COMBINATION TREATMENTS FOR HYPERTENSION (Part 1 of 3)

Generic	Brand & Company	Strengths	Formulation	Usual Adult Dose
****ACE INHIBITOR + THIAZIDE DIURETIC**				
benazepril + HCTZ	**LOTENSIN HCT** *(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	**CAPOZIDE** *(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	**VASERETIC** *(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	**PRINZIDE** *(Merck)*	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.
	ZESTORETIC *(AstraZeneca)*			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	**UNIRETIC** *(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	**ACCURETIC** *(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.
ACE INHIBITOR + CALCIUM CHANNEL BLOCKER (DIPHENYLALKYLAMINE)				
trandolapril + verapamil (ext-rel)	**TARKA** *(AbbVie)*	1mg/240mg 2mg/180mg 2mg/240mg 4mg/240mg	tabs	Not for initial therapy. Titrate individual components. Take with food. ≥18yrs: 1 tab daily.
****ANGIOTENSIN II RECEPTOR BLOCKER + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE)**				
telmisartan + amlodipine	**TWYNSTA** *(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).
ANGIOTENSIN II RECEPTOR BLOCKER + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + THIAZIDE DIURETIC				
olmesartan + amlodipine + HCTZ	**TRIBENZOR** *(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.
****ANGIOTENSIN II RECEPTOR BLOCKER + THIAZIDE DIURETIC**				
azilsartan + chlorthalidone	**EDARBYCLOR** *(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	**ATACAND HCT** *(AstraZeneca)*	16mg/12.5mg 32mg/12.5mg 32mg/25mg	scored 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
****ANGIOTENSIN II RECEPTOR BLOCKER + THIAZIDE DIURETIC (continued)**				
eprosartan + HCTZ	**TEVETEN HCT** *(AbbVie)*	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	**AVALIDE** *(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 ≤30mL/min: not recommended.
losartan + HCTZ	**HYZAAR** *(Merck)*	50mg–12.5mg 100mg–12.5mg 100mg–25mg	tabs	≥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	**BENICAR HCT** *(Daiichi Sankyo)*	20mg/12.5mg 40mg/12.5mg 40mg/25mg	tabs	Not for initial therapy. May be substituted for titrated components. Individualize. ≥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 ≤30mL/min: not recommended. Volume depleted: reduce dose.
telmisartan + HCTZ	**MICARDIS HCT** *(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 ≤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	**DIOVAN HCT** *(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 ≤30mL/min: not recommended.
β-BLOCKER + THIAZIDE DIURETIC				
atenolol + chlorthalidone	**TENORETIC** *(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	**ZIAC** *(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	**LOPRESSOR HCT** *(Novartis)*	50mg/25mg 100mg/25mg 100mg/50mg	scored tabs	Titrate individual components.
metoprolol succinate extended-release + HCTZ	**DUTOPROL** *(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	**CORZIDE** *(King)*	40mg/5mg 80mg/5mg	scored tabs	Titrate components. Renally impaired: increase dosing interval; see literature.
propranolol + HCTZ	**INDERIDE** *(Akrimax)*	40mg/25mg	scored tabs	Titrate individual components.
****CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + ACE INHIBITOR**				
amlodipine + benazepril	**LOTREL** *(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 ≤30mL/min per $1.73m^2$: not recommended. Hepatic impairment, or small, elderly, or frail patients: initially 2.5mg/10mg strength.

(continued)

COMBINATION TREATMENTS FOR HYPERTENSION (Part 3 of 3)

Generic	Brand & Company	Strengths	Formulation	Usual Adult Dose
****CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + ANGIOTENSIN II RECEPTOR BLOCKER**				
amlodipine + olmesartan	**AZOR** *(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	**EXFORGE** *(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.
CENTRAL α-AGONIST + THIAZIDE DIURETIC				
methyldopa + HCTZ	**ALDORIL** *(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.
	ALDORIL D *(Merck)*	500mg/30mg 500mg/50mg		
DIRECT RENIN INHIBITOR + ANGIOTENSIN II RECEPTOR BLOCKER				
aliskiren + valsartan	**VALTURNA** *(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.
DIRECT RENIN INHIBITOR + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE)				
aliskiren + amlodipine	**TEKAMLO** *(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.
DIRECT RENIN INHIBITOR + CALCIUM CHANNEL BLOCKER (DIHYDROPYRIDINE) + THIAZIDE DIURETIC				
aliskiren + amlodipine + HTCZ	**AMTURNIDE** *(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.
DIRECT RENIN INHIBITOR + THIAZIDE DIURETIC				
aliskiren + HCTZ	**TEKTURNA HCT** *(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.
DIURETIC COMBINATION (K^+ SPARING + THIAZIDE)				
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	**ALDACTAZIDE** *(Pfizer)*	25mg/25mg 50mg/50mg†	tabs († = scored)	Usual maintenance: 50–100mg each of spironolactone and HCTZ daily in single or divided doses.
triamterene + HCTZ	**DYAZIDE** *(GSK)*	37.5mg/25mg	caps	1–2 caps once daily.
	MAXZIDE *(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[1]

****Preferred Combination**
- ACEI + thiazide
- ACEI + dihydropyridine CCB
- ARB + thiazide
- ARB + dihydropyridine CCB

Acceptable Combination
- CCB + thiazide
- Thiazide + potassium-sparing diuretic
- Aliskiren + thiazide or CCB
- β-blocker + diuretic or dihydropyridine CCB

NOT Preferred Combination
- ACEI + ARB
- β-blocker + ACEI or ARB
- β-blocker + Nondihydropyridine CCB
- β-blocker + Central acting (clonidine, etc)

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

[1] 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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