ADOPTING FABHALTA® (iptacopan) INTO CLINICAL PRACTICE

> When I learned about the FDA approval for FABHALTA and clinical trial results that led to its approval, **I was excited about the possibilities for the patients in my practice.**

— **Belal Firwana, MD, MS**
Missouri Baptist Medical Center
St. Louis, MO

> **If the patient and physician both believe that a treatment option like FABHALTA is necessary, the patient should be given the opportunity to start FABHALTA.**

— **Srinivasa Sanikommu, MD**
Atrium Health Levine Cancer Institute
Charlotte, NC

Dr Sanikommu and Dr Firwana discuss their personal experiences with prescribing FABHALTA and key considerations for adopting FABHALTA into any clinical practice. They share their perspectives on the onboarding process, key points to review with patients, and tips on getting patients started on FABHALTA.

The perspectives provided within this newsletter by Dr Sanikommu and Dr Firwana are their own and not reflective of their affiliations. Dr Sanikommu and Dr Firwana have been paid by Novartis to provide their perspectives. This newsletter is not intended to be and does not serve as medical advice, guidance, or recommendations from Novartis.

FDA, US Food and Drug Administration.

INDICATION

FABHALTA is indicated for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH).

FABHALTA® (iptacopan) 200 mg capsules

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

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.

Please see additional Important Safety Information throughout this newsletter. Please click here for full Prescribing Information, including Boxed WARNING and Medication Guide.

CLICK BELOW TO SEE DR SANIKOMMU AND DR FIRWANA'S PERSPECTIVES ON THESE QUESTIONS

HEAR MORE EXPERT PERSPECTIVES AT
https://www.FABHALTA-hcp.com/pnh/medical-expert-perspectives

Why did you decide to start using FABHALTA in your practice?

FABHALTA® (iptacopan) 200 mg capsules

KEY TAKEAWAYS

FABHALTA is indicated for adults with PNH

FABHALTA is indicated for the treatment of adults with PNH.[1] **When I learned about the FDA approval for FABHALTA and clinical trial results that led to its approval,[1] I was excited about the possibilities for the patients in my practice. The indication for adults with PNH allows me to manage PNH in my patients who have previously been treated with C5 inhibitors** (eculizumab or ravulizumab) **or are new to complement inhibitor treatments.**[1]

— **Dr Firwana**

FABHALTA can help deliver comprehensive hemolysis control (IVH and EVH)

I believe that addressing EVH is an important unmet need. **FABHALTA is an oral complement Factor B inhibitor that acts proximally in the alternative complement pathway to control both C3b-mediated EVH and terminal complement-mediated IVH, making it the first FDA-approved oral monotherapy of its kind** for adults with PNH.[1-6]

— **Dr Sanikommu**

Some patients prefer an oral monotherapy option

Patient preference for an oral monotherapy is also an important deciding factor for choosing FABHALTA. **Many of my patients may not want to travel to infusion sites or the doctor's office. I listen to their concerns and help them select the treatment option that can best meet their needs and schedule.** Oral FABHALTA is taken twice daily.

— **Dr Firwana**

SEE ADDITIONAL TAKEAWAYS

C5, complement component 5; EVH, extravascular hemolysis; FDA, US Food and Drug Administration; IVH, intravascular hemolysis; PNH, paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

- 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.

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FABHALTA was studied in both C5i-experienced (eculizumab or ravulizumab) and complement inhibitor–naive adults with PNH[1]

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APPLY[1,15]

A head-to-head study of C5i-experienced (eculizumab or ravulizumab) adults with PNH

APPLY was a 24-week, randomized,* open-label, active comparator–controlled, phase 3 trial to assess the efficacy and safety of switching to FABHALTA 200 mg twice daily compared with continuing on intravenous C5i therapy (US-approved and non–US-approved eculizumab or ravulizumab) in adults with PNH and residual anemia (mean Hb <10 g/dL) despite previous treatment with a stable regimen of C5i treatment for at least 6 months; 97 patients were randomized in an 8:5 ratio to either switch to FABHALTA 200 mg taken orally twice daily (n=62) or continue their C5i regimen (n=35: eculizumab, n=23; ravulizumab, n=12). In the 24-week extension period of the APPLY trial, 61 of the 62 patients in the FABHALTA arm continued taking FABHALTA and 34 of the 35 patients in the C5i-to-FABHALTA arm switched to FABHALTA.

Superior and substantial Hb increases were achieved with FABHALTA over C5is through the 24-week randomized treatment period

PRIMARY END POINTS

Patients with **Hb increase of ≥2 g/dL**[§] from baseline in the absence of RBC transfusions[‖] after 24 weeks

Response rates

82.3% FABHALTA (n=51/62; 95% CI, 70.5-90.8)

vs

0% C5is (eculizumab or ravulizumab) (n=0/35; 95% CI, 0-10.0)

(Difference[¶]: 81.5%; 95% CI, 71.6-91.4; *P*<0.0001)

Patients with **normalized Hb**[§] of ≥12 g/dL* in the absence of RBC transfusions[‖] after 24 weeks

Response rates

67.7% FABHALTA (n=42/62; 95% CI, 54.7-79.1)

vs

0% C5is (eculizumab or ravulizumab) (n=0/35; 95% CI, 0-10.0)

(Difference[¶]: 66.6%; 95% CI, 54.6-78.6; *P*<0.0001)

APPOINT[1]

Designed to evaluate the efficacy and safety of an oral monotherapy for complement inhibitor–naive patients

APPOINT was a 24-week, phase 3, single-arm, open-label, uncontrolled study of FABHALTA 200 mg twice daily in adults (N=40) with PNH who were complement inhibitor–naive and had an RBC clone size ≥10%, a mean Hb <10 g/dL,[†] and an LDH level >1.5 x ULN.[‡] All 40 patients from the core period completed the 24-week extension period of the trial, as well.

With FABHALTA oral monotherapy, substantial Hb improvements without the need for RBC transfusions are within reach

PRIMARY END POINT

Patients with **sustained Hb increase of ≥2 g/dL****
from baseline in the absence of RBC transfusions[‖] after the 24-week core period

Response rate

Based on central laboratory Hb values

77.5% FABHALTA (n=31/40; 95% CI, 61.5-89.2)

Sensitivity analysis

87.5% (n=35/40; 95% CI, 73.2-95.8)

Response rate based on the inclusion of local laboratory values when central laboratory values were not available

C5i, complement component 5 inhibitor; CI, confidence interval; Hb, hemoglobin; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell.

*Randomization was stratified based on prior C5i treatment and transfusion history within the last 6 months.[1]
†Confirmed by 2 measurements 2 to 8 weeks apart for patients not receiving an RBC transfusion during screening, or by 1 measurement during the first screening visit for patients receiving an RBC transfusion.[16]
‡Confirmed by at least 2 measurements 2 to 8 weeks apart during the screening period.[16]
§Adjusted mean assessed between Weeks 18 and 24 (Days 126 and 168). Excludes values within 30 days post-transfusion.[1]
‖Assessed between Days 14 and 168. Requiring RBCs refers to any patient receiving transfusions or meeting protocol-defined criteria.[15,16]
¶Adjusted difference in proportion.[1]
#Normalization defined as meeting the primary end point of Hb ≥12 g/dL. Normal Hb levels vary, but generally are between 12-16 g/dL for women and 13-18 g/dL for men.[15,17]
**Assessed between Days 126 and 168.[1]

IMPORTANT SAFETY INFORMATION (continued)

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. 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.

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What was your experience with getting patients started on FABHALTA?

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KEY TAKEAWAYS

Get REMS certified to prescribe FABHALTA

Because of the risk of serious infections caused by encapsulated bacteria, FABHALTA is only available through a REMS program that requires vaccinations. Health care professionals will need to become certified in the FABHALTA REMS and fulfill its requirements.[1] **The FABHALTA REMS process took me a few minutes, and the process was very straightforward.** For me, the interface is user-friendly, and I give credit to those who made it so seamless.

— **Dr Sanikommu**

Completing or updating vaccinations before starting patients on FABHALTA

For the vaccination requirements, physicians need to comply with the most current ACIP recommendations for vaccinations against encapsulated bacteria in patients receiving complement inhibitors. Complete or update patients' vaccinations at least 2 weeks before starting treatment with FABHALTA.[1] **Patients switching from C5is may already be up to date with the required meningococcal vaccine, leaving just the required *Streptococcus pneumoniae* vaccination to fulfill this requirement.**

— **Dr Firwana**

The process of prescribing FABHALTA through a specialty network of pharmacies was smooth for me

Pharmacies that dispense FABHALTA must be certified in the FABHALTA REMS and verify that prescribers are certified.[1] **My part is informing patients which specialty pharmacy will be dispensing their FABHALTA prescription and telling them to expect a phone call to arrange delivery of their prescription.**[1]

— **Dr Sanikommu**

ACIP, Advisory Committee on Immunization Practices; C5i, complement component 5 inhibitor; PNH, paroxysmal nocturnal hemoglobinuria; REMS, Risk Evaluation and Mitigation Strategy.

CLICK HERE TO VIEW THE FULL PROCESS FOR STARTING PATIENTS ON FABHALTA

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Serious Infections Caused by Encapsulated Bacteria (continued)

- 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.

Please see additional Important Safety Information throughout this newsletter. Please click here for full Prescribing Information, including Boxed WARNING and Medication Guide.

CLICK BELOW TO SEE DR SANIKOMMU AND DR FIRWANA'S PERSPECTIVES ON THESE QUESTIONS

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What was your experience with getting patients started on FABHALTA? (continued)

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1 Get REMS certified to prescribe FABHALTA[1]

Because of the risk of serious infections caused by encapsulated bacteria, you will need to become certified in the FABHALTA REMS and fulfill its requirements.

TO ENROLL IN THE REMS

- **Review** the FABHALTA Prescribing Information and REMS materials
- **Submit** the completed Prescriber Enrollment Form to the FABHALTA REMS at **www.FABHALTA-REMS.com**, or by fax to **1-877-206-3255**

AFTER ENROLLMENT

- **Counsel** patients about the risk of serious infections caused by encapsulated bacteria, the need for vaccinations, and the early signs and symptoms of serious infections.
- **Provide** patients with REMS educational materials and the Patient Safety Card. Instruct patients to always carry this card with them during treatment and for 2 weeks following the last dose of FABHALTA

FABHALTA, a complement inhibitor, increases the risk of serious infections, 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.

Additional information is available by telephone at **1-833-99FABHA** or online at **www.FABHALTA-REMS.com**.

2 Complete or update vaccinations before starting treatment with FABHALTA[1]

Comply with the most current ACIP recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor.

Required vaccinations: *Streptococcus pneumoniae* and *Neisseria meningitidis* (serogroups A, C, W, Y, and B). Complete or update vaccinations for encapsulated bacteria at least 2 weeks prior to starting FABHALTA, unless the risks of delaying FABHALTA outweigh the risk of developing a serious infection.

- If urgent FABHALTA therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. For additional details on antibacterial drug prophylaxis, please see the FABHALTA Prescribing Information, Warnings and Precautions (Section 5.1)

During treatment with FABHALTA:

As vaccination does not eliminate the risk of serious encapsulated bacterial infections, closely monitor patients for early signs and symptoms. Inform patients of these signs and symptoms, and instruct patients to seek immediate medical care if they occur.

- Evaluate and treat immediately if infection is suspected, as serious infection may rapidly become life-threatening or fatal if not recognized and treated early. Promptly treat known infections
- Consider interruption of FABHALTA in patients who are receiving treatment for serious infections, depending on the risks of interrupting treatment in the disease being treated
- While on therapy, patients are required to be revaccinated as needed

3 Prescribe FABHALTA: Choose between 2 specialty pharmacies[1]

Inform your patient which specialty pharmacy will be dispensing their FABHALTA prescription, and tell them to expect a phone call to arrange delivery of their prescription. Pharmacies that dispense FABHALTA must be certified in the FABHALTA REMS and must verify that prescribers are certified.

Onco360®
- Website: **onco360.com**
- Phone: **1 (877) 662-6633**; Fax: **1 (877) 662-6355**

Biologics by McKesson
- Website: **biologics.mckesson.com**
- Phone: **1 (800) 850-4306**; Fax: **1 (800) 823-4506**

PNH, paroxysmal nocturnal hemoglobinuria; REMS, Risk Evaluation and Mitigation Strategy.

IMPORTANT SAFETY INFORMATION (continued)

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. Prescribers must 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 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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What key points about getting started with FABHALTA do you discuss with your patients?

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KEY TAKEAWAYS

The efficacy and safety of FABHALTA

When discussing FABHALTA with patients, I communicate the efficacy and safety of the drug. I review the changes they might experience based on the clinical trial end points such as Hb increase of ≥2 g/dL from baseline in the absence of RBC transfusions after 24 weeks and normalized Hb of ≥12 g/dL in the absence of RBC transfusions after 24 weeks.[1] **In terms of safety, I inform patients of the serious risks associated with FABHALTA and let them know that we will manage adverse events as they arise.**[1] Additionally, I will inform them that they will be given a Patient Safety card that they carry with them at all times during and for 2 weeks after treatment with FABHALTA.

— **Dr Firwana**

With oral monotherapy dosing, FABHALTA can fit into patients' lifestyles

In general, **I discuss all treatment options available, including FABHALTA.**[1-6] Since this may be their first time hearing about these treatments, I give them time to understand and consider their options. **In choosing a therapy, I work with patients to consider their management needs as well as their lifestyle.** They have to be on board with taking the medicine twice daily long term.

— **Dr Sanikommu**

Patients won't fully grasp the potential impact of FABHALTA until they experience it firsthand

Sometimes my patients don't want to complain, and may say things like "I'm doing okay," even when they are not. It can take some additional questions to get to an open dialogue about how they are really doing. When I have a patient who could benefit from a treatment switch, I now bring the experiences of my patients on FABHALTA into that conversation.

— **Dr Sanikommu**

CLICK HERE TO VIEW FABHALTA SAFETY DATA

ADDITIONAL TAKEAWAYS TO DISCUSS

Hb, hemoglobin; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell.

IMPORTANT SAFETY INFORMATION (continued)

Monitoring of PNH Manifestations After FABHALTA Discontinuation

- After discontinuing FABHALTA, closely monitor patients for at least 2 weeks after the last dose for signs and symptoms of hemolysis. These signs include elevated lactate dehydrogenase (LDH) levels along with sudden decrease in hemoglobin or PNH clone size, fatigue, hemoglobinuria, abdominal pain, dyspnea, major adverse vascular events (such as thrombosis, stroke, and myocardial infarction), dysphagia, or erectile dysfunction. If discontinuation of FABHALTA is necessary, consider alternative therapy.

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FABHALTA safety in the APPLY and APPOINT trials

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APPLY[1,15]

Adverse reactions reported in >5% of adults with PNH treated with FABHALTA (24-week randomized treatment period)

ADVERSE REACTIONS[1]	FABHALTA (N=62) n (%)	C5is (eculizumab or ravulizumab) (N=35) n (%)
Headache[a]	12 (19)	1 (3)
Nasopharyngitis[b]	10 (16)	6 (17)
Diarrhea	9 (15)	2 (6)
Abdominal pain[a]	9 (15)	1 (3)
Bacterial infection[c]	7 (11)	4 (11)
Nausea	6 (10)	1 (3)
Viral infection[d]	6 (10)	11 (31)
Arthralgia	5 (8)	1 (3)
Thrombocytopenia[a]	4 (6)	0
Dizziness	4 (6)	0
Systemic hypertension[a]	4 (6)	0
Lipid disorder[e]	4 (6)	0

- Serious adverse reactions were reported in 2 (3%) patients with PNH who received FABHALTA. They included pyelonephritis, urinary tract infection, and COVID-19[1]
- Rash was reported in 2 patients (3%)[1]
- Of the 37 FABHALTA-treated patients who had normal platelet counts at baseline, 43% experienced any grade thrombocytopenia[1]
- Three FABHALTA-treated patients experienced decreased platelets that worsened to grade ≥3 from baseline (1 patient with normal platelets that worsened to grade 4; 1 patient with baseline grade 1 that worsened to grade 4; and 1 patient with baseline grade 3 that worsened to grade 4)[1]

No patient discontinued FABHALTA or C5is due to an adverse reaction during the 24-week randomized treatment period. One patient discontinued FABHALTA due to pregnancy.[15]

APPOINT[1]

Adverse reactions reported in >5% of adults with PNH treated with FABHALTA in APPOINT (24-week core treatment period)

ADVERSE REACTIONS[1]	FABHALTA (N=40) n (%)
Headache[a]	11 (28)
Viral infection[d]	7 (18)
Nasopharyngitis[b]	6 (15)
Rash[f]	4 (10)
Abdominal pain[a]	3 (8)
Diarrhea	3 (8)
Lipid disorder[e]	3 (8)

- Serious adverse reactions were reported in 2 (5%) patients with PNH who received FABHALTA. They included COVID-19 and bacterial pneumonia[1]
- Bacterial infection[f] and nausea were reported in 2 patients each (5%). Dizziness and urticaria were reported in 1 patient each (3%)[1]

No patient discontinued FABHALTA due to an adverse reaction during the 24-week core treatment period.[16]

ADDITIONAL TAKEAWAYS TO DISCUSS

C5i, complement component 5 inhibitor; PNH, paroxysmal nocturnal hemoglobinuria.

[a]Includes similar terms.[1]
[b]Nasopharyngitis contains: rhinitis allergic, upper respiratory tract infection, pharyngitis, rhinitis.[1]
[c]Bacterial infection contains: pyelonephritis, urinary tract infection, bronchitis bacterial, bronchitis haemophilus, cholecystitis, folliculitis, cellulitis, arthritis bacterial, sepsis, *Klebsiella* infection, staphylococcal infection, *Pseudomonas* infection, hordeolum, pneumonia bacterial.[1]
[d]Viral infection contains: COVID-19, herpes zoster, oral herpes, nasal herpes, influenza A virus test positive, influenza.[1]
[e]Lipid disorder contains: dyslipidemia, blood cholesterol increased, low-density lipoprotein increased, hypercholesterolemia, blood triglycerides increased, hyperlipidemia.[1]
[f]Rash contains: dermatitis allergic, acne, erythema multiforme, rash maculopapular, rash erythematous.[1]

IMPORTANT SAFETY INFORMATION (continued)

Monitoring of PNH Manifestations After FABHALTA Discontinuation

- After discontinuing FABHALTA, closely monitor patients for at least 2 weeks after the last dose for signs and symptoms of hemolysis. These signs include elevated lactate dehydrogenase (LDH) levels along with sudden decrease in hemoglobin or PNH clone size, fatigue, hemoglobinuria, abdominal pain, dyspnea, major adverse vascular events (such as thrombosis, stroke, and myocardial infarction), dysphagia, or erectile dysfunction. If discontinuation of FABHALTA is necessary, consider alternative therapy.
- If hemolysis occurs after discontinuation of FABHALTA, consider restarting treatment with FABHALTA, if appropriate, or initiating another treatment for PNH.

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What key points about getting started with FABHALTA do you discuss with your patients? (continued)

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KEY TAKEAWAYS

Explain the timing of switching from a C5i (eculizumab or ravulizumab) to FABHALTA

> **For patients switching from C5 inhibitors** (eculizumab or ravulizumab), **I explain the timing of starting FABHALTA to reduce the potential risk of hemolysis with abrupt discontinuation of other PNH therapies.**[1]

— **Dr Firwana**

Instruct patients to take FABHALTA as prescribed

> I always communicate the need to take FABHALTA twice daily, as prescribed, with or without food,[1] and work with patients to identify and address any barriers to treatment. **In my experience, once patients are on FABHALTA, they are motivated to stay on therapy.**
>
> If my patient misses a dose, I instruct them to take one dose of FABHALTA as soon as possible, even if it's close to the next scheduled dose, and then continue with their regular dosing schedule.

— **Dr Firwana**

Switching from C5is (eculizumab or ravulizumab)[1]

To reduce the potential risk of hemolysis with abrupt discontinuation of other PNH therapies:

Eculizumab → **FABHALTA**

Start FABHALTA no later than 1 week after the last dose of eculizumab

Ravulizumab → **FABHALTA**

Start FABHALTA no later than 6 weeks after the last dose of ravulizumab

There is no available information regarding the time frame for initiation of FABHALTA after stopping other PNH therapies.

C5i, complement component 5 inhibitor; PNH, paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (continued)

Hyperlipidemia

- FABHALTA may increase total cholesterol, LDL cholesterol, and serum triglycerides.
- Of 88 FABHALTA-treated patients who had normal total cholesterol at baseline, 31 developed grade 1 hypercholesterolemia during the randomization or core treatment period and 1 patient worsened from baseline grade 1 to grade 2.
- Of 96 FABHALTA-treated patients with LDL cholesterol ≤ 130 mg/dL at baseline during the randomization or core treatment period, 14 patients developed LDL cholesterol > 130-160 mg/dL, 6 patients developed LDL cholesterol > 160-190 mg/dL and 4 patients developed LDL cholesterol > 190 mg/dL.

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What does incorporating FABHALTA into your clinical practice look like?

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KEY TAKEAWAYS

I closely monitor patients after starting them on FABHALTA

In my practice, after starting patients on FABHALTA, I follow them closely in clinic and have them come in 2 weeks later to monitor for adverse events. At 4 weeks after initiating treatment, I check their lab work, including a CBC. If everything looks good, the next checkup is at 8 weeks. Initially, we monitor patients closely, but the frequency of visits decreases over time.

— Dr Firwana

I continue to follow patients on FABHALTA regularly

In my practice, if a patient is doing well with stable blood counts and lab work, I see them periodically, every 2 to 3 months. I typically check for PNH lab work, keeping an eye out for any signs of hemolysis.[18] During checkup, I assess how the patient feels and ask if they can perform their regular activities. I make sure that patients communicate any signs or symptoms of infections or any conditions that may activate complement, such as surgery,[19] so that I can monitor them more closely.

— Dr Sanikommu

SEE ADDITIONAL TAKEAWAYS

CBC, complete blood count; PNH, paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (continued)

Hyperlipidemia (continued)

- Of 89 FABHALTA-treated patients with normal triglycerides during the randomization or core treatment period, 22 patients developed grade 1 elevated triglycerides. Three patients experienced an increase in triglycerides from grade 1 to grade 2.
- Of the 102 FABHALTA-treated patients in APPLY-PNH and APPOINT-PNH, 2 patients required cholesterol-lowering medications.
- Monitor serum lipid parameters periodically during treatment with FABHALTA and initiate cholesterol-lowering medications, if indicated.

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CLICK BELOW TO SEE DR SANIKOMMU AND DR FIRWANA'S PERSPECTIVES ON THESE QUESTIONS

HEAR MORE EXPERT PERSPECTIVES AT https://www.FABHALTA-hcp.com/pnh/medical-expert-perspectives

What does incorporating FABHALTA into your clinical practice look like? (continued)

FABHALTA® (iptacopan) 200 mg capsules

KEY TAKEAWAYS

I familiarize the practice with Novartis Patient Support services

There are financial support options available to eligible patients with private insurance. One of my patients who had private insurance was able to enroll in the $0 Co-Pay Plus* program.

— **Dr Firwana**

I advocate for the patient's opportunity to receive FABHALTA

If the patient and physician both believe that a treatment option like FABHALTA[1] is necessary, they should be given the opportunity. You can reach out to the insurance company to understand why they're recommending one treatment over another, and if they require it, I personally feel that pursuing a peer-to-peer review is in the patient's best interest. **Advocating for patients who could benefit from FABHALTA also means discussing FABHALTA with your peers.** I've been discussing the 48-week safety data with my colleagues and anyone interested since it was released last year.

— **Dr Sanikommu**

Novartis Patient Support is a comprehensive program that can help your eligible patients start and stay on treatment

Novartis Patient Support can help support your patients every step of the way

- **Insurance Support**
- **Vaccination Support**
- **Financial Support**
- **Ongoing Support**

For more information, please visit https://www.fabhalta.com/pnh/savings-support or speak to your local Novartis representative to learn more.

PNH, paroxysmal nocturnal hemoglobinuria.

*Co-Pay Plus: Limitations apply. Patients with commercial insurance coverage for FABHALTA may receive up to $20,000 in annual co-pay benefits for the cost of FABHALTA and up to $1,000 for qualifying vaccination costs (excluding administrative fees). Patient is responsible for any costs once limit is reached in a calendar year. Program not valid (i) under Medicare, Medicaid, TRICARE, VA, DoD, or any other federal or state health care program, (ii) where patient is not using insurance coverage at all, (iii) where the patient's insurance plan reimburses for the entire cost of the drug, or (iv) where product is not covered by patient's insurance. The value of this program is exclusively for the benefit of patients and is intended to be credited towards patient out-of-pocket obligations and maximums, including applicable co-payments, coinsurance, and deductibles. Patient may not seek reimbursement for the value received from this program from other parties, including any health insurance program or plan, flexible spending account, or health care savings account. Patient is responsible for complying with any applicable limitations and requirements of their health plan related to the use of the Program. Valid only in the United States, Puerto Rico and select territories. Void where prohibited by law. Additional restrictions may apply. This program is not health insurance. Program may not be combined with any third-party rebate, coupon, or offer. Proof of purchase may be required. Novartis reserves the right to rescind, revoke, or amend the Program and discontinue support at any time without notice.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

- The most common adverse reactions (≥10%) in adults with PNH receiving FABHALTA were headache, nasopharyngitis, diarrhea, abdominal pain, bacterial infection, viral infection, nausea, and rash.

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 increased risk for adverse reactions with FABHALTA. Coadministration with a strong CYP2C8 inhibitor is not recommended.

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What is the one thing every health care professional should know when starting their adult patients with PNH on FABHALTA?

FABHALTA® (iptacopan) 200 mg capsules

KEY TAKEAWAYS

Consider the options and offer patients the one that best meets their needs

Based on my experience with FABHALTA, I want to tell providers, physicians, and the PNH patient community that there is an opportunity to do more for patients with PNH. Patients can become accustomed to living with PNH and may not attribute how they're feeling to their disease. Physicians managing adults with PNH should find ways to gauge how they are doing. There is a need to better assess the impact of PNH on patients' day-to-day and manage with treatment options like FABHALTA[1] when appropriate.

FABHALTA should be considered for adults with PNH who are experiencing anemia or requiring RBC transfusions

If I have an adult patient with ongoing anemia or who requires RBC transfusions, I discuss FABHALTA as a potential treatment option.

— Dr Sanikommu

FABHALTA is a treatment option for appropriate adult patients with PNH who experience signs and symptoms of PNH[1]

I believe the biggest barrier to wider adoption of FABHALTA is that some physicians may stick to their usual treatments out of habit. **It's important to spread the word and encourage more physicians to consider FABHALTA.**

Novartis offers educational support for both HCPs and patients

Physicians should be familiar with the efficacy and safety profile of FABHALTA. **The education materials about FABHALTA on the Novartis website are helpful in understanding the considerations for treatment and support.**

— Dr Firwana

HCP, health care professional; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell.

IMPORTANT SAFETY INFORMATION (continued)

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.

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INDICATION

FABHALTA is indicated for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH).

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

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

- 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 influenza*e 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. 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. Prescribers must 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 last dose of FABHALTA.
- Further information is available by telephone: 1-833-993-2242 or online at www.FABHALTA-REMS.com.

Monitoring of PNH Manifestations After FABHALTA Discontinuation

- After discontinuing FABHALTA, closely monitor patients for at least 2 weeks after the last dose for signs and symptoms of hemolysis. These signs include elevated lactate dehydrogenase (LDH) levels along with sudden decrease in hemoglobin or PNH clone size, fatigue, hemoglobinuria, abdominal pain, dyspnea, major adverse vascular events (such as thrombosis, stroke, and myocardial infarction), dysphagia, or erectile dysfunction. If discontinuation of FABHALTA is necessary, consider alternative therapy.
- If hemolysis occurs after discontinuation of FABHALTA, consider restarting treatment with FABHALTA, if appropriate, or initiating another treatment for PNH.

Hyperlipidemia

- FABHALTA may increase total cholesterol, LDL cholesterol, and serum triglycerides.
- Of 88 FABHALTA-treated patients who had normal total cholesterol at baseline, 31 developed grade 1 hypercholesterolemia during the randomization or core treatment period and 1 patient worsened from baseline grade 1 to grade 2.
- Of 96 FABHALTA-treated patients with LDL cholesterol ≤ 130 mg/dL at baseline during the randomization or core treatment period, 14 patients developed LDL cholesterol > 130-160 mg/dL, 6 patients developed LDL cholesterol > 160-190 mg/dL and 4 patients developed LDL cholesterol > 190 mg/dL.
- Of 89 FABHALTA-treated patients with normal triglycerides during the randomization or core treatment period, 22 patients developed grade 1 elevated triglycerides. Three patients experienced an increase in triglycerides from grade 1 to grade 2.
- Of the 102 FABHALTA-treated patients in APPLY-PNH and APPOINT-PNH, 2 patients required cholesterol-lowering medications.
- Monitor serum lipid parameters periodically during treatment with FABHALTA and initiate cholesterol-lowering medications, if indicated.

ADVERSE REACTIONS

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