OPTIMIZING PNH MANAGEMENT: A CASE STUDY OF AN ADULT PATIENT WHO SWITCHED TO FABHALTA® (iptacopan)

FABHALTA may offer an effective treatment option for adults with PNH who were previously on C5 inhibitors (eculizumab or ravulizumab).[1] It also is an oral option that can fit well with patients with an active lifestyle.[1] One of my patients was able to replace PNH infusions with an oral monotherapy and take control of her treatment journey—something that wouldn't have been possible without the switch to FABHALTA.[1]

— **Jaroslaw Maciejewski, MD, PhD**
Chairman, Department of Translational Hematology and Oncology Research, Taussig Cancer Center, Professor, Cleveland Clinic Lerner College of Medicine, Case Western Reserve University Cleveland, OH

In this edition, Dr Maciejewski shares his clinical decision-making process for a patient in his practice who switched to FABHALTA. Join us as he shares how he approached this treatment-switch decision and discusses why FABHALTA was the right treatment option for his adult patient with PNH.

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

C5, complement component 5; C5i, complement component 5 inhibitor; Hb, hemoglobin PNH, paroxysmal nocturnal hemoglobinuria.

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.

READ ON TO FIND OUT HOW DR MACIEJEWSKI ANSWERS THESE QUESTIONS (CLICK BELOW)

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Can you tell us about a patient's case where you decided to switch them to FABHALTA® from a C5i?

FABHALTA® (iptacopan) 200 mg capsules

Kate*

31-year-old female

Administrative assistant at a local college

*The case presented here is based on a real patient treated by Dr Maciejewski. The patient's name has been changed to protect their privacy.

	1 Initial Presentation	2 6-Month Follow-Up
Initial visit	• Distance runner who recently stopped due to "not feeling like her usual self"	• Patient was "not feeling right" • Yellow eyes, LUQ tenderness, and palpable spleen[2-4]
Medical history	• Initially diagnosed with hypochromic anemia • No history of thrombosis	
Laboratory values	• Hb 10.5-11.0 g/dL • LDH 400 U/L	• Hb 8 g/dL • LDH 1200 U/L • ARC 154 × 10^9/L • Bilirubin 3 mg/dL[3-5] • Transaminase 120 U/L[3-5]
Diagnosis	• Flow cytometry confirmed PNH with clone size 67%	• Spiral CT scan with contrast confirmed chronic Budd-Chiari syndrome
Treatment plan	• Discussed C5i therapy; vaccinated in preparation for C5i, but patient refused treatment	• Started on a C5i and an anticoagulant

"**Kate was a physically active distance runner who recently stopped due to "not feeling like her usual self." She adjusted to a "new normal" by reducing her activity level.** There was no history of thrombosis, and routine lab tests revealed hypochromic anemia. Further workup led to a diagnosis of PNH. Given that she was not transfusion dependent and presenting with mild anemia and manageable symptoms, it was not unreasonable to hold off on treatment.

During subsequent visits, I explained the potential risks and complications of not being on a complement inhibitor therapy, but **the idea of requiring IV infusions was a significant psychological hurdle for her. I completed the required vaccinations in anticipation of an acute crisis.** Six months later, she requested an urgent visit and presented with intra-abdominal thrombotic complications, likely triggered by acute hemolysis. I started her on a C5i to control hemolysis and an anticoagulant to prevent further thromboembolic complications."

— **Jaroslaw Maciejewski, MD, PhD**

ARC, absolute reticulocyte count; C5i, complement component 5 inhibitor; CT, computed tomography; Hb, hemoglobin; IV, intravenous; LDH, lactate dehydrogenase; LUQ, left upper quadrant; 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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When did you realize FABHALTA® was the right option for this patient?

FABHALTA® (iptacopan) 200 mg capsules

Kate*

31-year-old female

Administrative assistant at a local college

*The case presented here is based on a real patient treated by Dr Maciejewski. The patient's name has been changed to protect their privacy.

3 **C5i** (eculizumab or ravulizumab) **Treatment Response** (8-month follow-up)

Presentation	• Declining response to C5i
Laboratory values	• Hb 8-9 g/dL • ARC 193 × 10^9/L • Coombs testing: positive
Diagnosis	• Extravascular hemolysis
Treatment plan	• After discussing alternative treatment options to address EVH, the decision was made to switch to FABHALTA and discontinue C5i†

†When switching from C5is (eculizumab or ravulizumab) to FABHALTA: To reduce the potential risk of hemolysis with abrupt discontinuation of other PNH therapies: For patients switching from eculizumab, initiate FABHALTA no later than 1 week after the last dose of eculizumab. For patients switching from ravulizumab, initiate FABHALTA no later than 6 weeks after the last dose of ravulizumab. There is no available information regarding the timeframe for initiation of FABHALTA after other PNH therapies.

ARC, absolute reticulocyte count; C5i, complement component 5 inhibitor; EVH, extravascular hemolysis; Hb, hemoglobin; PNH, paroxysmal nocturnal hemoglobinuria.

"**The patient improved while on the C5i for 8 months, but the initial improvements were not sustained.** Despite treatment, her hemoglobin continued to fluctuate between 8 and 9 g/dL, with an ARC of 193 × 10^9/L. A positive Coombs test indicated she was experiencing extravascular hemolysis.[2]

When patients undergo treatment, we expect improved hemolysis control. In the past, with fewer treatment options, we had limited choices. Now, we have more options for managing PNH and mitigating the risks of ongoing hemolysis."

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.
- 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.

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READ ON TO FIND OUT HOW DR MACIEJEWSKI ANSWERS THESE QUESTIONS (CLICK BELOW)

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How did you discuss FABHALTA® with your patient?

FABHALTA® (iptacopan) 200 mg capsules

My patient contacted our office to inquire about FABHALTA as a potential option.

We discussed how FABHALTA addresses both types of hemolysis, intravascular and extravascular,[1] which is important given the patient's declining response to C5i and extravascular hemolysis.

An important consideration was the oral administration of FABHALTA, which means no need for injections or infusions—an appealing option for this patient who did not want to manage an infusion schedule.[1] While discussing all treatment options, I emphasized the importance of adhering to an oral monotherapy such as FABHALTA, which is 1 capsule taken twice daily.

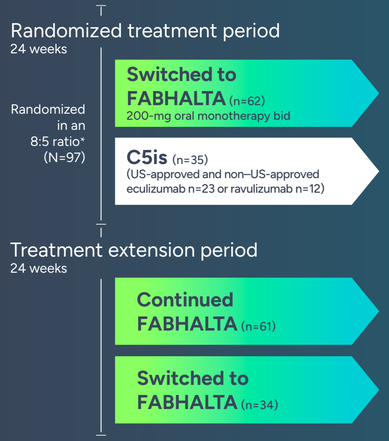
We reviewed the key data from the APPLY trial supporting the use of FABHALTA in adults with PNH.[1] **After extensive discussion of the risks and benefits, we ultimately chose FABHALTA for its ability to help comprehensively control both types of hemolysis (IVH and EVH), impact Hb levels,[1] and better suit her active lifestyle and personal needs.**

— **Jaroslaw Maciejewski, MD, PhD**

APPLY

A Phase 3, open-label, active comparator–controlled study evaluating FABHALTA in C5i-experienced (eculizumab or ravulizumab) **adults with PNH and residual anemia (mean Hb <10 g/dL) despite a stable regimen of C5i treatment for at least 6 months prior to randomization (N=97).**[1,6,7*]

Inclusion criteria included a PNH diagnosis (RBC and WBC clone size ≥10%), and reticulocytes ≥100 × 10^9/L.



Primary end points: randomized treatment period[1]

- Proportion of patients achieving sustained Hb increase of ≥2 g/dL† from baseline without a need for RBC transfusions‡ after 24 weeks
- Proportion of patients achieving sustained Hb level of ≥12 g/dL† without a need for RBC transfusions‡ after 24 weeks

Additional end points: randomized treatment period[1,7]

- RBC transfusion avoidance§
- Change from baseline† in Hb levels (g/dL)‖ | FACIT-Fatigue scores | Absolute reticulocyte count (ARC) (10^9/L) | LDH level
- Occurrence of major adverse vascular events¶
- Occurrence of clinical breakthrough hemolysis¶,#
- Safety

In the APPLY study analysis:

- All end points were based on central laboratory data; 95% CIs were based on the Sato variance estimator[8]

C5i, complement component 5 inhibitor; CI, confidence interval; EVH, extravascular hemolysis; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; Hb, hemoglobin; IVH, intravascular hemolysis; LDH, lactate dehydrogenase; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell; REMS, Risk Evaluation and Mitigation Strategy; US, United States; WBC, white blood cell.

*Randomization was stratified based on prior C5i treatment and transfusion history within the last 6 months.[1]
†Assessed between Days 126 and 168.[1]
‡Assessed between Days 14 and 168. Requiring RBCs refers to any patient receiving transfusions or meeting protocol-defined criteria.[7]
§Transfusion avoidance is defined as absence of administration of packed-RBC transfusions between Days 14 and 168.[1]
‖Excludes values within 30 days post-transfusion in the randomized period.[1]
¶Throughout the study.[7]
#As per the protocol definition.[7]

Have a patient in mind for FABHALTA?
Learn about the FABHALTA REMS program and required vaccinations

REMS PROGRAMS AND VACCINATION

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Serious Infections Caused by Encapsulated Bacteria (continued)

- 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.

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How did you discuss FABHALTA® with your patient? (continued)

FABHALTA® (iptacopan) 200 mg capsules

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, 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**

ACIP, Advisory Committee on Immunization Practices; C5i, complement component 5 inhibitor; Hb, hemoglobin; REMS, Risk Evaluation and Mitigation Strategy.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (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 was the effect on Hb levels after switching to FABHALTA®?

FABHALTA® (iptacopan) 200 mg capsules

Kate*

31-year-old female

Administrative assistant at a local college

*The case presented here is based on a real patient treated by Dr Maciejewski. The patient's name has been changed to protect their privacy.

4 FABHALTA Treatment Response (4-week follow-up)

Presentation

- **Patient reported overall improvement and return to running**

Laboratory values

- **Hb 11.5 g/dL**
- **ARC 52 × 10^9/L**
- **LDH 200-300 U/L**

After switching to FABHALTA, Kate's Hb improved to 11.5 g/dL. **Hb is an important measure as it's an objective index of improvement, which reassured us that the switch to FABHALTA was the right choice for Kate.**[4]

During our visit, she reported feeling better and was able to return to running, which was really important to her. My patient always had a positive attitude and rarely complained, so hearing about **her improvement was encouraging and rewarding as a physician.**

SEE HOW KATE'S RESPONSE ALIGNS WITH THE APPLY TRIAL

ARC, absolute reticulocyte count; C5i, complement component 5 inhibitor; Hb, hemoglobin; LDH, lactate dehydrogenase.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (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.

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 was the effect on Hb levels after switching to FABHALTA®? (continued)

FABHALTA® (iptacopan) 200 mg capsules

> **I truly believe that FABHALTA offers superior and substantial Hb improvements in appropriate patients and is an effective option for those who don't respond well to C5i.**[1] It also comes as an oral option that can fit well with patients with an active lifestyle.[1] This patient was adherent to her regimen of one 200-mg capsule of FABHALTA twice daily without issues.[1]

APPLY: PRIMARY END POINTS

Superior and substantial Hb increases were achieved with FABHALTA over C5is (eculizumab or ravulizumab) **through the 24-week randomized treatment period**

Significantly more patients achieved Hb improvements in the absence of RBC transfusions with FABHALTA vs C5is (eculizumab or ravulizumab)[1]

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)

*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.[7]
‡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.[7,9,10]

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

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (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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Was there any other impact of FABHALTA® on disease activity that stood out in this patient?

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In addition to improved Hb levels on FABHALTA, Kate's ARC decreased.* The results were not surprising, given the greater reductions seen in APPLY compared to C5is.[1]

Additionally, Kate's LDH remained stable between 200 and 300 U/L (<1.5 × ULN). These lab values are important markers of hemolysis and represent the underlying cause of RBC destruction.[2,11]

When markers like hemoglobin, ARC, and LDH fall within normal ranges, it's a sign for me that the patient is doing better.[4] **All these results confirm that the switch to FABHALTA was the right choice for my patient.**

APPLY: ADDITIONAL END POINTS

More patients achieved RBC transfusion avoidance†‡ with FABHALTA vs C5is (eculizumab or ravulizumab)[1]

- RBC transfusion avoidance assessed between Weeks 2 and 24: **95.2% of patients on FABHALTA (n=59/62; 95% CI, 86.5-99.0)** and **45.7% of patients on C5is** (eculizumab or ravulizumab) (n=16/35; 95% CI, 28.8-63.4) had this response; difference§: 49.5% (95% CI, 32.5-66.6; *P*<0.0001)[1]

FABHALTA delivered greater reductions in ARC vs C5is (eculizumab or ravulizumab)[1]

- Adjusted mean change from baseline assessed between Weeks 18 and 24‖ (10^9/L): **-116 × 10^9/L for patients on FABHALTA** (N=62; 95% CI, -127 to -105; baseline mean: 193 × 10^9/L) and **0 x 10^9/L for patients on C5is** (N=35; 95% CI, -13 to -14; baseline mean: 191 × 10^9/L); adjusted mean difference: -116 × 10^9/L (95% CI, -132 to -100; *P*<0.0001)[1]
- Values include post-transfusion data[8]

No statistically significant difference in LDH was seen between FABHALTA and C5is (eculizumab or ravulizumab)[1,8]

- The data from this additional analysis of LDH are descriptive in nature, presented for observation only. No formal conclusions or comparisons between the 2 treatment arms can be made
- Adjusted geometric mean ratio to baseline assessed between Weeks 18 and 24‖: **0.96 for patients on FABHALTA (N=62, baseline mean: 269 U/L)** and **0.97 for patients on C5is** (N=35, baseline mean: 273 U/L)[1,8]
- In both the FABHALTA- and C5i-treated groups, the mean (SD) (FABHALTA: 275.2 U/L [117.6]; C5is: 280.7 U/L [128.2]) and median (range) (FABHALTA: 251 U/L [150-859]; C5is: 242 U/L [142-815]) LDH values at Day 168 of the randomized treatment period were <1.5 × ULN[8]

ARC, absolute reticulocyte count; C5i, complement component 5 inhibitor; CI, confidence interval; Hb, hemoglobin; LDH, lactate dehydrogenase; RBC, red blood cell; SD, standard deviation; ULN, upper limit normal.

*In the APPLY trial, ARC within normal limits is defined based on the central lab normal ranges between 13.5-123 × 10^9/L.[7]
†Assessed between Days 14 and 168.[1]
‡Transfusion avoidance is defined as absence of packed RBC transfusions between Days 14 and 168.[1]
§Adjusted difference in proportion.[1]
‖Assessed between Days 126 and 168.[1]

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.

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What can you tell us about the safety profile of FABHALTA® and your experience with monitoring this patient?

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Safety profile of FABHALTA in the APPLY trial

Adverse reactions reported in >5% of adults with PNH treated with FABHALTA in APPLY (24-week randomized treatment period)[1]

ADVERSE REACTIONS	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 randomized treatment period.** One patient discontinued FABHALTA due to pregnancy[7]

[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]

C5i, complement component 5 inhibitor; Hb, hemoglobin; LDL, low density lipoprotein; PNH, paroxysmal nocturnal hemoglobinuria.

"**So far, my patient has had a positive experience with FABHALTA.** I'm keeping an eye on her cholesterol levels and typically manage any rise in LDL or cholesterol with therapy, if needed. We checked her cholesterol and lipids 3 months after starting FABHALTA, and everything looked normal. The patient also hasn't reported any side effects.

It's crucial to talk to your patients about watching for any potential side effects during treatment. If they notice any signs of infection, they should reach out to their physician immediately."

IMPORTANT SAFETY INFORMATION (continued)

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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READ ON TO FIND OUT HOW DR MACIEJEWSKI ANSWERS THESE QUESTIONS (CLICK BELOW)

Home

1 Can you tell us about a patient's case where you decided to switch them to FABHALTA from a C5i?

2 When did you realize FABHALTA was the right option for this patient?

3 How did you discuss FABHALTA with your patient?

4 What was the effect on Hb levels after switching to FABHALTA?

5 Was there any other impact of FABHALTA on disease activity that stood out in this patient?

6 **What can you tell us about the safety profile of FABHALTA and your experience with monitoring this patient?**

7 How do you see the role of FABHALTA evolving in your practice and in the broader medical community?

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

How do you see the role of FABHALTA® evolving in your practice and in the broader medical community?

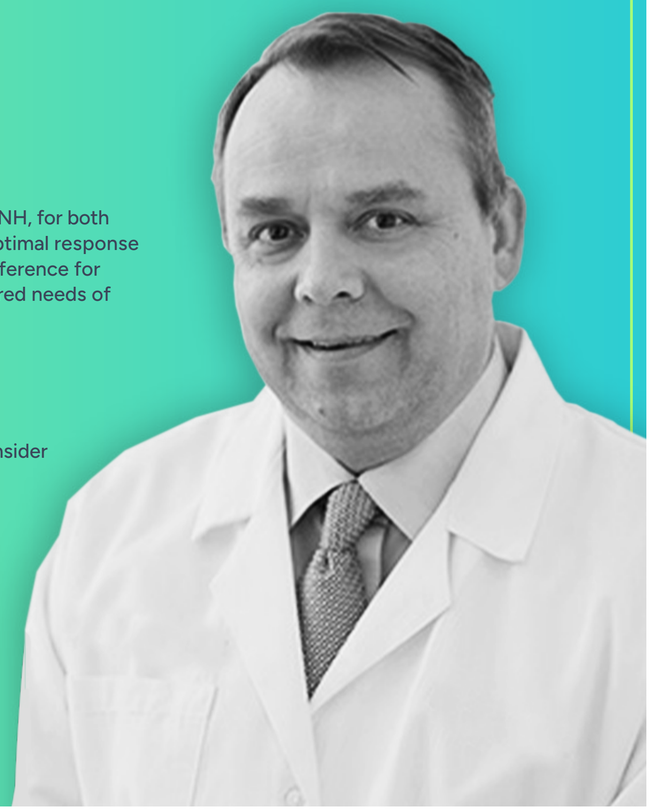
FABHALTA® (iptacopan) 200 mg capsules

Overall, I think FABHALTA is a valuable option for managing PNH, providing a different approach for patients and physicians.

For me, FABHALTA is a no-brainer. Having more treatment choices is always a good thing for managing PNH, for both physicians and patients. FABHALTA is particularly helpful for adult patients with PNH who have a suboptimal response to C5is, as it can address extravascular hemolysis.[1] Plus, the oral administration can really make a difference for patients and clinicians managing PNH because it allows a treatment experience that meets the preferred needs of some patients.[1]

FABHALTA has also been studied in the APPOINT trial for adult patients new to complement inhibitors, showing its potential as a first-line treatment. With its indication in adult patients with PNH, we can consider FABHALTA and offer patients a treatment option that can meet their needs and schedule.[1]

FABHALTA has an important place in my practice and will continue to be a valuable option for managing PNH. I believe that FABHALTA can make a real difference in patient care by helping to deliver comprehensive hemolysis control (IVH and EVH).



C5i, complement component 5 inhibitor; EVH, extravascular hemolysis; Hb, hemoglobin; IVH, intravascular hemolysis; PNH, paroxysmal nocturnal hemoglobinuria.

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® (iptacopan) 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

- 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

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