To reduce proteinuria in adults with primary IgAN at risk of rapid disease progression (generally a UPCR ≥1.5 g/g),[1,2]

YOU HAVE OPTIONS **FOR PATIENTS WITH IgA NEPHROPATHY (IgAN)**

VANRAFIA™ (atrasentan) tablets 0.75 mg

Meet Vince: A patient with IgAN and persistent proteinuria[1]

Learn more

Hypothetical patient case and portrayal.

INDICATION

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.

IMPORTANT SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY

VANRAFIA is contraindicated for use in pregnant patients; it may cause major birth defects, based on animal data. Exclude pregnancy prior to initiation of treatment with VANRAFIA. Advise use of effective contraception before the initiation of treatment, during treatment, and for 2 weeks after discontinuation of treatment with VANRAFIA. Stop VANRAFIA as soon as possible if the patient becomes pregnant.

CONTRAINDICATIONS

Pregnancy

Use of VANRAFIA is contraindicated in patients who are pregnant.

Hypersensitivity

VANRAFIA is contraindicated in patients with a history of a hypersensitivity reaction to atrasentan or any component of the product.

IgAN, immunoglobulin A nephropathy; UPCR, urine protein-to-creatinine ratio.

Please click here for full Important Safety Information. Please click here for full Prescribing Information, including Boxed WARNING and Medication Guide.

FABHALTA® (iptacopan) 200 mg capsules

Meet Fiona: A patient with IgAN, persistent proteinuria, and glomerular inflammation[2]

Learn more

Hypothetical patient case and portrayal.

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FABHALTA, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life threatening or fatal if not recognized and treated early.

- **Complete or update vaccinations for encapsulated bacteria at least 2 weeks prior to the first dose of FABHALTA, unless the risks of delaying therapy with FABHALTA outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor.**
- **Patients receiving FABHALTA are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, FABHALTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FABHALTA REMS.

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FABHALTA and VANRAFIA are two different drugs and were not studied for combination use.
The Prescribing Information for each drug does not mention the other drug, nor that the drugs can be used together.

How would you manage Vince's or Fiona's persistent proteinuria?

VANRAFIA™ (atrasentan) tablets 0.75 mg

Meet Vince:

A 45-year-old Asian male with IgAN and persistent proteinuria[1,3,4]

Hypothetical patient case and portrayal.

Initial presentation to nephrologist

Proteinuria (g/g): 1.9 **eGFR (mL/min/1.73 m²):** 63 **BP (mm Hg):** 131/85 **Comorbidities:** None

Vince's nephrologist suspects IgAN and sends him for a biopsy. The biopsy confirms an IgAN diagnosis, so he is started on an ACEi and lifestyle changes (low-sodium diet and exercise). His nephrologist dose adjusts to the maximally tolerated and stable dose of his ACEi.

6-month follow-up with nephrologist shows proteinuria is still persistent

Proteinuria (g/g): 1.5 **eGFR (mL/min/1.73 m²):** 62 **BP (mm Hg):** 125/80

There could be another option to reduce proteinuria for patients like Vince

Learn more about how VANRAFIA could help patients like Vince

ACEi, angiotensin-converting enzyme inhibitor; BP, blood pressure; eGFR, estimated glomerular filtration rate.

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Meet Fiona:

A 34-year-old Asian female with IgAN, persistent proteinuria, and glomerular inflammation[2,5,6]

Hypothetical patient case and portrayal.

Initial presentation to PCP

Proteinuria | Hematuria | Edema | Hypertension

Presentation to nephrologist

Proteinuria (g/g): 1.8 **eGFR (mL/min/1.73 m²):** 75 **BP (mm Hg):** 140/90 **Persistent microscopic hematuria**

Her nephrologist prescribed an ACEi and lifestyle changes (low-sodium diet and exercise)

Fiona's kidney biopsy at diagnosis

The biopsy revealed complement activation **MEST-C score:** M1, E1, S1, T0, C0

3-month follow-up after IgAN diagnosis

Proteinuria (g/g): 1.7 Fiona was prescribed a course of steroids

After completion of a 6-month course of steroids

Proteinuria (g/g): 1.5

3 months after steroid completion

Proteinuria (g/g): 1.5

Fiona and her nephrologist were not satisfied after completion of her course of steroids

Learn more about how FABHALTA could help patients like Fiona

MEST-C, mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S), tubular atrophy (T), and crescents (C); PCP, primary care provider.

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Meet Vince: A patient with IgAN and persistent proteinuria[1,3,4]

45-year-old Asian male | Hypothetical patient case and portrayal.

Initial presentation to nephrologist

Proteinuria (g/g): 1.9
BP (mm Hg): 131/85
eGFR (mL/min/1.73 m²): 63
Comorbidities: None

Vince's nephrologist suspects IgAN and sends him for a biopsy. The biopsy confirms an IgAN diagnosis, so he is started on an ACEi and lifestyle changes (low-sodium diet and exercise). His nephrologist dose adjusts to the maximally tolerated and stable dose of his ACEi.

6-month follow-up with nephrologist shows proteinuria is still persistent

Proteinuria (g/g): 1.5
BP (mm Hg): 125/80
eGFR (mL/min/1.73 m²): 62

There could be another option to reduce proteinuria for patients like Vince

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Meet Fiona: A patient with IgAN, persistent proteinuria, and glomerular inflammation[2,5,6]

34-year-old Asian female | Hypothetical patient case and portrayal.

Initial presentation to PCP

Proteinuria | Hematuria | Edema | Hypertension

Presentation to nephrologist

Proteinuria (g/g): 1.8
BP (mm Hg): 140/90
eGFR (mL/min/1.73 m²): 75
Persistent microscopic hematuria

Her nephrologist prescribed an ACEi and lifestyle changes (low-sodium diet and exercise)

Fiona's kidney biopsy at diagnosis

The biopsy revealed complement activation
MEST-C score: M1, E1, S1, T0, C0

3-month follow-up after IgAN diagnosis

Proteinuria (g/g): 1.7

Fiona was prescribed a course of steroids

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Hypersensitivity

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WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

Based on data from animal reproduction studies, VANRAFIA may cause fetal harm when administered to a pregnant patient and is contraindicated during pregnancy. The available human data for endothelin receptor antagonists (ERAs) do not establish the presence or absence of major birth defects related to the use of VANRAFIA. Counsel patients who can become pregnant of the potential risk to a fetus. Exclude pregnancy prior to initiation of treatment with VANRAFIA. Advise patients to use effective contraception prior to initiation of treatment, during treatment, and for 2 weeks after discontinuation of treatment with VANRAFIA. When pregnancy is detected, discontinue VANRAFIA as soon as possible.

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FABHALTA, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life threatening or fatal if not recognized and treated early.

- **Complete or update vaccinations for encapsulated bacteria at least 2 weeks prior to the first dose of FABHALTA, unless the risks of delaying therapy with FABHALTA outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor.**
- **Patients receiving FABHALTA are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, FABHALTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FABHALTA REMS.

CONTRAINDICATIONS

- In patients with serious hypersensitivity to FABHALTA or any of the excipients.
- For initiation in patients with unresolved serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, or *Haemophilus influenzae* type b.

WARNINGS AND PRECAUTIONS

Serious Infections Caused by Encapsulated Bacteria

- FABHALTA, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by encapsulated bacteria, including *Streptococcus pneumoniae, Neisseria meningitidis* (caused by any serogroup, including nongroupable strains), and *Haemophilus influenzae* type b.

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hepatotoxicity

Some ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure. Asymptomatic and transient transaminase elevations have been observed with VANRAFIA. Obtain liver enzyme testing before initiating VANRAFIA, and repeat during treatment as clinically indicated. In patients with elevated aminotransferases at baseline (>3 × upper limit of normal [ULN]), consider periodic liver test monitoring. Do not initiate VANRAFIA in patients with severe hepatic impairment.

Advise patients to report symptoms suggesting hepatic injury (eg, nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching). If clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 × ULN, or by clinical symptoms of hepatotoxicity, discontinue VANRAFIA. Consider reinitiation of VANRAFIA when hepatic enzyme levels normalize in patients who have not experienced clinical symptoms of hepatotoxicity or jaundice.

Fluid Retention

Fluid retention may occur with ERAs and has been observed in clinical studies with VANRAFIA. VANRAFIA has not been evaluated in IgAN patients with heart failure. If clinically significant fluid retention develops, consider initiating or increasing diuretic treatment and interrupting VANRAFIA treatment.

Decreased Sperm Counts

VANRAFIA, similar to other ERAs, may have an adverse effect on spermatogenesis. Counsel men about the potential effects on fertility.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥5%) with VANRAFIA were peripheral edema and anemia.

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FABHALTA® (iptacopan) 200 mg capsules

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Serious Infections Caused by Encapsulated Bacteria (continued)

Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors. The initiation of FABHALTA is contraindicated in patients with unresolved serious infections caused by encapsulated bacteria.

- Complete or update vaccination against encapsulated bacteria at least 2 weeks prior to the start of FABHALTA, according to the current ACIP recommendations for patients receiving a complement inhibitor. Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with FABHALTA. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent FABHALTA therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. The benefits and risks of treatment with FABHALTA, as well as the benefits and risks of antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by encapsulated bacteria.
- Vaccination does not eliminate the risk of serious encapsulated bacterial infections, despite development of antibodies following vaccination. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections. Serious infection may become rapidly life threatening or fatal if not recognized and treated early. Consider interruption of FABHALTA in patients who are undergoing treatment for serious infections, depending on the risks of interrupting treatment in the disease being treated.

FABHALTA REMS

- FABHALTA is available only through a restricted program under a REMS called FABHALTA REMS, because of the risk of serious infections caused by encapsulated bacteria.
- Under the FABHALTA REMS, prescribers must enroll in the program; counsel patients about the risks, signs, and symptoms of serious infections caused by encapsulated bacteria; provide patients with the REMS educational materials; ensure patients are vaccinated against encapsulated bacteria; prescribe antibacterial drug prophylaxis if patients' vaccine status is not up to date and treatment must be started urgently; and provide instructions to always carry the Patient Safety Card during treatment and for 2 weeks following the last dose of FABHALTA.
- Further information is available by telephone: 1-833-993-2242 or online at www.FABHALTA-REMS.com.

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VANRAFIA™ (atrasentan) tablets 0.75 mg

IMPORTANT SAFETY INFORMATION (continued)

EFFECT OF OTHER DRUGS ON VANRAFIA

Strong or Moderate CYP3A Inducers: Avoid concomitant use with a strong or moderate CYP3A inducer. Atrasentan is a CYP3A substrate. Concomitant use with a strong and moderate CYP3A inducer is expected to decrease atrasentan exposure, which may reduce VANRAFIA efficacy.

OATP1B1/1B3 Inhibitors: Avoid concomitant use with organic anion transporting polypeptides (OATP) 1B1/1B3 (OATP1B1/1B3) inhibitors. Atrasentan is an OATP1B1/1B3 substrate. Concomitant use with an OATP1B1/1B3 inhibitor increases atrasentan exposure, which may increase the risk of VANRAFIA adverse reactions.

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FABHALTA® (iptacopan) 200 mg capsules

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hyperlipidemia

- FABHALTA may increase total cholesterol, LDL cholesterol, and serum triglycerides. Some patients required cholesterol-lowering medications.
- Monitor serum lipid parameters periodically during treatment with FABHALTA and initiate cholesterol-lowering medications, if indicated.

ADVERSE REACTIONS

- The most common adverse reactions (≥5%) in adults with IgAN receiving FABHALTA were upper respiratory tract infection, lipid disorder, and abdominal pain.

DRUG INTERACTIONS

- Concomitant use of CYP2C8 inducers (eg, rifampin) may decrease iptacopan exposure, which may result in loss of or reduced efficacy of FABHALTA. Monitor the clinical response and discontinue use of the CYP2C8 inducer if loss of efficacy of FABHALTA is evident.
- Concomitant use of strong CYP2C8 inhibitors (eg, gemfibrozil) may increase iptacopan exposure, which may result in an increased risk for adverse reactions with FABHALTA. Coadministration with a strong CYP2C8 inhibitor is not recommended.

USE IN SPECIFIC POPULATIONS

- Because of the potential for serious adverse reactions in a breastfed child, breastfeeding should be discontinued during treatment and for 5 days after the final dose.
- FABHALTA is not recommended in patients with severe hepatic impairment (Child-Pugh class C). No dose adjustment is required for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment.

Please click here for full Prescribing Information, including Boxed WARNING and Medication Guide.

References: 1. Vanrafia. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Fabhalta. Prescribing information. Novartis Pharmaceuticals Corp. **3.** Rovin BH, Adler SG, Barratt J, et al; Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int*. 2021;100(suppl 4):S1-S276. doi:10.1016/j.kint.2021.05.021 **4.** Heerspink HJL, Jardine M, Kohan DE, et al. Atrasentan in patients with IgA nephropathy. *N Engl J Med*. 2024;1-11. doi:10.1056/NEJMoa2409415 **5.** Rizk DV, Rovin BH, Zhang H, et al. Targeting the alternative complement pathway with iptacopan to treat IgA nephropathy: design and rationale of the APPLAUSE-IgAN study. *Kidney Int Rep.* 2023;8(5):968-979. doi:10.1016/j.ekir2023.01.041 **6.** Data on file. APPLAUSE Sub Analysis. Novartis Pharmaceuticals Corp; July 2024.

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