Iptacopan and Danicopan for Paroxysmal Nocturnal Hemoglobinuria: Effectiveness and Value

Public Meeting — February 16th, 2024

Meeting materials available at: https://icer.org/assessment/paroxysmal-nocturnal-hemoglobinuria-2024/

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

AN ICER PROGRAM
CTAF
CALIFORNIA TECHNOLOGY ASSESSMENT FORUM

Patient Experts

Leigh Clark, BCPA, Director, Patient Services, Aplastic Anemia and MDS International Foundation

- *AAMDSIF has received <25% of funding from healthcare companies.*

Jeri Keiller, Certified Public Accountant

- *No conflicts to disclose.*

Clinical Experts

Irina Murakhovskaya, MD, Associate Professor, Albert Einstein College of Medicine/Montefiore Medical Center

- *Dr. Murakhovskaya has received more than $5,000 in honoraria or consulting fees from Novartis and Alexion. Dr. Murakhovskaya has also received >25% of funding from WAIHA Warriors and has served as the Principal Investigator for the Novartis CLNP023C12303 trial.*

Caroline Piatek, MD, Associate Professor of Clinical Medicine, University of Southern California

- *Dr. Piatek has received more than $5,000 in honoraria or consulting fees from Argenx, Omeros, Janssen, Novartis, AstraZeneca/Alexion, Rigel, Apellis, Sanofi, Sobi. Dr. Piatek has also received manufacturer support through AstraZeneca/Alexion, Apellis.*

Why are we here today?

“My family worries about me a lot…anytime I tell them I’m not feeling well, I can see in their face their concern, because when I was diagnosed, they [doctors] said I’d be lucky to live 10 years, so that is in their mind. So, they expect any day that something could go wrong….I never know when I’m not going to feel well, that’s probably the toughest part because I don’t know when I’m going to have a bad day.”

“So, What’s it like? First of all, I look really healthy and so when I tell somebody that I don’t feel well, or that I can’t stay any longer because I’m tired…it’s like they don’t believe me. And I’m one of the lucky ones who do not have a lot of side effects, you know, I do get tired and a lot of abdominal pain…but nobody believes me. I have a disability sticker. So, if I have a bad day, I can’t really walk very far.”

Person Living with PNH

Why Are We Here Today?

What happens the day these treatments receive FDA approval?

Questions about:

- What are the risks and benefits?
- How do new treatments fit into the evolving landscape?
- What are reasonable prices and costs to patients, the health system, and the government?
- What lessons are being learned to guide our actions in the future?

The Impact on Rising Health Care Costs for Everyone

DIAGNOSIS: DEBT

100 Million People in America Are Saddled With Health Care Debt

By Noam N. Levey

JUNE 16, 2022

Why Delaware is eying a 27% premium hike on state employees' health insurance

Amanda Fries

Delaware News Journal

Published 4:35 a.m. ET Feb. 1, 2024 | **Updated 9:29 p.m. ET Feb. 6, 2024**

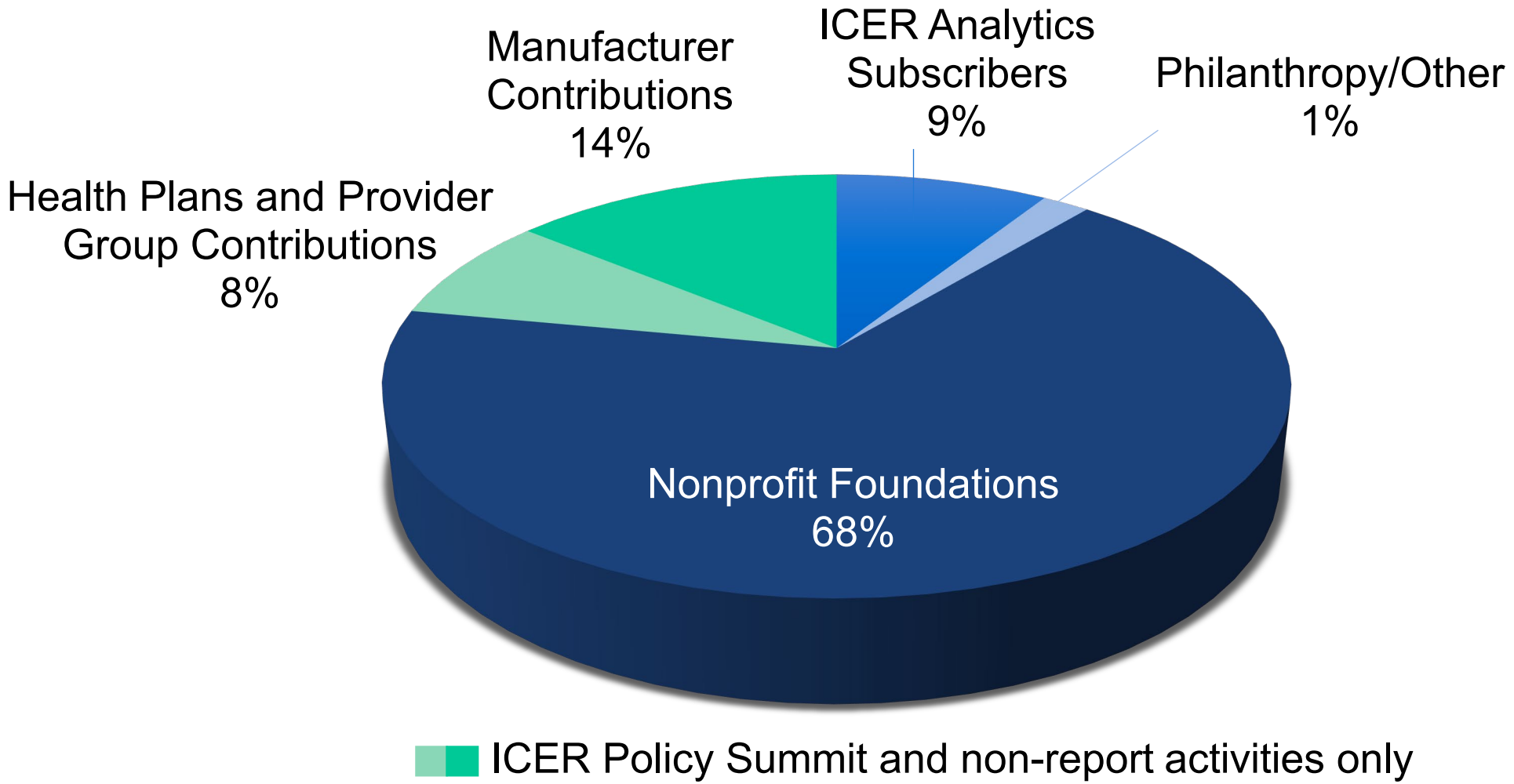
100 Million People in America Are Saddled With Health Care Debt (KFF Health News)

Why Delaware is eying a 27% premium hike on state employees' health insurance (Delaware Online)

Organizational Overview

- California Technology Assessment Forum (CTAF)
- Institute for Clinical and Economic Review (ICER)

Funding 2024



How Was the ICER Report Developed?

- Scoping with guidance from patients, clinical experts, manufacturers, and other stakeholders
- Internal ICER evidence analysis and cost-effectiveness modeling done by University of Washington School of Medicine
- Public comment and revision
- Expert reviewers:
  - **Robert Brodsky, MD,** Director, Division of Hematology; Professor of Medicine, Johns Hopkins University
  - **Leigh Clark, BCPA,** Director, Patient Services, AAMDSIF
  - **Doug Coyle, PhD,** Professor, School of Epidemiology and Public Health, University of Ottawa
  - **Ilene Weitz, MD,** Professor of Medicine, Jane Anne Nohl Division of Hematology, Keck-USC School of Medicine
- How is the evidence report structured to support CTAF voting and policy discussion?

Agenda (PT)

9:00 AM	Meeting Convened and Opening Remarks
9:20 AM	Presentation of the Clinical Evidence
10:00 AM	Presentation of the Economic Model
10:40 AM	Public Comments and Discussion
11:00 AM	Lunch Break
11:50 AM	CTAF Deliberation and Vote
12:50 PM	Break
1:00 PM	Policy Roundtable Discussion
2:30 PM	Reflections from CTAF
3:00 PM	Meeting Adjourned

Presentation of the Clinical Evidence

Anil Makam, MD, MAS

Associate Professor of Medicine

University of California, San Francisco (UCSF)

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Key Collaborators

- **Shahariar Mohammed Fahim, PhD,** Research Lead, ICER
- **Belen Herce-Hagiwara, BA,** Senior Research Assistant, ICER

Disclosures:

UCSF, on behalf of Dr. Makam, received funding from ICER for this report.

Researchers have no conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.

PNH is a Rare, Acquired Blood Disorder Characterized by Chronic Destruction of Red Blood Cells and Blood Clots

Key Symptoms

Anemia causes fatigue, and if severe, lifelong transfusion dependence.

Thrombosis occurs in 30% and it is the most common cause of death.

Epidemiology

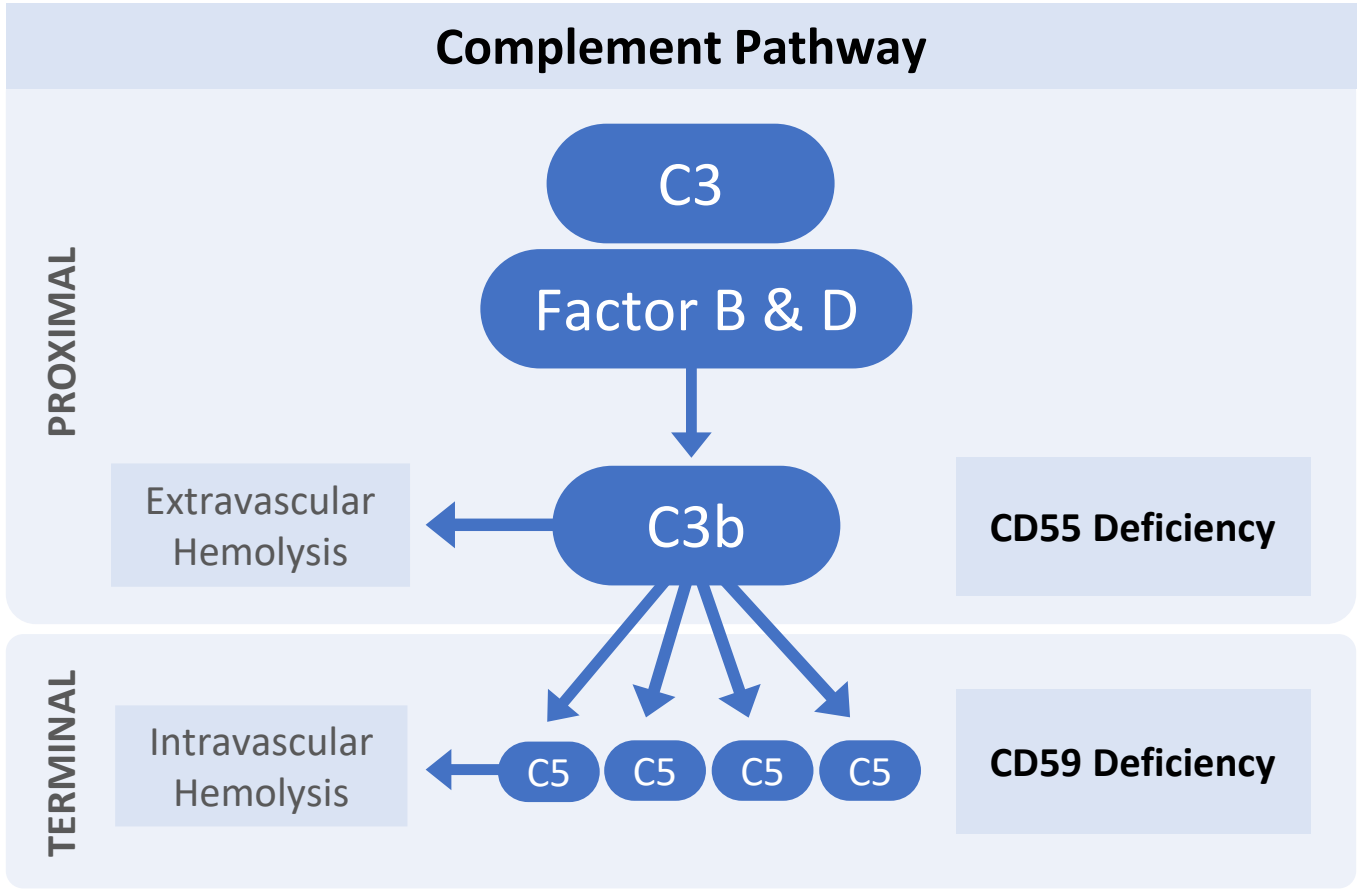
Prevalence: 10-20 cases per million

Incidence: 1-2 new cases per million annually

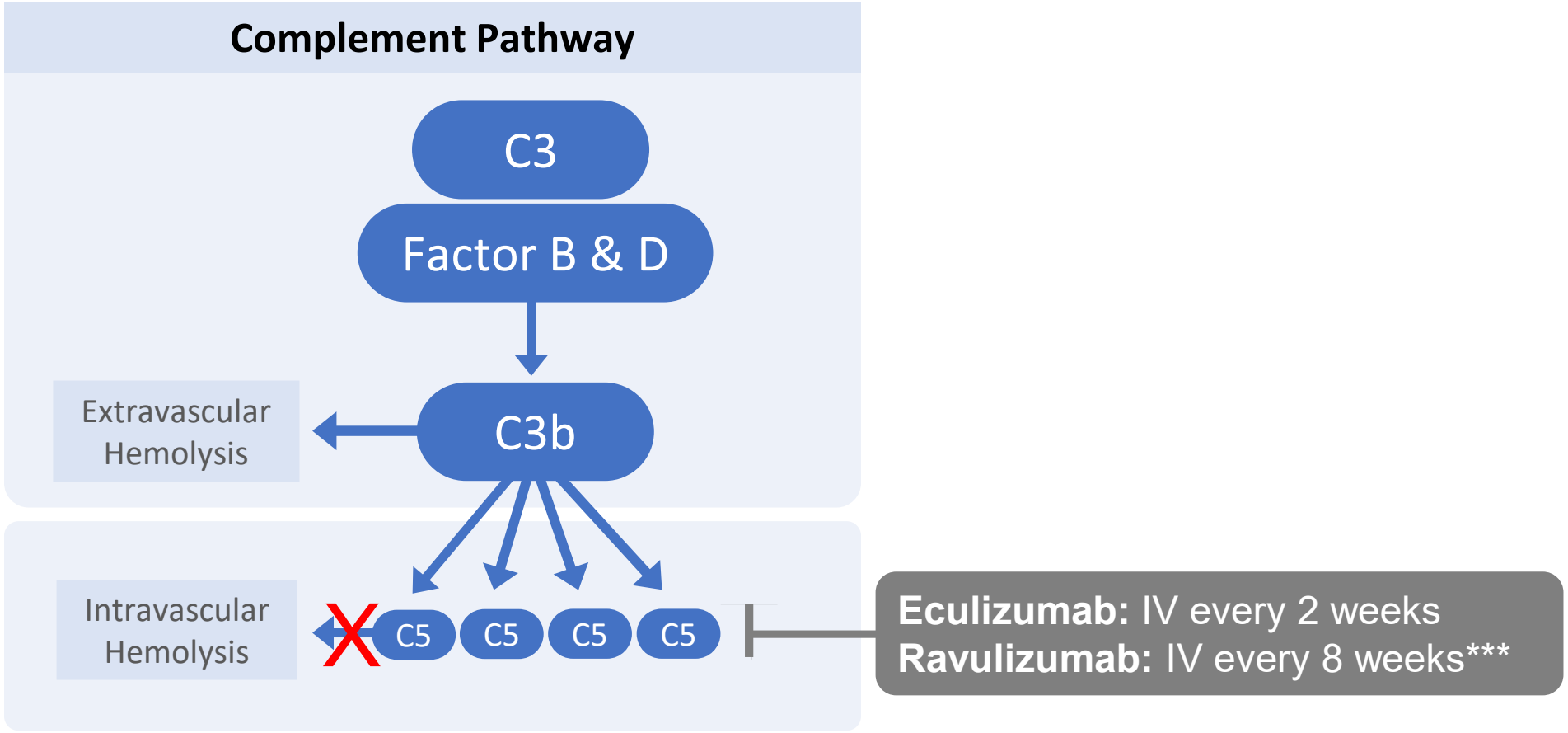
Treatment

No "real" cure as bone marrow transplant is too toxic for most.

PNH is Caused by the Deficiency of 2 Proteins Which Normally Prevent Hemolysis by the Immune System

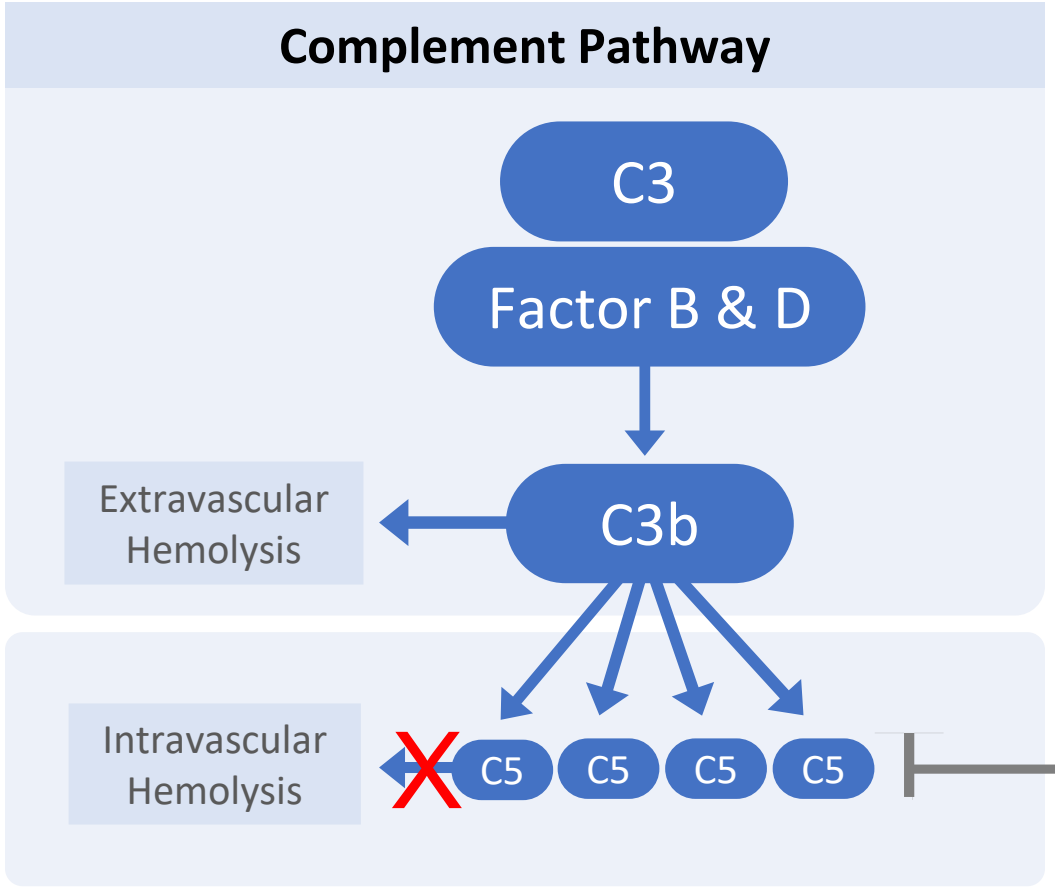


C5 Inhibitors are Standard of Care



IV: intravenous

C5 Inhibitors are Standard of Care



Recommended in **symptomatic PNH** (60%)

- **1st line** in treatment-naïve PNH

Greatly **reduces** anemia, thrombosis, death

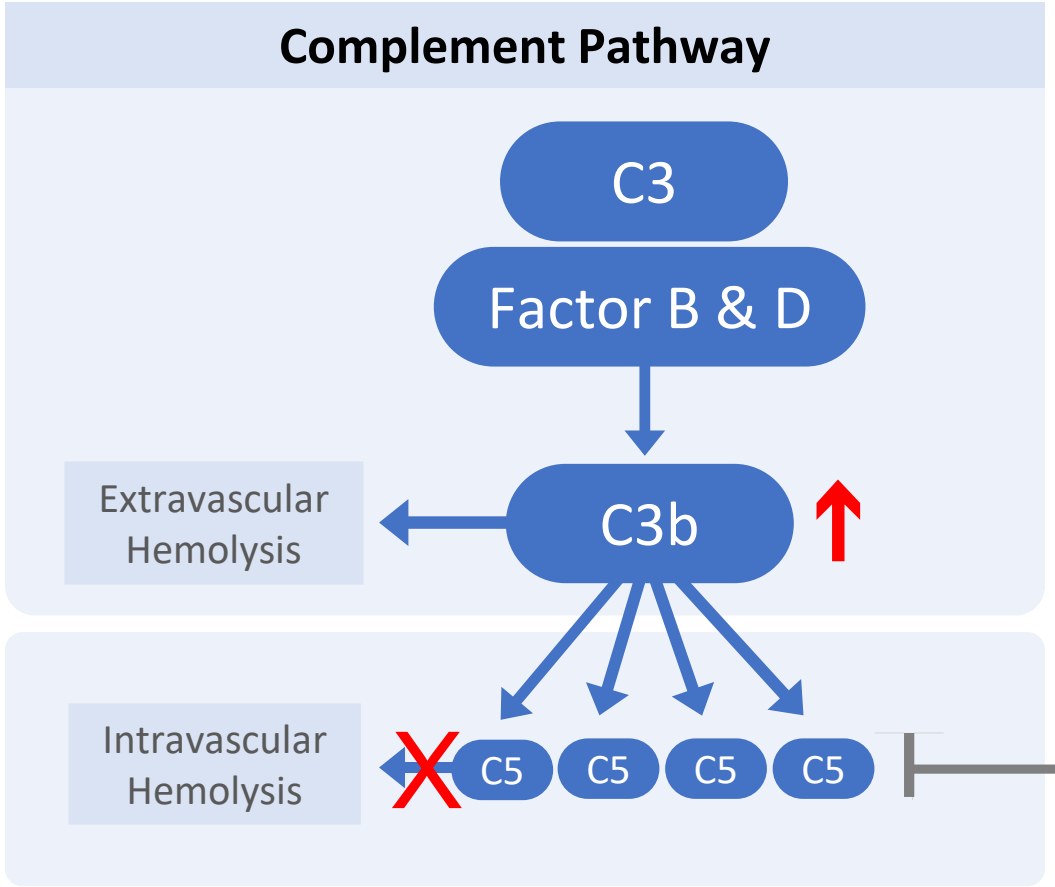
- Life expectancy ≈ general population

Costly: lifelong costs over $9 million

- ~$500,000 per year

Eculizumab: IV every 2 weeks
Ravulizumab: IV every 8 weeks***

Clinically Significant Extravascular Hemolysis (EVH)



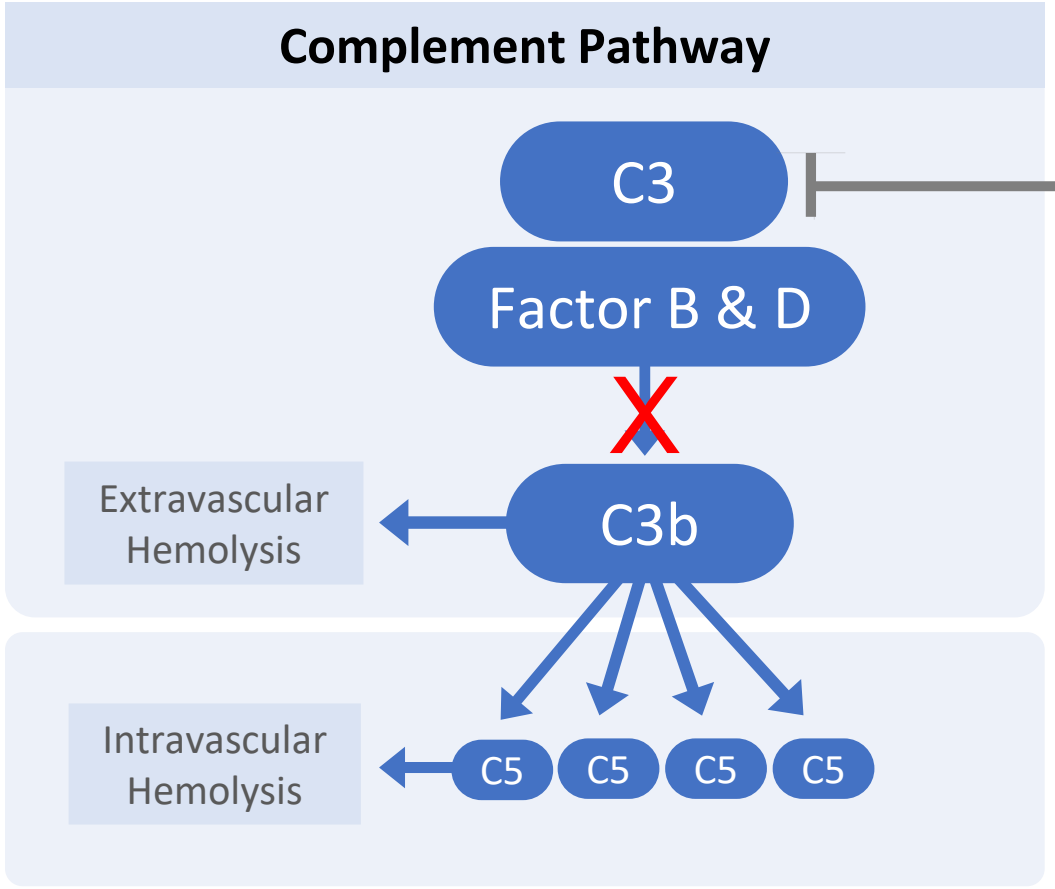
~1/3rd have **symptomatic anemia**

20% are **transfusion dependent** in part due to EVH

Eculizumab: IV every 2 weeks
Ravulizumab: IV every 8 weeks***

EVH: extravascular hemolysis, **IV**: intravenous

Pegcetacoplan: Option for Clinically Significant EVH



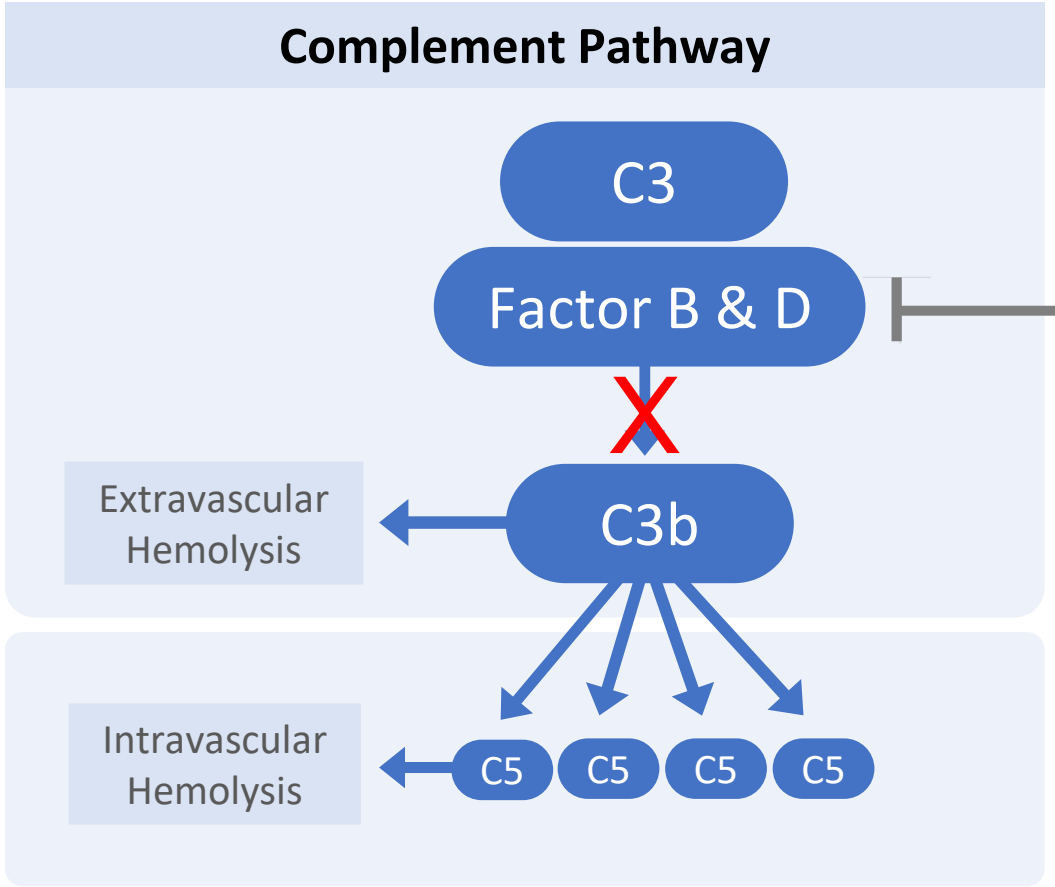
Pegcetacoplan
SQ twice weekly

FDA-approved for the treatment of **all PNH**

Recommend for **clinically significant EVH**

EVH: extravascular hemolysis, **SQ:** subcutaneous

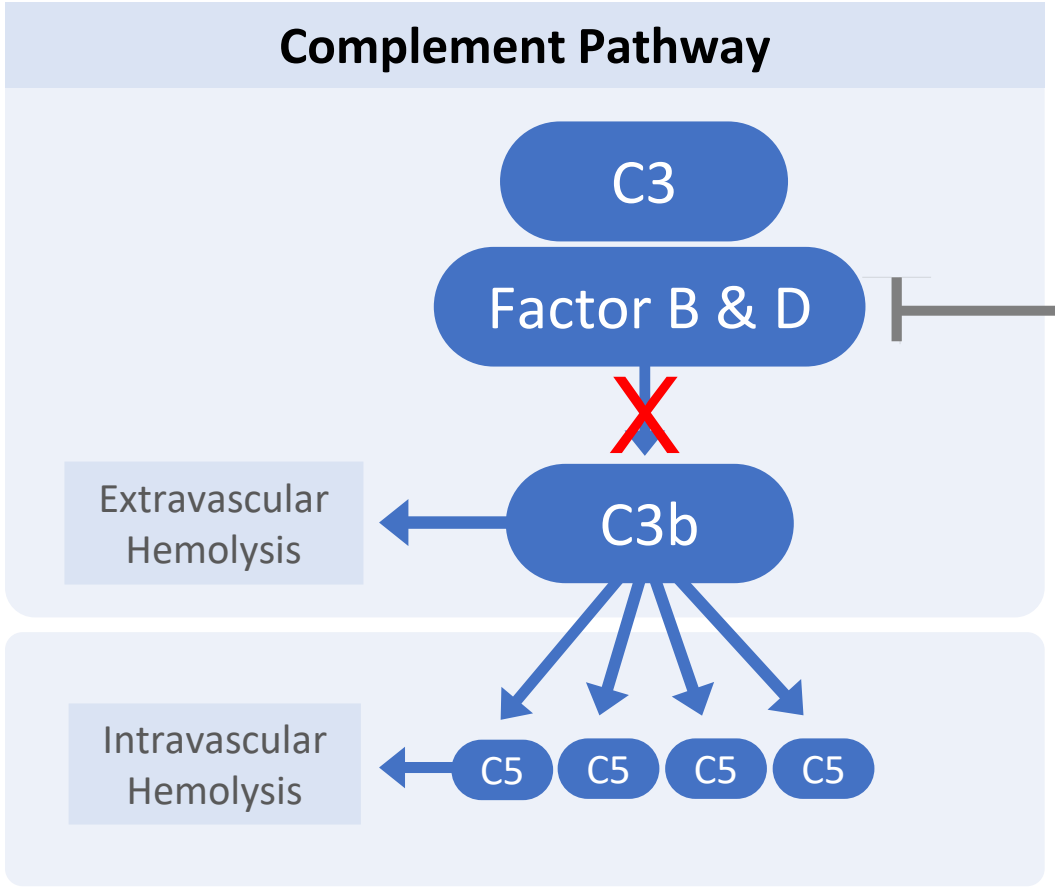
Two New Proximal Complement Inhibitor Medications



Oral twice daily **factor B inhibitor**

FDA-approved for **all PNH** on 12/6/23

Two New Proximal Complement Inhibitor Medications



Oral 3x daily **factor D inhibitor**

Considered by FDA as **add-on** to a C5 inhibitor for only **treatment-experienced** patients with **clinically significant EVH**

EVH: extravascular hemolysis

Insights from Discussions with Patients

Diverse range of experiences ranging from no symptoms to severe illness.

PNH is often an "invisible" illness, even if severely symptomatic.

Satisfaction with C5 inhibitors for treatment-naïve patients for disease control and peace of mind of not worrying about missed doses, and durable protection against thrombosis.

Would consider switching treatments if has cs-EVH but concerns about affordability.

Scope of Review

The comparative clinical effectiveness of **iptacopan monotherapy** or **danicopan added-on to a C5 inhibitor** for the treatment of PNH

Populations of PNH

- Treatment-naïve
- Treatment-experienced with clinically significant extravascular hemolysis (cs-EVH)

Comparators

- C5 inhibitors (eculizumab or ravulizumab)
- No head-to-head comparison with pegcetacoplan or to each other
- Evidence base was too limited to conduct an indirect network meta-analysis

Outcomes

Primary – Hematologic response

- Hemoglobin level (Hb) ± avoidance of red blood cell transfusions

Secondary

- Lactase dehydrogenase (LDH): biomarker of intravascular hemolysis (IVH)
- Fatigue using the FACIT-Fatigue score (lower = worse; MCID of 5 points in PNH)

Safety

- Breakthrough intravascular hemolysis (BTH)
- Major adverse vascular event (MAVE): includes thrombosis

FACIT: Functional Assessment of Chronic Illness Therapy,
MCID: minimal clinically important difference

Clinical Evidence

Iptacopan: Overview of Evidence

Treatment-Naïve: APPOINT-PNH Trial (N=40)

- **Single-arm**, open-label multinational phase 3 trial of 24-week duration
- Confirmed PNH with hemolysis without bone marrow failure
- Mean age of 42, mean Hb ~8 g/dL, 70% transfused in prior 6 months

Treatment-Experienced with cs-EVH: APPLY-PNH Trial (N=97)

- **RCT**, open-label, multinational, 2:1 of iptacopan vs continued C5 inhibitor for 24 weeks
- Confirmed PNH with EVH on a stable C5i regimen ≥6 months w/o bone marrow failure
- Mean age of 51, mean Hb ~9 g/dL, 58% transfused in prior 6 months

EVH: extravascular hemolysis, **g/dL**: grams per deciliter, **Hb**: hemoglobin, **N**: number

Iptacopan: Key Results in Treatment-Naïve PNH

from the single arm APPOINT-PNH trial

Primary outcome

- 94% had sustained ↑ Hb ≥ 2 g/dL without transfusion.

Secondary outcomes

- 58% had Hb ≥ 12 g/dL without a transfusion.
- 100% avoided transfusion.
- Mean LDH 1582 → 261 IU/L; 95% achieved normal or near-normal levels.
- FACIT-Fatigue score increased by ~11 points (MCID=5 pts).

FACIT: Functional Assessment of Chronic Illness Therapy, **g/dL**: grams per deciliter, **Hb**: hemoglobin, **IU/L**: international units per liter, **LDH**: lactate dehydrogenase, **MCID**: minimal clinically important difference

Iptacopan: Key Results in Treatment-Experienced

from the open-label APPLY-PNH RCT

Achieved co-primary endpoints of hematologic response

- 85% had sustained ↑ Hb ≥ 2 g/dL without transfusion vs. 0% for C5 inhibitor group.
- 70% achieved Hb ≥ 12 g/dL without transfusion vs. 0% for C5 inhibitor group.

Secondary outcomes

- 95% achieved transfusion avoidance vs. 40% for C5 inhibitor group.
- LDH levels similarly controlled: Mean 277 vs. 283 IU/L for C5 inhibitor group.
- FACIT-Fatigue score increased by 8.6 points vs. 0.3 points for C5 inhibitor group.

FACIT: Functional Assessment of Chronic Illness Therapy, **g/dL**: grams per deciliter, **Hb**: hemoglobin, **IU/L**: international units per liter, **LDH**: lactate dehydrogenase

Iptacopan: Durability in Treatment-Experienced

24-week uncontrolled extension with 97% participant retention:

Benefits for iptacopan were sustained at 48 weeks:

- Mean Hb 12.2 g/dL, 94% avoided transfusion, FACIT-Fatigue +10 points

C5 inhibitor crossover to iptacopan showed similar beneficial trend 24 → 48 weeks:

- Mean Hb 12.1 g/dL, 94% avoided transfusion, FACIT-Fatigue +11 points

FACIT: Functional Assessment of Chronic Illness Therapy, **g/dL**: grams per deciliter, **Hb**: hemoglobin

Harms of Iptacopan

Most common harms: Headache, diarrhea, and nasopharyngitis

Serious harms: Minimal during randomized phase without discontinuation

- 1 participant had a MAVE in the APPLY-PNH trial
- **Mortality:** 1 patient died from an encapsulated bacterial infection

BTH: Occurred in **5%** of iptacopan arm vs **23%** of C5 inhibitor arm

- Defined more broadly than intravascular hemolysis
- Not available by type of C5 inhibitor (1/3rd of C5 inhibitor arm used ravulizumab)

Uncertainties and Controversies for Iptacopan

- Two **small, short-term clinical trials** conducted outside of the US
- Concerns persist for **BTH** and **thrombosis** from nonadherence and complement-activating conditions (i.e., infections)
- **Open-label design** may bias fatigue ascertainment
- **Lack comparative efficacy** to a C5 inhibitor for treatment-naïve and pegcetacoplan for treatment-experienced

ICER Evidence Ratings for Iptacopan

Population	Comparator	Evidence Rating
Treatment-Naïve	C5 inhibitor	I
Treatment-Experienced with cs-EVH	Pegcetacoplan	I
Treatment-Experienced with cs-EVH	Continuing a C5 inhibitor	P/I

Insufficient (I) – Low certainty due to lack of comparative efficacy data.

Promising but Inconclusive (P/I) – Moderate to substantial net benefit but uncertainty about long-term safety, particularly BTH and thrombosis.

BTH: breakthrough hemolysis
csEVH: clinically significant extra vascular hemolysis

Danicopan add-on: Overview of Evidence

Treatment-Experienced with cs-EVH: ALPHA Trial (n=86)

- **RCT,** double-blind, placebo-controlled, multinational, 2:1 add-on danicopan vs add-on placebo to a C5 inhibitor for 12 weeks
- Confirmed PNH with EVH on a stable C5i ≥6 months w/o bone marrow failure
- Mean age of ~52, mean Hb of ~8 g/dL, 100% transfused in prior 6 months
- Outcome data available for ~75% participants in a prespecified interim analysis

C5i: C5 inhibitors, **csEVH**: clinically significant extra vascular hemolysis, **Hb**: hemoglobin, **RCT:** randomized controlled trial

Danicopan: Results in Treatment-Experienced

Primary outcome: between-group mean Hb change of +2.4 g/dL

Secondary outcomes:

- 60% had sustained ↑ Hb ≥ 2 g/dL without transfusions vs. 0% for placebo add-on.
- 83% achieved transfusion avoidance vs. 38% for placebo add-on.
- LDH levels remained similarly controlled in both groups.
- FACIT-Fatigue score increased by 8.0 vs. 1.9 points for placebo add-on (MCID=5 pts).

FACIT: Functional Assessment of Chronic Illness Therapy, **g/dL**: grams per deciliter, **Hb**: hemoglobin, **LDH**: lactate dehydrogenase, **MCID**: minimal clinically important difference

Danicopan add-on: Durability

12-week uncontrolled extension with 93% participant retention:

Benefits for danicopan add-on were sustained at 24 weeks

- Mean Hb change of +3.2 g/dL, 78% avoided transfusion, FACIT-Fatigue +6.1 points (MCID=5 pts)

Placebo crossover to danicopan add-on had similar beneficial trend 12→24 weeks

- Mean Hb change of +2.3 g/dL, 90% avoid transfusion, FACIT-Fatigue +6.4 points

FACIT: Functional Assessment of Chronic Illness Therapy, **g/dL**: grams per deciliter, **Hb**: hemoglobin, **MCID**: minimal clinically important difference

Harms of Danicopan

Minimal serious harms: No deaths; low discontinuation rate

Most common harms: Headache and elevated liver enzymes

Non-serious hemolysis in 4% vs. 0% of placebo

- In 80 treated participants, 1 clinical breakthrough hemolysis without discontinuation

Uncertainties and Controversies for Danicopan

- 1 **small, short-duration trial** with efficacy data available for ~75%
- No concern for **BTH** and **thrombosis** since added to a C5 inhibitor
- **No head-to-head comparison** to pegcetacoplan
  - Qualitatively all proximal complement inhibitors appear similar

ICER Evidence Ratings for Danicopan add-on to C5i

Population	Comparator	Evidence Rating
Treatment-Experienced with cs-EVH	Pegcetacoplan	I
Treatment-Experienced with cs-EVH	Continuing a C5 inhibitor	C++

Insufficient (I) – Low certainty due to lack of comparative efficacy data.

Comparable or Better (C++) – Moderate certainty of a modest to substantial net benefit.

Potential Other Benefits and Contextual Considerations

Oral iptacopan

- More convenient and could improve access to care, especially for patients who do not live near an infusion center.

Danicopan add-on

- Does not provide greater convenience or access.

Public Comments Received

Iptacopan | Consider other potential benefits (access, time, travel) and productivity loss from C5 inhibitor infusions

Danicopan | Interim analysis of the first 75% of randomized patients was pre-specified as the primary analysis set of the study

Both | Improvements in fatigue were…considered clinically meaningfully

Summary

Iptacopan appears well tolerated and may have moderate to substantial net benefit for treatment-experienced patients with cs-EVH.

- Uncertainty about long-term safety, particularly BTH and thrombosis
- Lack comparative data to pegcetacoplan, or to C5 inhibitor for treatment-naïve

Danicopan added on to a C5 inhibitor appears safe with moderate certainty for modest to substantial net benefit.

- No concerns for BTH and thrombosis, but no gain in convenience or access to care

Questions?

Iptacopan and Danicopan for Paroxysmal Nocturnal Hemoglobinuria: Effectiveness and Value

Kangho Suh, PharmD, PhD
Assistant Professor
University of Pittsburgh School of Pharmacy

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Key Review Team Members

- **Josh Carlson, PhD, MPH**, Professor, University of Washington
- **Ronald Dickerson, MA, MPH**, Research Assistant, University of Washington
- **Marina Richardson, PhD, MSc**, Associate Director of HTA Methods and Health Economics, ICER
- *Disclosures:*

Financial support was provided to the University of Washington and Pittsburgh from the Institute for Clinical and Economic Review.

Drs. Suh and Carlson have no conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.

Objective

To evaluate the cost-effectiveness of **iptacopan** or **add-on danicopan compared to ravulizumab** for the treatment of paroxysmal nocturnal hemoglobinuria in **treatment experienced patients** with clinically significant extravascular hemolysis.

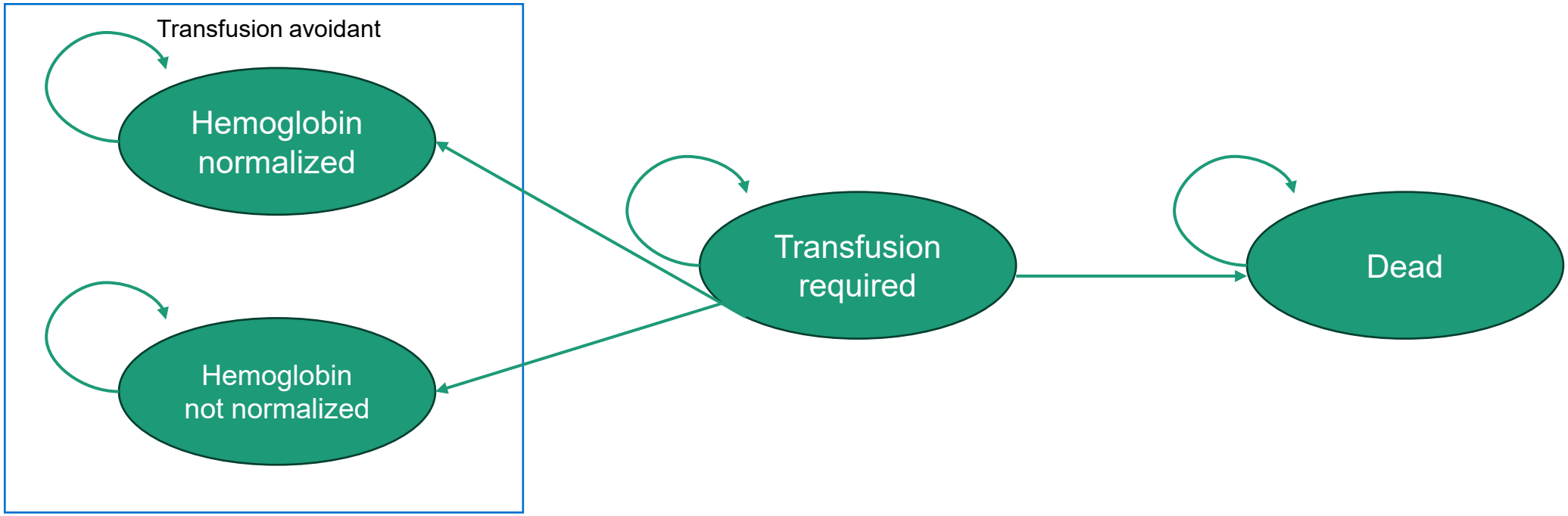
Methods in Brief

Methods Overview

- **Model:** Markov
- **Setting:** United States
- **Perspective:** Health Care Sector Perspective
- **Time Horizon:** 5-year
- **Discount Rate:** 3% per year (costs and outcomes)
- **Cycle Length:** 24 week
- **Primary Outcome:** Cost per quality-adjusted life year (QALY) gained; cost per evLY gained; cost per LY gained

evLY: equal value life year, **LY**: life year

Model Schematic



Hemoglobin normalized defined as ≥12 g/dL

Figure adapted from Fishman J et al. J Comp Eff Res. 2023;12(10):e230055

Model Characteristics

Baseline Characteristic	Iptacopan vs. Ravulizumab	Danicopan Add-on vs. Ravulizumab Alone
Age, mean	51.0	52.8
Female, %	69.1	62.8
Mean Hemoglobin, g/dL	8.9	7.8
Source	APPLY trial	ALPHA trial

g/dL: gram per deciliter

Key Assumptions

- Patients do not transition between non death health states after initial treatment initiation.
- Treatment efficacy holds for the duration of the 5-year time horizon.
- Utility values are consistent across definitions of hemoglobin normalization.
- Ravulizumab is equivalent to eculizumab with respect to efficacy.
- Model assumes patients remain adherent for full time horizon.

Key Model Inputs: Treatment-Related Efficacy

	Iptacopan (APPLY)	Ravulizumab (APPLY)
Transfusion Avoidant and Hgb Normalized	68.8%	1.8%
Transfusion Avoidant and Hgb Not Normalized	27.6%	24.3%
Transfusion Required	3.6%	73.9%
Breakthrough Hemolysis	5.0%	2.3%*
MAVE	1.6%	0%

*Weighted average from Study 301 and 302
Hgb: hemoglobin, MAVE: major adverse vascular event

Key Model Inputs: Treatment Costs

Intervention (Dosage)	Net Unit Price	Net Annual Cost	Source
Iptacopan	$753	$550,377	Redbook
Danicopan	$137*	$150,000*	IPD Analytics
Ravulizumab, 10mg/mL (30 mL)†	$222	First year: $518,000 Second year onwards: $477,000	Redbook

Mg: milligram, mL: milliliter
*placeholder price
†Assuming a mean body weight of 69 kg (Lee et al 2019), loading dose (2700mg), maintenance dose (3300mg) every eight weeks starting two weeks after loading dose.

Key Model Inputs: PNH-Related Costs

	Cost	Source
IV Administration Cost (First Hour)	$132	CMS Fee Schedule
IV Administration Cost (Subsequent Hours)	$28	CMS Fee Schedule
Hematologist Visit Cost	$143	CMS Fee Schedule
Blood Tests	$9	CMS Fee Schedule
Blood Transfusion Unit Cost	$2,772	Cheng 2021

Key Model Inputs: Health State Utilities

Health State	Utility	Source
Transfusion Avoidant and Hgb normalized*	0.869	PRINCE trial
Transfusion Avoidant and Hgb not normalized*	0.820	PRINCE trial
Transfusion required	0.818	PRINCE trial
General population	Age-adjusted	Jiang R. et al 2021

*Hgb normalized defined as Hgb ≥ 12g/dl for females and ≥ 13.6g/dl for males

Results

Base-Case Results for Iptacopan

Drug	Drug Cost	Total Cost	LYs	QALYs	evLYs
Iptacopan	$2,360,000	$2,375,000	4.29	3.65	3.65
Ravulizumab	$2,088,000	$2,175,000	4.29	3.50	3.50
Incremental Results*	$273,000	$200,000	0.00	0.15	0.15

Drug	Comparator	Cost per QALY gained	Cost per evLY gained
Iptacopan	Ravulizumab	$1,368,000	$1,368,000

*any discrepancies in incremental results due to rounding
evLYs: equal value of life years, LYs: life years, QALYs: quality-adjusted life years

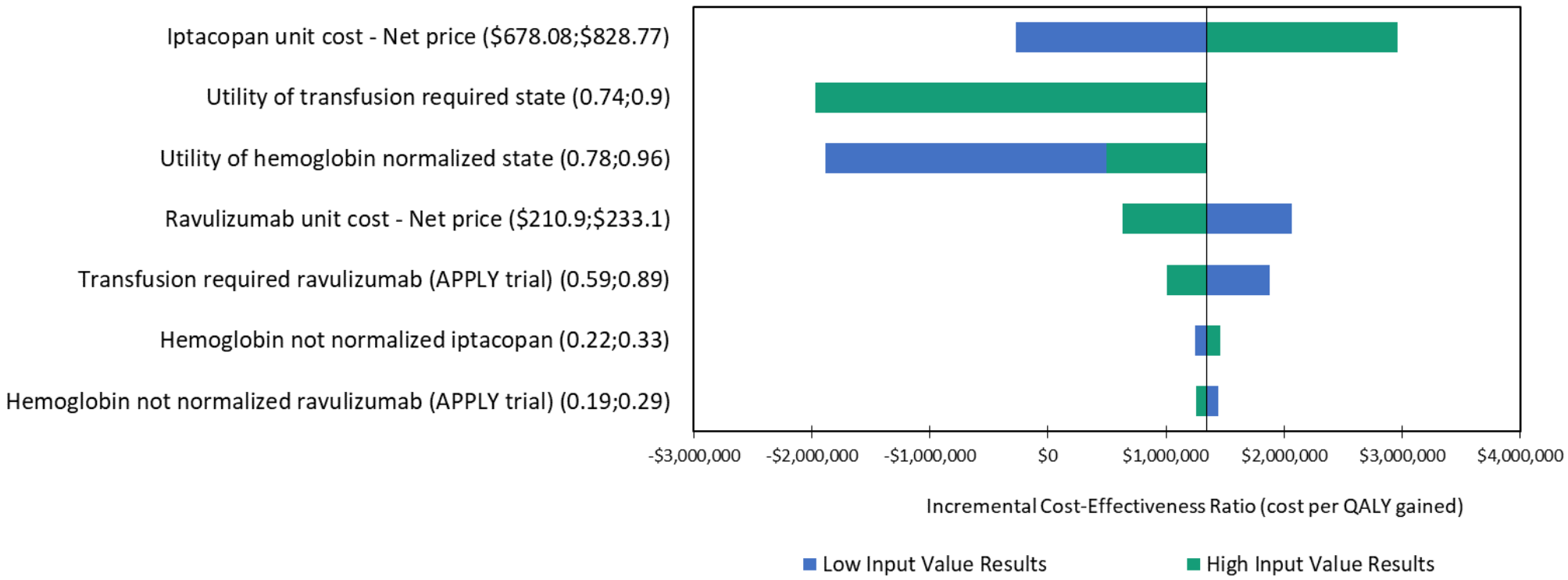
Base-Case Results for Add-on Danicopan

Drug	Drug Cost	Total Cost	LYs	QALYs	evLYs
Danicopan + Ravulizumab	$2,712,000*	$2,737,000*	4.26	3.51	3.51
Ravulizumab	$2,073,000	$2,144,000	4.26	3.45	3.45
Incremental Results	$639,000	$593,000	0.00	0.06	0.06

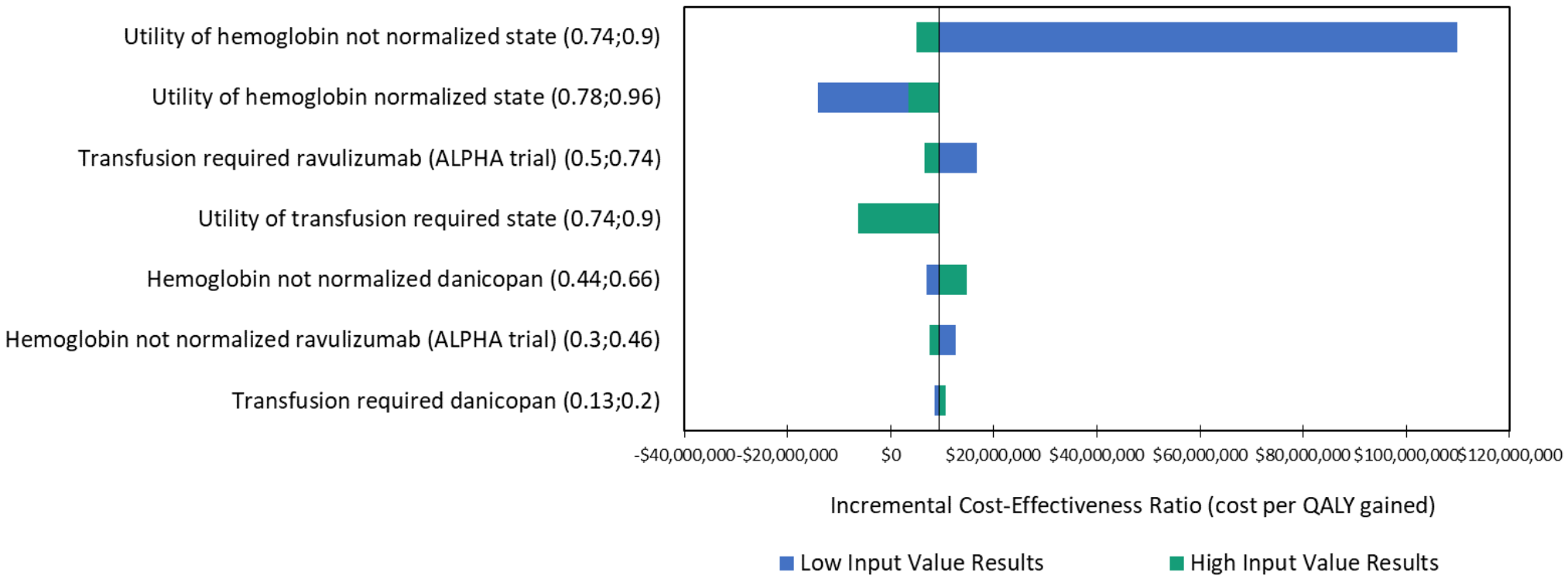
Drug	Comparator	Cost per QALY gained	Cost per evLY gained
Danicopan + Ravulizumab	Ravulizumab	$9,457,000*	$9,457,000*

*Based on placeholder price
evLYs: equal value of life years, LYs: life years, QALYs: quality-adjusted life years

One Way Sensitivity Analysis for Iptacopan



One Way Sensitivity Analysis for Add-on Danicopan



Probabilistic Sensitivity Analysis

Drug	$50,000 per QALY	$100,000 per QALY	$150,000 per QALY
Iptacopan	13.10%	13.80%	15.60%
Add-on Danicopan	0.00%	0.00%	0.00%

QALY: quality-adjusted life year

Threshold Prices

Intervention	Annual WAC	Annual Price at $100,000 Threshold	Annual Price at $150,000 Threshold	Discount from WAC to Reach Threshold Prices
Iptacopan	$550,377	$507,000	$509,000	7.54% - 7.85%
Add-on Danicopan	Not available	$12,300	$13,100	Not available

WAC: wholesale acquisition cost

Scenario Analyses

- Modified Societal
- Lifetime time horizon
- Alternative set of utility values
- Higher rate of breakthrough hemolysis rate for ravulizumab
- $150,000 cost-offset cap

Health System Cost-Offset Cap Scenario

- Cost-offset cap scenario in which health system cost-offsets generated by a new treatment are capped at $150,000 per year.
- Health Benefit Price Benchmarks estimated using the cost-offset cap may be considered when:
  - A large percentage of the traditional value-based price comes from the cost-offsets of comparator (e.g. standard of care) therapy.
    - ~97% of annual threshold price for iptacopan was from comparator cost-offsets.
  - Comparator therapy price is not known to meet common cost-effectiveness thresholds.
    - Prior models of C5 inhibitors vs. supportive treatment did not result in favorable incremental cost-effectiveness ratios ($2.27 million/QALY gained).

Health Benefit Price Benchmarks (HBPBs)

Intervention	Annual WAC	Annual Price at $100,000 Threshold	Annual Price at $150,000 Threshold	Discount from WAC to Reach Threshold Prices
Iptacopan*	$550,377	$178,000	$180,000	67.30% - 67.61%
Add-on Danicopan	Not available	$12,300	$13,100	Not available

*Based on the $150,000 cost-offset cap scenario
WAC: wholesale acquisition cost

Limitations

- Limited amount of publicly available data:
  - Reduced to estimating the initial cycle (24 weeks) and limited between health state transition probabilities
  - Only able to evaluate in treatment-experienced population
- Clinical data used to inform model parameters limited to small sample sizes and short follow-up periods

Comments Received

- Breakthrough hemolysis rate used for ravulizumab in iptacopan comparison
- Modified societal costs especially around productivity
- Non-drug medical costs for PNH patients

Conclusions

- Iptacopan and add-on danicopan provide important clinical benefits, but there are uncertainties regarding long-term efficacy and safety.
- At the current wholesale acquisition cost, iptacopan would not meet commonly cited cost-effectiveness thresholds.
- Conventional annual threshold price analysis results for iptacopan are driven by high prices of C5 inhibitors.
- At the currently assumed placeholder price, add-on danicopan would not meet commonly cited cost-effectiveness thresholds.

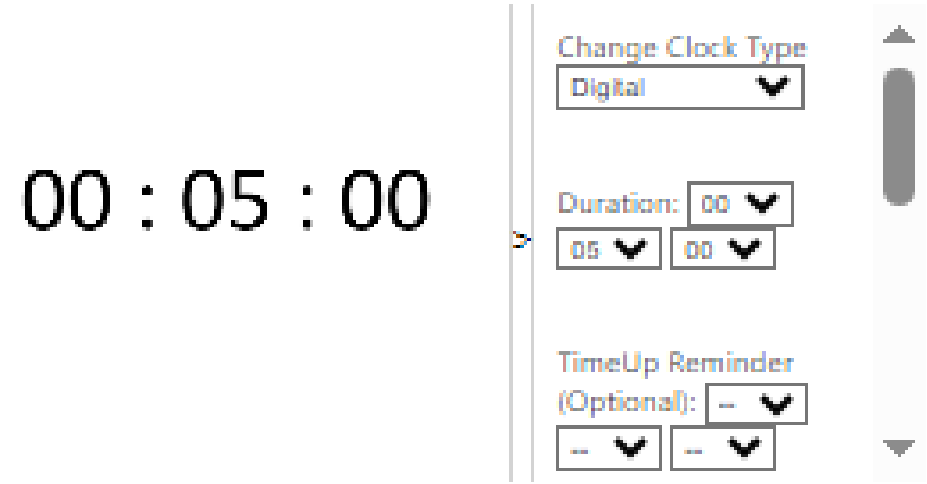
Questions?

Manufacturer Public Comment and Discussion

Anita Hill, MD, PhD
Head of Medical Affairs, Hematology and Nephrology, Alexion

Conflicts of Interest:

- *Dr. Hill is a full-time employee at Alexion.*



Public Comment and Discussion

Evan Rossman, Individual Living with PNH Onboarding Specialist/Solution Expert

Conflicts of Interest:

- *No conflicts to disclose.*

Snooze Options: 30 Seconds | 1 Minute | 5 Minutes | 10 Minutes

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Lunch

Meeting will resume at 11:50 AM PT (2:50 PM ET)

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Clinical Evidence

Patient Population: Treatment-naïve PNH patients.

slido

1. Is the currently available evidence adequate to demonstrate that the net health of iptacopan is superior to that provided by C5 inhibitor therapies (eculizumab, ravulizumab)?

ⓘ Start presenting to display the poll results on this slide.

Patient Population: Treatment-experienced on a stable C5 Inhibitor regimen with clinically significant extravascular hemolysis

slido

2. Is the currently available evidence adequate to demonstrate that the net health benefit of switching to iptacopan is superior to that provided by continuing a C5 inhibitor?

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slido

3. Is the currently available evidence adequate to demonstrate that the net health of switching to iptacopan is superior to that provided by switching to pegcetacoplan?

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slido

4. Is the currently available evidence adequate to demonstrate that the net health benefit of adding danicopan to a C5 inhibitor is superior to that provided by continuing a C5 inhibitor alone?

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slido

5. Is the currently available evidence adequate to demonstrate that the net health benefit of adding danicopan to a C5 inhibitor is superior to that provided by switching to pegcetacoplan?

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Contextual Considerations and Potential Other Benefits or Disadvantages

When making judgments of overall long-term value for money, what is the relative priority that should be given to any effective new treatment for PNH, on the basis of the following contextual considerations:

slido

1. Acuity of need for treatment of individual patients based on short-term risk of death or progression to permanent disability

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slido

2. Magnitude of the lifetime impact on individual patients of the condition being treated

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Patient Population: Treatment-experienced on a stable C5 Inhibitor regimen with clinically significant extravascular hemolysis

What are the relative effects of switching to iptacopan versus continuing C5 inhibitors on the following outcomes that inform the judgment of the overall long-term value for money of iptacopan?

slido

3. Patients’ ability to achieve major life goals related to education, work, or family life

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slido

4. Caregivers’ quality of life and/or ability to achieve major life goals related to education, work, or family life

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slido

5. Patients’ ability to manage and sustain treatment given the complexity of regimen

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slido

6. Society’s goal of reducing health inequities

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Patient Population: Treatment-experienced on a stable C5 Inhibitor regimen with clinically significant extravascular hemolysis

What are the relative effects of adding danicopan to C5 inhibitors versus C5 inhibitors alone on the following outcomes that inform judgment of the overall long-term value for money of danicopan?

slido

7. Patients’ ability to achieve major life goals related to education, work, or family life

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slido

8. Caregivers’ quality of life and/or ability to achieve major life goals related to education, work, or family life

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slido

9. Patients’ ability to manage and sustain treatment given the complexity of regimen

ⓘ Start presenting to display the poll results on this slide.

slido

10. Society’s goal of reducing health inequities

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Long-Term Value for Money

Patient Population: Treatment-experienced on a stable C5 Inhibitor regimen with clinically significant extravascular hemolysis

Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment at current pricing with iptacopan versus C5 inhibitors?

slido

1. What is the long-term value for money of treatment at current pricing with iptacopan versus C5 inhibitors?

ⓘ Start presenting to display the poll results on this slide.

Break

Meeting will resume at 1:00 PM PT (4:00 PM ET)

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Policy Roundtable

Policy Roundtable

Participant	Conflict of Interest
Leigh Clark, BCPA, Director, Patient Services, Aplastic Anemia and MDS International Foundation	AAMDSIF has received <25% of funding from healthcare companies.
Eve Hindin, PharmD, MS, Executive Director, Clinical Formulary, CVS Health	Dr. Hindin is a full-time employee at CVS Health.
Jeri Keiller, Certified Public Accountant	No conflicts to disclose.
Irina Murakhovskaya, MD, Associate Professor, Albert Einstein College of Medicine/Montefiore Medical Center	Dr. Murakhovskaya has received more than $5,000 in honoraria or consulting fees from Novartis and Alexion. Dr. Murakhovskaya has also received >25% of funding from WAIHA Warriors and has served as the Principal Investigator for the Novartis CLNP023C12303 trial.
Caroline Piatek, MD, Associate Professor of Clinical Medicine, University of Southern California	Dr. Piatek has received more than $5,000 in honoraria or consulting fees from Argenx, Omeros, Janssen, Novartis, AstraZeneca/Alexion, Rigel, Apellis, Sanofi, Sobi. Dr. Piatek has also received manufacturer support through AstraZeneca/Alexion, Apellis.
Emily Tsiao, PharmD, BCPS, Clinical Pharmacist of Medical Policies, Premera	Dr. Tsiao is a full-time employee at Premera.

CTAF Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around March 14, 2024
    - Includes description of CTAF votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/paroxysmal-nocturnal-hemoglobinuria-2024/

Adjourn

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