USING THE ORPHAR-SEFH MCDA FRAMEWORK TO ASSESS THE VALUE CONTRIBUTION OF PEGCETACOPLAN IN ULTRA-RARE KIDNEY DISEASES

HTA358

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CONCLUSIONS

- The Rare Diseases and Orphan Drugs Working Group of the Spanish Society of Hospital Pharmacy (Orphar-SEFH) Multi-Criteria Decision Analysis (MCDA) framework has been weighted by a multidisciplinary panel of 7 experts for its use in the evaluation of specific treatments for C3 glomerulopathy (C3G) and primary immune complex-mediated membranoproliferative glomerulonephritis (primary IC-MPGN). The relative importance of criteria was consistent across profiles, with efficacy/effectiveness, unmet needs and disease severity among the most relevant criteria, and cost-related criteria among the least, likely reflecting difficulties of capturing accurate cost estimates.
- Pegcetacoplan was perceived as a more effective targeted treatment option for the ultra-rare kidney diseases C3G and primary IC-MPGN than iptacopan. Its demonstrated efficacy in the reduction of proteinuria (UPCR), conservation of the estimated glomerular filtration rate (eGFR) and improvements in histological variables, which have been directly associated with the prognosis of the disease, is expected to modify the course of both diseases avoiding the progression to final stages of kidney disease[1].

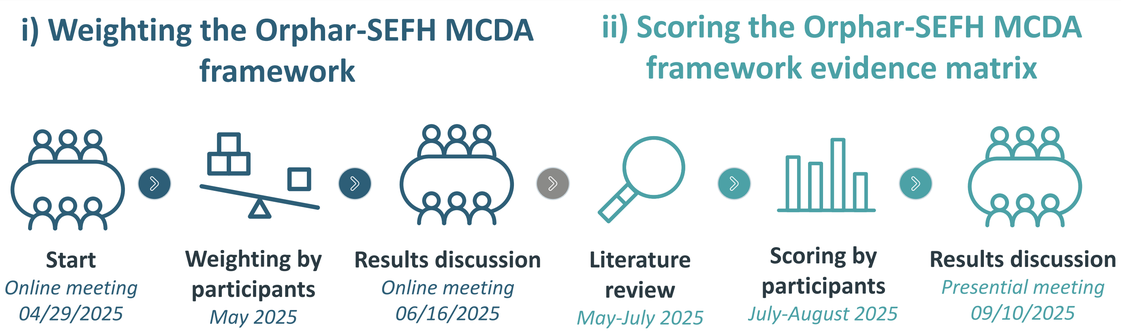
OBJECTIVES

- To evaluate the relative importance of different criteria used to assess the value of targeted therapies for the ultra-rare kidney diseases C3 glomerulopathy (C3G) and primary immune complex–mediated membranoproliferative glomerulonephritis (primary IC-MPGN) using a Multi-Criteria Decision Analysis (MCDA) approach in the Spanish context.
- To assess the value contribution of pegcetacoplan vs iptacopan for the treatment of C3G and primary IC-MPGN using the weighted Orphar-SEFH MCDA framework.

METHODS

- The project was conducted in two main steps: i) weighting the Orphar-SEFH MCDA framework (Table 1), and ii) scoring the MCDA evidence matrix; a panel of 7 experts participated: 3 nephrology experts, 2 hospital pharmacists, 1 national ex-payer and 1 patient representative (Figure 1).

Figure 1: Methodological approach



The adapted EVIDEM framework, developed by Orphar-SEFH for orphan drug evaluation in Spain[2-4] was weighted according to the relative importance of its constituent criteria, considering its usefulness in the assessment and decision-making process for the treatment of the ultra-rare kidney diseases C3G and primary IC-MPGN in Spain (Table 1).

Non-comparative quantitative criteria were scored on a scale of 0 to 5, and comparative quantitative criteria on a scale of -5 to 5 (-5 favourable to iptacopan and 5 favourable to pegcetacoplan). Contextual criteria were scored qualitatively: i) positive impact, ii) neutral impact, iii) negative impact.

Table 1: Quantitative and qualitative criteria of the Orphar-SEFH MCDA framework

QUANTITATIVE DIMENSION*
Disease related criteria
• Severity of the disease
• Unmet needs
Treatment related criteria
• Efficacy/effectiveness
• Safety/tolerability
• Patient Reported Outcomes (PROs)
• Therapeutic Impact
• Other medical costs
• Non-medical/indirect costs
• Quality of evidence or Level of evidence and Grade of recommendation
QUALITATIVE/CONTEXTUAL DIMENSION
• Population access priorities
• Established objectives and specific interests
• System capacity and appropriate use of the intervention

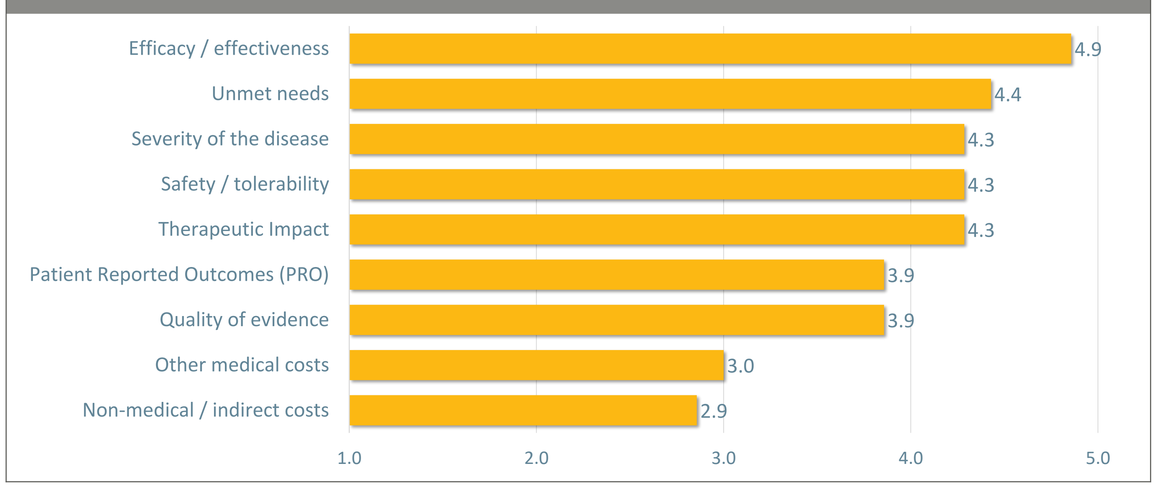
**Only the quantitative criteria were weighted. Each quantitative criterion was scored on a scale of 1 to 5 (1=very unimportant, 5=very important)*

RESULTS

Weighting of the Orphar-SEFH framework

- Comparative efficacy/effectiveness was rated the most relevant criterion, mean score (4.9) followed by the unmet needs (4.4). Disease severity, comparative safety/tolerability and therapeutic impact were also perceived as highly relevant criteria (4.3 each). PROs and quality of the evidence were scored with a 3.9; cost criteria, including other medical costs and non-medical/indirect costs, received a score of 3 and 2.9, respectively (Figure 2).
- Comparative efficacy/effectiveness was considered the most relevant criterion due to its clinical and prognostic impact, since key variables (i.e., UPCR, eGFR) have been directly associated with the long-term evolution of both diseases[1].
- Unmet needs was the second most relevant criterion, especially due to the lack of targeted treatments and the physical and emotional burden of both diseases.
- Disease severity, comparative safety/tolerability and therapeutic impact were also considered highly relevant criteria due to the poor prognosis and high morbidity/mortality of both diseases, the importance of treatment safety profile in chronic diseases, and the expected outcome on modifying the course of the disease, respectively.

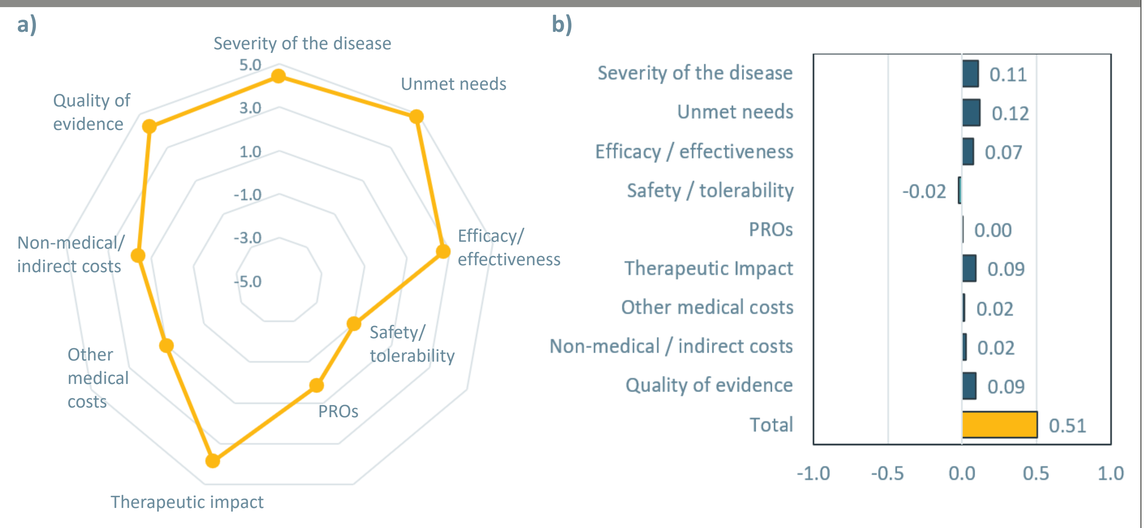
Figure 2: Mean score of the quantitative criteria, in descending order according to their relative importance



Scoring of the Orphar-SEFH framework – quantitative criteria

- Regarding non-comparative criteria, unmet needs received the highest mean score (4.9), followed by disease severity (4.4). Quality of evidence and therapeutic impact received a mean score of 4.3 and 3.9, respectively. As for the comparative criteria, efficacy/effectiveness was rated with a mean score of 2.7, followed by the indirect costs (1.6) and other medical costs (1.0). PROs and safety received a mean score of 0.1 and -1.0, respectively (Figure 3a and Table 2).
- Pegcetacoplan was perceived as a more effective treatment than iptacopan for C3G and primary IC-MPGN, diseases with lack of targeted therapies and poor prognosis; showing a high reduction of UPCR, stabilisation of the eGFR, and improvements in histological variables, which are associated with the improved prognosis of both diseases. Efficacy results were consistent across all subgroups (i.e., transplanted and non-transplanted patients, adults and adolescents) included in the study. The safety profile of pegcetacoplan was considered acceptable, with transient adverse events attributable to the route of administration and demonstrated with real world experience in the treatment of paroxysmal nocturnal haemoglobinuria.
- The sustained efficacy of pegcetacoplan in the open label period (OLP) demonstrated its capacity to modify the course of C3G and primary IC-MPGN in adults and adolescents, avoiding the progression to final stages of kidney disease and the necessity of renal replacement therapy (i.e., dialysis) and transplant.
- The quality and robustness of the Phase 3 VALIANT and long-term extension VALE studies supported the expected impact of pegcetacoplan to modify the course of C3G and primary IC-MPGN.
- The overall value contribution of pegcetacoplan, obtained through the normalised weights and the adjusted scores, was 0.51 (on a scale of -1 to 1); demonstrating a positive value contribution compared to iptacopan, as well as meaningful contribution in non-comparative criteria (Figure 3b).

Figure 3: a) Mean scores of the quantitative criteria and b) overall value contribution of pegcetacoplan vs iptacopan



Comparative criteria (efficacy, safety, PROs and cost-related criteria) were scored on a scale of -5 to 5 (-5 favourable to iptacopan and 5 favourable to pegcetacoplan); and non-comparative criteria on a scale of 0 to 5.

Table 2: Mean scores of the evidence matrix, quantitative criteria

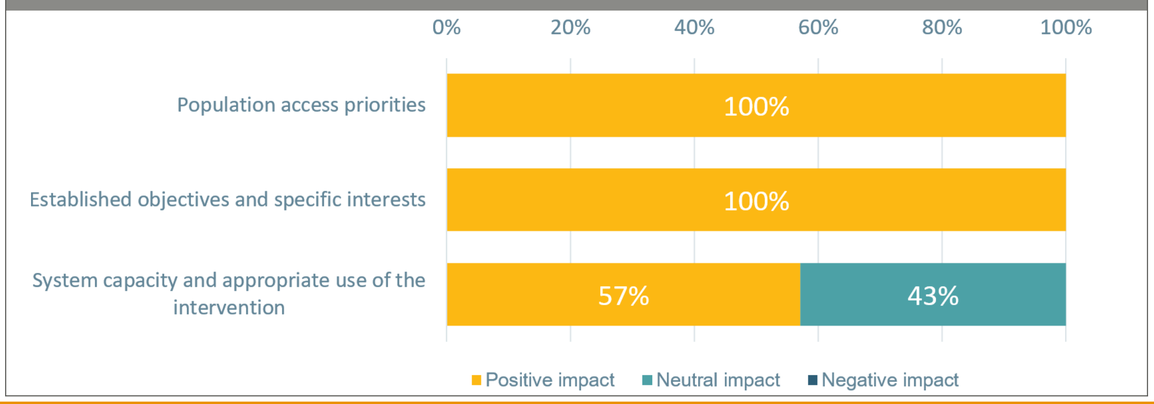
Criterion	Mean	Median	SD	Min	Max	n
Severity of the disease	4.4	4.0	0.5	4.0	5.0	7
Unmet needs	4.9	5.0	0.4	4.0	5.0	7
Efficacy/effectiveness	2.7	3.0	1.0	1.0	4.0	7
Safety/tolerability	-1.0	-1.0	1.0	-3.0	0.0	7
PROs	0.1	0.0	0.4	0.0	1.0	7
Therapeutic impact	3.9	4.0	0.4	3.0	4.0	7
Other medical costs	1.0	2.0	2.1	-2.0	4.0	7
Non-medical/indirect costs	1.6	1.0	1.5	0.0	4.0	7
Quality of evidence	4.3	4.0	0.5	4.0	5.0	7

Comparative criteria (efficacy, safety, PROs and cost-related criteria) were scored on a scale of -5 to 5 (-5 favourable to iptacopan and 5 favourable to pegcetacoplan); and non-comparative criteria on a scale of 0 to 5.

Scoring of the Orphar-SEFH framework – contextual criteria

- The inclusion of pegcetacoplan for the treatment of C3G and primary IC-MPGN would be aligned with Spanish population access priorities, patient demands, and with the Spanish National Healthcare System (NHS) capacity for its appropriate use (Figure 4).

Figure 4: Qualitative scores of contextual criteria (% of responses)



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