Impact of the use of cost-effectiveness analysis (CEA) on patient access to medicines: A comparison of CEA vs non-CEA markets

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Background and objectives

- Approaches to determining patient access to new medicines, including the use of health technology assessment (HTA), vary around the world.
- HTA can impact which patients are able to access a medicine in clinical practice. As part of their HTA/reimbursement process, some markets apply CEA as a key determinant of their value assessments.
- Previous publications have reported variability in market access decisions; however, analyses were based only on the initial assessment of the first indication,[1] or identified that market-specific processes started at different times across markets but did not fully explore the implications of this.[2]
- The current study aimed to identify the impact of CEA on the extent and timing of patient access to innovative medicines, including initial reviews, reassessments, and subsequent indications. The impact of market access decisions on patients' access was assessed for 10 markets:
  - CEA markets (Australia, Canada, England, Scotland, Sweden).
  - Non-CEA markets (France, Germany, Italy, Spain, US).

Methods

Sample based on regulatory approvals

- All oncology and orphan drugs with initial European Medicines Agency (EMA) regulatory approval of the first indication between January 2016 and December 2019 were included in the analysis set; any subsequent indications that received EU regulatory approval up to the end of December 2021 were also included. Generic drugs, diagnostic medications, devices, biosimilars, and hybrid products were excluded.
- For all drugs/indications included, the corresponding regulatory approvals from the US Food and Drug Administration (FDA), Australian Therapeutic Goods Administration (TGA), and Health Canada were identified.

Identifying the HTA/reimbursement assessments and data

- For each drug/indication, the relevant published HTA (decision, date, and/or restrictions applied) was identified and linked to the relevant regulatory approval.
- Comparison between the patient population from the regulatory label and HTA eligible population provided us with the market access outcomes. Market access outcomes were classified as full access (green), restricted access (amber), no access (red), or in development (grey) (Table 1).

Table 1: Types of market access outcomes

Market access outcome	Description
Full access	Unrestricted patient access in accordance with approved regulatory indication
Restricted access	Restricted patient access compared with approved regulatory indication (e.g., sub-population)
No access	No patient access for approved regulatory indication
In development	Assessment is in progress

- For a drug/indication to be included in the analysis, at least one market access outcome had to be identified to the end of 2021 (Table 2).
- Given the differences in HTA/reimbursement systems across markets, no single metric captures all aspects of every market – the main focus was on a "successful" market access outcome, defined as the first HTA outcome recommending some access (full or restricted) or a decision of no access based on a negative outcome.
- All assumptions made were validated with external experts and Janssen market experts.
- "Time to access", defined as the time from regulatory approval to a "successful" market access outcome, was also estimated.

Table 2: Number of regulatory and market access decisions per agency

	Agency	N[a] with regulatory approval	N[b] completed market access decisions
		Total	Total
CEA	NICE	116	80
CEA	SMC	116	80
CEA	TLV	116	67
CEA	CADTH	88	64
CEA	PBAC	80	61
Non-CEA	HAS	116	101
Non-CEA	AIFA	116	97
Non-CEA	AEMPS	116	85
Non-CEA	G-BA	116	116
Non-CEA	US (FDA)	110	110[c]

[a]Drug/indications, [b]drug/indications with regulatory approval, [c]in the US, regulatory approval provides access to the market

Results

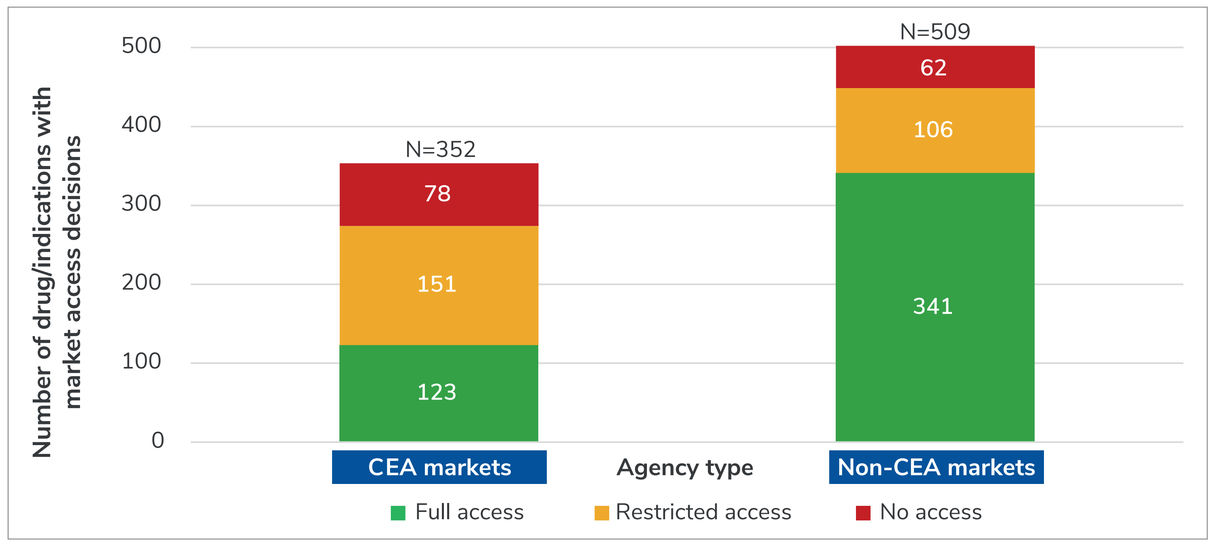
Sample based on regulatory approvals

- The sample included 129 unique drug/indication combinations across 70 individual drugs.
- Of the 129 drug/indication regulatory approvals, 68 (53%) had been approved by all four regulatory agencies; the FDA was often the first agency to grant regulatory approval (76%).

HTA/reimbursement decisions

- Across the HTA/reimbursement agencies, a total of 861 market access decisions were included in the analysis (Figure 1).

Figure 1: Overall market access decisions by agency type

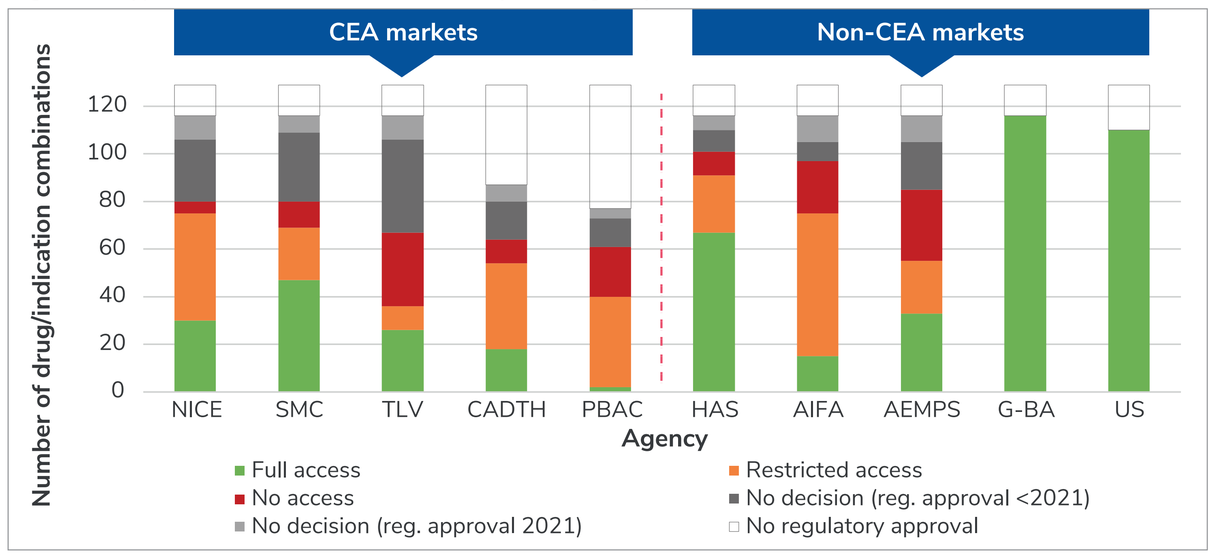


- The number of market access decisions in the non-CEA markets (n=509) was markedly higher (by over 100) than in the CEA markets (n=352) (Figure 1), partly driven by differences in regulatory approvals (Table 2 and Figure 1). The number of full access decisions in non-CEA markets was also higher (difference was over 200).
  - There were fewer confirmed market access decisions (green and amber) in the CEA markets than in the non-CEA markets.
    - Potential factors influencing this were the lower number of regulatory approvals from Health Canada and the TGA within the selected time window, and the reimbursement processes in Germany and the US, which prioritize national-level access after regulatory approval.
    - The same conclusions hold for EMA markets when these 4 markets are excluded.

Assessment outcomes

- Market access decisions varied across markets/agencies; in CEA markets patients had less access to medicines than in non-CEA markets.
  - The number and proportion of restricted market access decisions was greater in the CEA markets than in the non-CEA markets (n=151 [42.9%] vs n=106 [20.8%]) (Figure 1).
  - The number and proportion of unrestricted market access decisions (i.e., aligned with the regulatory label) was greater in the non-CEA markets than in the CEA markets (n=341 [67.9%] vs n=123 [34.9%]) (Figure 1).

Figure 2: Type of market access decisions by HTA agency



- The level of "successful" market access differs across agencies, and the differences among agencies are greater than the differences between CEA and non-CEA markets (Figure 2). Some of the variability is process-driven.
- The decision of "restricted access" is not used in Germany or at a national level in the US and is used to a varying extent in the other markets.
- Among the CEA markets, PBAC, NICE, and CADTH restricted reimbursement more often than granting full access.
  - A wide range of restriction criteria were applied, most commonly in the CEA markets, focusing on patient characteristics and/or disease- or treatment-related factors.
  - Multiple restriction criteria were often applied to each individual decision; the average number of discrete restriction criteria per decision ranged from 1.1 for the TLV to 2.7 for CADTH.
- The time to a market access outcome was highly variable across markets, with no systematic difference between CEA and non-CEA markets.
  - However, within Europe, all non-CEA markets reported more market access outcomes than CEA markets (283 vs 227), suggesting CEA market processes are longer.

Conclusions

- Patient access to innovative oncology and rare medicines is more limited in CEA than in non-CEA markets.
- Restrictions beyond the regulatory label are often used in market access outcomes. Restrictions were more often applied in CEA markets than non-CEA markets.
- Overall, there is significant variability in the time to patient access to medicines across markets, highlighting the importance of ensuring that any approach to value assessment is locally tailored, timely, and fit-for-purpose.

References

1. Wang T, Sola B, McAuslane N. 2022. R&D Briefing 83: Review of HTA outcomes and timelines in Australia, Canada and Europe 2016 -2020. Centre for Innovation in Regulatory Science. London, UK.
2. The root cause of unavailability and delay to innovative medicines: Reducing the time before patients have access to innovative medicines. Available at: https://www.efpia.eu/media/554527/root-causes-unavailability-delay-cra-final-300620.pdf

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