

atrasentan (VanrafiaTM)

Policy # 00936

Original Effective Date: 08/01/2025

Current Effective Date: 08/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider atrasentan (VanrafiaTM)[†] for the treatment of primary immunoglobulin A nephropathy to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for atrasentan (Vanrafia) will be considered when the following criteria are met:

Initial

- Patient has a diagnosis of primary immunoglobulin A nephropathy (IgAN); AND
- Patient is greater than or equal to 18 years of age; AND
- Diagnosis has been confirmed by biopsy; AND
- Patient is at high risk of disease progression, defined by meeting the following criteria:
 - Patient meets ONE of the following:
 - Proteinuria greater than or equal to 0.5 g/day; OR
 - Urine protein to creatinine ratio greater than or equal to 0.44g/g; AND
 - Patient has been receiving the maximally tolerated dose of an angiotensin converting enzyme inhibitor (ACEi) (e.g., lisinopril, enalapril, benazepril, captopril, fosinopril, moexipril, perindopril, quinapril, ramipril, trandolapril) or angiotensin receptor blocker (ARB) (e.g., candesartan, irbesartan, losartan, olmesartan, telmisartan, valsartan) for greater than or equal to 90 days; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73 m²;
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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Continuation

- Patient has received an initial authorization for Vanrafia; AND
- According to the prescriber, patient is continuing to derive benefit from Vanrafia. Examples of treatment benefits include reduction in urine protein to creatinine ratio from baseline or reduction in proteinuria from baseline.

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of atrasentan (Vanrafia) when the patient has not been receiving the maximally tolerated dose of an ACEi or ARB for at least 90 days, or the patient has an estimated glomerular filtration rate less than 30 mL/min/1.73 m² to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of atrasentan (Vanrafia) when the patient is not deriving benefit from the therapy (as evidenced by a reduction in urine protein to creatinine ratio or reduction in proteinuria) to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of atrasentan (Vanrafia) when the patient selection criteria are not met (except those noted above as **not medically necessary****) to be **investigational.***

Background/Overview

Vanrafia is a once-daily, nonsteroidal, oral, endothelin receptor antagonist indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression. Vanrafia can be added to supportive care that includes a renin-angiotensin system inhibitor with or without a sodium glucose co-transporter 2 inhibitor (SGLT2i). It is a selective antagonist for the endothelin type A receptor. Endothelin-1 is thought to contribute to the pathogenesis of IgAN via the endothelin type A receptor.

IgAN is the most common cause of primary glomerulonephritis in resource-abundant settings. Around 25% of patients with this condition have a slow progression to end-stage kidney disease (ESKD) within 25 years of presentation. The remaining patients enter a sustained remission or have persistent low-grade hematuria and/or proteinuria. Some of the proposed risk factors for disease progression include proteinuria above 0.5 g/day, hypertension, reduced eGFR, hematuria, certain histologic predictors on kidney biopsy, and modifiable factors such as obesity, hypertriglyceridemia, and smoking. The goal of treating IgAN is to prevent disease progression to ESKD by reducing proteinuria to less than 0.5 to 1 g/day and resolving microscopic hematuria. The first-line treatment options to achieve this goal are supportive care with blood pressure control, maximally tolerated

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renin-angiotensin system blockade, treatment with a SGLT2i, and lifestyle modification. After 3-6 months of optimized supportive care, patients at high risk may require further therapy to reduce risk. Several agents that target IgAN-specific pathogenic mechanisms have been approved recently for the treatment of IgAN in patients at risk of disease progression. These include budesonide (TarpeyoTM)[‡], iptacopan (Fabhalta[®])[‡], sparsentan (FilspariTM)[‡], atrasentan (VanrafiaTM)[‡], and sibeprenlimab (Voyxact).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Vanrafia was approved 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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The effect of Vanrafia on proteinuria was assessed in a randomized, double-blind, placebo-controlled multicenter, global study (ALIGN) in adults with biopsy-proven primary IgAN, an eGFR ≥ 30 mL/min/1.73 m², and urine protein ≥ 1 g/day on a stable dose of maximally tolerated renin angiotensin system inhibitor. The study included two cohorts: a main cohort of 340 patients and an exploratory cohort of 64 patients who were also on a stable dose of sodium glucose co-transporter 2 inhibitor (SGLT2i) at baseline. Patients with chronic kidney disease due to another condition in addition to IgAN or those who had been recently treated with systemic immunosuppressants were excluded. Patients were randomized (1:1) to receive either Vanrafia 0.75 mg or placebo once daily. RAS inhibitor therapy was continued throughout the study. Rescue immunosuppressive treatment could be initiated per investigator discretion during the trial.

The efficacy analysis included the first 270 patients in the main cohort who reached the Week 36 visit. The primary endpoint was the percent reduction in UPCR at Week 36 relative to baseline. For the Vanrafia group (n = 135), the % reduction in UPCR was 38% (95% CI: 32%, 44%). For the placebo group (n = 135), the % reduction in UPCR was 3% (95% CI: -7%, 12%).

References

1. Vanrafia [package insert]. Novartis Pharmaceuticals Corporation. East Hanover, NJ. Updated June 2025.
2. Vanrafia (atrasentan) New Drug Review. IPD Analytics. Updated May 2025.
3. Kidney Disease: Improving Global Outcomes (KDIGO) IgAN/IgAV Work Group. KDIGO 2025 clinical practice guideline for the management of immunoglobulin A nephropathy (IgAN) and immunoglobulin A vasculitis (IgAV). *Kidney Int.* 2025;108(4 Suppl):S1-S71.

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07/03/2025 Medical Policy Committee review

07/09/2025 Medical Policy Implementation Committee approval. New policy.

07/21/2026 Pre Pharmacy and Therapeutics Committee approval

07/22/2026 Pharmacy and Therapeutics Committee approval. Updated criteria and background information to align with other treatments for this condition and reflect recent guideline updates.

Next Scheduled Review Date: 07/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.