Clinical Policy: Atrasentan (Vanrafia)

Reference Number: CP.PHAR.727
Effective Date: 06.01.25
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Atrasentan (Vanrafia®) is an endothelin receptor antagonist.

FDA Approved Indication(s)

Vanrafia is 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.*

**This indication is approved under accelerated approval based on a reduction of proteinuria. 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.*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Vanrafia is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Immunoglobulin A Nephropathy (must meet all)**:**

1. Diagnosis of IgAN confirmed via kidney biopsy;
2. Prescribed by or in consultation with a nephrologist;
3. Age ≥ 18 years;
4. Documentation of both of the following (a and b):
   a. Proteinuria of ≥ 0.5 g/day or UPCR ≥ 1.5 g/g;
   b. Estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m^2;
5. Member is currently receiving therapy with a renin-angiotensin-aldosterone system (RAAS) inhibitor (e.g., irbesartan, losartan, lisinopril, benazepril; *see Appendix D*) at up to maximally tolerated doses for at least 12 weeks, unless contraindicated or clinically significant adverse effects are experienced;
6. Vanrafia is prescribed in combination with a RAAS inhibitor (*see Appendix* D), unless contraindicated or clinically significant adverse effects are experienced;
7. Failure of a 12 week trial of a sodium-glucose cotransporter-2 (SGLT2) inhibitor (e.g., empagliflozin, dapagliflozin) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;*
   **For Illinois HIM requests, the step therapy requirements above do not apply per IL HB 5395*
8. Dose does not exceed 0.75 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Immunoglobulin A Nephropathy (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Decrease in UPCR from baseline;
   b. Reduction of proteinuria as evidenced by a lower total urine protein per day from baseline;
3. If request is for a dose increase, new dose does not exceed 0.75 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the

relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACEI: angiotensin-converting-enzyme inhibitor
ARB: angiotensin receptor blocker
eGFR: estimated glomerular filtration rate
ERA: endothelin receptor antagonist
FDA: Food and Drug Administration
IgAN: immunoglobulin A nephropathy
RAS: renin-angiotensin system
UPCR: urine protein-to-creatinine ratio

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Maximum Dose
RAS inhibitors	
Angiotensin-converting enzyme (ACE) inhibitors (e.g., benazepril, captopril, enalapril, lisinopril, quinapril)	Varies
Angiotensin-receptor blockers (ARB) (e.g., candesartan, irbesartan, losartan, olmesartan, telmisartan, valsartan)	Varies
SGLT2 Inhibitors	
dapagliflozin (Farziga®)	10 mg/day
Jardiance® (empagliflozin)	10 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): pregnancy, hypersensitivity
- Boxed warning(s): embryo-fetal toxicity

Appendix D: General Information

- The 2025 Kidney Disease Improving Global Outcomes (KDIGO) guideline recommends initial therapy with a RAS inhibitor (ACEI or ARB) for all patients, except patients with

contraindications such as low blood pressure, bilateral renal artery stenosis, or hyperkalemia, especially due to advanced chronic kidney disease (CKD).

- The 2025 KDIGO guideline recommends initial therapy with an SGLT2 inhibitor, for patients with proteinuria > 0.5 g per day, regardless of whether the patient has hypertension.
- Patients with IgAN who are considered high risk for progressive CKD despite maximum supportive care (defined as blood pressure control, reduction of proteinuria, and lifestyle modifications) may consider treatment with corticosteroids or immunosuppressive drugs; however, there is current uncertainty over the safety and efficacy of existing immunosuppressive treatment choices. For all patients in whom immunosuppression is being considered, a detailed discussion of the risks and benefits of each drug should be undertaken with the patient recognizing that adverse treatment effects are more likely in patients with eGFR < 50 mL/min/1.73 m^2.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
IgAN	0.75 mg PO QD with or without food	0.75 mg/day

VI. Product Availability

Tablet: 0.75 mg

VII. References

1. Vanrafia Prescribing Information. Novartis Pharmaceuticals Corporation; East Hanover, New Jersey: April 2025. Available at: https://www.vanrafia-hcp.com/. Accessed May 7, 2026.
2. Heerspink HJL, Jardine M, Kohan DE, et al; ALIGN Study Investigators. Atrasentan in patients with IgA nephropathy. *N Engl J Med*. 2025 Feb 6;392(6):544-554. doi: 10.1056/NEJMoa2409415.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. Kidney nt. 2021 Oct;100(4S):S1-S276. doi: 10.1016/j.kint.2021.05.021
4. Caster DJ and Lafayette RA. The treatment of primary IgA nephropathy: change, change, change. *Am J Kidney Dis.* 2024 Feb;83(2):229-240.
5. KDIGO 2025 Clinical Practice Guideline for the management of immunoglobulin A nephropathy (IgAN) and immunoglobulin A vasculitis (IgAV). Kidney International 2025 October;108(45):S1-S71.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.22.25	05.25
2Q 2026 annual review: revised proteinuria criterion from 1 g/day to 0.5 g/day per updated 2025 KDIGO guidelines; extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition; references reviewed and updated. Added ICHRA line of business.	03.30.26	05.26

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2026 annual review: added redirection to SGLT2i per updated 2025 KDIGO guidelines; references reviewed and updated.	05.07.26	08.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.