Pharmacy Policy Bulletin: J-1278 Filspari (sparsentan) and Vanrafia (atrasentan) – Commercial and Healthcare Reform	
Number: J-1278	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1278-004	**Original Date:** 04/05/2023
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Filspari (sparsentan) • Vanrafia (atrasentan)

FDA-Approved Indication(s):	• Filspari (sparsentan)
	  ○ To slow kidney function decline in adults with primary immunoglobulin A nephropathy (IgAN) who are at risk for disease progression.
	• Vanrafia (atrasentan)
	  ○ To reduce proteinuria in adults with primary IgAN at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g.

Background:	• Filspari acts as an antagonist at the endothelin type A receptor and the angiotensin II type 1 receptor, while Vanrafia acts as an antagonist at only the endothelin type A receptor (ET_AR). Antagonism at these receptors blocks the action of endothelin-1 and angiotensin II, potent vasoconstrictors thought to contribute to the pathogenesis of IgAN. • IgAN, also known as Berger's disease, is an autoimmune disorder where there are increased levels of a galactose-deficient immunoglobulin A (IgA) variant in the blood. Galactose-deficient IgA antibodies produced on mucosal B-cells in the ileum form immune complexes around the IgA. As the kidneys filter blood, these immune complexes damage the glomeruli and cause inflammation, kidney remodeling, and proteinuria. IgAN can lead to end-stage renal disease (ESRD) as the damage progresses; up to 40% of adults with IgAN will develop ESRD after 20 years. It is estimated that 60,000 people in the United States have IgAN. • The 2024 KDIGO Clinical Practice Guideline for the Management of IgA Nephropathy (IgAN) and IgA Vasculitis (IgAV) recommends that all patients with IgAN and proteinuria > 0.5 g/day be treated with a maximally tolerated dose of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) (category 1B recommendation), or sparsentan (category 2B recommendation), in addition to blood pressure management and lifestyle modifications (e.g., smoking cessation, dietary sodium restriction, and regular

exercise). The guidelines define high risk of progression in IgAN as proteinuria > 0.5 g/day.

- The KDIGO guidelines state that IgAN can only be diagnosed with a kidney biopsy; there are no validated diagnostic serum or urine biomarkers for IgAN. In patients with IgAN, results of immunofluorescence or immunoperoxidase staining upon renal biopsy will demonstrate the presence of dominant or codominant deposition of IgA.
- In clinical trials, both Filspari and Vanrafia were studied in patients with total urine protein ≥ 1 g/day. Patients in the Filspari clinical trials were receiving a maximized stable dose of renin-angiotensin system inhibitors (ACE inhibitors/ARBs) prior to the study, and patients in the Vanrafia clinical trials concomitantly used maximally tolerated ACE inhibitors/ARBS. The primary endpoint, relative change from baseline in UPCR, was measured at 36 weeks.
- ICD-10 Code Information:
    - ICD-10: N02.3 “Recurrent and persistent hematuria with diffuse mesangial proliferative glomerulonephritis” may apply to Filspari; however, the prescriber must confirm that the member has a specific diagnosis of primary IgAN at risk of rapid disease progression.
- Prescribing Considerations:
    - Filspari has a black box warning (BBW) and Risk Evaluation and Mitigation Strategies (REMS) for hepatotoxicity and embryo-fetal toxicity. The REMS requirements for Filspari include pregnancy testing before, during, and after treatment; and measurement of liver aminotransferases and total bilirubin prior to initiation of treatment and measurement of alanine transaminase (ALT) and aspartate transaminase (AST) monthly for 12 months, then every 3 months thereafter during treatment.
    - Vanrafia has a BBW for embryo-fetal toxicity. Vanrafia does not have any REMS requirements.
    - Filspari has warnings and precautions for hepatotoxicity, embryo-fetal toxicity, hypotension, acute kidney injury, hyperkalemia, and fluid retention. Vanrafia also has warnings or precautions for fluid retention and hepatotoxicity and carries an additional warning for decreased sperm counts.
    - Prior to initiating treatment with Filspari, renin-angiotensin-aldosterone system inhibitors (specifically, ACE inhibitors, ARBs, and aliskiren) and endothelin receptor antagonists must be discontinued. Concomitant use of Filspari with these agents is contraindicated.
    - Filspari has drug interactions with strong and moderate cytochrome P450 (CYP) 3A inhibitors; strong CYP3A inducers; antacids/acid reducing agents; nonsteroidal anti-inflammatory drugs (NSAIDs); CYP2B6, 2C9, and 2C19 substrates; sensitive p-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) substrates; and agents that increase serum potassium. Vanrafia has drug interactions with strong or moderate CYP3A inducers and OATP1B1/1B3 inhibitors.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Filspari or Vanrafia may be approved when all of the following criteria are met **(A. through E.)**:

A. The member is 18 years of age or older.

B. The member has a diagnosis of primary immunoglobulin A nephropathy (IgAN), confirmed by biopsy (No ICD-10 code).

C. The member is at risk for rapid disease progression, evidenced by proteinuria ≥ 0.5 g/day.

D. If the request is for Filspari, the member meets both of the following criteria **(1. and 2.)**:
   1. The member has experienced therapeutic failure, contraindication, or intolerance to a maximally tolerated dose of one (1) of the following **(a. or b.)**:
      a. Angiotensin converting enzyme (ACE) inhibitor
      b. Angiotensin receptor blocker (ARB)
   2. The member will not be using Filspari in combination with a renin-angiotensin system inhibitor (specifically, ACE inhibitor, ARB, aliskiren) or endothelin receptor antagonist (for example, Letairis (ambrisentan), Opsumit (macitentan), Tracleer (bosentan)).

E. If the request is for Vanrafia, the member is concurrently taking, or has experienced intolerance or contraindication to, a maximally tolerated dose of one (1) of the following **(1. or 2.)**:
   1. Angiotensin converting enzyme (ACE) inhibitor
   2. Angiotensin receptor blocker (ARB)

II. Reauthorization

When a benefit, reauthorization of Filspari or Vanrafia may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member has experienced a reduction in proteinuria from baseline.

B. If the request is for Filspari, the member will not be using in combination with a renin-angiotensin system inhibitor (specifically, ACE inhibitor, ARB, aliskiren) or endothelin receptor antagonist (for example, Letairis (ambrisentan), Opsumit (macitentan), Tracleer (bosentan)).

C. If the request is for Vanrafia, the member will be concurrently taking, or have experienced contraindication or intolerance to, one (1) of the following **(1. or 2.)**:
   1. Angiotensin converting enzyme (ACE) inhibitor
   2. Angiotensin receptor blocker (ARB)

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Filspari [package insert]. San Diego, CA: Travere Therapeutics, Inc.; September 2024.
2. Vanrafia [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2025.
3. National Institute of Diabetes and Digestive and Kidney Diseases. IgA Nephropathy. Available at: https://www.niddk.nih.gov/health-information/kidney-disease/iga-nephropathy. Accessed February 23, 2023.

4. National Kidney Foundation. Hundreds of IgA Nephropathy Patients Share Experience with FDA, Professionals, Drug-Makers. Available at: https://www.kidney.org/news/hundreds-iga-nephropathy-patients-share-experience-fda-professionals-drug-makers. Accessed February 23, 2023.
5. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. 2024 KDIGO Clinical Practice Guideline for the Management of IgA Nephropathy (IgAN) and IgA Vasculitis (IgAV) Public Review Draft. Available at: https://kdigo.org/wp-content/uploads/2024/08/KDIGO-2024-IgAN-IgAV-Guideline-Public-Review-Draft.pdf. Accessed October 16, 2024.