Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCGEN009.0825	**GENITOURINARY PRODUCTS** **FILSPARI®** (sparsentan tablet) **VANRAFIA®** (atrasentan tablet)
Effective Date: 10/1/2025	**Review/Revised Date**: 01/24, 12/24, 01/25, 08/25 (kn)
Original Effective Date: 10/23	**P&T Committee Meeting Date**: 08/23, 02/24, 12/24, 02/25, 08/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
For initial authorization, all the following criteria must be met:
1. Diagnosis of primary immunoglobulin A nephropathy (IgAN), confirmed by biopsy
2. Patient has been receiving a stable dose of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blockers (ARB), at a maximally tolerated dose
3. Patient is at high risk of disease progression, defined as meeting one of the following criteria (a or b):
    a. Proteinuria of more than 1.0 g/day; OR
    b. Urine protein-to-creatinine ratio of 1.5 g/g or more
4. eGFR greater than or equal to 30 mL/min1.73m^2
5. For sparsentan (Filspari®): provider attestation that ACE inhibitor or ARB will be discontinued before sparsentan therapy is initiated

Reauthorization: Documentation of positive response to therapy defined as improvement in proteinuria.

EXCLUSION CRITERIA:
- For sparsentan only: Concurrent therapy with angiotensin receptor blockers, endothelin receptor antagonists, or aliskiren

AGE RESTRICTIONS:
May be approved for patients aged 18 years and older.

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, a nephrologist.

COVERAGE DURATION:
Initial authorization and reauthorization will be approved for one year.

QUANTITY LIMIT:
Filspari 200mg: 60 tablets per 30 days
Filspari 400mg: 30 tablets per 30 days
Vanrafia 0.75 mg tablet: 30 tablets per 30 days

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Sparsentan (Filspari®) is the second FDA approved medication for adults with IgAN at risk of rapid disease progression (Tarpeyo® being the first FDA approved medication).

Atrasentan (Vanrafia®) is an endothelin type A (Eta) receptor antagonist indicated to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression. Endothelin (ET)-1 is thought to contribute to the pathogenesis of IgAN via the ETAR

FDA APPROVED INDICATIONS:

Sparsentan (Filspari®) is indicated to slow kidney function decline in adults with primary immunoglobulin A nephropathy (IgAN) who are at risk for disease progression.

Atrasentan (Vanrafia®) is indicated to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression.

POSITION STATEMENT:

- Primary IgAN impairs the kidney's ability to filter, causing blood and protein to leak into the urine. Patients will usually present with red-colored urine (hematuria), flank pain, swelling in the ankles, and high blood pressure. After living with IgAN for greater than or equal to 10 years, up to 40% of patients will develop end state renal disease (ESRD), requiring dialysis or renal transplant. Therefore, the goal in treating IgAN is to prevent or delay progression to ESRD.[4]
- IgAN is a rare disease but is the most common primary glomerular disease worldwide (incidence estimated at 2 to 10 per 100,000). IgAN can present at any age but is most commonly diagnosed in patients in their 20s and 30s. Diagnosis is made by a kidney biopsy and is usually performed once a patient has persistent proteinuria.[4]
- Other treatments approved for IgAN include budesonide delayed-release capsule (Tarpeyo®) and iptacopan capsule (Fabhalta®). Tarpeyo® is a corticosteroid 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) greater than or equal to 1.5 g/g. Fabhalta® is an oral factor B inhibitor of the alternative complement pathway 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.
- The approval of sparsentan was based on the results from one randomized, double-blind, active-control, unpublished trial (PROTECT trial) that demonstrated that sparsentan had statistically significant relative change from baseline in urine protein-to-creatinine ratio (UPCR) at week 36 when compared to irbesartan (-45% [95% CI, -51% to -38%] in the sparsentan group and -15% [95% CI, -24% to -4%] in the irbesartan group, with a p-value of <0.0001).[1,5]
    - Primary endpoint was the relative change from baseline in urine protein-to-creatinine ratio (UPCR) at week 36.
    - Key study inclusion criteria included:
        - Biopsy-proven primary IgAN
        - Proteinuria equal to or greater than 1 g/day at screening
        - eGFR of equal to or greater than 30 mL/min/1.73m^2 at screening

        - Currently on stable dose of ACEI and/or ARB therapy, for at least 12 weeks prior to screening (maximum tolerated dose and at least one-half of the maximum labeled dose)
    - Key study exclusion criteria included:
        - IgAN secondary to another condition
        - Presence of cellular glomerular crescents in >25% of glomeruli on renal biopsy (if biopsy available within 6 months of screening)
        - CKD in addition to IgAN
        - Treatment of systemic immunosuppressive medications (including corticosteroids) for >2 weeks within three months of screening
        - Jaundice, hepatitis, or known hepatobiliary disease or elevations of transaminases (ALT/AST) >2 times ULN at screening
        - Potassium greater than 5.5 mEq/L (5.5 mmol/L) at screening
        - History of serious side effect or allergic response to any angiotensin II antagonist or endothelin receptor antagonist, including sparsentan or irbesartan, or has a hypersensitivity to any of the excipients in the study medications
    - Contraindications include: pregnancy, coadministration with angiotensin receptor blockers, endothelin receptor antagonists, or aliskiren
    - Warnings and precautions include: hepatotoxicity, embryo-fetal toxicity, hypotension, acute kidney injury, hyperkalemia, and fluid retention
    - Filspari REMS: For all patients, only available only through a restricted program under a REMS called the FILSPARI REMS because of the risk of hepatotoxicity and embryo-fetal toxicity
- Accelerated approval of atrasentan was based a prespecified interim analysis of the ALIGN trial, a single phase 3, multinational, double-blind, randomized, placebo-controlled trial of 270 adults with biopsy proven IgAN, which found that 0.75 mg of atrasentan per day reduced the urinary protein-tocreatinine ratio by 38.1% at week 36 compared to a 3.1% reduction in the placebo group. Final study results will review the benefit of atrasentan in 404 patients at 136 weeks. Continued approval will depend on verification of clinical benefit
    - Primary efficacy endpoint: Change in the 24-hour UPCR by week 36
    - Key study inclusion criteria
        - Biopsy-proven IgAN
        - Total urinary protein excretion of at least 1 g/day
        - Estimated eGFR of at least 30 mL/min/1.73 m^2
        - Use of a RAS inhibitor (ACEi or ARB) at a maximally tolerated and stable dose for at least 12 weeks
    - Key study exclusion criteria
        - Secondary IgAN
        - Diagnosis or hospitalization for heart failure
        - B-type natriuretic peptide (BNP) of at least 200 pg/mL

  - Boxed Warning: Embryo-Fetal Toxicity
  - Warnings/Precautions: Hepatotoxicity, fluid retention, decreased sperm counts[8]
- The Kidney Disease: Improving Global Outcomes (KDIGO) 2024 Clinical Practice Guidelines recommend patients who are at risk of progressive kidney function loss with IgAN to be treated with an optimized maximally tolerated dose of either angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB), a sodium-glucose cotransporter-2 inhibitor (SGLT2i), and sparsentan. As sparsentan is a dual endothelin angiotensin receptor antagonist (DEARA), it should not be prescribed in combination with an ACEi or ARB.[6]

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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.
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7. The Filspari™ REMS (Risk Evaluation and Mitigation Strategy). Available at: https://filsparirems.com/#Main. Accessed on: January 12, 2025.
8. Heerspink HJL, Jardine M, Kohan DE, et al. Atrasentan in Patients with IgA Nephropathy. *N Engl J Med*. 2025;392(6):544-554. doi:10.1056/NEJMoa2409415