09-J5000-20

Original Effective Date: 07/01/25

Reviewed: 05/14/25

Revised: 00/00/00

Subject: Atrasentan (Vanrafia) tablet

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Primary IgA nephropathy (IgAN) is due to the deposition of IgA immune complexes in the mesangial cells of the glomeruli, causing mesangial proliferation. It most commonly affects young adults and is more common in East or Pacific Asia. Patients may be asymptomatic, with microscopic hematuria and minimal proteinuria at first, but potential symptoms can include gross hematuria – hypertension, significant proteinuria, and decline in renal function may occur as the disease progresses. Definitive diagnosis requires a kidney biopsy showing IgA deposition in the mesangium confirmed by immunohistology.

In patients with normal blood pressure, normal estimated GFR, and consistent urinary protein to creatinine ratio of < 0.2, treatment may not be necessary. However, once proteinuria exceeds 1 g/day, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are recommended. In those with an inadequate response or rapidly progressive crescentic IgAN, a six-month course of corticosteroids, combination cyclophosphamide with corticosteroids, or single agent cyclophosphamide, azathioprine, or cyclosporine are recommended depending on severity of disease and GFR. Transplant is the treatment of choice for those with progressive kidney failure due to IgAN. Recurrence of IgAN after transplant appears to be time-dependent, with rates of recurrence increasing as time from transplant lengthens. A retrospective study from the ANZDATA registry showed that among a cohort of 2501 kidney transplant patients with biopsy-proven IgAN as the primary disease, 5% 10%, and 15% of recipients experienced disease recurrence at 5, 10 and 15 years after transplant, respectively. However, this may be underreported, and recurrence may be as high as 25% at 5 years and 50% at years.

Atrasentan (Vanrafia) oral tablets were approved by the U.S. Food and Drug Administration (FDA) in April 2025 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. This indication was approved under accelerated approval based on a reduction in proteinuria. It has not been

established whether atrasentan 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.

Atrasentan is an endothelin type A receptor antagonist. In kidney diseases like IgAN and focal segmental glomerulosclerosis (FSGS), blockade of ETA pathways have been shown to reduce proteinuria.

The safety and efficacy of atrasentan were evaluated in a phase 3, double-blind, randomized, controlled trial involving adults with biopsy-proven IgA nephropathy (ALIGN, NCT: NCT04573478). Patients were required to have a total urinary protein excretion of at least 1 g per day, and an estimated glomerular filtration rate of at least 30 ml per minute per 1.73 m2 of body-surface area. Patients (n=340, including 270 patients evaluated for the primary outcome) were randomly assigned to receive atrasentan (0.75 mg per day) or matched placebo for 132 weeks.

The primary outcome, assessed at a prespecified interim analysis of data from the first 270 patients in the main stratum, was the change in the 24-hour urinary protein-to-creatinine ratio from baseline to week 36; the change was estimated with the use of a repeated-measures model.

The mean change in 24-hour urinary protein-to-creatinine ratio (UPCR) from baseline to week 36 was significantly improved with atrasentan therapy (1450.2 vs 882.2; -38.1%; 95% CI, -43.9% to -31.7%) compared with placebo (1484.3 vs 1374.8; -3.1%; 95% CI, -12.4% to 7.3%), resulting in a significant treatment difference of -36.1 percentage points between groups (95% CI, -44.6 to -26.4 percentage points). In the atrasentan group, decrease in UPCR was apparent at week 6 and sustained through week 36.

From baseline to week 36, the mean change in blood pressure with atrasentan compared with placebo was -3.94 vs 2.67 mmHg (systolic) and -4.25 vs 2.25 mmHg (diastolic), and the mean change in body weight was -0.2 vs -0.1 kg; at week 24, the mean change in B-type natriuretic peptide level was 4 vs -0.6 picograms/mL Nasopharyngitis (10.1% vs 5.9%), peripheral edema (8.9% vs 6.5%), anemia (6.5% vs 1.2%), pyrexia (6.5% vs 4.1%), and upper respiratory tract infection (6.5% vs 5.3%) occurred more frequently in the atrasentan group compared with the placebo group. The incidence of severe (7.1% vs 5.9%) or serious (5.9% vs 6.5%) adverse events and patients who discontinued treatment due to an adverse event (3.6% vs 3.5%) were similar with atrasentan compared with placebo.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of atrasentan (Vanrafia) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with IgA nephropathy – documentation from the medical record must be provided

2. Member's diagnosis is confirmed with kidney biopsy – biopsy report must be provided
3. Member's current (within 90 days) urine protein-to-creatinine ratio (UPCR) is greater than or equal to 1.5 g/g – laboratory documentation must be provided
4. Atrasentan is prescribed by a nephrologist
5. Atrasentan is not used concomitantly with budesonide delayed-release capsules (Tarpeyo), iptacopan (Fabhalta), or sparsentan (Filspari)
6. Dose does not exceed 0.75 mg (one tablet) daily

Approval duration: 12 months

Continuation of atrasentan (Vanrafia) **meets the definition of medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue in the past two years for IgA nephropathy OR the member has previously met all indication-specific initiation criteria
2. Member has (or maintains) a beneficial response to treatment with atrasentan (Vanrafia) as evidenced by a 20% or greater reduction in UPCR from baseline (i.e., prior to treatment with sparsentan) – laboratory documentation must be provided
3. Atrasentan is prescribed by a nephrologist
4. Atrasentan is not used concomitantly with budesonide (Tarpeyo), iptacopan (Fabhalta), or sparsentan (Filspari)
5. Dose does not exceed 0.75 mg (one tablet) daily

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

- Tablets: 0.75 mg
- 0.75 mg orally once daily with or without food

PRECAUTIONS:

- Pregnancy
- Hypersensitivity
- Hepatotoxicity
- Fluid Retention
- Decreased Sperm Counts

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

N02.B1	Recurrent and persistent immunoglobulin A nephropathy with glomerular lesion
N02.B2	Recurrent and persistent immunoglobulin A nephropathy with focal and segmental glomerular lesion
N02.B3	Recurrent and persistent immunoglobulin A nephropathy with diffuse membranoproliferative glomerulonephritis
N02.B4	Recurrent and persistent immunoglobulin A nephropathy with diffuse membranous glomerulonephritis
N02.B5	Recurrent and persistent immunoglobulin A nephropathy with diffuse mesangial proliferative glomerulonephritis
N02.B6	Recurrent and persistent immunoglobulin A nephropathy with diffuse mesangiocapillary glomerulonephritis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

Budesonide (Tarpeyo), 09-J4000-14

Sparsentan (Filspari), 09-J4000-48

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 5/1/25]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2025 [cited 5/1/25]. Available from: http://clinicaltrials.gov/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex 2024 [cited 5/1/25].
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 5/1/25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

07/01/25	New Medical Coverage Guideline.