol sulfate with doses of 10–80 mg qd reduced supine and standing SBP/DBP by 5–8/3–5 mm Hg greater than placebo, measured</p>	<p>Sinus bradycardia, atrioventricular block, hypotension, shortness of breath, depression, dizziness, fatigue, vivid dreams, diarrhea, nausea, vomiting, can increase the risk of developing type 2 diabetes, increased triglycerides, sexual dysfunction, pruritus, skin hyperpigmentation, alopecia, xerosis, and urticaria.</p>	<p>Beta-blockers are indicated in the treatment of mild-to-moderate arterial hypertension and may be used in combination with other antihypertensive agents, especially thiazide-type diuretics.</p>

		hydrochloride: 40–160 mg bid	24 hrs after dosing ¹³		
<p>Combined Alpha- and Beta-Adrenergic Blockers:</p> <ol style="list-style-type: none"> 1. Carvedilol (Coreg[®], Coreg CR[®]) 2. Labetalol (Normodyne[®], Trandate[®]) 	Antagonizes both alpha- and beta-receptors to cause vasodilation and decreased peripheral resistance, resulting in decreased BP without decreasing resting heart rate, cardiac output, or stroke volume.	<p>Carvedilol: 12.5–50 mg bid</p> <p>Labetalol: 200–800 mg bid</p>	Studies have shown that carvedilol reduced SBP/DBP by 6–11/4–9.2 mm Hg, depending on dose. Decreases in mean trough at 24 hrs were 3.3–8.4/2.8–7.4 mm Hg, depending on dose. ¹⁴	Vertigo, headache, bronchospasm, fatigue, rash, abdominal pain, diarrhea, peripheral edema, insomnia, somnolence, and palpitations.	Combined alpha- and beta-blockers are indicated for the treatment of essential hypertension, and can be combined with other antihypertensive agents, especially thiazide-type diuretics.
<p>Direct Vasodilators:</p> <ol style="list-style-type: none"> 1. Hydralazine hydrochloride (Apresoline[®], Hydra-Zide[®]) 2. Minoxidil (Loniten[®]) 	Direct vasodilatory effect in arterial smooth muscle causing a reduction in peripheral resistance and BP.	<p>Hydralazine hydrochloride: 25–100 mg bid</p> <p>Minoxidil: 2.5–80 mg qd or bid</p>	In patients who cannot tolerate ACEIs or angiotensin-receptor blockers (ARBs), hydralazine in combination with isosorbide dinitrate is an acceptable alternative in the treatment of heart failure.	Peripheral edema, headache, tachycardia, angina, hypertrichosis, mastalgia, and bullous rash.	Commonly used for hypertension in pregnancy. Injectable hydralazine is used as a first-line agent in the treatment of hypertensive emergencies.
<p>Calcium Antagonists (calcium channel blockers):</p> <ol style="list-style-type: none"> 1. Diltiazem hydrochloride (eg, Cardizem SR[®], Cardizem CD[®], Tiazac[®]) 2. Verapamil hydrochloride (eg, Isoptin[®] SR, Verelan[®], Calan[®]) 3. Amlodipine besylate (Norvasc[®]) 4. Felodipine (Plendil[®]) 5. Isradipine (DynaCirc[®], DynaCirc[®] CR[®]) 6. Nicardipine (Cardene[®], Cardene SR[®]) 7. Nifedipine (eg, Procardia[®], Adalat[®], Nifedical[®] XL) 8. Nisoldipine (Sular[®]) 	Inhibits the influx of extracellular calcium across the myocardial and vascular smooth muscle cell membranes causing the dilation of the coronary artery and systemic arteries.	<p>Diltiazem hydrochloride: 150–420 mg qd</p> <p>Verapamil hydrochloride: 120–480 mg qd or bid</p> <p>Amlodipine besylate: 2.5–10 mg qd</p> <p>Felodipine: 2.5–20 mg qd</p> <p>Isradipine: 2.5–10 mg bid</p> <p>Nicardipine: 60–120 mg bid</p> <p>Nifedipine: 30–60 mg qd</p> <p>Nisoldipine: 10–40 mg qd</p>	<p>Studies have shown that:</p> <p>Diltiazem hydrochloride reduced supine DBP in an apparent linear manner over the entire dose range; measured at trough, the reductions were 2.9–10.5 mm Hg¹⁵</p> <p>Amlodipine besylate reduced supine and standing SBP/DBP in patients with mild-to-moderate hypertension at 24 hours post-dose by about 13/7 mm Hg (standing) and 12/6 mm Hg (supine)¹⁶</p> <p>Felodipine reduced SBP/DBP at mean peak response by 9.4–18/4.7–10.8 mm Hg and at</p>	Peripheral edema, headache, dizziness, flushing, palpitations, fatigue, nausea/vomiting, abdominal pain, drowsiness, and angina.	Calcium antagonists or calcium channel blockers are indicated for the treatment of hypertension and may be used alone or in combination with other antihypertensive medications.

			<p>mean trough response by 2.7–10.0/2.5–6.0 mm Hg, depending on dose¹⁷</p> <p>Isradipine reduced SBP/DBP by 5.2–5.6/2.8–11.8 mm Hg, depending on dose¹⁸</p> <p>Nifedipine reduced mean trough supine SBP/DBP by 5.3–2.5/2.9–8.1 mm Hg, depending on dose¹⁹</p> <p>Nisoldipine reduced mean supine trough SBP/DBP by 8–15/3–10 mm Hg, depending on dose²⁰</p>		
<p>Angiotensin-Converting Enzyme Inhibitors (ACEIs):</p> <ol style="list-style-type: none"> 1. Benazepril hydrochloride (Lotensin[®] HCT) 2. Captopril (Capoten[®]) 3. Enalapril maleate (Vasotec[®], Vaseretic[®]) 4. Fosinopril sodium (Monopril[®]) 5. Lisinopril (Prinivil[®], Zestril[®]) 6. Moexipril (Univasc[®]) 7. Quinapril hydrochloride (Accupril[®]) 8. Ramipril (Altace[®]) 9. Trandolapril (Mavik[®]) 	<p>Competes with ACE or angiotensin I, blocking its conversion to angiotensin II, causing a decrease in BP and increased renin activity through lower angiotensin II plasma levels. Decreases peripheral vascular resistance and causes arterial dilation.</p>	<p>Benazepril hydrochloride: 10–40 mg qd</p> <p>Captopril: 25–100 mg bid</p> <p>Enalapril maleate: 5–40 mg qd or bid</p> <p>Fosinopril sodium: 10–40 mg qd</p> <p>Lisinopril: 10–40 mg qd</p> <p>Moexipril: 7.5–30 mg qd</p> <p>Quinapril hydrochloride: 10–80 mg qd</p> <p>Ramipril: 2.5–20 mg qd</p> <p>Trandolapril: 1–4 mg qd</p>	<p>Studies have shown that: Benazepril hydrochloride decreased supine SBP/DBP, 24 hours after dosing, by about 6–12/4–17 mm Hg, depending on dose²¹</p> <p>Enalapril lowered SBP/DBP by 14.8/14.1 mm Hg⁷</p> <p>Fosinopril sodium lowered supine or seated SBP/DBP at 24 hrs post-dosing by an average of 8–9/6–7 mm Hg more than placebo, depending on dose²²</p> <p>Lisinopril lowered SBP/DBP by 10.5/8.7 mm Hg¹</p> <p>Moexipril reduced sitting SBP/DBP effects at</p>	<p>Orthostatic hypotension, sinus tachycardia, fatigue, dizziness, syncope, headache, hyperkalemia, renal insufficiency, elevated serum creatinine or blood urea nitrogen, and cough.</p>	<p>ACEIs are indicated for the treatment of hypertension and may be used alone or in combination with thiazide diuretics.</p> <p>ACEIs have been shown to have less effect in African-Americans than in non-African-Americans.</p>

			<p>trough by 3–6/4–11 mm Hg, depending on dose²³</p> <p>Quinapril hydrochloride lowered SBP/DBP with a trough affect of about 5–11/3–7 mm Hg, depending on dose²⁴</p> <p>Ramipril lowered mean SBP/DBP by 3/3 mm Hg (HOPE)²⁵</p> <p>Trandolapril lowered supine or standing SBP/DBP 24 hours post-dose by an average of 7–10/4–5 mm Hg below placebo responses in non–African-Americans patients, and 4–6/3–4 mm Hg in African-American patients, depending on dose²⁶</p>		
<p>Angiotensin-Receptor Blockers (ARBs):</p> <ol style="list-style-type: none"> 1. Losartan (Cozaar[®]) 2. Valsartan (Diovan[®]) 3. Irbesartan (Avapro[®]) 4. Candesartan (Atacand[®]) 5. Olmesartan (Benicar[®]) 6. Telmisartan (Micardis[®]) 7. Eprosartan (Teveten[®]) 	<p>Blocks angiotensin II to decrease systemic vascular resistance without a marked change in heart rate.</p>	<p>Losartan: 25–100 mg qd or bid</p> <p>Valsartan: 80–320 mg qd or bid</p> <p>Irbesartan: 150–300 mg qd</p> <p>Candesartan: 8–32 mg qd</p> <p>Olmesartan: 20–40 mg qd</p> <p>Telmisartan: 20–80 mg qd</p> <p>Eprosartan: 400–800 mg qd or bid</p>	<p>Studies have shown that:</p> <p>The average for the range of placebo-corrected DBP/SBP reduction for losartan was 8.0/5.5 mm Hg; valsartan 7.5/4.0 mm Hg; irbesartan 10.0/6.5 mm Hg; for candesartan 10.0/6.0 mm Hg; for telmisartan 9.5/6 mm Hg; and for eprosartan 7.5/4.5 mm Hg²⁷</p> <p>Olmesartan reduced trough sitting SBP/DBP over placebo by approximately 10–12/6–7 mm Hg²⁸</p> <p>All reductions depend on dosage</p>	<p>Diarrhea, dyspepsia, orthostatic hypotension, syncope, dizziness, insomnia, angioedema, vasculitis, hyperkalemia, hyponatremia, elevated hepatic enzymes, hyperbilirubinemia, decreased hematocrit and hemoglobin.</p>	<p>ARBs are indicated for the treatment of hypertension and may be used alone or in combination with other antihypertensive agents.</p>

ALLHAT=Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; ASCOT=Anglo-Scandinavian Cardiac Outcomes Trial; bid=twice daily; BUFUL=BUmetanide and FUroseamide on Lipid profile study; HOPE=Heart Outcomes Prevention Evaluation Study; LDL-C=low-density lipoprotein cholesterol; PATS=Post-stroke Antihypertensive Treatment study; qd=once daily; tid=three times daily; VLDL-C=very low-density lipoprotein cholesterol

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