EE303

Cost-Utility Analysis of Iptacopan Versus C5 Inhibitors in Adult Patients With Paroxysmal Nocturnal Hemoglobinuria Naïve to Complement Inhibitors in the Brazilian Private Healthcare System

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BACKGROUND

- Paroxysmal nocturnal hemoglobinuria (PNH) is an ultra-rare disease characterized by chronic hemolytic anemia. In Brazil's private healthcare system, C5 inhibitors (C5i) are the standard treatment for PNH.[1]
- Ravulizumab, a C5i administered intravenously every 8 weeks, is currently the only complement inhibitor included in the mandatory coverage list under Law 14,307/2022.[1]
- Iptacopan is an oral factor B inhibitor that showed efficacy in treatment-naïve patients in the phase 3 APPOINT-PNH trial.[2] Although iptacopan and other new complement inhibitors have recently been approved in Brazil (e.g., crovalimab, pegcetacoplan, danicopan), they are not yet part of the mandatory coverage list.[1]

OBJECTIVE

- To evaluate the cost-utility of iptacopan compared to C5i (eculizumab, ravulizumab, crovalimab) for the treatment of PNH in patients naïve to complement inhibitors, 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 were derived from hemoglobin (Hb) and transfusion avoidance endpoints of APPOINT-PNH.[2]
- Transition probabilities for eculizumab and ravulizumab were derived from APPEX, a real-world cohort who received C5i, adjusted to align with APPOINT-PNH population characteristics.[3]
- An indirect treatment comparison of iptacopan versus crovalimab in patients naïve to complement inhibitors was not available at the time this model was developed. In COMMODORE-2, crovalimab demonstrated non-inferior efficacy compared to eculizumab.[4] Therefore, the same efficacy parameters were applied to all C5i in the model.

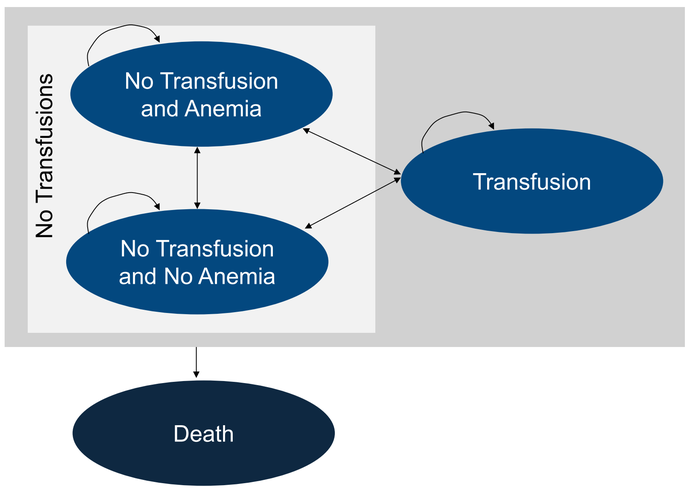
Safety

- In APPOINT-PNH and APPLY-PNH, no adverse events (AE) led to discontinuation or death in the iptacopan arm; therefore, AEs were not included in the model.[2]
- Breakthrough hemolysis (BTH) rates were extracted from APPOINT-PNH and APPLY-PNH for iptacopan (3.2%)[2], from ALXN1210-PNH-301 for eculizumab and ravulizumab (11% and 4%, respectively)[5], and from COMMODORE-2 for crovalimab (10.4%)[4]. BTH was associated with a disutility; however, no costs related to BTH were included in the model.

Treatment Discontinuation

- In APPOINT-PNH and APPLY-PNH, no patients discontinued treatment due to AEs in either the iptacopan or C5i arms; therefore, no discontinuation was considered for any treatment.[2]

Figure 1. Semi-Markov Model Structure



Note: Anemia was defined as hemoglobin <10.0 g/dL for all treatments.

METHODS

Utilities

- Health state utilities were treatment- and health state-specific.
- For iptacopan, eculizumab, and ravulizumab, utilities were derived from APPOINT-PNH and APPLY-PNH.[2] Utilities for crovalimab were assumed to be equivalent to those of eculizumab/ravulizumab.
- The utilities applied in the model for iptacopan 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.[6]

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).[7] Procedure costs were sourced from the Brazilian Hierarchical Classification of Medical Procedures (CBHPM).[8]
- Transfusion costs were derived from the Brazilian study by Magro *et al.,* 2025 and updated to current CBHPM tariffs.[8,9]
- 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	- 833,647	+1.89	Dominant
Ravulizumab	- 656,181	+ 1.88	Dominant
Crovalimab	- 3,802	+ 1.90	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 (QALYs; 13.43). 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 1.89 and 1.88 additional QALYs with cost savings of USD 833,647 and USD 656,181, respectively. Compared to crovalimab, iptacopan achieved 1.90 additional QALYs and savings of USD 3,802.
- Iptacopan's greater effectiveness and lower costs compared to C5i reflect reduced transfusion requirements and a lower list price.

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 >71% of simulations across comparators.

CONCLUSION

- This model demonstrated that iptacopan potentially generates more QALYs than C5i in treating PNH patients naïve to complement inhibitors.
- 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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