PRIOR AUTHORIZATION POLICY

POLICY: Nephrology – Filspari Prior Authorization Policy
- Filspari™ (sparsentan tablets – Travere)

REVIEW DATE: 02/22/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Filspari, an endothelin and angiotensin II receptor antagonist, is indicated to reduce proteinuria in adults with **primary immunoglobulin A nephropathy** (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g.[1] This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether Filspari slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

Filspari is contraindicated for use with renin-angiotensin-aldosterone system (RAAS) inhibitors, endothelin receptor antagonists (ERAs), or aliskiren.[1] RAAS inhibitors, ERAs, and/or aliskiren must be discontinued prior to initiation of Filspari.

Clinical Efficacy

The efficacy of Filspari is being assessed in an ongoing Phase III trial in adults with biopsy-proven IgAN, proteinuria ≥ 1.0 g/day at screening, and estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m^2 (PROTECT, n = 404).[2] Additionally patients were receiving the maximum tolerated dose (at least one-half of the maximum labeled dose) of an angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) for ≥ 12 weeks prior to study entry and had blood

pressure of ≤ 150/100 mmHg (managed according to standard of care). Patients with use of immunosuppressive medications (including corticosteroids for > 2 weeks within 3 months of screening), chronic kidney disease (CKD) in addition to IgAN, or IgAN secondary to other conditions were excluded. Per study protocol, patients discontinued their ACEi or ARB 1 day prior to the start of Filspari.[2]

The primary efficacy endpoint was the change from baseline in urine protein-to-creatinine ratio (based on 24-hour urine sample) at Week 36.[2] The primary analysis was based on an interim data cutoff of August 1, 2021. At Week 36, the primary endpoint was significantly greater with Filspari vs. irbesartan in the interim analysis set (comprised of the first 281 patients randomized in the study, including 2 patients who were not treated); the geometric least squares mean percent change in UPCR from baseline was -45% vs. -15%, respectively. This resulted in a statistically significant relative reduction from baseline in UPCR for the Filspari vs. irbesartan (geometric mean ratio 0.7; 95% confidence interval [CI]: 0.6, 0.8; P < 0.0001), corresponding to a 35% relative reduction with Filspari. Supportive secondary endpoints for changes in UPCR from baseline to Week 94 and urine albumin-to-creatinine ratio (UACR) from baseline to Weeks 36 and 94, were significantly greater with Filspari. A confirmed 40% reduction in eGFR, end-stage kidney disease, or death was reported in a smaller proportion of patients treated with Filspari (3.5%) vs. irbesartan (6.4%) [P = not estimable].

Several exploratory endpoints also favored Filspari over irbesartan. At interim analysis (Week 36), the proportion of patients in the Filspari group who achieved partial proteinuria remission (< 1 g/day) was significantly higher with Filspari vs. irbesartan (55% vs. 24%, respectively) and numerically more patients in the Filspari vs. irbesartan group (11% vs. 4%, respectively) achieved complete proteinuria remission (< 0.3 g/day) at Week 36.

Guidelines

Kidney Diseases: Improving Global Outcomes (KDIGO) clinical practice guidelines for the management of glomerular diseases (2021) mention Filspari as an investigational agent.[3] Therapeutic strategies that minimize or avoid systemic glucocorticoid exposure are considered areas of priority for future research to improve the treatment and outcomes of patients with IgAN, and the PROTECT trial is mentioned. Filspari is also mentioned for children with steroid-resistant nephrotic syndrome. For children with calcineurin inhibitor-resistant steroid resistant nephrotic syndrome, consideration for entry into clinical trials evaluating novel therapies on the horizon should be strongly considered.

Following biopsy-confirmed diagnosis of IgAN, the guidelines recommend assessment of disease progression.[3] The primary focus of IgAN treatment should include multiple modalities such as RAAS blockage (maximum dose or maximum tolerated dose), blood pressure control, cardiovascular risk minimization, and adherence to lifestyle advice (i.e., dietary counseling, smoking cessation, weight control, and exercise as appropriate). RAAS blockade (with either an ACEi or ARB) is recommended regardless of hypertension if a patient has proteinuria > 0.5 g/day (500 mg/day). There are no data to suggest that dual blockade with an ACEi and ARB is superior to

single blockade. In patients who remain at high risk of progressive CKD despite maximal supportive care, a 6-month course of glucocorticoid therapy should be considered.

Safety

Filspari has a Black Box Warning and Risk Evaluation and Mitigation Strategy (REMS) program around hepatotoxicity and embryo-fetal toxicity associated with Filspari.[1,4] The three objectives of the REMS are to monitor for elevations in liver enzymes in patients exposed to Filspari, ensure that patients who can become pregnant are not pregnant before initiating Filspari, and to minimize exposure in patients who may become pregnant while taking Filspari.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Filspari. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Filspari as well as the monitoring required for adverse events and long-term efficacy, approval requires Filspari to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Filspari™ (sparsentan tablets (Travere)
is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Primary Immunoglobulin A Nephropathy.** Approve for the duration noted if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 9 months if the patient meets the following criteria (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The diagnosis has been confirmed by biopsy; AND
     - **iii.** Patient is at high risk of disease progression, defined by meeting the following criteria (a and b):
       - **a)** Patient meets ONE of the following [(1) or (2)]:
         - **(1)** Proteinuria > 1.0 g/day; OR
         - **(2)** Urine protein-to-creatinine ratio ≥ 1.5 g/g; AND
       - **b)** Patient has received the maximum or maximally tolerated dose of ONE of the following for ≥ 12 weeks prior to starting Filspari [(1) or (2)]:
         - **(1)** Angiotensin converting enzyme inhibitor; OR
         - **(2)** Angiotensin receptor blocker; AND
     - **iv.** Patient has received ≥ 3 months of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification, according to the prescriber; AND
     - **v.** Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 m^2; AND

vi. The medication will not be used in combination with any renin-angiotensin-aldosterone antagonists (e.g., angiotensin converting enzyme inhibitors or angiotensin receptor blockers), endothelin receptor antagonists, or aliskiren; AND
Note: Examples of angiotensin converting enzyme inhibitors include but are not limited to lisinopril, fosinopril, enalapril, benazepril. Examples of angiotensin receptor blockers include but are not limited to irbesartan, losartan, candesartan, valsartan.

vii. The medication is prescribed by or on consultation with a nephrologist.

B) Patient is Currently Receiving Filspari. Approve for 1 year if the patient meets the following criteria (i, ii, iii, iv, v, and vi):

i. Patient is ≥ 18 years of age; AND

ii. The diagnosis has been confirmed by biopsy; AND

iii. Patient has had a response to Filspari, according to the prescriber; AND
Note: Examples of a response are a reduction in urine protein-to-creatinine ratio from baseline, reduction in proteinuria from baseline.

iv. Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 m^2; AND

v. The medication is not being used in combination with any renin-angiotensin-aldosterone antagonists (e.g., angiotensin converting enzyme inhibitors or angiotensin receptor blockers), endothelin receptor antagonists, or aliskiren; AND
Note: Examples of angiotensin converting enzyme inhibitors include but are not limited to lisinopril, fosinopril, enalapril, benazepril. Examples of angiotensin receptor blockers include but are not limited to irbesartan, losartan, candesartan, valsartan.

vi. The medication is prescribed by or on consultation with a nephrologist.

CONDITIONS NOT COVERED

Filspari™ (sparsentan tablets (Travere) is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Filspari™ tablets [prescribing information]. San Diego, CA: Travere; February 2023.
2. Sparsentan for Primary IgAN, Formulary Dossier. Version 4.1 Travere. February 18, 2023
3. Kidney Diseases: Improving Global Outcomes (KDIGO) 2021 clinical practice guidelines for the management of glomerular diseases. *Kidney Int.* 2021;100:S1-S276. Available at: https://www.kidney-international.org/action/showPdf?pii=S0085-2538%2821%2900562-7. Accessed on February 20, 2023.
4. The Filspari™ REMS (Risk Evaluation and Mitigation Strategy). Available at: https://filsparirems.com/#Main. Accessed on: February 20, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	02/22/2023