

COMBINATION HYPERTENSION TREATMENT (Part 1 of 4)

RECOMMENDATION FOR DRUG COMBINATION IN UNCOMPLICATED HYPERTENSION†

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

*ACE INHIBITOR + THIAZIDE DIURETIC

Generic	Brand	Strength	Form	Usual Adult Dose
benazepril/HCTZ	Lotensin HCT	5mg/6.25mg, 10mg/12.5mg, 20mg/12.5mg, 20mg/25mg	scored tabs	<i>To switch from benazepril monotherapy:</i> initially 10/12.5mg once daily. Or, titrate individual components.
captopril/HCTZ	Capozide	25mg/15mg, 25mg/25mg, 50mg/15mg, 50mg/25mg	scored tabs	Take 1hr before meals. <i>As initial therapy:</i> one 25/15 tab daily; adjust at 6wk intervals. <i>Previously titrated:</i> use same doses as individual components. Usual max 150mg captopril, 50mg HCTZ daily.
enalapril/HCTZ	Vaseretic	10mg/25mg	tabs	<i>Switching from monotherapy with either component:</i> start with 10/25 once daily, then adjust; max 20mg enalapril/day and 50mg HCTZ/day. Allow 2–3wks for titration of HCTZ component. Or, substitute for individually titrated components.
lisinopril/HCTZ	Prinzide	10mg/12.5mg, 20mg/12.5mg+	tabs	Not for initial therapy. Initially 10mg/12.5mg or 20mg/12.5mg; increase HCTZ dose 2–3wks after. Max 80mg/50mg daily. <i>CrCl <30mL/min:</i> not recommended.
	Zestoretic	10mg/12.5mg, 20mg/12.5mg, 20mg/25mg	tabs	<i>Switching from monotherapy with either component:</i> initially 10/12.5 or 20/12.5 once daily, then after 2–3wks titrate HCTZ component. <i>If on diuretic:</i> if possible, suspend diuretic for 2–3 days, then adjust. Or, substitute for individually titrated components.
moexipril/HCTZ	Uniretic	7.5mg/12.5mg, 15mg/12.5mg, 15mg/25mg	scored tabs	Take 1hr before a meal. <i>Switching from monotherapy with either component:</i> 1 tab once daily; adjust at 2–3-week intervals; usual max 30mg/50mg per day. Or, substitute for individually titrated components.
quinapril/HCTZ	Accuretic	10mg/12.5mg+, 20mg/12.5mg+, 20mg/25mg	tabs	Not for initial therapy. <i>Previously titrated:</i> use same doses as individual components. <i>Switching from quinapril monotherapy:</i> initially one 10/12.5 tab or one 20/12.5 tab once daily; allow 2–3wks before increasing HCTZ component. <i>Switching from HCTZ 25mg/day monotherapy:</i> initially one 10/12.5 tab daily or one 20/12.5 tab once daily. Adjust based on response and serum potassium. <i>CrCl ≤30mL/min:</i> not recommended.

ACE INHIBITOR + CALCIUM CHANNEL BLOCKER (DIPHENYLALKYLAMINE)

trandolapril/ verapamil (ext-rel)	Tarka	1mg/240mg, 2mg/180mg, 2mg/240mg, 4mg/240mg	tabs	Titrate individual components. Take with food. 1 tab daily.
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ANGIOTENSIN II RECEPTOR BLOCKER + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + THIAZIDE DIURETIC

olmesartan/ amlodipine/HCTZ	Tribenzor	20mg/5mg/12.5mg, 40mg/5mg/12.5mg, 40mg/5mg/25mg, 40mg/10mg/12.5mg, 40mg/10mg/25mg	tabs	One tab daily. Titrate at 2-week intervals; max one 40/10/25mg tablet daily. <i>Replacement therapy:</i> may be substituted for individually titrated components. <i>Add-on/switch therapy:</i> 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.
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*ANGIOTENSIN II RECEPTOR BLOCKER + THIAZIDE DIURETIC

azilsartan/ chlorthalidone	Edarbyclor	40mg/12.5mg, 40mg/25mg	tabs	Initially 40/12.5mg once daily. May increase to 40/25mg after 2–4wks as needed. <i>Max:</i> 40/25mg. <i>Patients titrated to the individual components:</i> may give corresponding dose of Edarbyclor. See full labeling.
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COMBINATION HYPERTENSION TREATMENTS (Part 2 of 4)

Generic	Brand	Strength	Form	Usual Adult Dose
*ANGIOTENSIN II RECEPTOR BLOCKER + THIAZIDE DIURETIC (continued)				
candesartan/HCTZ	Atacand HCT	16mg/12.5mg, 32mg/12.5mg, 32mg/25mg	scored tabs	Not for initial therapy. May be substituted for titrated components. <i>BP not controlled on HCTZ 25mg once daily, or controlled but serum potassium decreased:</i> one 16/12.5 tab once daily. <i>BP not controlled on candesartan 32mg per day:</i> initially one 32/12.5 tab once daily; may increase to 32/25 once daily. <i>CrCl</i> $\leq 30\text{mL/min}$: not recommended.
eprosartan/HCTZ	Teveten HCT	600mg/12.5mg, 600mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. One 600mg/12.5mg tab once daily; after 2–3wks may increase to one 600mg/25mg tab once daily. May add eprosartan 300mg once daily in the PM if additional BP control is needed at trough.
irbesartan/HCTZ	Avalide	150mg/12.5mg, 300mg/12.5mg	tabs	Take once daily. <i>Not controlled on monotherapy:</i> initially 150/12.5mg, titrate to 300/12.5mg then 300/25mg if needed. <i>Replacement therapy:</i> may be substituted for titrated components. <i>Initial therapy:</i> start at 150/12.5mg for 1–2wks, then titrate as needed up to max 300/25mg. Maximum effects within 2–4wks after dose change. <i>CrCl</i> $\leq 30\text{mL/min}$: not recommended.
losartan/HCTZ	Hyzaar	50mg/12.5mg, 100mg/12.5mg, 100mg/25mg	tabs	One 50/12.5mg tab once daily; may increase after about 3wks (2–4wks for severe HTN) to two 50/12.5mg tabs once daily or one 100/25mg tab once daily. <i>Titrate components:</i> see literature. <i>HTN with LVH:</i> switch from losartan monotherapy (see literature). <i>CrCl</i> $< 30\text{mL/min}$: not recommended.
olmesartan/HCTZ	Benicar HCT	20mg/12.5mg, 40mg/12.5mg, 40mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. Individualize. <i>BP not controlled on olmesartan or HCTZ alone:</i> one tab once daily; may titrate at 2–4-week intervals; usual max 40mg/25mg once daily. <i>CrCl</i> $\leq 30\text{mL/min}$: not recommended. <i>Volume depleted:</i> reduce dose.
telmisartan/HCTZ	Micardis HCT	40mg/12.5mg, 80mg/12.5mg, 80mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. <i>BP not controlled on telmisartan 80mg/day:</i> one 80mg/12.5mg tab once daily; may titrate to 160mg/25mg. <i>BP not controlled on HCTZ 25mg/day:</i> one 80mg/12.5mg tab or 80mg/25mg tab once daily; may titrate to 160mg/25mg if BP uncontrolled after 2–4wks. <i>BP controlled on HCTZ 25mg/day but hypokalemic:</i> One 80mg/12.5mg tab once daily. <i>CrCl</i> $\leq 30\text{mL/min}$: not recommended. <i>Hepatic insufficiency or biliary obstruction:</i> initially one 40mg/12.5mg tab once daily; monitor closely. <i>Severe renal or hepatic impairment:</i> not recommended.
valsartan/HCTZ	Diovan HCT	80mg/12.5mg, 160mg/12.5mg, 160mg/25mg, 320mg/12.5mg, 320mg/25mg	tabs	Take once daily. <i>Add-on or initial therapy and not volume-depleted:</i> Initially 160mg/12.5mg; may increase after 1–2wks up to max 320mg/25mg. <i>Replacement therapy:</i> may be substituted for the titrated components. Maximum effects within 2–4wks after dose change. <i>CrCl</i> $\leq 30\text{mL/min}$: not recommended.
BETA-BLOCKER + THIAZIDE DIURETIC				
atenolol/ chlorthalidone	Tenoretic	50mg/25mg+, 100mg/25mg	tabs	<i>Switching from monotherapy:</i> initially one 50mg/25mg tab daily; may increase to one 100mg/25mg tab daily. <i>CrCl</i> 15–35mL/min: max 50mg atenolol/day. <i>CrCl</i> $< 15\text{mL/min}$: max 50mg atenolol every other day.
bisoprolol/HCTZ	Ziac	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 once daily.

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COMBINATION HYPERTENSION TREATMENTS (Part 3 of 4)

Generic	Brand	Strength	Form	Usual Adult Dose
BETA-BLOCKER + THIAZIDE DIURETIC (continued)				
metoprolol tartrate/ HCTZ	 Lopressor HCT	50mg/25mg, 100mg/25mg, 100mg/50mg	scored tabs	Titrate individual components.
metoprolol succinate extended-release/ HCTZ	Dutoprol	25mg/12.5mg, 50mg/12.5mg, 100mg/12.5mg	tabs	Individualize. Take once daily. Titrate as needed every 2wks up to max 200/25mg. <i>Severe renal impairment:</i> not recommended. <i>Moderate hepatic impairment:</i> consider initiating with lower HCTZ component.
nadolol/ bendroflumethiazide	Corzide	40mg/5mg, 80mg/5mg	scored tabs	Titrate components. <i>Renally impaired:</i> increase dosing interval; see literature.
propranolol/HCTZ	Inderide	40mg/25mg	scored tabs	Titrate individual components.
*CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + ACE INHIBITOR				
amlodipine/ benazepril	Lotrel	2.5mg/10mg, 5mg/10mg, 5mg/20mg, 5mg/40mg, 10mg/20mg, 10mg/40mg	caps	<i>Not adequately controlled with dihydropyridine CCB, ACE inhibitor, unable to achieve BP control with amlodipine without developing edema:</i> Initially 2.5mg/10mg once daily; may titrate up to 10mg/40mg once daily if BP remains uncontrolled. <i>Replacement therapy:</i> may be substituted for titrated components. <i>CrCl</i> \leq 30mL/min: not recommended.
*CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + ANGIOTENSIN II RECEPTOR BLOCKER				
amlodipine/ olmesartan	Azor	5mg/20mg, 5mg/40mg, 10mg/20mg, 10mg/40mg	tabs	Take once daily. <i>Initial therapy:</i> initially 5/20mg; may increase after 1–2wks up to max 10mg/40mg; \geq 75yrs old or hepatic impairment: not recommended. <i>Replacement therapy:</i> may be substituted for titrated components. <i>Add-on therapy:</i> 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 2wks after dose change.
amlodipine/ telmisartan	Twynsta	5mg/40mg, 5mg/80mg, 10mg/40mg, 10mg/80mg	tabs	Take once daily. <i>Initial therapy:</i> 5/40mg or 5/80mg; may titrate at 2-week intervals to max 10/80mg. <i>Add-on therapy:</i> may be used if not controlled on monotherapy; if dose-limiting adverse reactions with amlodipine 10mg, switch to 5/40mg tab. <i>Replacement therapy:</i> may be substituted for the titrated components. <i>Renal and/or hepatic impairment:</i> titrate slower. \geq 75yrs, or hepatic impairment: not for initial use (initially use amlodipine alone, or add amlodipine 2.5mg to telmisartan).
amlodipine/ valsartan	Exforge	5mg/160mg, 5mg/320mg, 10mg/160mg, 10mg/320mg	tabs	Take once daily. <i>Initial therapy and not volume depleted:</i> Initially 5/160mg; may increase after 1–2wks up to max 10/320mg. <i>Add-on therapy:</i> may be used if not controlled on monotherapy; if inadequate response after 3–4wks, may titrate up to max 10/320mg. <i>Replacement therapy:</i> may be substituted for the titrated components. Maximum effects within 2wks after dose change.
CENTRAL ALPHA-AGONIST + THIAZIDE DIURETIC				
methylodopa/HCTZ	—	250mg/15mg, 250mg/25mg	tabs	Titrate individual components. Initially one 250mg/15mg tab 2–3 times daily or one 250mg/25mg tab 2 times daily.
DIRECT RENIN INHIBITOR + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE)				
aliskiren/amlodipine	Tekamlo	150mg/5mg, 150mg/10mg, 300mg/5mg, 300mg/10mg	tabs	Take once daily, consistently with regard to meals. Initially one 150mg/5mg tab daily. <i>Add-on:</i> switch when BP is not controlled with aliskiren or any DHP CCB alone. <i>Replacement therapy:</i> switch from previously-titrated components. Titrate at 2–4-week intervals (slow titration in hepatic impairment or heart failure); max one 300mg/10mg tab daily.

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COMBINATION HYPERTENSION TREATMENTS (Part 4 of 4)

Generic	Brand	Strength	Form	Usual Adult Dose
DIRECT RENIN INHIBITOR + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + THIAZIDE DIURETIC				
aliskiren/amlodipine/ HCTZ	Amturnide	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 tab daily. <i>Replacement:</i> may substitute for individually titrated components. <i>Add-on/switch:</i> 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 yrs or severe hepatic impairment: initially amlodipine 2.5mg/day (not available). <i>Concomitant simvastatin:</i> see Interactions
DIRECT RENIN INHIBITOR + THIAZIDE DIURETIC				
aliskiren/HCTZ	Tekturna HCT	150mg/12.5mg 150mg/25mg 300mg/12.5mg 300mg/25mg	tabs	Take consistently with regard to meals. 1 tab once daily. <i>Add-on or initial therapy and not volume-depleted:</i> initially 150mg/12.5mg; may increase after 2–4wks up to max 300mg/25mg. <i>Replacement therapy:</i> substitute for the titrated components.
K⁺ SPARING DIURETIC + THIAZIDE DIURETIC				
amiloride/HCTZ	—	5mg/50mg	scored tabs	Initially 1 tab daily with food. May increase to 2 tabs daily in single or divided doses.
spironolactone/HCTZ	Aldactazide	25mg/25mg, 50mg/50mg+	tabs	<i>Usual maintenance:</i> 50/100mg each of spironolactone and HCTZ daily in single or divided doses.
triamterene/HCTZ	Dyazide Maxzide	37.5mg/25mg 37.5mg/25mg, 75mg/50mg	caps scored tabs	1–2 caps once daily. 1–2 tabs of 37.5/25 daily or 1 tab of 75/50 daily.

NOTES

Key: HCTZ = hydrochlorothiazide; + = scored.

Not an inclusive list of medications, official indications, and/or dosing details. Please see drug monograph at www.eMPR.com and/or contact company for full drug labeling.

REFERENCES

†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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