Paroxysmal Nocturnal Hemoglobinuria 2024

ICER SNAPSHOT

The ICER Snapshot is a summary designed to help patients and the broader community learn about the key results and recommendations from ICER's 2024 Final Evidence Report on Treatments for Paroxysmal Nocturnal Hemoglobinuria.

The information included is up to date as of March 2024. New information about these therapies may become available, but is not captured here.

Let's Take a Look

What is Paroxysmal Nocturnal Hemoglobinuria?

Impact on Individuals and Families

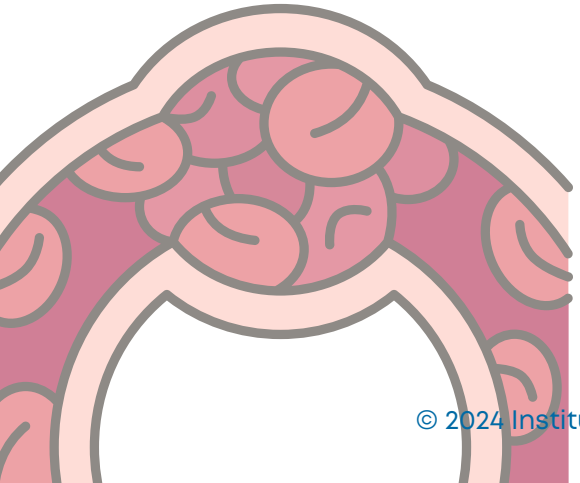
Treatments: Benefits and Risks

Treatments: What's A Fair Price?

Policy Recommendations & Impact of Engagement

What is Paroxysmal Nocturnal Hemoglobinuria?

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare blood disorder most common in adults that destroys red blood cells (hemolytic anemia). PNH is named for one of its symptoms: suddenly peeing dark-colored urine at night, with “paroxysmal” meaning sudden onset, “nocturnal” meaning at night, and “hemoglobinuria” meaning blood in the urine.



Because red blood cells are destroyed, this condition causes severe fatigue (tiredness) and may require life-long blood transfusions depending on how bad the condition is. Thrombosis (blood clots), which occurs in up to 30% of PNH patients, is the most common cause of death for people with PNH.

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Impact on Patients and Families

What ICER Learned from the Community



PNH is an **"invisible" illness** in which patients do not appear sick nor need significant help from caregivers. However, severe fatigue and not knowing when a blood clot may occur can **cause anxiety and strain relationships.**

PNH is a chronic disease and **current treatments are costly** (about $500,000/year). Since patients require lifelong therapy costing more than $9 million, they are concerned about the **access and affordability of PNH treatments.**

The current available treatments put strain on patients and caregivers who need to **go into a hospital to receive infusions** every few weeks.

The process to be approved for another year of PNH treatment can be very burdensome for patients and **delays can lead to missed doses** and return of PNH symptoms.

PNH Clinical Context

PNH is caused by a deficiency in two proteins that lead to red blood cell destruction both inside and outside blood vessels. Unfortunately, there are no clinical guidelines for PNH.

Currently Available PNH Treatments

C5 Inhibitors: The most common and effective FDA-approved treatments for PNH that help reduce red blood cell destruction inside blood vessels, blood clots, and death.

Pegcetacoplan: An FDA-approved treatment for PNH that helps reduce red blood cell destruction both inside and outside blood vessels, and works in a similar way to iptacopan and danicopan.

Helpful Clinical Terms

Extravascular hemolysis (EVH): Red blood cell destruction that happens outside the blood vessels (such as in the spleen, liver, or bone marrow)

Treatment-naïve: Patients who have never been treated with a C5 inhibitor

Treatment-experienced: Patients treated with a C5 inhibitor for at least 6 months

Clinically significant: Experiencing symptoms from the effect of EVH which may include fatigue and dependence on blood transfusions

Breakthrough hemolysis: Return of PNH symptoms due to missing doses or due to triggers for PNH symptoms in a real-world setting (such as surgery or infection)

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ICER's Review of Iptacopan

Iptacopan

Iptacopan, made by Novartis, is a new treatment that any adult with PNH can take orally twice a day without taking a C5 inhibitor. Iptacopan works by preventing the destruction of red blood cells.

Iptacopan was FDA approved in December 2023.

What Did Clinical Trials Show?



Iptacopan in the APPOINT-PNH Trial

- **Studied in 40 treatment-naïve PNH patients**

INCREASED	INCREASED	DECREASED
Transfusion Independence	Hemoglobin	Fatigue

Iptacopan in the APPLY-PNH Trial

- **Compared to continuing C5 inhibitors**
- **Studied in 97 treatment-experienced PNH patients with clinically significant EVH**

INCREASED	INCREASED	DECREASED
Transfusion Independence	Hemoglobin	Fatigue

OUTCOMES

Transfusion Independence: No longer needing blood transfusions

Hemoglobin: Most important component of red blood cells; more hemoglobin means less red blood cell destruction

These represent some, but not all outcomes that were measured in the clinical trials.

What We Still Don't Know

- How well iptacopan works compared to a C5 inhibitor in a treatment-naïve PNH population
- How well iptacopan works when compared to pegcetacoplan in treatment-experienced patients with clinically significant EVH
- How well iptacopan works in a real-world setting that includes triggers (e.g., surgery, infection) for PNH symptoms
- Iptacopan's long-term safety and efficacy

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ICER's Review of Danicopan



Danicopan

Danicopan, made by Alexion Pharmaceuticals, is a new treatment to be added to C5 inhibitor therapy. Danicopan is to be taken orally three times a day by PNH patients who are currently on C5 inhibitors but also experiencing clinically significant EVH. Danicopan works similarly to iptacopan.

Danicopan is under FDA review as of March 2024.

What Did Clinical Trials Show?

Danicopan added to C5 Inhibitors in the ALPHA Trial

- **Compared to C5 inhibitors alone**
- **Studied in 63 treatment-experienced PNH patients with clinically significant EVH**

INCREASED	INCREASED	DECREASED
Transfusion Independence	Hemoglobin	Fatigue

These represent some, but not all outcomes that were measured in the clinical trials.

OUTCOMES

Transfusion Independence: No longer needing blood transfusions

Hemoglobin: Most important component of red blood cells; more hemoglobin means less red blood cell destruction

What We Still Don't Know

- How well danicopan works when compared to pegcetacoplan in treatment-experienced patients with clinically significant EVH
- Danicopan's long-term safety and efficacy

Safety of Iptacopan & Danicopan

Both iptacopan and danicopan had few serious harms based on the clinical trials, although both drugs have the risk of serious infection. There were a few cases of breakthrough hemolysis and blood clots with iptacopan.

ICER's report findings are NOT recommendations that support the use of iptacopan or danicopan. Individuals and families should always talk with their doctors to make shared decisions about treatment for PNH.

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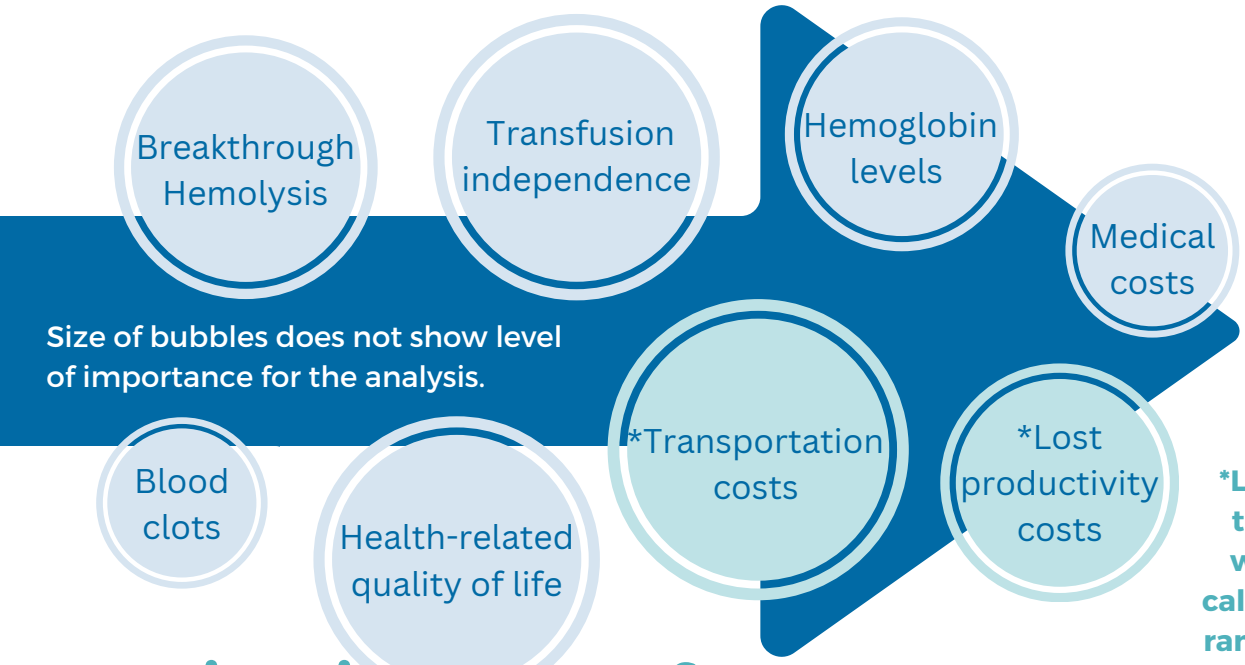
How Did ICER Calculate a Fair Price?

A fair price is how much a treatment should cost based on how well it works for patients. Using economic modeling, we calculated the cost effectiveness of iptacopan and add-on danicopan compared to current standard of care. See below for what types of information ICER considered to calculate a fair price range for these treatments.

Population

Adult patients with PNH who are on a C5 inhibitor but still experiencing clinically significant EVH

Factors Included in ICER's Economic Analysis





*Lost productivity and transportation costs were not included in calculating the fair price range. See full report for how these inputs were factored into other economic results.

Fair Price Range for Iptacopan

180,000 per year

Our economic analysis concluded that the fair-price range for **iptacopan** is between $178,000 to $180,000 per year. Since the comparator drug was not considered cost effective, this was calculated using a cost-offset cap scenario analysis (see page 33 of full report for details).

Fair Price Range for Add-On Danicopan

$12,300 - 13,100 per year

Our economic analysis concluded that the fair-price range for **danicopan** as an add-on to C5 inhibitor is between $12,300 to $13,100 per year.

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Key Policy Recommendations

The Policy Roundtable at the ICER public meeting informed several policy recommendations for pricing, access, and future research in PNH. A few key recommendations are summarized below.

1 Annual insurance coverage renewal requirements for PNH therapies should either be eliminated or implemented using a separate time-sensitive pathway to avoid missing doses.

Since symptomatic and high-risk patients with PNH require lifetime therapy to prevent life-threatening symptoms, coverage policies related to annual renewal for existing and new PNH therapies should be designed to avoid unnecessary disruptions to treatment. Similarly, improvement in hemoglobin levels should not lead to a denial of continued coverage, because stopping treatment will result in the return of symptoms like red blood cell destruction and blood clots.



2 Payers should allow patients and clinicians to choose from multiple treatment options until there is greater certainty about long-term safety, durability, and effectiveness.

For treatment-naïve patients, clinical experts and patients argued that C5 inhibitors are seen as the first treatment patients are given for PNH. They emphasized the importance of customizing treatment options given the important benefits and risks involved with choosing between older, more proven intravenous (injected through the veins) treatments and newer oral (taken as a pill) treatments.

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3 Manufacturers should set prices that will foster affordability and good access for all patients.

By aligning prices with the benefits patients receive from treatments, manufacturers can improve affordability and access. Drug prices that are set above the cost-effective range cause financial burden for patients and families. This may lead to being forced out of insurance coverage or taking smaller doses of treatment, ultimately causing harm to patients.

4 Identify subpopulations of patients who may benefit from specific treatment strategies for PNH by developing biomarkers or prediction models.

Clinical experts shared that a gap in the current management of PNH patients was an inability to identify which patients are at risk for red blood cell destruction or blood clots if treated with a C5 inhibitor alone. While the percentage of PNH cells versus normal cells (clone size) is the best way to understand a patient's severity of illness, patients with the same clone size can have very different courses of disease. Thus, new biomarkers or the development of more accurate predictors may better guide treatment selection before complications develop.

Impact of Patient Engagement

A **Share Your Story Form submission** from a PNH patient led to continued engagement throughout the review and **participation as a patient expert panelist** for ICER's public meeting.

Collaboration with the PNH community allowed ICER to gain a **deep understanding of the lived experience** of individuals with PNH and their families.

Testimony from PNH patients at the public meeting helped shape ICER's recommendations for payers to **reduce barriers to annual insurance coverage renewal.**

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit organization that does research on how well new treatments work and what a fair price should be. Patients and families should always talk with their doctor to make shared decisions about the best treatment option for them.

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