PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 02/28/2024; selected revision 10/02/2024

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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. 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 slow kidney function decline in adults with **primary immunoglobulin A nephropathy** (IgAN) who are at risk of rapid disease progression.[1]

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 group (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 the 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.

Following the 36 week randomized, treatment period, patients were followed until the patient reached Week 110.[5] The significant reduction in proteinuria at Week 36 was maintained through Week 110. The UPCR at Week 110 was 40% lower in the Filspari group compared to the irbesartan group (-42·8% with Filspari versus -4·4% with irbesartan). Filspari also reduced the rate of decline in kidney function from baseline to Week 110 when compared with irbesartan (-3.0 mL/min/1.73 m^2 per year for Filspari vs. 4.2 mL/min/1.73 m^2 per year for irbesartan) with a corresponding treatment effect of 1.2 mL/min/1.73 m^2 per year (P = 0.0168).

Guidelines

Kidney Diseases: Improving Global Outcomes (KDIGO) clinical practice guidelines for the management of IgAN and immunoglobulin A vasculitis (2024) recommend Filspari for patients who are at risk of progressive kidney function loss with IgAN.[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.

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.[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 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (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 BOTH of the following criteria (a and b):
       - **a)** Patient meets ONE of the following [(1) or (2)]:
         - **(1)** Proteinuria ≥ 0.5 g/day; OR
         - **(2)** Urine protein-to-creatinine ratio ≥ 0.8 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 if the patient meets ALL of the following (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); criteria will be updated as new published data are available.

REFERENCES

1. Filspari™ tablets [prescribing information]. San Diego, CA: Travere; September 2024.
2. Sparsentan for Primary IgAN, Formulary Dossier. Version 4.1 Travere. February 18, 2023
3. Kidney Diseases: Improving Global Outcomes (KDIGO) 2024 clinical practice guidelines for the management of immunoglobulin A nephropathy (IgAN) and immunoglobulin A vasculitis (IgAV). *Draft published online ahead of print.* Available at: https://kdigo.org/wp-content/uploads/2024/08/KDIGO-2024-IgAN-IgAV-Guideline-Public-Review-Draft.pdf. Accessed on September 23, 2024.

4. The Filspari™ REMS (Risk Evaluation and Mitigation Strategy). Available at: https://filsparirems.com/#Main. Accessed on: February 12, 2024.
5. Rovin BH, Barratt J, Heerspink HJL, et al. Efficacy and safety of sparsentan versus irbesartan in patients with IgA nephropathy (PROTECT): 2-year results from a randomised, active-controlled, phase 3 trial. *Lancet*. 2023;402(10417):2077-2090.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	02/22/2023
Annual Revision	No criteria changes.	02/28/2024
Selected Revision	**Primary Immunoglobulin A Nephropathy:** The criterion requiring that the patient is at high risk of disease progression, defined by ONE of the following: urine-to-protein-creatinine ratio ≥ 1.5 g/g OR proteinuria ≥ 1 g/day was revised to require that the patient is at high risk of disease progression, defined by urine-to-protein-creatinine ratio ≥ 0.8 g/g OR proteinuria ≥ 0.5 g/day. The approval duration was changed to 1 year for initial and continuation therapy (previously the approval duration was 9 months for initial and 1 year for continuation therapy).	10/02/2024