# Budget Impact of Pegcetacoplan, a Complement C3 Inhibitor, for the Treatment of Paroxysmal Nocturnal Hemoglobinuria in US Adults

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Talbird SE,[1] Anderson S,[1] Fishman J[2], Mody-Patel N,[2] Sarda SP[2]

[1]RTI Health Solutions, Research Triangle Park, NC, United States
[2]Apellis Pharmaceuticals, Inc., Waltham, MA, United States

## Background

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare blood disease that may result in hemolysis, anemia, blood clots, bone marrow failure, and thrombosis.[1]
- PNH is diagnosed in approximately 5.7 people per million each year.[2]
- Two intravenous C5 inhibitor treatments (C5i) for PNH are available: eculizumab and ravulizumab.
- In May 2021, pegcetacoplan received Food and Drug Administration (FDA) approval for the treatment of adults with PNH based on head-to-head clinical data. Pegcetacoplan is a C3 inhibitor administered subcutaneously for treatment of PNH in adults who (1) are treatment naïve or (2) are currently treated with a C5i (treatment-switch).

## Objective

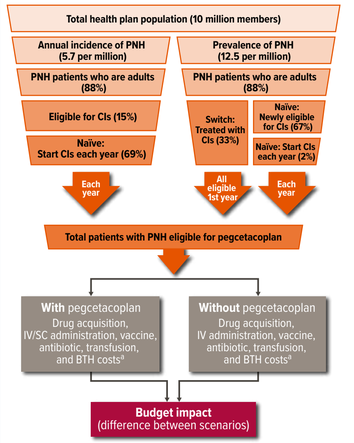
- This study estimates the budget impact of introducing pegcetacoplan to a health plan's formulary for the treatment of PNH among adults in the United States (US).

## Methods

### Model Structure

- A budget-impact model was developed using a 3-year time horizon and US health plan perspective (Figure 1).
- The model compared the current market scenario using C5i to a scenario introducing pegcetacoplan within a health plan's formulary (with future treatments excluded).
- The patient population was adults diagnosed with PNH who are eligible for treatment with a complement inhibitor (Figure 1).

**Figure 1.** Budget-Impact Model Structure




BTH = breakthrough hemolysis; CI = C5 inhibitors; IV = intravenous; PNH = paroxysmal nocturnal hemoglobinuria; SC = subcutaneous.
[a] BTH costs capture the increased drug costs (due to increased frequency or higher dosing for patients experiencing BTH) and costs for additional transfusions and hospitalizations. Vaccination costs apply only to the naïve population.

## Model Inputs

**Table 1.** Patient Population

| Input | Input value | Number of people | Source/assumption |
|---|---|---|---|
| Plan size | 10,000,000 | 10,000,000 | Assumption |
| PNH prevalence per million population | 12.5 | 125 | 2 |
| Percentage of prevalent patients who are adults | 88.1% | 110 | 3 |
| Percentage of prevalent adults treated with C5is | 33% | 36.4 | 4,5 |
| **Treatment-switch patients eligible for pegcetacoplan treatment** | | **36.4** | **Calculated** |
| Percentage of prevalent patients who are C5i naïve | 67% | 74 | Residual of 33% of patients currently treated |
| Annual net uptake of C5is in this group | 2% | 1.5 | Assumed 5% discontinuation and 3% newly eligible for C5is annually due to disease progression |
| **Prevalent treatment-naïve patients eligible for pegcetacoplan treatment annually** | | **1.5** | **Calculated** |
| PNH incidence per million population | 5.7 | 57 | 2 |
| Percentage of incident patients who are adults | 88.1% | 50 | 3 |
| Percentage of incident adults eligible for C5is | 15% | 8 | 4 |
| Incident adults who start C5is each year | 68.7% | 5.2 | 2; calculated: 10.3% of 15% eligible to start treatment with C5is |
| **Incident treatment-naïve patients eligible for pegcetacoplan treatment annually** | | **5.2** | **Calculated from inputs above** |

- In the without-pegcetacoplan scenario, 80% of patients were treated with ravulizumab and 20% with eculizumab.
- Forecasted market shares were based on existing C5i market shares and treatment response:
  - Estimated annual pegcetacoplan market uptake was varied for both the naive and switch populations from approximately 10%.
  - It was assumed that patients switched from C5i treatments equally to pegcetacoplan, preserving the 80/20 market share split for ravulizumab and eculizumab.
- Drug-acquisition costs for each treatment are based on US wholesale acquisition costs[6]:
  - Pegcetacoplan: $4,403.84 for 1,080 mg/20 mL
  - Eculizumab: $6,523.00 per 300 mg/30 mL
  - Ravulizumab: $6,404.00 per 300 mg/3 mL
- Monthly drug-acquisition costs were calculated for each treatment weighted by the proportion of patients on each dosage strength observed in the PEGASUS trial (Table 2).[7]

**Table 2.** Monthly Drug-Acquisition Costs

| | Treatment switch | Treatment naïve |
|---|---|---|
| Pegcetacoplan | | |
| First month | $76,698[a] | $38,628 |
| Subsequent months | $38,628 | $38,628 |
| Eculizumab | | |
| First month | $71,753 | $87,852 |
| Subsequent months | $46,672 | $46,778 |
| Ravulizumab | | |
| First month | $131,309 | $131,309 |
| Subsequent months | $36,313 | $36,313 |

[a] This includes drug-acquisition costs for the 4-week run-in dose with pegcetacoplan and the previously prescribed C5i treatment.

**Table 3.** Administration, Transfusion, and BTH Unit Costs

| Parameter | Unit/event cost | Source |
|---|---|---|
| Home infusion (50% of infusions for eculizumab and ravulizumab) | $250 | 8 |
| Clinic infusion (50% of infusions for eculizumab and ravulizumab) | $661 | 8 |
| Infusion pump | $0 | Assumed |
| Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular | $14.44 | (CPT 96372)[b] |
| PNH transfusion cost (outpatient) | $438 | Analysis of MarketScan data with 392 outpatient and 23 inpatient PNH transfusions |
| PNH transfusion cost (inpatient) | $40,264 | |
| Hospitalization cost per BTH event[a] | $20,812 | 10 |

CMS = Centers for Medicare and Medicaid Services; CPT = Current Procedural Terminology.
[a] Cost assumed to be covered by manufacturer.

- The model also included costs for drug administration, transfusion, breakthrough hemolysis (BTH), vaccines, and antibiotics but excluded physician visits and supportive treatments that were assumed equal across treatments (Table 3).
- Transfusion and BTH rates for treatment-switch patients:
  - Annualized transfusion and BTH rates were derived from the head-to-head phase 3 PEGASUS trial (NCT03500549) for pegcetacoplan and eculizumab for patients switching from previous C5i treatment (referred to as "treatment-switch").
  - Annualized transfusion and BTH rates for ravulizumab were assumed to equal that for eculizumab based on noninferiority trial results (Table 4).[11]
- Transfusion and BTH rates for treatment-naïve patients:
  - Annualized transfusion and BTH rates were derived from the phase 1b, open-label PADDOCK trial (NCT02588833) for pegcetacoplan for patients without previous C5i treatment (referred to as "treatment-naïve").
  - Annualized transfusion and BTH rates for eculizumab and ravulizumab were estimated from the pivotal phase 3 trial comparing ravulizumab with eculizumab in treatment-naïve patients (Table 4).[12]

**Table 4.** Transfusion and BTH Model Inputs

| Parameter | Pegcetacoplan | Eculizumab | Ravulizumab |
|---|---|---|---|
| **Value for treatment-naïve** | | | |
| Rate of transfusions per person per year | 0.80[a] | 2.43[b] | 1.73[b] |
| Rate of BTH events per person per year | 0.25[a] | 0.25[b] | 0.08[b] |
| **Value for treatment-switch** | | | |
| Rate of transfusions per person per year | 1.32[c] | 7.92[d] | 7.92 |
| Rate of BTH events per person per year | 0.37[c] | 1.25[d] | 1.25 |

[a] Calculated from 52-week PADDOCK trial data (n = 20).[13-15]
[b] Calculated from 26-week CHAMPION trial data (n = 121 for eculizumab, n = 125 for ravulizumab) using the reported average number of red blood cell units per transfusion (1.56 for eculizumab and 1.46 for ravulizumab) and extrapolating linearly the number of BTH events and the average red blood cell units transfused per person from 26 weeks to 52 weeks.[15]
[c] Calculated using 48-week, head-to-head PEGASUS data (n = 41) and extrapolated linearly from 48 to 52 weeks.[7,15,18]
[d] Calculated using 16-week, head-to-head PEGASUS data (n = 39) and extrapolated linearly from 16 to 52 weeks.[15,18]

### Model Outcomes and Analyses

- The following outcomes were estimated annually and cumulatively over 3 years for the eligible health plan population:
  - Total costs in 2020 US dollars for each market scenario, with and without pegcetacoplan on formulary
  - Total budget impact
  - Number of transfusions avoided
  - Number of BTH events avoided
- Scenario analyses were conducted on pegcetacoplan uptake, as well as transfusion rates, BTH rates, BTH hospitalization costs, and drug costs (accounting for increased dosages and frequencies) for each treatment.

## Results

- For a health plan of 10 million members, the total annual costs ranged from $24.0-$27.1 million each year with pegcetacoplan and $24.5-$27.8 million each year without pegcetacoplan (Figure 2).
- In all 3 years, introducing pegcetacoplan to a health plan's formulary reduced drug and administration costs (–$1.2 million), transfusion costs (–$441,500), and BTH costs (–$56,000) as well as reduced transfusions (–167) and BTH events (–19). The cumulative budget impact was –$1.7 million (Figure 3).

**Figure 2.** Total Annual Costs of PNH Treatment by Scenario

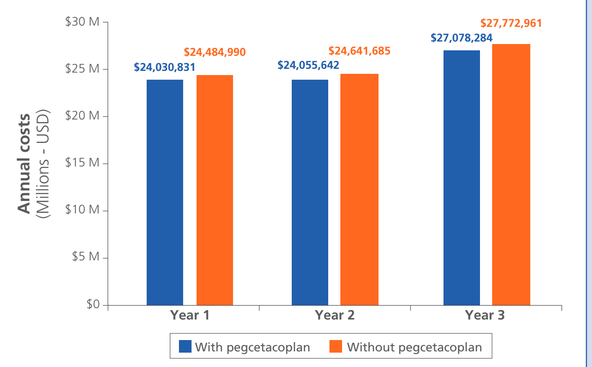
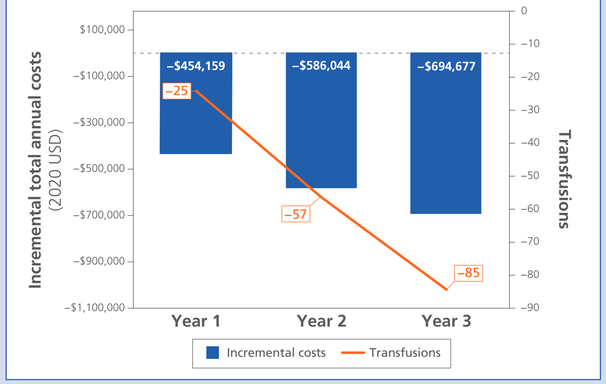



**Figure 3.** Annual Budget Impact and Transfusions Avoided




- All scenario analyses found that introducing pegcetacoplan was cost saving (range, –$1.2 to –$2.2 million cumulatively over 3 years). Results were most sensitive to drug-acquisition costs, market share, and percentage of patients requiring higher doses or increased dose frequencies (Table 5).

**Table 5.** Scenario Analyses Results

| Scenario description | Cumulative budget impact over 3 years |
|---|---|
| Base case | –$1,734,879 |
| Lower pegcetacoplan uptake (–20%) | –$1,225,127 |
| Higher pegcetacoplan uptake (+20%) | –$2,244,640 |
| Lower eculizumab and ravulizumab transfusion rate (–30%) | –$1,570,125 |
| Higher eculizumab and ravulizumab transfusion rate (+30%) | –$1,899,634 |
| Eculizumab/ravulizumab transfusion rate based on real-world data[a] | –$1,370,106 |
| BTH rate for all treatments based on real-world data[b] | –$1,691,350 |
| Lower BTH hospitalization cost (–20%) | –$1,723,695 |
| Higher BTH hospitalization cost (+20%) | –$1,746,064 |
| Lower drug costs for all treatments, 100% label dosing only | –$1,181,842 |
| More ravulizumab patients receive increased dose frequency (+20%) | –$1,999,530 |
| No loading-dose costs for eculizumab/ravulizumab among treatment-switch patients | –$1,508,467 |

[a] Analysis of MarketScan data showing patients treated with eculizumab experienced a mean of 3.1 transfusions per person over 19.1 months (i.e., 1.95 transfusions per person per year).[17]
[b] This scenario tests a reduced BTH rate for treatment-switch patients and an increased BTH rate for treatment-naïve patients, with: 13 of 35 (37.1%) and 34 of 87 (39.1%) patients treated with eculizumab and ravulizumab, respectively, reporting experiencing ≥ 1 BTH event[16] and 11 of 41 (26.8%) patients treated with pegcetacoplan experiencing ≥ 1 BTH event.[16]

## Discussion

- This analysis, which uses head-to-head clinical trial data, shows that the introduction of pegcetacoplan has the potential to reduce US health plan costs for the treatment of adults with PNH by reducing both drug costs and administration costs (i.e., site-of-care costs) due to its lower price and subcutaneous administration.
- In addition, pegcetacoplan is estimated to lead to a reduction in medical costs by avoiding transfusions and BTH events, which are both costly and represent a substantial burden on patients with PNH currently treated with C5i.

**DISCLOSURES**

Funding for this study was provided by Apellis Pharmaceuticals. Authors maintained independent scientific control of the study design and analyses.

**CONTACT INFORMATION**

**Seri Anderson, MPH, PhD**
Senior Research Health Economist

RTI Health Solutions

Phone: +1.919.541.7427
Email: saanderson@rti.org

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