Cost-Utility Analysis of Iptacopan for Adult Patients With Paroxysmal Nocturnal Hemoglobinuria Previously Treated With C5 Inhibitor in the Brazilian Private Healthcare System

EE302

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BACKGROUND

- Paroxysmal nocturnal hemoglobinuria (PNH) is an ultra-rare disease characterized by chronic hemolytic anemia. In the Brazilian Private Healthcare System, treatment with complement C5 inhibitors (C5i) is the standard of care. Ravulizumab is currently the only C5i included in the mandatory coverage list due to Law 14,307/2022.[1]
- Despite the advances in PNH care, the burden of with persistent anemia and frequent treatment infusions remain. Iptacopan, an oral factor B inhibitor, demonstrated superior efficacy compared to C5i in the phase 3 APPLY-PNH trial.[2,3]
- New complement inhibitors have recently been registered in Brazil, including iptacopan, pegcetacoplan and crovalimab; however, they are not included in the mandatory coverage list.[1]

OBJECTIVE

- To conduct a cost-utility analysis of iptacopan compared to C5i (eculizumab, ravulizumab, crovalimab) and pegcetacoplan (C3 inhibitor) for the treatment of PNH in patients previously treated with C5i, from the perspective of the Brazilian Private Healthcare System.

METHODS

Model Structure

- A semi-Markov model simulated the clinical course of PNH across health states for transfusion avoidance (with and without anemia), transfusion dependence, and death, over a 25-year lifetime horizon (**Figure 1**).

Efficacy Parameters

- Transition probabilities for iptacopan, eculizumab, and ravulizumab were derived from APPLY-PNH.[3] As the trial had a C5i arm that included eculizumab/ravulizumab, aggregated results for hemoglobin (Hb) level and transfusion avoidance were used for both eculizumab and ravulizumab.
- An indirect treatment comparison of iptacopan versus crovalimab was not feasible, as crovalimab has not been studied in patients with Hb <10 g/dL despite prior C5i treatment. In COMMODORE-1, crovalimab sustained the efficacy after switch from eculizumab.[4] Therefore, the same efficacy parameters were applied to all C5i in the model.
- For the pegcetacoplan comparison, transition probabilities were extracted from a matching-adjusted indirect comparison (MAIC) available on literature. The weights were used to adjust the transition probabilities for iptacopan and the C5i.[5]

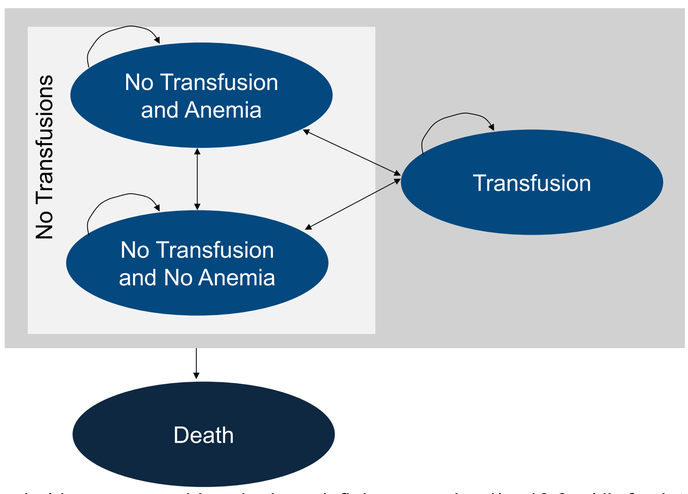
Safety

- In APPLY-PNH, no adverse events (AE) led to discontinuation or death in either the iptacopan or C5i arms; therefore, AEs were not included in the model.[3]
- Breakthrough hemolysis (BTH) rates were extracted from APPLY-PNH (3.2% for iptacopan and 17.1% for C5i), COMMODORE-1 (10.3% for crovalimab), and PEGASUS (9.8% for pegcetacoplan).[3,4,6] BTH was associated with a disutility; however, no costs related to BTH were included in the model.

Treatment Discontinuation

- In APPLY-PNH, there were no patients who discontinued treatment due to AEs in either the iptacopan or C5i arms; therefore, no discontinuation was considered.[3]
- For pegcetacoplan, an annual treatment discontinuation rate of 17.5% was used based on the PEGASUS trial and applied to all health states.[6] Patients who discontinued pegcetacoplan were assumed to switch to ravulizumab.

Figure 1. Semi-Markov Model Structure



Note: Two hemoglobin thresholds were considered when defining anemia: 1) <10.0 g/dL for iptacopan vs. C5 inhibitors, to align with the inclusion criteria in APPLY-PNH; and 2) <10.5 g/dL for iptacopan vs. pegcetacoplan, to algin with the definition used in PEGASUS.

METHODS

Utilities

- Health state utilities were treatment- and health state-specific.
- For iptacopan, eculizumab, and ravulizumab, utilities were derived from APPLY-PNH.[3] Utilities for crovalimab were assumed to be equivalent to those of eculizumab/ravulizumab. For pegcetacoplan, despite differences in treatment administration, utilities were assumed to be the same as iptacopan, given that both are proximal complement inhibitors.
- The utilities applied in the model for iptacopan and pegcetacoplan vs. C5i were:
  - No transfusion and anemia: 0.82 vs. 0.74.
  - No transfusion and no anemia: 0.88 vs. 0.79.
  - Transfusion: 0.79 vs. 0.69.
- A disutility of -0.4 over 6 days was applied per BTH event, based on O'Connell *et al*., 2020.[7]

Healthcare Resource Use and Costs

- The model included direct medical costs: drug acquisition, administration, disease monitoring, transfusion, and prophylaxis (vaccines and antibiotics).
- Healthcare resource use per health state and treatment was estimated based on the Brazilian Ministry of Health PNH guidelines and validated by a clinician experienced in PNH management in the private system.
- Drug and vaccine costs were based on publicly available list prices published by the Brazilian Drugs Market Regulation Chamber (CMED).[8] Procedure costs were sourced from the Brazilian Hierarchical Classification of Medical Procedures (CBHPM).[9]
- Transfusion costs were derived from the Brazilian study by Magro *et al.,* 2025 and updated to current CBHPM tariffs.[9,10]
- All costs were estimated in BRL and converted to USD using a 5.66 exchange rate.

Sensitivity Analyses

- Parameter uncertainty was explored via one-way sensitivity analyses (OWSA), using 95% confidence intervals when available or ±10% of the mean.
- Model robustness was assessed through a probabilistic sensitivity analysis (PSA; 1,000 iterations).

Table 1. Cost-utility results

Iptacopan vs.	Incremental Costs (USD)	Incremental QALYs	ICUR
Eculizumab	- 729,022	+ 2.03	Dominant
Ravulizumab	- 516,833	+ 2.03	Dominant
Crovalimab	- 150,516	+ 2.01	Dominant
Pegcetacoplan	- 69,761	+ 0.30	Dominant

Notes: QALY: quality-adjusted life years; ICUR: incremental cost-utility ratio.

RESULTS & DISCUSSION

Base Case

- Iptacopan dominated all comparators, providing the highest total quality-adjusted life-years (QALY; 12.03). QALY gains were primarily driven by iptacopan's superior efficacy in increasing Hb levels and avoiding transfusions (Table 1).
- Versus eculizumab and ravulizumab, iptacopan yielded 2.03 additional QALYs with cost savings of USD 729,022 and USD 516,833, respectively. Compared to crovalimab, iptacopan achieved 2.01 additional QALYs and savings of USD 150,516.
- Iptacopan's greater effectiveness and lower costs compared to C5i reflect reduced transfusion requirements and a lower list price.
- Compared to pegcetacoplan, iptacopan yielded 0.30 additional QALYs and savings of USD 69,761, primarily due to reductions in transfusion rates and treatment discontinuation.

Sensitivity Analyses

- One-way sensitivity analyses showed that drug acquisition costs and health state utilities were key drivers of model outcomes.
- PSA confirmed robustness, with iptacopan remaining cost-saving and more effective in >96% of simulations across comparators.

CONCLUSION

- Iptacopan demonstrated incremental QALYs compared to C5i and pegcetacoplan in treating PNH patients with Hb <10 g/dL despite prior C5i treatment.
- In the Brazilian Private Healthcare System, iptacopan demonstrated greater effectiveness and potential cost-savings, helping reduce both economic and logistical burdens associated with PNH management.

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