Medication Policy Manual **Policy No:** dru333

Topic: Non-Preferred Branded Renin-Aldosterone-System-Antagonist-Containing Medications:
- aliskiren (Tekturna®)
- aliskiren/hydrochlorothiazide (Tekturna HCT®)
- azilsartan (Edarbi™)
- azilsartan/chlorthalidone (Edarbyclor™)
- olmesartan/amlodipine (generic, Azor®)
- olmesartan/amlodipine/hydrochlorothiazide (generic, Tribenzor®)

Date of Origin: March 14, 2014

Committee Approval Date: March 11, 2016 **Next Review Date:** March 2017

Effective Date: October 13, 2016

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Aliskiren (Tekturna) and aliskiren/hydrochlorothiazide (Tekturna HCT) are direct renin inhibitor (DRI) containing medications taken by mouth for treatment of high blood pressure. Azilsartan (Edarbi), azilsartan/chlorthalidone (Edarbyclor), olmesartan/amlodipine (Azor), and olmesartan/amlodipine/hydrochlorothiazide (Tribenzor) are angiotensin receptor blocker (ARB) containing medications taken by mouth for the treatment of high blood pressure. This policy does not apply to generically available eprosartan (please see High Cost Generically Available ARBs dru335).

Policy/Criteria

I. Most contracts require prior authorization approval of brand name aliskiren (Tekturna), aliskiren/hydrochlorothiazide (Tekturna HCT), azilsartan (Edarbi), azilsartan/chlorthalidone (Edarbyclor), olmesartan/amlodipine (Azor), and olmesartan/amlodipine/ hydrochlorothiazide (Tribenzor) prior to coverage. These medications may be considered medically necessary when both criteria A and B below are met.

A. A best value generic angiotensin receptor blocker (ARB) listed in Appendix 1 has been ineffective, not tolerated, or is contraindicated.

AND

B. A preferred/formulary angiotensin receptor blocker (ARB) listed in Appendix 2 has been ineffective, not tolerated, or is contraindicated.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers the medications in this policy to be self-administered.

B. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

Position Statement

- There are many generic angiotensin receptor blockers (ARBs) available (see Appendices 1 and 2).
- Generic treatments provide the best value. The medications included in this policy have not been proven to be safer or more effective than generically available ARBs, but are more costly.
- As a class, the ARBs are similar to the angiotensin converting enzyme inhibitors ACEIs with regard to blood pressure lowering and in reducing morbidity/mortality in specific subpopulations (e.g. preventing progression of kidney disease in diabetic patients, preventing recurrent stroke, and decreasing the risk of cardiovascular morbidity and mortality). There are numerous ACEIs available generically.
- ARBs are recognized as a treatment option in patients who develop intolerance to ACEI therapy (e.g. non-productive cough).
- Combining an ARB with an ACEI results in little additional blood pressure lowering; however, it increases the risk of adverse effects such as hyperkalemia.
- The combination of aliskiren, a direct renin inhibitor, with an ARB or an ACEI may increase the risk of non-fatal stroke and end-stage renal disease in some patients with type 2 diabetes. Concomitant use of these medications in not recommended.

Clinical Efficacy

- The angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and aliskiren are all used in the treatment of hypertension. [1]
- Reduction in cardiovascular morbidity and mortality, prevention of recurrent strokes, and prevention of progression of kidney disease are not unique to any ARB or ACEI and have been demonstrated with many of the available products. [2, 3]
- No single ARB has been shown to be better than another with regard to improving long-term outcomes (none of the outcomes studies compare one ARB versus another).
- The 2014 Eighth Joint National Committee (JNC8) treatment guidelines recommend initial treatment of hypertension with either a thiazide diuretic, calcium channel blocker, ACEI, or ARB. No distinction is made between products. [4]
- There is no high quality evidence to show that combining an ARB and an ACEI is superior to either one alone with regard to improving long-term outcomes.
    * A single high quality study (ONTARGET study) concluded that there was no difference between telmisartan or ramipril, or the combination of each for the composite endpoint death from cardiovascular causes, myocardial infarction, or stroke. [5]
    * Three additional studies with combination ACEI and ARB arms were appraised as being of low quality because of high discontinuation rates and confounding medications. [6-8]
- There is currently no evidence that aliskiren, a direct renin inhibitor, has a beneficial impact on long-term clinical outcomes.
- A study combining aliskiren with an ACEI or an ARB in patients with type 2 diabetes and renal impairment was terminated due to an increased incidence of non-fatal stroke, renal complications, hyperkalemia, and hypotension after 18 to 24 months. [9] Concomitant administration of aliskiren with ACEIs and ARBs is not recommended.

Safety

- Both ARBs and aliskiren (along with ACEIs) carry a boxed warning regarding use in pregnancy (all can cause injury and even death to a developing fetus). [1]
- Adverse effects reported with ACEIs, ARBs, and aliskiren include dizziness, fatigue, hypotension, diarrhea, dry cough, and elevated serum potassium. [1]
- The incidence of dry cough with ACEIs ranges from 7% to 15%; whereas the reported incidence with ARBs is generally around 1% (similar to placebo). [1]
- Concomitant use of ACEIs or ARBs with aliskiren is not recommended because it may increase the risk of non-fatal stroke, renal complications, hyperkalemia, and hypotension. [9]

Appendix 1: Best Value Generic Angiotensin Receptor Blockers (ARBs)
Best Value Generic ARBs
irbesartan (generic Avapro®)
losartan (generic Cozaar®)
Best Value Generic ARB Combination Products
irbesartan + HCTZ (generic Avalide®)
losartan + HCTZ (generic Hyzaar®)

Appendix 2: Other Preferred Angiotensin Receptor Blockers (ARBs)
High Cost Generically Available ARBs
candesartan (generic Atacand®)
eprosartan (generic Teveten®)
telmisartan (generic Micardis®)
valsartan (generic Diovan®)
Other Generically Available ARB Combination Products
candesartan + HCTZ (generic Atacand® HCT)
telmisartan + amlodipine (generic Twynsta®)
telmisartan + HCTZ (generic Micardis HCT®)
valsartan + amlodipine (generic Exforge®)
valsartan + amlodipine + HCTZ (generic Exforge HCT®)
valsartan + HCTZ (generic Diovan HCT®)
Preferred/ Formulary Brand Name ARBs
olmesartan (Benicar®)
Preferred/ Formulary Brand Name ARB Combination Products
olmesartan + HCTZ (Benicar HCT®)

Cross References
High-Cost Generically Available ARBs, dru335
Preferred Branded ARB-Containing Medications, dru334

Codes	Number	Description
N/A		

References

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Revision History

Revision Date	Revision Summary
10/13/2016	Clarified that policy also applies to generic Azor and Tribenzor products.
03/11/2016	Removal of aliskiren/amlodipine/ hydrochlorothiazide (Amturnide), aliskiren/amlodipine (Tekamlo), and eprosartan/hydrochlorothiazide (Teveten HCT) from policy