

# COMBINATION TREATMENTS FOR HYPERTENSION (part 1 of 3)

Generic	Brand & Company	Strengths	Formulation	Usual Adult Dose
<b>**ACE INHIBITOR + THIAZIDE DIURETIC</b>				
benazepril + HCTZ	<b>LOTENSIN HCT</b> (Novartis)	5mg/6.25mg 10mg/12.5mg 20mg/12.5mg 20mg/25mg	scored tabs	To switch from benazepril monotherapy: see literature. Or, titrate individual components.
captopril + HCTZ	<b>CAPOZIDE</b> (Par)	25mg/15mg 25mg/25mg 50mg/15mg 50mg/25mg	scored tabs	Take 1 hr before meals. As initial therapy: one 25/15 tab daily; adjust at 6 wk intervals. Previously titrated: use same doses as individual components. Usual max 150mg captopril, 50mg HCTZ daily.
enalapril + HCTZ	<b>VASERETIC</b> (Valeant)	5mg/25mg	tabs	Switching from monotherapy with either component: start with Vaseretic 10-25 once daily, then adjust; max 20mg enalapril/day and 50mg HCTZ/day. Allow 2-3 weeks for titration of HCTZ component. Or, substitute for individually titrated components.
lisinopril + HCTZ	<b>PRINZIDE</b> (Merck) <b>ZESTORETIC</b> (AstraZeneca)	10mg-12.5mg 20mg-12.5mg 20mg-25mg	tabs	Not for initial therapy. Usual maintenance: 1-2 tabs of 20-12.5 or 20-25 once daily, or 1 tab of 10-12.5 once daily. Switching from monotherapy with either component: start with Zestoretic 10-12.5 or 20-12.5 once daily, then adjust. Allow 2-3 weeks for titration of HCTZ component. If on diuretic: if possible, suspend diuretic for 2-3 days, then adjust. Or, substitute for individually titrated components.
moexipril + HCTZ	<b>UNIRETIC</b> (UCB)	7.5mg/12.5mg 15mg/12.5mg 15mg/25mg	scored tabs	Not for initial therapy. Take 1 hour before a meal. Switching from monotherapy with either component: 1 tab once daily; adjust at 2-3 week intervals; usual max 30mg/50mg per day. Or, substitute for individually titrated components.
quinapril + HCTZ	<b>ACCURETIC</b> (Pfizer)	10mg/12.5mg† 20mg/12.5mg† 20mg/25mg	tabs († = scored)	Not for initial therapy. Previously titrated: use same doses as individual components. Switching from quinapril monotherapy: initially one Accuretic 10/12.5 tab or one Accuretic 20/12.5 tab once daily; allow 2-3 weeks before increasing HCTZ component. Switching from HCTZ 25mg/day monotherapy: initially one Accuretic 10/12.5 tab daily or one Accuretic 20/12.5 tab once daily. Adjust based on response and serum potassium. CrCl ≤30mL/min: not recommended.
<b>ACE INHIBITOR + CALCIUM CHANNEL BLOCKER (DIPHENYLALKYLAMINE)</b>				
trandolapril + verapamil (ext-rel)	<b>TARKA</b> (Abbott)	1mg/240mg 2mg/180mg 2mg/240mg 4mg/240mg	tabs	Not for initial therapy. Titrate individual components. Take with food. ≥18yrs: 1 tab daily.
<b>**ANGIOTENSIN II RECEPTOR BLOCKER + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE)</b>				
telmisartan + amlodipine	<b>TWYNSTA</b> (Boehringer Ingelheim)	40mg/5mg 40mg/10mg 80mg/5mg 80mg/10mg	tabs	Take once daily. Initial therapy: 40/5mg or 80/5mg; may titrate at 2-week intervals to max 80/10mg. Add-on therapy: may be used if not controlled on monotherapy; if dose-limiting adverse reactions with amlodipine 10mg, switch to 40/5mg tab. Replacement therapy: may be substituted for the titrated components. Renal and/or hepatic impairment: titrate slower. ≥75yrs, or hepatic impairment: not for initial use (initially use amlodipine alone, or add amlodipine 2.5mg to telmisartan).
<b>ANGIOTENSIN II RECEPTOR BLOCKER + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + THIAZIDE DIURETIC</b>				
olmesartan + amlodipine + HCTZ	<b>TRIBENZOR</b> (Daiichi Sankyo)	20mg/5mg/12.5mg 40mg/5mg/12.5mg 40mg/5mg/25mg 40mg/10mg/12.5mg 40mg/10mg/25mg	tabs	One tablet daily. Titrate at 2-week intervals; max one 40/10/25mg tablet daily. Replacement therapy: may be substituted for individually titrated components. Add-on/switch therapy: may be used to provide additional BP lowering for patients not adequately controlled on max tolerated, labeled or usual doses of any two antihypertensive classes: ARBs, CCBs, and diuretics.
<b>**ANGIOTENSIN II RECEPTOR BLOCKER + THIAZIDE DIURETIC</b>				
azilsartan + chlorthalidone	<b>EDARBYCLOR</b> (Takeda)	40mg/12.5mg 40mg/25mg	tabs	Initially 40/12.5mg once daily. May increase to 40/25mg after 2-4 weeks as needed. Max: 40/25mg. Patients titrated to the individual components: may give corresponding dose of Edarbyclor. See literature.
candesartan + HCTZ	<b>ATACAND HCT</b> (AstraZeneca)	16mg/12.5mg 32mg/12.5mg 32mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. BP not controlled on HCTZ 25mg once daily, or controlled but serum potassium decreased: one Atacand HCT 16-12.5 tab once daily. BP not controlled on candesartan 32mg per day: initially one Atacand HCT 32-12.5 tab once daily; may increase to 32-25 once daily. CrCl ≤30mL/min: not recommended.

(continued)

# COMBINATION TREATMENTS FOR HYPERTENSION (part 2 of 3)

Generic	Brand & Company	Strengths	Formulation	Usual Adult Dose
<b>**ANGIOTENSIN II RECEPTOR BLOCKER + THIAZIDE DIURETIC (continued)</b>				
eprosartan + HCTZ	<b>TEVETEN HCT</b> (Abbott)	600mg/12.5mg 600mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. One Teveten HCT 600mg/12.5mg tab once daily; after 2-3 weeks may increase to one Teveten HCT 600mg/25mg tab once daily. May add eprosartan 300mg once daily in the PM if additional BP control is needed at trough.
irbesartan + HCTZ	<b>AVALIDE</b> (Sanofi Aventis)	150mg/12.5mg 300mg/12.5mg	tabs	Take once daily. Not controlled on monotherapy: initially 150/12.5mg, titrate to 300/12.5mg then 300/25mg if needed. Replacement therapy: may be substituted for titrated components. Initial therapy: start at 150/12.5mg for 1-2 weeks, then titrate as needed up to max 300/25mg. Maximum effects within 2-4 weeks after dose change. CrCl $\leq$ 30mL/min: not recommended.
losartan + HCTZ	<b>HYZAAR</b> (Merck)	50mg-12.5mg 100mg-12.5mg 100mg-25mg	tabs	$\geq$ 18yrs: One 50-12.5mg tab once daily; may increase after about 3 weeks (2-4 weeks for severe HTN) to two 50-12.5mg tabs once daily or one 100-25mg tab once daily. Titrate components: see literature. HTN with LVH: switch from losartan monotherapy (see literature). CrCl <30mL/min: not recommended.
olmesartan + HCTZ	<b>BENICAR HCT</b> (Daichi Sankyo)	20mg/12.5mg 40mg/12.5mg 40mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. Individualize. $\geq$ 18yrs: BP not controlled on olmesartan or HCTZ alone: one tab once daily; may titrate at 2-4 week intervals; usual max 40mg/25mg once daily. CrCl $\leq$ 30mL/min: not recommended. Volume depleted: reduce dose.
telmisartan + HCTZ	<b>MICARDIS HCT</b> (Boehringer Ingelheim)	40mg/12.5mg 80mg/12.5mg 80mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. BP not controlled on telmisartan 80mg/day: one Micardis HCT 80mg/12.5mg tab once daily; may titrate to 160mg/25mg. BP not controlled on HCTZ 25mg/day: one Micardis HCT 80mg/12.5mg tab or 80mg/25mg tab once daily; may titrate to 160mg/25mg if BP uncontrolled after 2-4 weeks. BP controlled on HCTZ 25mg/day but hypokalemic: One Micardis HCT 80mg/12.5mg tab once daily. CrCl $\leq$ 30mL/min: not recommended. Hepatic insufficiency or biliary obstruction: initially one Micardis HCT 40mg/12.5mg tab once daily; monitor closely. Severe hepatic impairment: not recommended.
valsartan + HCTZ	<b>DIOVAN HCT</b> (Novartis)	80mg/12.5mg 160mg/12.5mg 160mg/25mg 320mg/12.5mg 320mg/25mg	tabs	Take once daily. Add-on or initial therapy and not volume-depleted: Initially 160mg/12.5mg; may increase after 1-2 weeks up to max 320mg/25mg. Replacement therapy: may be substituted for the titrated components. Maximum effects within 2-4 weeks after dose change. CrCl $\leq$ 30mL/min: not recommended.
<b><math>\beta</math>-BLOCKER + THIAZIDE DIURETIC</b>				
atenolol + chlorthalidone	<b>TENORETIC</b> (AstraZeneca)	50mg/25mg† 100mg/25mg	tabs († = scored)	Switching from monotherapy: initially one Tenoretic 50 tab daily; may increase to one Tenoretic 100 tab daily. CrCl 15-35mL/min: max 50mg atenolol/day. CrCl <15mL/min: max 50mg atenolol every other day.
bisoprolol + HCTZ	<b>ZIAC</b> (Teva)	2.5mg/6.25mg 5mg/6.25mg 10mg/6.25mg	tabs	Initially one 2.5mg/6.25mg tab once daily. Adjust at 14-day intervals; max two 10mg/6.25mg tabs (20mg bisoprolol + 12.5mg HCTZ) once daily.
metoprolol tartrate + HCTZ	<b>LOPRESSOR HCT</b> (Novartis)	50mg/25mg 100mg/25mg 100mg/50mg	scored tabs	Titrate individual components.
metoprolol succinate extended-release + HCTZ	<b>DUTOPROL</b> (AstraZeneca)	25mg/12.5mg 50mg/12.5mg 100mg/12.5mg	tabs	Individualize. Take once daily. Titrate individual components. Severe renal impairment: not recommended. Moderate hepatic impairment: consider initiating with lower HCTZ component.
nadolol + bendroflumethiazide	<b>CORZIDE</b> (King)	40mg/5mg 80mg/5mg	scored tabs	Titrate components. Renally impaired: increase dosing interval; see literature.
propranolol + HCTZ	<b>INDERIDE</b> (Akrimax)	40mg/25mg	scored tabs	Titrate individual components.
<b>**CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + ACE INHIBITOR</b>				
amlodipine + benazepril	<b>LOTREL</b> (Novartis)	2.5mg/10mg 5mg/10mg 5mg/20mg 5mg/40mg 10mg/20mg 10mg/40mg	caps	Not for initial therapy. Titrate components (amlodipine or another dihydropyridine CCB, or benazepril or another ACEI). CrCl $\leq$ 30mL/min per 1.73m <sup>2</sup> : not recommended. Hepatic impairment, or small, elderly, or frail patients: initially 2.5mg/10mg strength.

(continued)

# COMBINATION TREATMENTS TREATMENTS (part 3 of 3)

Generic	Brand & Company	Strengths	Formulation	Usual Adult Dose
<b>**CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + ANGIOTENSIN II RECEPTOR BLOCKER</b>				
amlodipine + olmesartan	<b>AZOR</b> (Daiichi Sankyo)	5mg/20mg 5mg/40mg 10mg/20mg 10mg/40mg	tabs	Take once daily. Initial therapy: initially 5/20mg; may increase after 1–2 weeks up to max 10mg/40mg; ≥75yrs old or hepatic impairment: not recommended. Replacement therapy: may be substituted for titrated components. Add-on therapy: may be used if not controlled on monotherapy. Individualize; titrate at 2-week intervals up to max 10/40mg once daily, usually by increasing dose of one or both components if BP not controlled on prior therapy. Maximum effects within 2 weeks after dose change.
amlodipine + valsartan	<b>EXFORGE</b> (Novartis)	5mg/160mg 5mg/320mg 10mg/160mg 10mg/320mg	tabs	Take once daily. Initial therapy and not volume depleted: Initially 5/160mg; may increase after 1–2 weeks up to max 10/320mg. Add-on therapy: may be used if not controlled on monotherapy; if inadequate response after 3–4 weeks, may titrate up to max 10/320mg. Replacement therapy: may be substituted for the titrated components. Maximum effects within 2 weeks after dose change.

<b>CENTRAL α-AGONIST + THIAZIDE DIURETIC</b>				
methylodopa + HCTZ	<b>ALDORIL</b> (Merck)	250mg/15mg 250mg/25mg	tabs	Titrate individual components. Initially 1 Aldoril 15 tab 2–3 times daily or 1 Aldoril 25 tab twice daily or 1 Aldoril D30 tab once daily or 1 Aldoril D50 tab once daily.
	<b>ALDORIL D</b> (Merck)	500mg/30mg 500mg/50mg		

<b>DIRECT RENIN INHIBITOR + ANGIOTENSIN II RECEPTOR BLOCKER</b>				
aliskiren + valsartan	<b>VALTURNA</b> (Novartis)	150mg/160mg 300mg/320mg	tabs	Take consistently with regard to meals. 1 tablet once daily. Add-on or initial therapy and not volume-depleted: initially 150/160mg; may increase after 2–4 weeks to max 300/320mg. Replacement therapy: substitute for the titrated components.

<b>DIRECT RENIN INHIBITOR + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE)</b>				
aliskiren + amlodipine	<b>TEKAMLO</b> (Novartis)	150mg/5mg 150mg/10mg 300mg/5mg 300mg/10mg	tabs	Give once daily, consistently with regard to meals. Initial therapy: One 150mg/5mg tablet daily. Add-on: switch when BP is not controlled with aliskiren or any DHP CCB alone. Replacement therapy: switch from previously-titrated components. Titrate at 2 to 4-week intervals (slow titration in hepatic impairment or heart failure); max one 300mg/10mg tablet daily.

<b>DIRECT RENIN INHIBITOR + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + THIAZIDE DIURETIC</b>				
aliskiren + amlodipine + HCTZ	<b>AMTURNIDE</b> (Novartis)	150/5/12.5mg 300/5/12.5mg 300/5/25mg 300/10/12.5mg 300/10/25mg	tabs	Take once daily. Titrate at 2-week intervals; max one 300/10/25mg tablet daily. Replacement: may substitute for individually titrated components. Add-on/switch: if not adequately controlled on any two of the following: aliskiren, dihydropyridine CCB, thiazide diuretics. May switch with a lower dose of any component that causes dose-limiting ADRs. ≥75 years or severe hepatic impairment: initially amlodipine 2.5mg/day (not available). Concomitant simvastatin: see Interactions.

<b>DIRECT RENIN INHIBITOR + THIAZIDE DIURETIC</b>				
aliskiren + HCTZ	<b>TEKTURNA HCT</b> (Novartis)	150mg/12.5mg 150mg/25mg 300mg/12.5mg 300mg/25mg	tabs	Take consistently with regard to meals (absorption reduced by high-fat meals). ≥18yrs: 1 tablet once daily. Add-on or initial therapy and not volume-depleted: initially 150mg/12.5mg; may increase after 2–4 weeks up to max 300mg/25mg. Replacement therapy: substitute for the titrated components. Max effect usually seen at 4 weeks.

<b>DIURETIC COMBINATION (K<sup>+</sup> SPARING + THIAZIDE)</b>				
amiloride + HCTZ	(Various)	5mg/50mg	scored tabs	Initially 1 tab daily with food. May increase to 2 tabs daily in single or divided doses.
spironolactone + HCTZ	<b>ALDACTAZIDE</b> (Pfizer)	25mg/25mg 50mg/50mg†	tabs († = scored)	Usual maintenance: 50–100mg each of spironolactone and HCTZ daily in single or divided doses.
triamterene + HCTZ	<b>DYAZIDE</b> (GSK)	37.5mg/25mg	caps	1–2 caps once daily.
	<b>MAXZIDE</b> (Bertek)	37.5mg/25mg 75mg/50mg	scored tabs	1–2 tab(s) of 37.5/25 daily or 1 tab of 75/50 daily.

## NOTES

Caps = capsules; tabs = tablets; ext-rel = extended-release; HCTZ = hydrochlorothiazide. Regimens shown are from manufacturer's suggested guidelines. Doses should be individualized. Some of the products listed above have additional indications. See Alphabetical and Section indexes.

## RECOMMENDATION FOR DRUG COMBINATION IN UNCOMPLICATED HYPERTENSION<sup>1</sup>

**Preferred Combination	Acceptable Combination	NOT Preferred Combination
<ul style="list-style-type: none"> <li>• ACEI + thiazide</li> <li>• ACEI + dihydropyridine CCB</li> <li>• ARB + thiazide</li> <li>• ARB + dihydropyridine CCB</li> </ul>	<ul style="list-style-type: none"> <li>• CCB + thiazide</li> <li>• Thiazide + potassium-sparing diuretic</li> <li>• Aliskiren + thiazide or CCB</li> <li>• β-blocker + diuretic or dihydropyridine CCB</li> </ul>	<ul style="list-style-type: none"> <li>• ACEI + ARB</li> <li>• β-blocker + ACEI or ARB</li> <li>• β-blocker + Nondihydropyridine CCB</li> <li>• β-blocker + Central acting (clonidine, etc)</li> </ul>

ACEI = angiotensin-converting enzyme inhibitor; CCB = calcium channel blocker; ARB = angiotensin II receptor blocker

<sup>1</sup> Adapted from Gradman AH, Basile JN, Carter BL, et al. Combination therapy in hypertension. *Journal of the American Society of Hypertension* 2010; 4:42-50.

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