Italian perspective on rare disease, new treatments and HTA: insights from iptacopan multidimensional evaluation in PNH

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Rationale of the study & Objective

- Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare, life-threatening hematologic disorder characterized by hemolysis, thrombosis, and bone marrow failure
- C5 inhibitors (eculizumab and ravulizumab) and C3 inhibitor pegcetacoplan have improved outcomes. However, many patients (in particular those treated with C5 inhibitors) remain anemic and transfusion-dependent [1-2]
- Iptacopan, an oral factor B inhibitor, represents a promising alternative; its oral administration may lower adverse events, reduce healthcare costs, and ease organizational burdens—ultimately improving patient outcomes, access to care, and hospital resources utilization

To define the incremental and multidimensional benefits of oral iptacopan as treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH) compared to current treatments (C5-inhibitors eculizumab or ravulizumab, and the C3-inhibitor pegcetacoplan) in Italy

Materials and Methods

A multidimensional evaluation, conducted through a Health Technology Assessment approach, grounding on the **EUnetHTA Core Model**, was performed in the years 2023-2024

Different data sources were utilized:

- **literature evidence,** to define efficacy and safety comparative indicators considering the different PNH treatments
- **quantitative tools,** to estimate potential economic, organizational, and social benefits of shifting from infusion-based therapy to oral one
- **qualitative questionnaires,** administered to 14 healthcare professionals (HCPs) and 8 PNH patients, using a 7-item Likert scale (from -3 to +3), to investigate iptacopan's perceived multidimensional advantages over current treatments. ANOVA inferential testing was conducted to evaluate statistically significant differences in perceived benefits

Results

From the economic evaluation of the single procedure, to the demonstration of the financial sustainability

- Accounting for all direct healthcare costs, **iptacopan resulted in a 10% cost-reduction per patient *versus* ravulizumab, however a 5% and 47% increase versus pegcetacoplan and eculizumab** (including biosimilar)
- Excluding drug costs, **iptacopan required fewer resources with per-patient cost-savings ranging from 15% to 52%**

Annual economic assessment	ECU	RAVU	PEG	IPT
Diagnosis	1,284.40 €	1,284.40 €	1,284.40 €	1,284.40 €
PNH monitoring (specialist visits and lab exams)	1,171.78 €	626.60 €	692.13 €	801.09 €
Adverse events	442.57 €	411.42 €	125.87 €	51.80 €
RCB transfusion	2,878.43 €	2,878.43 €	583.46 €	194.49 €
Other direct costs (Vaccinations, antibiotic prophylaxis, and supportive therapy such as folic acid and anticoagulant treatment)	819.49 €	819.49 €	819.49 €	819.49 €
Drug cost (derived from the published Italian NHS price list, considering ex-factory prices) – including administration cost	228,440.59 €	375,818.88 €	325,136.43 €	342,092.63 €
Total	**235,037.24 €**	**381,839.21 €**	**328,641.78 €**	**345,243.89 €**
Total, excluding drug cost	**6,596.65 €**	**6,020.33 €**	**3,505.35 €**	**3,151.26 €**

ECU: eculizumab; RAVU: ravulizumab; PEG: pegcetacoplan; IPT: iptacopan

At national level, routine adoption of iptacopan would generate economic annual savings of 2% (-3,157,784 €) for treating 452 PNH patients

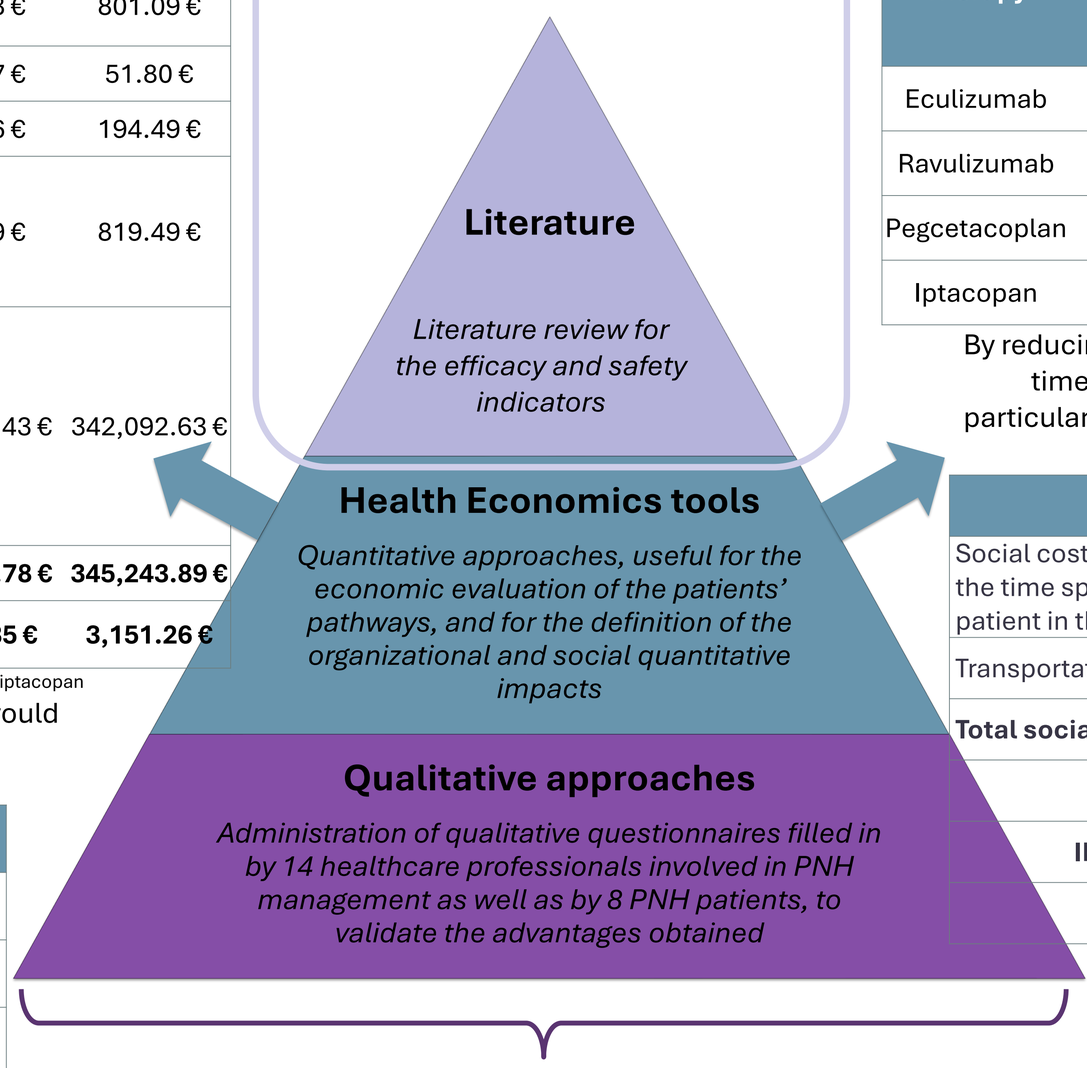
	Including drug acquisition (€)	Excluding drug costs (€)
Baseline scenario (AS IS)*	157,198,922 €	2,743,120 €
Innovative scenario (TO BE)**	154,041,139 €	1,861,389 €
Difference	-3,157,784 €	-881,731 €
Difference (%)	-2.01%	-32.14%

**Scenario AS IS*: 22% of patients received eculizumab, 75% ravulizumab, and 3% of pegcetacoplan with no use of iptacopan

***Scenario TO BE*: iptacopan was assumed to reach a 67% market share, reducing the distribution of eculizumab, ravulizumab and pegcetacoplan to 10%, 22% and 1%, respectively

Literature demonstrates a superior efficacy (% of patients achieving a hematologic response after 24 weeks of treatment, without the need for transfusions) and safety (development of any drug-related adverse events) profile of iptacopan *vs* C5i [3-4]

No head-to-head study has been conducted to date comparing iptacopan and pegcetacoplan



From the organizational sustainabilty to the assessment of the social benefits

- The analysis of cumulative time and hospital activities demonstrates that treatment selection directly affects hospital capacity
- Compared to the other therapies, iptacopan can significantly reduce the time spent per patient per year, freeing 32 hours compared to eculizumab, 14 hours compared to ravulizumab, and 71 hours compared to pegcetacoplan
- This reduction represents an opportunity to reallocate healthcare professional time and infusion slots to other patients or services

Therapy	Infusion & Monitoring Time (hours/year)	Assessment & Visit Time – not linked to drug administration - (hours/year)	Total Time (hours/year)	Time Saved vs Iptacopan (hours; %)
Eculizumab	29.16	10.76	39.92	-32.42; -81%
Ravulizumab	16.92	4.59	21.51	-14.01; -65%
Pegcetacoplan	73.17	5.91	79.08	-71.58; -91&
Iptacopan	0	7.5	7.5	

By reducing hospital visits and travel time, iptacopan generates time savings that lower patients' overall social costs, particularly for those of working age whose treatment time may interfere with work

	ECU	RAVU	PEG*	IPT
Social cost, related to the time spent by the patient in the hospital	€ 1,589.09	€ 448.37	€ 2,892.77	€ 312.57
Transportation cost	€ 1,281.39	€ 391.83	€ 2,298.03	€ 603.63
Total social cost	**€ 2,870.48**	**€ 840.20**	**€ 5,190.80**	**€ 916.20**
IPT vs ECU	**-€ 1,954.28 (-68%)**			
IPT vs RAVU	**€ 76.00 (9%)**			
IPT vs PEG	**-€ 4.274.60 (-82%)**			

ECU: eculizumab; RAVU: ravulizumab; PEG: pegcetacoplan; IPT: iptacopan

* Weighted social cost, assuming 50% PEG administration in hospital setting and 50% self-administration at home by trained patients

- **Patients acknowledged iptacopan's potential to reduce fatigue and PNH-related symptoms, to improve emotional health, family and social life, and ability to perform daily activities** (p-value <0.05)
- HCPs reported **their preference towards iptacopan, declaring better perceived safety and effectiveness**
- In addition, HCPs declared the potential ability of iptacopan to **reduce hospital waiting lists** by eliminating the need for infusions, easing pressure on healthcare resources (p = 0.006) and **to decrease reliance on blood transfusions**, supporting a more sustainable management of blood supply (p = 0.021), **with positive organizational impact** (p = 0.031)

HCPs perceptions	ECU	RAV	PEG	IPT	p-value
Effectiveness	0.93	1.21	1.41	2.25	0.009
Safety	0.13	0.40	0.40	1.40	0.004
Equity Impact	0.13	0.36	0.51	0.80	0.089
Legal Impact	0.43	0.43	0.33	-0.05	0.456
Organizational Impact	-0.95	-0.80	0.31	1.13	0.031

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Patients' perceptions	RAV	PEG	IPT	p-value
Impact on patients' autonomy	1.75	1	2.86	0.018
Impact on performing usual daily activities requiring physical effort	-0.5	1.67	2.14	0.016
Impact on performing usual work activities	-0.25	1	2.14	0.026
Impact on the patient's emotional state	0	2	2.71	<0.001
Impact on family and social life	1.25	2.67	3	<0.001
Impact on overall perceived quality of life	1	2.67	3	<0.001
Impact on life satisfaction	1.75	1.67	3	0.004
Impact on persistent fatigue	1.5	1	2.86	0.001
Impact on PNH signs and symptoms	1	2	2.57	0.017
Impact on adherence	1.5	2	3	0.002
Impact on perceived anxiety	-0.25	2	2.71	<0.001

Conclusions

The findings highlights iptacopan's potential to redefine the management of PNH by offering clinically effective, economically sustainable, and social benefits

Its adoption could generate multidimensional benefits and value for patients, hospitals, and the broader health system

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