OFF-LABEL COMPARATORS IN HEALTH TECHNOLOGY ASSESSMENT DECISION MAKING IN PORTUGAL

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HTA148

OBJECTIVES

Health Technology Assessment (HTA) anchors in the accurate definition of the scope for the assessment PICO: P-Populations; I-Interventions; C-Comparators; O-Outcomes. Since October 2022, INFARMED - National Authority of Medicines and Health Products has included in the methodological guidelines for pharmacotherapeutic assessment of Health Technologies, the possibility to consider off-label medication as standard of care to new interventions[1]. This study aimed to assess INFARMED patterns of off-label comparators use in the HTA in Portugal and its expected implications.

METHODS

All pricing and reimbursement (P&R) decisions issued from 01/01/2023 to 30/05/2024 were reviewed. Off-label comparators were identified as those that were being used outside their approved indications according to the European Medicines Agency. Data was collected relative to the outcome of the therapeutic value grouped as no value, equivalent value and added therapeutic value. Economic value assessment and ultimately P&R appraisal was also recorded. When the outcome of HTA was P&R withdrawal it was assumed marketing authorization holder´s decision[2].

RESULTS

Of 91 HTA and P&R reports published between January 2023 and May 2024, 20 (22,0%) included a comparison to at least one off-label comparator.

Table 1. Main characteristics in the comparators considered in the P&R processes

Characteristics	Overall N=91	Off-label	
		0 N=71	≥1 N=20
Comparators, mean (SD)	2.38 (2.02)	2.17 (2.01)	3.15 (1.90)
Number of comparators off-label, n (%)			
0	71 (78)	71 (100)	-
1	14 (15)	-	14 (70)
2	4 (4.4)	-	4 (20)
3	1 (1.1)	-	1 (5)
4	1 (1.1)	-	1 (5)
Type of therapeutic decision in the P&R process, n (%)			
Added therapeutic value	49 (53.8)	41 (57.8)	8 (40)
Equivalent therapeutic value	35 (38.5)	25 (35.2)	10 (50)
Both	2 (2.2)	2 (2.8)	0
No value	5 (5.5)	3 (4.2)	2 (10)
Type of public financing decision in the P&R process, n (%)			
Reimbursed	73 (80.2)	61 (85.9)	12 (60)
Not reimbursed	7 (7.7)	4 (5.6)	3 (15)
Withdrawal	11 (12.1)	6 (8.5)	5 (25)
Year of P&R decision, n (%)			
2023	48 (53)	38 (54)	10 (50)
2024	43 (47)	33 (46)	10 (50)

RESULTS (cont.)

Overall, two innovative medicines were rejected when compared with, at least, one off-label alternative. Equivalent therapeutic value was the most common HTA outcome to 10 new medicines (50.0%) of scopes with off-label comparators use. In the P&R decisions that presented added therapeutic value (40.0%), all the medicines evaluated were considered not cost-effective in the Portuguese context. Consequently, 5 (25.0%) market authorization holders decided to withdraw P&R applications (Table 1).

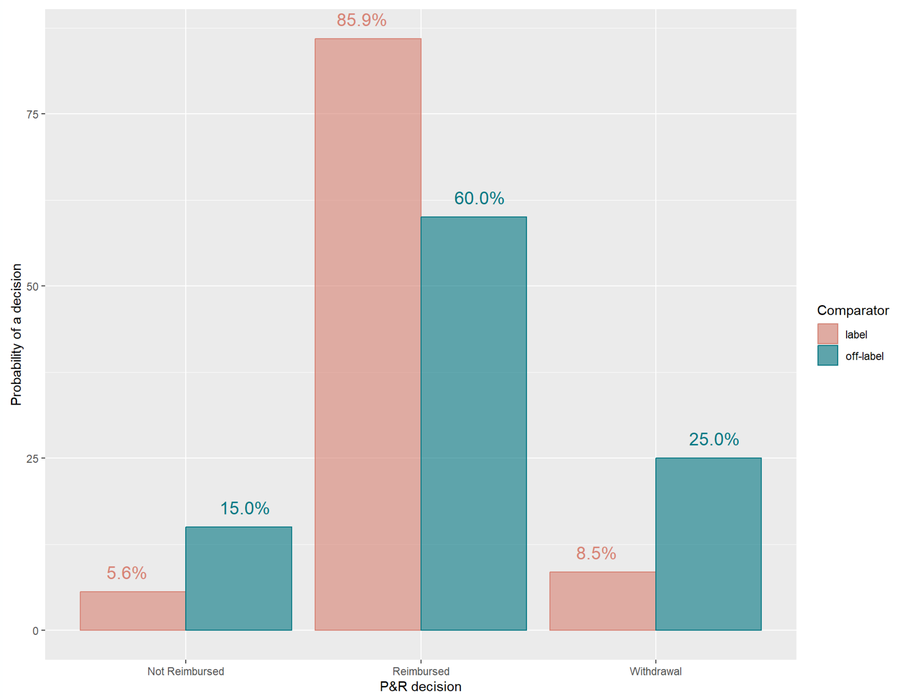

Figure 1. Probability of a P&R decision (reimbursed, not reimbursed or withdrawal) stratified by the type of comparators included

P&R processes with off-label comparators were more likely to be not reimbursed (OR=3.8, p-value=0.105) or to be withdrawal (OR=4.2, p-value=0.035) when compared to P&R processes with label comparators (Figure 1). Additionally, the probability of a reimbursed P&R decision was superior when all the comparators were labelled (Figure 2).

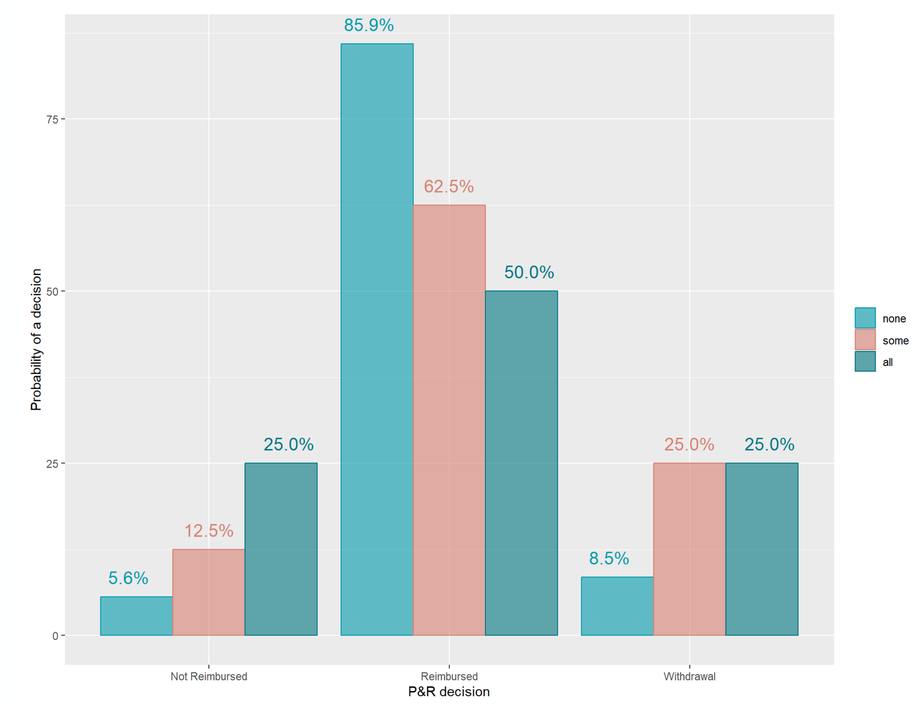

Figure 2. Probability of a P&R decision stratified by the quantity of off-label comparators included

CONCLUSION

The use of off-label comparators poses significant HTA challenges, making it increasingly difficult to demonstrate new medicines cost-effectiveness. The broader implications of having off-label use indirectly validated by HTA Authorities, such as off-label prescription encouragement or R&D disincentive should not be neglected. Expected barriers on access to innovation is also a major concern.

REFERENCES: 1. INFARMED, Orientações metodológicas nacionais na avaliação farmacoterapêutica, versão 3.0. 2022. 2. INFARMED. Lista de novas DCI/ indicações terapêuticas com financiamento público. 2024 [30/05/2024]; Available from: https://www.infarmed.pt/web/infarmed/relatorios-de-avaliacao-de-financiamento-publico.