# Clinical Policy: Atrasentan (Vanrafia)

Reference Number: PA.CP.PHAR.727
Effective Date: 08/2025
Last Review Date: 04/2026

## 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 PA Health & Wellness® 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. Dose does not exceed 0.75 mg (1 tablet) per day.

**Approval duration: 12 months**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**II. Continued Therapy**

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## 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 – PA.CP.PMN.53

## 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
RAAS: renin-angiotensin-aldosterone 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 and may require prior authorization.*

| Drug Name | Maximum Dose |
|---|---|
| ***ACEIs*** | |
| benazepril (Lotensin®) | 80 mg/day |
| captopril (Capoten®) | 450 mg/day |
| enalapril (Vasotec®, Epaned®) | 40 mg/day |
| fosinopril (Monopril®) | 80 mg/day |
| lisinopril (Prinivil®, Zestril®, Qbrelis®) | 80 mg/day |
| moexipril (Univasc®) | 30 mg/day |
| perindopril (Aceon®) | 16 mg/day |
| quinapril (Accupril®) | 80 mg/day |

| Drug Name | Maximum Dose |
|---|---|
| ramipril (Altace®) | 20 mg/day |
| trandolapril (Mavik®) | 8 mg/day |
| ***ARBs*** | |
| azilsartan (Edarbi®) | 80 mg/day |
| candesartan (Atacand®) | 32 mg/day |
| eprosartan (Teveten®) | 900 mg/day |
| irbesartan (Avapro®) | 300 mg/day |
| losartan (Cozaar®) | 100 mg/day |
| olmesartan (Benicar®) | 40 mg/day |
| telmisartan (Micardis®) | 80 mg/day |
| valsartan (Diovan®) | 320 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 2021 Kidney Disease Improving Global Outcomes (KDIGO) recommends initial therapy with a RAAS inhibitor (ACEI or ARB) 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 chronic kidney disease 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 January 23, 2026.
2. ClinicalTrials.gov. Atrasentan in patients with IgA nephropathy (ALIGN). Available at: https://clinicaltrials.gov/study/NCT04573478. Accessed January 23, 2026.

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 |
|---|---|
| Policy created | 07/2025 |
| 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. | 04/2026 |