Horizon Scanning for Paroxysmal Nocturnal Hemoglobinuria in Brazil: Insights on Past Trends and Future Prospects

HTA36

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BACKGROUND

- Paroxysmal Nocturnal Hemoglobinuria (PNH) is an ultra-rare, life-threatening disease that lacked approved therapies in Brazil until 2017, despite the U.S. Food and Drug Administration (FDA) approving the first specific therapy in 2007. Collaboration between Brazil's Agência Nacional de Vigilância Sanitária (ANVISA) and the U.S. FDA has promised accelerated approvals, reducing regulatory timelines.
- By March 2025, six therapies have achieved regulatory approval, rapidly transforming PNH management. This expanding therapeutic landscape presents challenges for differentiating therapies and guiding clinical and policy decisions.

OBJECTIVES

- Conduct Horizon scanning for PNH therapies.
- Assess the time from U.S. FDA approval to Brazil's ANVISA regulatory approval.
- Analyze the time from ANVISA approval to submission and final reimbursement decisions by the Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde (CONITEC).
- Investigate reimbursement status of PNH therapies approved in Brazil by the National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK).

METHODS

- PNH therapies were identified through an advanced search of Phase 3 clinical trials in the Cortellis database on December 16, 2024.
- Regulatory approval dates were collected directly from the FDA and ANVISA websites.
- CONITEC website records were reviewed to collect submission dates and the final reimbursement decision status in Brazil. Additionally, NICE decisions were collected from the NICE website to enable a comparison with CONITEC's outcomes.
- All searches and data were updated on March 15, 2025.

RESULTS

- The HS identified ten therapies for PNH. Of these, four therapies – cemdisiran (C5 inhibitor, subcutaneous), nomacopan (second-generation C5 inhibitor, subcutaneous), pozelimab (C5 inhibitor, subcutaneous), and HRS-5965 (Factor B inhibitor, oral) – are currently in Phase 3 clinical trials and have not yet received regulatory approval from either the FDA or ANVISA. The remaining six therapies have been approved by both the FDA and ANVISA, and their characteristics are presented in detail in **Table 1**.
- The median time from FDA approval to ANVISA approval was 355 days (range: 235–3650 days) for the six therapies approved, while the median time from ANVISA approval to CONITEC submission for three of these therapies was 394 days (range: 266–1374 days). For the three therapies evaluated by CONITEC, the median time from submission to final reimbursement decision was 274 days (range: 250–293 days). Positive reimbursement decisions were granted for eculizumab and ravulizumab, while pegcetacoplan received a negative recommendation **(Table 2)**.
- Three therapies that have yet to be reviewed by CONITEC – iptacopan, danicopan, and crovalimab – received positive final recommendations from NICE in the UK in late 2024 (September, October, and November, respectively).

Table 1 – Characteristics of Approved PNH therapies.

Drug	Mechanism of Action	Route of Administration	Regimen	Posology
Crovalimab	C5 inhibitor	Intravenous (IV) / Subcutaneous (SC) injection	Monotherapy	Initial IV dose, then SC injection every 4 weeks
Danicopan	Factor D inhibitor	Oral	Combination therapy (with eculizumab or ravulizumab)	Oral – once daily
Eculizumab	C5 inhibitor	Intravenous	Monotherapy	IV – every 2 weeks
Iptacopan	Factor B inhibitor	Oral	Monotherapy	Oral – twice daily
Pegcetacoplan	C5 inhibitor	Subcutaneous infusion	Monotherapy	SC infusion – twice weekly
Ravulizumab	C5 inhibitor	Intravenous	Monotherapy	IV – every 8 weeks

Table 2 – Regulatory Approval Timeline and Reimbursement Status for PNH therapies.

Drug	FDA's Approval Date	ANVISA's Approval Date	CONITEC Submission Date	CONITEC's Final Decision Publication Date	Time from FDA to ANVISA's Approval (days)	Time from ANVISA to CONITEC Submission (days)	Time from CONITEC Submission to Final Decision (days)	Reimbursement Status	
								NICE	CONITEC
Crovalimab	June 20, 2024	February 10, 2025	Not yet submitted	–	235	–	–	Positive	Not yet assessed
Danicopan	March 29, 2024	January 13, 2025	Not yet submitted	–	290	–	–	Positive	Not yet assessed
Eculizumab	March 16, 2007	March 13, 2017	April 11, 2018	December 17, 2018	3650	394	250	Positive	Positive
Iptacopan	December 5, 2023	January 27, 2025	Not yet submitted	–	419	–	–	Positive	Not yet assessed
Pegcetacoplan	May 14, 2021	July 25, 2023	April 16, 2024	February 3, 2025	802	266	293	Positive	Negative
Ravulizumab	December 21, 2018	September 2, 2019	June 7, 2023	March 7, 2024	255	1374	274	Positive	Positive

DISCUSSION

- At the time of abstract submission, three therapies were approved in Brazil. Since then, danicopan, iptacopan, and crovalimab have gained approval, and the analyses have been updated accordingly.
- Among the recently approved therapies, iptacopan stands out as a key innovation due to its oral monotherapy regimen. Unlike danicopan, which must be administered with other IV C5 inhibitors like eculizumab or ravulizumab, iptacopan's unique pharmacological properties eliminate cold chain requirements and dependency on infusion centers. Additionally, crovalimab, the newest therapy approved this year, operates via the same mechanism of action as the old generation C5 inhibitors, but it is administered as a subcutaneous injection following the initial IV dose. This way, the logistical advantage of iptacopan is particularly impactful for patients in Brazil, who currently travel an average of 101 kilometers to access IV-based therapy (1).
- Over time, the intervals between FDA approval and ANVISA approval, and between ANVISA approval and CONITEC submission, have shown a decreasing trend. Additionally, CONITEC's median timeframe for reimbursement decisions was 274 days, closely aligning with its stated goal of completing the process within 270 days. These improved regulatory processes are crucial in reducing delays in the introduction of new therapies, ultimately benefiting patients by enabling faster access to innovative therapies.
- NICE decisions do not always reflect the same outcomes in CONITEC evaluations. For instance, pegcetacoplan received a positive decision from NICE but a negative decision from CONITEC.

CONCLUSION

ANVISA's approval of drugs for PNH is now aligned with those approved by the FDA, with regulatory timelines in Brazil becoming faster. While CONITEC's evaluations prioritize operational, logistical, and economic factors to meet national healthcare goals, positive recommendations from agencies like NICE do not necessarily translate into positive decisions by CONITEC. Looking ahead, innovative therapies such as oral monotherapy could transform pharmaceutical assistance by reducing reliance on infusion centers, simplifying logistics, and providing greater convenience for patients.

REFERENCE

1. Folha de S.Paulo. (2024, November). Pacientes com doença rara no sangue percorrem em média 101 km para tratamento, diz estudo. Retrieved from https://www1.folha.uol.com.br/equilibrioesaude/2024/11/pacientes-com-doenca-rara-no-sangue-percorrem-em-media-101-km-para-tratamento-diz-estudo.shtml