BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

FILSPARI™ (sparsentan) oral
Generic Equivalent (if available)

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 prior authorization 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:** Filspari (sparsentan) and/or generic equivalent (if available) are 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 a Nephrologist or Immunologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of primary immunoglobulin A nephropathy (IgAN) with persistent overt proteinuria who remain at high-risk for rapid disease progression despite use of stable doses of ACEI and/or ARB (see Definitions section)

ORIGINAL EFFECTIVE DATE: 05/18/2023 | ARCHIVE DATE: | LAST REVIEW DATE: 05/16/2024 | LAST CRITERIA REVISION DATE: 05/16/2024

4. Individual has documented failure (at least 12-weeks of a maximized stable dose that was at least one-half of the maximum labeled dose), contraindication per FDA label, intolerance, or is not a candidate for **ALL** of the following:
    a. Angiotensin converting enzyme inhibitor (ACEI such as lisinopril, enalapril, etc.) or angiotensin receptor blocker (ARB such as losartan, irbesartan, etc.) therapy
    b. A sodium-glucose cotransporter 2 (SGLT2) inhibitor (e.g., dapagliflozin)
    c. Immunosuppressive therapy (i.e., systemic glucocorticoids or mycophenolate mofetil)

5. If approved and prior to initiating Filspari (sparsentan), individual must discontinue use of renin-angiotensin-aldosterone system (RAAS) inhibitors, endothelin receptor antagonists (ERAs), and aliskiren

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. 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. Individual is enrolled in the Filspari REMS
    b. Liver aminotransferases and total bilirubin
    c. Negative pregnancy test in a woman of childbearing potential
    d. Woman of childbearing potential is using effective contraception
    e. Biopsy proven IgAN
    f. Estimated glomerular filtration rate is at least 30 mL/min/1.73m^2
    g. Proteinuria of at least 1 g/day
    h. Systolic BP ≤150 mmHg and diastolic BP ≤100 mmHg

8. There are **NO** FDA-label contraindications such as:
    a. Use in an individual who is pregnant
    b. Concurrent use with angiotensin receptor blockers (ARBs), endothelin receptor antagonists (ERAs), or aliskiren (see Definitions section)

9. Individual is not currently taking any drugs which may cause any significant drug interactions requiring discontinuation such as:
    a. Strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, others)
    b. Strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, others)
    c. Acid reducing agents (histamin-2 receptor antagonists, proton pump inhibitors) (see Definitions section)
    d. Sensitive P-gp and BCRP substrates (e.g., cyclosporine, everolimus, sirolimus, tacrolimus, methotrexate, mitoxantrone, rosuvastatin, others)
    e. Concurrent use with ACE inhibitors, ARBs, endothelin receptor antagonists (ERAs) or aliskiren (see Definitions section)

10. Individual does not have any degree of hepatic impairment (Child-Pugh A-C)

11. Individual does not have heart failure

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Filspari (sparsentan) and/or generic equivalent (if available) are 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 a Nephrologist or Immunologist

  2. Individual's condition has responded while on therapy with response defined as **TWO** of the following:
     a. Improvement in UPCR
     b. Improvement in eGFR
     c. Reduced need for rescue immunosuppressive treatment

  3. Individual has been adherent with the medication

  4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

  5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
     a. Elevated aminotransferases greater than 3x the upper limit of normal
     b. Individual who experienced clinical symptoms of hepatotoxicity or whose hepatic enzyme levels and bilirubin have not returned to pretreatment levels
     c. Clinically significant decrease in kidney function
     d. Significant hyperkalemia despite use of medication to control serum potassium levels

  6. Individual is not currently taking any drugs which may cause significant drug interactions requiring discontinuation such as:
     a. Strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, others)
     b. Strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, others)
     c. Acid reducing agents (histamin-2 receptor antagonists, proton pump inhibitors) (see Definitions section)
     d. Sensitive P-gp and BCRP substrates (e.g., cyclosporine, everolimus, sirolimus, tacrolimus, methotrexate, mitoxantrone, rosuvastatin, others)
     e. Concurrent use with ACE inhibitors, ARBs, endothelin receptor antagonists (ERAs) or aliskiren (see Definitions section)

  7. Individual does not have any degree of hepatic impairment (Child-Pugh A-C)

  8. Individual does not have heart failure

  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:

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

Description:

Filspari (sparsentan) is an endothelin and angiotensin II receptor antagonist indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) who are at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g. It is the first drug approved for treating IgAN that does not cause immune suppression. This indication is approved under accelerated approval. Accelerated approval of Filspari (sparsentan) is based on reduction of proteinuria seen in an unfinished clinical study. It has not been established whether Filspari (sparsentan) 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. Additional positive results, including its effects on overall kidney function, from the trial will be needed before full FDA approval is granted. Final results are expected by the end of 2023

IgAN is a rare form of autoimmune kidney disease; believed to affect 150,000 Americans. Patients who have IgAN make too much IgA, a normal component of the immune system. IgA generally attaches to bacteria and viruses. Excessive amounts of it forms large complexes that get trapped in the tiny blood vessels of the kidneys. The resulting inflammation, permeability, and scarring of the glomeruli attract more IgA and other substances, slowly increasing kidney damage. As many as 40% of patients who have IgAN eventually develop kidney failure that requiring dialysis or a kidney transplant.

Most patients with IgAN present with either gross hematuria (single or recurrent), usually accompanying an upper respiratory infection, or microscopic hematuria with or without mild proteinuria detected on a routine examination. Less commonly, patients may present with either nephrotic syndrome or an acute, rapidly progressive glomerulonephritis.

The diagnosis of IgAN should be suspected in any patient who presents with one or more episodes of gross hematuria (especially if accompanied by an upper respiratory infection), persistent microscopic hematuria with or without proteinuria, or slowly progressive kidney function impairment. The diagnosis is confirmed by kidney biopsy. However, a kidney biopsy is usually performed only if there are signs suggestive of more severe or progressive disease, such as persistent proteinuria of at least 500 mg per day or an elevated serum creatinine concentration.

Current pharmacologic treatment for IgAN includes corticosteroids, immunosuppressants, and antihypertensive drugs in the angiotensin-converting enzyme (ACE) inhibitor and angiotensin receptor blocker (ARB) therapy classes. In December 2021, Tarpeyo™ (budesonide) delayed-release capsules was given Accelerated Approval from the FDA to treat IgAN at risk of rapid progression. It also needs further clinical trial support for full FDA approval.

Treatment of IgAN is to optimize supportive care consisting of blood pressure control, reduction of proteinuria with maximally tolerated renin-angiotensin system blockade (either an angiotensin-converting enzyme [ACE] inhibitor or angiotensin receptor blocker [ARB]), treatment of dyslipidemia (if present), and lifestyle modification (such as dietary sodium and protein restriction, smoking cessation, weight control, and exercise as appropriate). Individuals with an eGFR >30 mL/min/1.73 m2, use of a sodium-glucose cotransporter 2 (SGLT2) inhibitor may be

added to this supportive regimen. Supportive care should be continued for a minimum of three months and ideally six months, unless there is evidence of rapid disease progression.

Individuals with proteinuria ≥1 g/day despite at least three months of optimized supportive care are considered to be at high risk for progressive disease. In such individuals, treatment with immunosuppressive therapy (i.e., oral systemic glucocorticoids) plus supportive care should be considered.

The role of oral budesonide in the treatment of IgAN has not been clearly established, it should be reserved for individuals with IgAN who do not respond to or cannot tolerate a six-month course of moderate-dose oral glucocorticoids and who have a persistent urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g or proteinuria ≥2 g/day.

Sparsentan is a single molecule with antagonism of the endothelin type A receptor (ET_A R) and the angiotensin II type 1 receptor (AT_1 R). Sparsentan has high affinity for both the ET_A R and the AT_1 R, and greater than 500-fold selectivity for these receptors over the endothelin type B and angiotensin II subtype 2 receptors. Endothelin-1 and angiotensin II are thought to contribute to the pathogenesis of IgAN via the ET_A R and AT_1 R, respectively.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Angiotensin Converting Enzyme (ACE) Inhibitors
Benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril

Angiotesin II Receptor Blockers (ARB)
Azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan

Endothelin Receptor Antagonists
Ambrisentan, bosentan, macitentan

Histamine-2 receptor antagonists
Cimetidine, famotidine, nizatidine, ranitidine

Proton pump inhibitors
Dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole

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Resources:

Filspari (sparsentan) product information, revised by Travere Therapeutics, Inc. 02-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 23, 2024.

Cheung CK, Barratt J. IgA nephropathy: Clinical features and diagnosis. In: UpToDate, Glassock RJ, Fervenza FC, Coppo R, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2024. Topic last updated January 05, 2024. Accessed March 23, 2024.

Cattran DC, Appel GB, Coppo R. IgA nephropathy: Treatment and prognosis. In: UpToDate, Glassock RJ, Fervenza FC, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2024. Topic last updated March 21, 2024. Accessed March 23, 2024.

Santos RD, Brennan DC. IgA nephropathy: Recurrence after transplantation. In: UpToDate, Vella J, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2024. Topic last updated July 28, 2023. Accessed March 23, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03762850: A Randomized, Multicenter, Double-blind, Parallel-group, Active-control Study of the Efficacy and Safety of Sparsentan for the Treatment of Immunoglobulin A Nephropathy. Available from: http://clinicaltrials.gov. Last update posted February 03, 2023. Last verified February 2023. Accessed March 06, 2023. Re-evaluated March 23, 2024.