VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Nephrology – Vanrafia Prior Authorization Policy
- Vanrafia™ (atrasentan tablets – Novartis)

REVIEW DATE: 04/09/2025

OVERVIEW

Vanrafia, an endothelin receptor antagonist, is 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 ration (UPCR) ≥ 1.5 g/g.[1]

Vanrafia was approved under accelerated approval based on reduction of proteinuria.[1] It has not been established whether Vanrafia 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.

Disease Overview

IgAN is the most common primary glomerular disease in the world and it is the leading cause of chronic kidney disease (CKD) and kidney failure.[2] The disease is slowly progressive; approximately 25% to 30% of patients develop kidney failure within 20 to 25 years of presentation. The management of IgAN is focused on supportive care to slow the rate of disease progression. IgAN is characterized by a single histopathologic criterion of predominant or co-dominant IgA deposits on kidney biopsy; however, it is well recognized that the disease exhibits heterogeneity in clinical and pathological features. Hypertension and proteinuria are major risk factors for the progression of CKD. Guidelines from Kidney Diseases: Improving Global Outcomes (KDIGO) [2024] note that proteinuria reduction to < 0.5 g/day, a surrogate marker of improved kidney outcomes in IgAN, is a reasonable target.

Clinical Efficacy

The efficacy of Vanrafia was evaluated in a 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 (ALIGN, n = 270).[1,3] Additionally, patients were receiving the maximum tolerated dose of an angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) for ≥ 12 weeks prior to study entry. 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. The majority of patients remained on a renin-angiotensin system inhibitor throughout the study.[1]

The primary efficacy endpoint was the change from baseline in urine protein-to-creatinine ratio (based on 24-hour urine sample) at Week 36.[1,3] At Week 36, the primary endpoint was significantly greater with Vanrafia in the interim analysis set (comprised of the first 270 patients randomized in the study, who completed 36 weeks of the trial). The geometric least squares mean percent change in UPCR from baseline was -38% for Vanrafia vs. -3% for placebo. This resulted in a statistically significant relative reduction from baseline in UPCR for the Vanrafia, corresponding to a 36% relative reduction with Vanrafia (P < 0.001). Exploratory efficacy endpoints for changes in UPCR from baseline to Week 36 in the sodium-glucose linked transporter (SGLT) 2 inhibitor stratum, was -39% for Vanrafia (14 patients) compared to -3% for placebo (15 patients).[3]

Safety

Vanrafia has a Black Box Warning for embryo-fetal toxicity.[1] Vanrafia may cause major birth defects if used during pregnancy. Effective contraception must be started before the start of treatment and continued for 2 weeks after treatment.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Vanrafia. 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 Vanrafia as well as the monitoring required for adverse events and long-term efficacy, approval requires Vanrafia to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Vanrafia is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Primary Immunoglobulin A Nephropathy.** Approve for 9 months 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, and vi):
     - **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 (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 ≥ 1.5 g/g; AND
       - **b)** Patient has received or is currently receiving the maximum or maximally tolerated dose of ONE of the following for ≥ 12 weeks prior to starting Vanrafia [(1) or (2)]:
         - **(1)** Angiotensin converting enzyme inhibitor; OR
         - **(2)** Angiotensin receptor blocker; AND
     - **iv.** According to the provider, patient has received ≥ 3 months of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification; AND
     - **v.** Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 m^2; AND
     - **vi.** The medication is prescribed by or on consultation with a nephrologist; OR
   - **B)** Patient is Currently Receiving Vanrafia. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The diagnosis has been confirmed by biopsy; AND
     - **iii.** According to the prescriber, patient has had a response to Vanrafia,; 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 prescribed by or on consultation with a nephrologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Vanrafia is not recommended in the following situations:

1. **Concurrent use with other medications indicated for the treatment of immunoglobulin A nephropathy (e.g., Fabhalta and Filspari).**
   The requested medication should not be administered in combination with other medications indicated for immunoglobulin A nephropathy. Combination therapy is generally not recommended due to a lack of controlled clinical trial data supporting additive efficacy.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Vanrafia™ tablets [prescribing information]. East Hanover, NJ: Novartis; April 2025.
2. 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 February 20, 2025.
3. Heerspink HJL, Jardine M, Kohan DE, et al. Atrasentan in Patients with IgA Nephropathy. *N Engl J Med*. 2025;392(6):544-554.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	04/09/2025