

Antihypertensive Medication Step Therapy Program Summary

FDA APPROVED INDICATIONS AND DOSAGE ARBs and ARB Combinations¹⁻²²

Agent(s)	Indication(s)	Dosage
ARBs and ARB Combinations		
Atacand® (candesartan) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension in adults and children 1 to < 17 years of age Treatment of heart failure (NYHA class II-IV) 	<p>Hypertension (HTN): 2-32 mg, usual starting recommended starting dose is 16 mg once daily. May be given once or twice daily with total daily doses from 8-32 mg. Larger doses do not appear to have greater effects; limited experience with such doses.</p> <p>Pediatric HTN: See package insert</p> <p>Heart Failure (HF): Recommended initial dose is 4 mg daily. Target dose is 32 mg daily as tolerated by the patient</p>
Atacand HCT® (candesartan/HCTZ) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension 	<p>HTN: Usual recommended starting dose is 16-12.5 mg once daily. Dose ranges from 8 mg to 32 mg of candesartan and 12.5 to 50 mg of HCTZ once to twice daily. Doses larger than 32 mg do not appear to have a greater BP lowering effect.</p>
Avalide® (irbesartan/HCTZ) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension: <ul style="list-style-type: none"> In patients not adequately controlled with monotherapy As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals 	<p>HTN: The usual starting dose is 150/12.5 mg once daily. The dosage can be increased to a maximum of 300/25 mg once daily.</p>
Avapro® (irbesartan) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension Treatment of diabetic nephropathy in hypertensive patients with type 2 diabetes, an elevated serum creatinine and proteinuria 	<p>HTN: Initially, 150 mg once daily; 75 mg in volume- or salt-depleted patients. Patients requiring further BP reduction may be titrated to a maximum dose of 300 mg once daily.</p> <p>Diabetic Nephropathy: Target dose is 300 mg/day.</p>

Agent(s)	Indication(s)	Dosage
<p>Azor[®] (olmesartan/ amlodipine)^a</p> <p>Tablet</p>	<ul style="list-style-type: none"> Treatment of hypertension, alone or with other antihypertensive agents May also be used as initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals 	<p>HTN: The recommended starting dose is 5/20 mg once daily. Titrate as needed up to a maximum of 10/40 mg once daily.</p>
<p>Benicar[®] (olmesartan)^a</p> <p>Tablet</p>	<ul style="list-style-type: none"> Treatment of hypertension in adult and pediatric patients six years of age and older, alone or with other antihypertensive agents 	<p>HTN: The usual recommended starting dose is 20 mg once daily. Doses more than 40 mg/day do not appear to have greater benefit; twice daily dosing has no advantage over the same dose given once daily.</p> <p>Pediatric HTN: The usual recommended starting dose is 10 mg once daily for patients who weigh 20 to < 35 kg or 20 mg once daily for patients who weigh ≥ 35 kg. May be increased to a maximum of 20 mg once daily for patients who weigh < 35 kg or 40 mg once daily for patients who weigh ≥ 35 kg.</p>
<p>Benicar HCT[®] (olmesartan/HCTZ)^a</p> <p>Tablet</p>	<ul style="list-style-type: none"> Treatment of hypertension 	<p>HTN: The recommended starting dose in patients whose blood pressure is not adequately controlled with olmesartan monotherapy is 40/12.5 mg. Recommended starting dose for patients whose BP is not adequately controlled with HCT monotherapy or who experience dose-limiting adverse reactions with hydrochlorothiazide is 20/12.5 mg. Dose can be titrated up to 40/25 mg if necessary.</p>
<p>Cozaar[®] (losartan)^a</p> <p>Tablet</p>	<ul style="list-style-type: none"> Treatment of hypertension in adults and pediatric patients 6 years of age and older To reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy Treatment of diabetic nephropathy with an elevated serum creatine and proteinuria in patients with type 2 diabetes and a history of hypertension 	<p>HTN: The usual starting dose is 50 mg once daily; can be increased to a maximum of 100 mg once daily as needed to control blood pressure. A starting dose of 25 mg is recommended for patients with possible intravascular depletion.</p> <p>Pediatric HTN: The usual recommended starting dose is 0.7 mg/kg once daily (up to 50</p>

Agent(s)	Indication(s)	Dosage
		<p>mg total). Dosage should be adjusted according to blood pressure response. Doses above 1.4 mg/kg (or in excess of 100 mg) daily have not been studied in pediatric patients.</p> <p>Hypertensive patients with left ventricular hypertrophy (LVH): The usual starting dose is 50 mg once daily. Hydrochlorothiazide (HCTZ) 12.5 mg daily should be added and/or the dose of Cozaar should be increased to 100 mg once daily followed by an increase in HCTZ to 25 mg once daily, based on blood pressure response.</p> <p>Nephropathy in type 2 diabetic patients: The usual starting dose is 50 mg once daily. The dose should be increased to 100 mg once daily based on blood pressure response.</p>

Agent(s)	Indication(s)	Dosage
<p>Diovan® (valsartan)^a</p> <p>Tablet</p>	<ul style="list-style-type: none"> • Treatment of hypertension in adults and pediatric patients one year of age and older • Treatment of heart failure (NYHA class II-IV) • Post-myocardial infarction in clinically stable patients with left ventricular failure or left ventricular dysfunction 	<p>HTN: The recommended starting dose is 80 or 160 mg once daily when used as monotherapy in patients who are not volume depleted. Patients requiring greater reduction may be started at the higher dose. The dose range is 80-320 mg once daily.</p> <p>Pediatric HTN: The usual recommended starting dose is 1 mg/kg once daily (up to 40 mg total). Maximum dose is 4 mg/kg once daily (160 mg).</p> <p>HF: The recommended starting dose is 40 mg twice daily. Uptitrate to 80 mg and 160 mg twice daily or to the highest dose tolerated by the patient. The maximum daily dose administered in clinical trials is 320 mg in divided doses.</p> <p>Post-myocardial infarction: The recommended starting dose is 20 mg twice daily. Patients may be uptitrated to a target maintenance dose of 160 mg twice daily, as tolerated by the patient.</p>
<p>Diovan HCT® (valsartan/HCTZ)^a</p> <p>Tablet</p>	<ul style="list-style-type: none"> • Treatment of hypertension in patients not adequately controlled with monotherapy, or as initial therapy in patients likely to need multiple drugs to achieve their BP goals. 	<p>HTN: The usual starting dose is valsartan/HCTZ 160/12.5 mg once daily. Titrate to maximum of 320/25 mg once daily.</p>
<p>Edarbi® (azilsartan)</p> <p>Tablet</p>	<ul style="list-style-type: none"> • Treatment of hypertension 	<p>HTN: The recommended dose is 80 mg once daily. Consider starting dose of 40 mg for patients who are treated with high doses of diuretics.</p>

Agent(s)	Indication(s)	Dosage
Edarbyclor® (azilsartan/ chorthalidone) Tablet	Treatment of hypertension in patients not adequately controlled with monotherapy or as initial therapy in patients likely to need multiple drugs to help achieve blood pressure goals	HTN: The recommended starting dose is 40/12.5 mg once daily. The dosage may be increased to 40/25 mg after 2 to 4 weeks as need to achieve blood pressure goals. Doses above 40/25 mg are probably not useful.
Eprosartan Tablet	<ul style="list-style-type: none"> • Treatment of hypertension 	HTN: The usual recommended dose is 600 mg once daily when used in patients not volume depleted. Give once or twice daily with total daily doses range 400-800 mg. There is limited experience with doses beyond 800 mg/day.
Exforge® (valsartan/ amlodipine) ^a Tablet	<ul style="list-style-type: none"> • Treatment of hypertension in patients not adequately controlled with monotherapy or as initial therapy in patients likely to need multiple drugs to achieve blood pressure goals 	HTN: Dose once daily. Increase as needed to a maximum dose of 10/320 mg once daily.
Exforge HCT® (valsartan/ amlodipine/HCTZ) ^a Tablet	<ul style="list-style-type: none"> • Treatment of hypertension <p>Limitation of use: Exforge HCT is not indicated for initial treatment of hypertension</p>	HTN: Initial dose 5/160 mg once daily. The maximum recommended dose is 10/320/25 mg.
Hyzaar® (losartan/HCTZ) ^a Tablet	<ul style="list-style-type: none"> • Treatment of hypertension • Reduction in the risk of stroke in patients with hypertension and left ventricular hypertrophy. 	<p>HTN: The usual starting dose is losartan/HCTZ 50/12.5 mg once daily. May increase to a maximum of losartan/HCTZ 100/25 once daily.</p> <p>HTN/LVH: In patients whose blood pressure is not adequately controlled on 50 mg losartan once daily, initiate treatment with Hyzaar 50/12.5 mg. If additional blood pressure reduction is needed, increase to 100/12.5 mg, followed by 100/25 mg once daily.</p>
Micardis® (telmisartan) ^a Tablet	<ul style="list-style-type: none"> • Treatment of hypertension • Cardiovascular risk reduction in patients unable to take ACE inhibitors 	<p>HTN: The usual starting dose is 40 mg once daily. Blood pressure response is dose-related over the range of 20 to 80 mg.</p> <p>Cardiovascular risk reduction: The recommended dose is 80 mg once daily.</p>

Agent(s)	Indication(s)	Dosage
Micardis HCT[®] (telmisartan/HCTZ) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension Limitation of use: Micardis HCT is not indicated for initial therapy	HTN: Initiate a patient whose blood pressure is not adequately controlled with telmisartan monotherapy 80 mg or HCTZ 25 mg on 80/12.5 mg. Dose can be titrated up to 160/25 mg if necessary.
Tribenzor[®] (olmesartan/ amlodipine/HCTZ) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension Limitation of use: Tribenzor is not indicated for initial therapy	HTN: Dose once daily. Dosage may be increased after 2 weeks. The maximum recommended dose is 40/10/25 mg.
Twynsta[®] (telmisartan/ amlodipine) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension Initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals 	HTN: The usual starting dose is 40/5 mg once daily. Patients requiring larger blood pressure reductions may be started on 80/5 mg once daily. The maximum recommended dose is 80/10 mg once daily.

HCTZ = hydrochlorothiazide

HTN = hypertension

a - generic available

Agent(s)	Indication(s)	Dosage
Renin Inhibitors, Renin Inhibitor Combinations		
Tekturna[®] (aliskiren) ^a Tablet	<ul style="list-style-type: none"> Treatment of hypertension in adults and in pediatric patients weighing 50 kg or greater who are at least 6 years of age 	HTN: Recommended starting dose is 150 mg once daily. In patients whose blood pressure is not adequately controlled, dose may be increased to 300 mg daily. Doses above 300 mg did not give an increased BP response.
Tekturna HCT[®] (aliskiren/HCTZ) Tablet	<ul style="list-style-type: none"> Treatment of hypertension As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals 	HTN: The usual recommended starting dose is 150/12.5 mg once daily. The dose may be titrated to a maximum of 300/25 mg.

HCTZ = hydrochlorothiazide

HTN = hypertension

a - generic available

CLINICAL RATIONALE

ACEIs & ARBs

Angiotensin Converting Enzyme Inhibitors (ACEIs) and Angiotensin II Receptor Blockers (ARBs) are recommended as a first-line pharmacotherapy options for adults with hypertension (HTN), for adults with hypertension and comorbid stable ischemic heart disease (SIHD), and heart failure with reduced ejection fraction (HFrEF). In adults with hypertension and heart failure with preserved ejection fraction (HFpEF), ACEI and ARBs are to be added once diuretics have managed volume overload. ACEIs are first-line options for adults with hypertension and chronic kidney disease (CKD). ARBs are a reasonable alternative if the patient is intolerant of ACEIs. For adults

who experience a stroke or transient ischemic attack (TIA) and are hypertensive, once stabilized, thiazide diuretics, ACEIs, ACEi and thiazide combinations, and ARBs are useful. In adults with hypertension and diabetes mellitus, ACEIs and ARBs are among first-line options. If albuminuria is present, ACEis or ARBs may be considered due to their best efficacy among the drug classes on urinary albumin excretion. Treatment of adults with hypertension with an ARB can be useful for prevention of recurrence of atrial fibrillation. The American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines did not differentiate ACEIs or ARBs within their pharmacological classes.²³

Pediatric guidelines state that pharmacologic treatment of hypertension in children and adolescents should be initiated with an ACEI, ARB, long-acting calcium channel blocker, or a thiazide diuretic. In children with hypertension and CKD, proteinuria, or diabetes mellitus, an ACEI or ARB is recommended as the initial antihypertensive agent unless there is an absolute contraindication.²⁴

Direct Renin Inhibitors

Aliskiren decreases plasma renin activity, a different mechanism than ACEIs and ARBs. Studies have shown aliskiren to be as effective as other antihypertensive drugs. It is unclear whether the PRA decrease provided by aliskiren has an impact on clinical outcomes and cardiovascular endpoints.²⁵

Safety

In patients with hypertension undergoing major surgery, discontinuation of ACEIs or ARBs perioperatively may be considered.²³

The FDA added a contraindication against the use of aliskiren with ARBs or ACEIs in patients with diabetes because of the risk of renal impairment, hypotension, and hyperkalemia. A warning was added to avoid use of aliskiren with ARBs or ACEIs in patients with moderate to severe renal impairment (i.e., where glomerular filtration rate [GFR] < 60 mL/min). The FDA stated that Valtorna (a combination containing aliskiren and valsartan) should not be used in patients with diabetes and Valtorna was removed from the market in July 2012.²⁶

All ARBs and Renin Inhibitors have a black box warning concerning fetal toxicity. When pregnancy is detected, the agent should be discontinued. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.¹⁻²²

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Antihypertensive Medication Step Therapy Criteria (1-Step)

TARGET AGENT(S)

Atacand[®] (candesartan)^a

Atacand HCT[®] (candesartan/hydrochlorothiazide)^a

Avalide[®] (irbesartan/hydrochlorothiazide)^a

Avapro[®] (irbesartan)^a

Azor[®] (olmesartan/amlodipine)^a

Benicar[®] (olmesartan)^a

Benicar HCT[®] (olmesartan/hydrochlorothiazide)^a

Cozaar[®] (losartan)^a

Diovan[®] (valsartan)^a

Diovan HCT[®] (valsartan/hydrochlorothiazide)^a

Edarbi[®] (azilsartan)

Edarbyclor[®] (azilsartan/chlorthalidone)

Eprosartan

Exforge[®] (valsartan/amlodipine)^a

Exforge HCT[®] (valsartan/amlodipine/hydrochlorothiazide)^a

Hyzaar[®] (losartan/hydrochlorothiazide)^a

Micardis[®] (telmisartan)^a

Micardis HCT[®] (telmisartan/hydrochlorothiazide)^a

Tekturna[®] (aliskiren)^a

Tekturna HCT[®] (aliskiren/hydrochlorothiazide)

Tribenzor[®] (olmesartan/amlodipine/hydrochlorothiazide)^a

Twynsta[®] (telmisartan/amlodipine)^a

a – generic available that is a prerequisite agent for step therapy program

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Target Agent(s) will be approved when ONE of the following is met:

1. Information has been provided that indicates the patient is currently being treated with the requested agent within the past 90 days.
OR
2. The prescriber states the patient is currently being treated with the requested agent within the past 90 days AND is at risk if therapy is changed
OR
3. The patient's medication history includes use of a generic ACEI, generic ACEI combination, generic ARB, generic ARB combination, or generic renin inhibitor product within the past 90 days
OR
4. The patient has an intolerance or hypersensitivity to a generic ACEI, generic ACEI combination, generic ARB, generic ARB combination, or generic renin inhibitor product
OR
5. The patient has an FDA labeled contraindication to ALL generic ACEIs, generic ACEI combinations, generic ARBs, generic ARB combinations, or generic renin inhibitor products

Length of Approval: 12 months