Angiotensin II Receptor Antagonists (ARBs), Renin Inhibitors, and Combinations Step Therapy and Quantity Limit Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed and Health Insurance Marketplace formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

FDA APPROVED INDICATIONS AND DOSAGE
ARBs and ARB Combinations [1-22,27]

Agent(s)	Indication(s)
Atacand® (candesartan)[a] Tablet	• Treatment of hypertension in adults and children 1 to <17 years of age • Treatment of heart failure (NYHA class II-IV)
Atacand HCT® (candesartan/HCTZ)[a] Tablet	• Treatment of hypertension

Avalide® (irbesartan/HCTZ)[a]
 	
Tablet
	• Treatment of hypertension:
	  ○ In patients not adequately controlled with monotherapy
	  ○ As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals

Avapro® (irbesartan)[a] Tablet	• Treatment of hypertension • Treatment of diabetic nephropathy in hypertensive patients with type 2 diabetes, an elevated serum creatinine and proteinuria

 Effective: 10/01/2023

Agent(s)	Indication(s)
Azor® (olmesartan/ amlodipine)[a] Tablet	• 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
Benicar® (olmesartan)[a] Tablet	• Treatment of hypertension in adult and pediatric patients six years of age and older, alone or with other antihypertensive agents
Benicar HCT® (olmesartan/HCTZ)[a] Tablet	• Treatment of hypertension

Agent(s)	Indication(s)
Cozaar® (losartan)[a] Tablet	• 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
Diovan® (valsartan)[a] Tablet	• 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
Diovan HCT® (valsartan/HCTZ)[a] Tablet	• 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.

Agent(s)	Indication(s)
Edarbi® (azilsartan) Tablet	• Treatment of hypertension
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
Exforge® (valsartan/ amlodipine)[a] Tablet	• 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
Exforge HCT® (valsartan/ amlodipine/ HCTZ)[a] Tablet	• Treatment of hypertension Limitation of use: Exforge HCT is not indicated for initial treatment of hypertension
Hyzaar® (losartan/HCTZ)[a] Tablet	• Treatment of hypertension • Reduction in the risk of stroke in patients with hypertension and left ventricular hypertrophy.
Micardis® (telmisartan)[a] Tablet	• Treatment of hypertension • Cardiovascular risk reduction in patients unable to take angiotensin-converting enzyme (ACE) inhibitors
Micardis HCT® (telmisartan/HCTZ)[a] Tablet	• Treatment of hypertension Limitation of use: Micardis HCT is not indicated for initial therapy
Tribenzor® (olmesartan/ amlodipine/HCTZ)[a] Tablet	• Treatment of hypertension Limitation of use: Tribenzor is not indicated for initial therapy

Agent(s)	Indication(s)
Twynsta® (telmisartan/ amlodipine)[a] Tablet	• Treatment of hypertension • Initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals

HCTZ = hydrochlorothiazide
HTN = hypertension
[a] – generic available

Agents	Indication(s)
Tekturna® (aliskiren)[a] Tablet	• Treatment of hypertension in adults and in pediatric patients weighing 50 kg or greater who are at least 6 years of age
Tekturna HCT® (aliskiren/HCTZ) Tablet	• Treatment of hypertension in patients not adequately controlled with monotherapy • As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals
Valsartan Solution	• Treatment of hypertension in adults and children six years and older to lower blood pressure; treatment of heart failure (NYHA class II-IV) to reduce the risk of hospitalization for heart failure in patients who are unable to swallow valsartan tablets; to reduce the risk of cardiovascular death in clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction who are unable to swallow valsartan tablets.

HCTZ = hydrochlorothiazide
HTN= hypertension
[a] – generic available

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

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 Cariology/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 (PRA), 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 Valturna (a combination containing aliskiren and valsartan) should not be used in patients with diabetes and Valturna 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, 27]

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Angiotensin II Receptor Antagonists (ARBs), Renin Inhibitors, and Combinations Step Therapy (1-Step)

TARGET AGENT(S)
Atacand® (candesartan) tablet[a]
Atacand HCT® (candesartan/hydrochlorothiazide) tablet[a]
Avapro® (irbesartan)[a]
Avalide® (irbesartan/hydrochlorothiazide) tablet[a]
Azor® (olmesartan/amlodipine) tablet[a]
Benicar® (olmesartan) tablet[a]
Benicar HCT® (olmesartan/hydrochlorothiazide) tablet[a]
Cozaar® (losartan) tablet[a]
Diovan® (valsartan) tablet[a]
Diovan HCT® (valsartan/hydrochlorothiazide) tablet[a]
Edarbi® (azilsartan) tablet
Edarbyclor® (azilsartan/chlorthalidone) tablet
Exforge® (valsartan/amlodipine) tablet[a]
Exforge HCT® (valsartan/amlodipine/hydrochlorothiazide) tablet[a]
Hyzaar® (losartan/hydrochlorothiazide) tablet[a]
Micardis® (telmisartan) tablet[a]
Micardis HCT® (telmisartan/hydrochrolothiazide) tablet[a]
Tribenzor® (olmesartan/amlodipine/hydrochlorothiazide) tablet[a]
Twynsta® (telmisartan/amlodipine) tablet[a]
Tekturna® (aliskiren) tablet[a]
Tekturna HCT® (aliskiren/hydrochlorothiazide) tablet
Valsartan oral suspension^
a – generic available included as a prerequisite agent for step therapy program
^ - Branded generic products available; targeted in the 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 is currently being treated with the requested agent as indicated by ALL of the following:
   A. A statement by the prescriber that the patient is currently taking the requested agent
      AND
   B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
      AND
   C. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   OR
4. The patient's medication history includes use of a generic ACEI, generic ACEI combination, generic ARB, generic ARB combination, or generic renin inhibitor product
   OR
5. 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

6. The patient has an FDA labeled contraindication to ALL generic ACEIs, generic ACEI combinations, generic ARBs, generic ARB combinations, or generic renin inhibitor products
   OR
7. BOTH of the following:
   A. The prescriber has stated that the patient has tried a generic ACEI, generic ACEI combination, generic ARB, generic ARB combination, or generic renin inhibitor product
      AND
   B. A generic ACEI, generic ACEI combination, generic ARB, generic ARB combination, or generic renin inhibitor product was discontinued due to lack of effectiveness or an adverse event

   OR
8. The prescriber has provided documentation that ALL generic ACEI, generic ACEI combination, generic ARB, generic ARB combination, or generic renin inhibitor products cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: 12 months

NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents.

