BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

KERENDIA® (finerenone) oral

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Kerendia (finerenone) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist or Nephrologist.

  2. Individual is 18 years of age or older.

  3. Individual has a confirmed diagnosis of Chronic Kidney Disease (CKD) associated with type 2 diabetes (T2D) to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure.

4. The individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Serum potassium is less than 4.8 mEq/L
    b. Estimated glomerular filtration rate (eGFR) greater than or equal to 25 mL/min/1.73m^2
    c. Urine albumin to creatinine ratio (UACR) is **ONE** of the following:
        i. Individual **with** diabetic retinopathy, greater than or equal to 30 but less than 300 mg/g
        ii. Individual **without** diabetic retinopathy, greater than or equal to 300 but less than or equal to 5,000 mg/g

5. Individual's medical regimen includes **ALL** of the following:
    a. **ONE** angiotensin converting enzyme inhibitor (e.g., lisinopril, enalapril, others) **OR ONE** angiotensin receptor blocker (e.g., candesartan, losartan, others)
    b. **ONE** Glucagon-like peptide 1 (GLP-1) receptor agonists (e.g., dulaglutide, liraglutide, semaglutide) where clinically indicated or has a documented failure, contraindication per FDA label or intolerance

6. For individual with eGFR greater than or equal to 45 mL/min/1.73m^2 there is a documented failure, contraindication per FDA label or intolerance to **ONE** of the following sodium-glucose co-transporter 2 (SGLT2) inhibitors:
    a. Invokana (canagliflozin)
    b. Farxiga (dapagliflozin)
    c. Jardiance (empagliflozin)

7. There are **NO** FDA-label contraindications, such as:
    a. Concomitant use with strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, ritonavir, clarithromycin)
    b. Patients with adrenal insufficiency

8. There are **NONE** of the following:
    a. Individual with an eGFR less than 25 mL/min/1.73m^2
    b. Individual with severe hepatic impairment (Child-Pugh Class C)

9. There are no significant interacting drugs such as concomitant use with strong or moderate CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, bosentan, efavirenz, nafcillin, rifabutin, rifapentine, others).

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Kerendia (finerenone) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist or Nephrologist.

2. Individual's condition has not worsened while on therapy with worsening defined as ANY of the following:
    a. A decline in eGFR of greater than or equal to 40%

b. Kidney failure defined as on chronic dialysis, required kidney transplantation or a sustained decrease in eGFR to less than 15 mL/min/1.73m^2
c. Experienced a nonfatal myocardial infarction
d. Hospitalized for heart failure
e. Evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication.

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant adverse effect such as Hyperkalemia

5. There are no significant interacting drugs such as concomitant use with:
   a. Strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, ritonavir, clarithromycin)
   b. Strong or moderate CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, bosentan, efavirenz, nafcillin, rifabutin, rifapentine, others)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Kerendia (finerenone) is a non-steroidal mineralocorticoid receptor antagonist (MRA) indicated to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).

Finerenone is a nonsteroidal, selective antagonist of the mineralocorticoid receptor (MR), which is activated by aldosterone and cortisol and regulates gene transcription. Finerenone blocks MR mediated sodium reabsorption and MR overactivation in both epithelial (e.g., kidney) and nonepithelial (e.g., heart, and blood vessels) tissues. MR overactivation is thought to contribute to fibrosis and inflammation. Finerenone has a high potency and selectivity for the MR and has no relevant affinity for androgen, progesterone, estrogen, and glucocorticoid receptors.

In meta-analyses of the cardiovascular disease (CVD) outcome trials for dapagliflozin, canagliflozin, and empagliflozin compared with placebo there was a reduction in the risk of major adverse cardiovascular (CV) events and a composite outcome of CV death or hospitalization for heart failure. The clinical benefit of the SGLT2 inhibitors in reducing the risk of major CV events of myocardial infarction, stroke, and CV death was limited to those patients with established atherosclerotic CVD, with no benefit in those with multiple risk factors for CVD. In

contrast to the findings for major adverse CV events, the meta-analyses showed a reduction in hospitalization for heart failure with use of sodium-glucose co-transporter 2 (SGLT2) inhibitors regardless of the presence of established atherosclerotic CVD or heart failure at baseline.

In a meta-analysis of the CVD outcome trials for dapagliflozin, canagliflozin, and empagliflozin, there was a reduction in the progression of diabetic kidney disease (DKD), with a similar effect observed in patients with established atherosclerotic CVD or multiple risk factors for CVD. DKD is a major cause of CKD and is the most common cause of end-stage kidney disease.

SGLT2 inhibitors reduce the risk of kidney disease progression and end-stage renal disease in patients with diabetic kidney disease, regardless of the degree of proteinuria. Patients with severely increased albuminuria (albumin-to-creatinine ratio ≥300 mg/g) are at higher risk for kidney disease progression and end-stage renal disease and therefore derive a greater absolute benefit from therapy with SGLT2 inhibitors.

SGLT2 inhibitors can have a role in patients with urine to creatinine ratio (UACR) greater than 300 mg/g and an eGFR of less than 90 mL/min/1.73m^2. However, dapagliflozin and empagliflozin should not be used for eGFR less than 45 mL/min/1.73m^2 and canagliflozin should not be used for eGFR less than 30 mL/min/1.73m^2.

Use of SGLT2 inhibitors should be avoided in patients with frequent bacterial urinary tract infections or genitourinary yeast infections, low bone density and high risk for falls and fractures, foot ulceration, and factors predisposing to diabetic ketoacidosis (DKA; e.g., pancreatic insufficiency, drug or alcohol abuse disorder) because of increased risk while using these agents.

Definitions:

Chronic Kidney Disease classification based upon Glomerular Filtration Rate and Albuminuris		
GFR Stages	GFR (mL/min/1.73m^2)	Terms
G1	≥ 90	Normal or high
G2	60-89	Mildly decreased
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	< 15	Kidney failure (if treated with dialysis: G5D)
Albuminuria Stages	Albumin Excretion Rate (AER mg/day)	
A1	< 30	Normal to mildly increased
A2	30-300	Moderately increased
A3	> 300	Severely increased

Staging of patients who meet the definition of Chronic Kidney Disease			
	Persistent albuminuria category		
GFR category	A1	A2	A3
G1	1 if CKD	1	2

PHARMACY COVERAGE GUIDELINE

KERENDIA® (finerenone) oral

G2	1 if CKD	1	2
G3a	1	2	3
G3b	2	3	3
G4	3	3	4+
G5	4+	4+	4+
GFR and albuminuria grid to reflect the risk of progression by intensity of coloring (green, yellow, orange, red, deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year).			

Resources:

Kerendia (finerenone) product information, revised by Bayer Healthcare Pharmaceuticals, Inc. 07-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 21,2022.

Rosenberg M. Management of chronic kidney disease in adults. In: UpToDate, Curhan GC, Forman JP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on April 21, 2022. Accessed July 21, 2022.

Mottl AK, Tuttle KR, Barkis GL. Diabetic kidney disease: Manifestations, evaluation, and diagnosis. In: UpToDate, Glassock RJ, Nathan DM, Forman JP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on November 13, 2020. Accessed July 21, 2022.

Perkovic V, Badve SV, Barkis GL. Treatment of diabetic kidney disease. In: UpToDate, Glassock RJ, Nathan DM, Forman JP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on February 09, 2022. Accessed July 21, 2022.

DeSantis A. Sodium-glucose co-transporter 2 inhibitors for the treatment of hyperglycemia in type 2 diabetes mellitus. In: UpToDate, Nathan DM, Mulder JE (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on May 31, 2022. Accessed July 21, 2022.

Berns JS. Management of hyperglycemia in patients with type 2 diabetes mellitus and advanced chronic kidney disease or end-stage kidney disease. In: UpToDate, Golper TA, Nathan DM, Lam AQ, Mulder JE (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on June 04, 2021. Accessed July 21, 2022.

Dungan K, DeSantis A. Glucagon-like peptide 1 based therapies for the treatment of type 2 diabetes mellitus. In: UpToDate, Golper TA, Nathan DM, Mulder JE (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on June 02, 2022. Accessed July 21, 2022.

American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes—2022. Diabetes Care 2022;45 (Suppl. 1): S125–S143. Accessed June 26, 2022.

American Diabetes Association Professional Practice Committee. 10. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes—2022. Diabetes Care 2022;45 (Suppl. 1): S144–S174. Accessed June 26, 2022.

American Diabetes Association Professional Practice Committee. 11. Chronic kidney disease and risk management: Standards of Medical Care in Diabetes—2022. Diabetes Care 2022;45 (Suppl. 1): S175–S184. Accessed June 26, 2022.