Health Technology Assessment (HTA), Reimbursement, and Funding Landscape Challenges for Oncology Companion Diagnostics (CDx) in Europe and Canada

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INTRODUCTION

- Use of precision oncology medicines requires patient selection through biomarker testing, often using companion diagnostic (CDx) tests[1]
- However, access to and reimbursement for CDx testing remain barriers to the use of innovative medicines across Europe and other geographies[1,2]
- Prior research indicates that there can be challenges in health technology assessment (HTA) processes and reimbursement for CDx, as well as insufficient funding for biomarker testing[1,2]
- Additionally, the introduction of the In Vitro Diagnostic Medical Devices Regulation (IVDR) in Europe is expected to largely restrict the use of laboratory-developed tests (LDTs),[3] which may further impede access to affordable testing alternatives
- Despite these current and future challenges, there is limited up-to-date research on the current status of HTA, reimbursement, and funding landscape for oncology CDx in Europe and Canada

OBJECTIVE

- We aimed to assess the current landscape of HTA, reimbursement, and funding for CDx in Europe and Canada and highlight associated challenges in HTA and funding for oncology biomarker testing

METHODS

- A hybrid, comprehensive targeted web and literature search was conducted using publicly accessible sources from government and HTA agency websites, as well as guidelines, policies, and databases from governmental organizations, health insurers, and other relevant institutions, with a focus on CDx and LDTs for immunohistochemistry in oncology
  - The detailed review was performed for the following countries: Belgium, Canada, France, Germany, Italy, Spain, Switzerland, and the United Kingdom (UK)
- Data were extracted based on predefined research questions and criteria for oncology CDx HTA, reimbursement, funding, and sponsorship (**Figure 1**)
- The targeted web and literature search was validated and supplemented with 3 to 5 qualitative interviews with relevant experts in each country, including payers, pathologists, and budget holders
- The literature review was conducted from September through October 2024, and validation interviews were conducted from December 2024 through February 2025

Figure 1. Scope of the Literature Review

HTA Processes for CDx	Evidence Requirements for CDx HTA and Reimbursement	Coding and Funding for CDx Reimbursement	Sponsorship of CDx
• Whether HTA is mandatory for CDx • Whether the CDx is reviewed alongside or separate from the corresponding targeted drug • Whether national and/or regional HTAs are required • Whether reimbursement systems coordinate the approval and coverage timelines for CDx with their associated drugs	• HTA evidence requirements for CDx and biomarkers (eg, CDx clinical evidence, economic data, clinical utility, and diagnostic, prognostic, or therapeutic value)	• Available IHC coding (specific coding for IHC CDx or biomarkers vs generic IHC code) • Reimbursement rate for biomarker testing and whether it is sufficient to cover CDx costs	• Whether pharmaceutical industry funding for CDx is permitted or prohibited • Whether CDx sponsorship by the pharmaceutical industry is critical

Abbreviations: CDx, companion diagnostic(s); HTA, health technology assessment; IHC, immunohistochemistry.

RESULTS

HTA process and evidence requirements for CDx

- The majority of countries assessed (5/8) required HTA for CDx reimbursement (**Table 1**)
  - Some countries required a submission for the CDx separate from the submission for the associated drug (Belgium, Canada, France, and Italy) and/or local or regional assessments (Canada, Italy, and Spain), which can lead to inconsistent access and adoption within a country or delays in reimbursement
  - National HTAs for CDx are conducted in Belgium, Canada, France, and the UK
- Broadly, evidence requirements for CDx were consistent across countries and included clinical utility, budget impact, and test performance (**Table 1**)
- Qualitative interviews confirmed the literature review findings on the CDx HTA process and evidence requirements for each country

Table 1. HTA Process and Evidence Requirements

Country	CDx HTA Required	Joint Review With Drug	IHC CDx HTA Process	Evidence Requirements for CDx HTA	References
Belgium	**Yes** (national)	**Separate**	• IHC CDx face prolonged multi-level evaluation processes through TMC and Royal Decree	• Description of the test, necessary infrastructure, and workflow; detailed price and costs; budget impact and cost-effectiveness; burden of disease, unmet need, test positioning, and competitive landscape; and test performance	4
Canada	**Yes** (national, provincial, local)	**Joint & separate**	• For Quebec, INESSS performs separate but simultaneous drug and test reviews • For other provinces, CDA conducts a joint review of drugs and CDx, then relies on provincial and/or hospital-based review processes following non-obligatory drug funding recommendations from the CDA	• CDA focuses on drug efficacy, with no formal evaluation process for CDx • Provincial evidence requirements lack harmony but often involve gap analyses and resource assessments • For Quebec, INESSS requires a separate CDx dossier detailing clinical evidence and budget impact modeling	5-7
France	**Yes** (national)	**Separate**	• Drugs and CDx require HTA through HAS by 2 committees with 2 separate dossiers: (1) CNEDiMTS, which evaluates diagnostic tests, and (2) CT, which evaluates drugs	• CDx require a separate dossier that focuses on analytical and clinical validity, clinical utility, and economic impact	8-10
Italy	**Yes** (regional)	**Separate**	• There is no national HTA process for CDx; responsibilities are delegated to regional authorities, which can create inconsistent and delayed reimbursement decisions across regions	• CDx HTA evidence requirements vary among regional healthcare authorities; some focus on budget impact assessments, while others also mandate cost-effectiveness analyses	11, 12
UK	**Yes** (national)	**Joint**	• CDx evaluation is integrated into the NICE TA for the associated drug; this is the only route to mandated NHS funding	• NICE assesses both clinical evidence and cost-effectiveness of the drug–CDx combination	13
Germany	**No**	**NA**	• The G-BA does not conduct HTAs for CDx, as CDx reimbursement becomes legally mandated within 6 months after drug launch	• Because HTAs are not conducted for CDx, no additional evidence is required	14, 15
Spain	**No** (local assessments performed instead)	**NA**	• There is no standardized national HTA framework for CDx; individual hospitals must assess, adopt, and fund CDx	• Local hospital assessments require budget impact models and clinical evidence, although evidence requirements vary by location	16-19
Switzerland	**No**	**NA**	• Once the FOPH approves coverage for the drug, the CDx benefits from a positive reimbursement status; no separate HTA is needed	• Because HTAs are not conducted for CDx, there are no evidence requirements	20-23

Green shading indicates a positive impact (eg, greater predictability or fewer resources required) and red shading indicates a negative impact (eg, less predictability or more time and resources required).
Abbreviations: CDA, Canada's Drug Agency; CDx, companion diagnostic(s); CNEDiMTS, National Committee for the Evaluation of Medical Devices and Health Technologies; CT, Transparency Committee; FOPH, Federal Office of Public Health; G-BA, Federal Joint Committee; HAS, Haute Autorité de Santé; HTA, health technology assessment; IHC, immunohistochemistry; INESSS, Institut National d'Excellence en Santé et en Services Sociaux; NA, not applicable; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; TA, technology appraisal; TMC, Technical Medical Council; UK, United Kingdom.

Alignment of CDx and targeted drug reimbursement

- In 3 countries (Belgium, Canada, and Italy), drug and CDx reimbursement timelines were not aligned, which can lead to substantial delays in access to testing (**Table 2**)
- Literature review findings were confirmed in the qualitative interviews

Table 2. Alignment of CDx–Drug Funding and Reimbursement

Country	Aligned CDx–Drug Funding/ Reimbursement	CDx–Drug Time Alignment on Funding/Reimbursement	References
Belgium	**No**	• Reimbursement decisions are not aligned; IHC CDx require extensive multi-commission reviews and Royal Decree, whereas drugs follow streamlined pathways • Competing budget priorities and lack of mandated timelines can cause delays	4
Canada	**No**	• Recommendations from CDA face separate provincial reimbursement assessments, creating significant delays in CDx–drug funding alignment, except in Quebec, where CDx–drug funding is aligned	7
Italy	**No**	• Although AIFA mandates CDx funding with drug approval, regional CDx reimbursement decisions can face prolonged delays	24
France	**Yes**	• Drug and CDx coverage decisions are generally aligned because they are assessed simultaneously by HAS	10
Germany	**Yes**	• CDx reimbursement is available within 6 months of drug launch, aligning with the G-BA's drug HTA; sick funds can cover CDx prior to HTA completion and EBM code assignment	25, 26
Spain	**Yes**	• CDx and drug coverage typically align due to pharmaceutical company sponsorship programs in select hospitals and/or delays from lengthy drug reimbursement processes across Spain	
Switzerland	**Yes**	• Drug and CDx reimbursement are aligned on timing; laboratories can use generic IHC codes via TARMED	27-29
UK	**Yes**	• CDx–drug funding is aligned, but a positive funding decision from NICE is dependent on cost-effectiveness of both the drug and the CDx, which often requires multiple rounds of negotiation with NICE	

Green shading indicates a positive impact (eg, greater predictability or fewer resources required) and red shading indicates a negative impact (eg, less predictability or more time and resources required).
Abbreviations: AIFA, Italian Medicines Agency; CDA, Canada's Drug Agency; CDx, companion diagnostic(s); EBM, German Uniform Assessment Standard; G-BA, Federal Joint Committee; HAS, Haute Autorité de Santé; HTA, health technology assessment; IHC, immunohistochemistry; NICE, National Institute for Health and Care Excellence; TARMED, Swiss Tariff System; UK, United Kingdom.

Funding challenges for CDx

- In all countries assessed, current reimbursement rates and budgets typically fail to cover the anticipated costs of CDx testing, which can force laboratories to develop LDTs, seek alternative funding sources, or request additional budget (**Table 3**)
- Three countries (Canada, Italy, and Spain) had geographic disparities in access to testing due to regional HTA/local assessments or siloed budget constraints
- Findings on barriers to CDx funding and reimbursement were confirmed in the qualitative interviews

Table 3. Funding and Reimbursement Barriers for CDx

Country	IHC Coding Available		Sufficient Budget/ Reimbursement for CDx	Funding/Reimbursement Barriers	References
	IHC CDx	Generic IHC			
Belgium	✓	✓	**No**	• IHC reimbursement rates fail to cover costs, forcing laboratories to absorb costs, ask for patient payment, develop LDTs, or deny testing	30
Germany	✓	✓	**No**	• Reimbursement rate decisions (from confidential negotiations) typically favor existing codes over new ones; rates typically fail to cover CDx costs	31-33
Italy	✓	✓	**No**	• Budget constraints can delay regional decisions; wealthier regions reimburse CDx more quickly, and resource-limited regions face delays	34-36
France	✗	✓	**No**	• IHC rates fail to cover the costs of CDx, creating a financial burden for laboratories, which must absorb costs or develop LDTs	37, 38
Switzerland	✗	✓	**No**	• IHC CDx are inadequately reimbursed through TARMED codes, imposing financial strain on laboratories; TARDOC aims to address this	39-41
Canada	**NA** (budget-based system)		**Insufficient budgets**	• CDx funding may come from different sources (eg, hospitals, provincial agencies, or pharmaceutical companies) • Provincial disparities in budgets and expertise create a starkly uneven landscape for CDx funding and reimbursement; regions with lower budgets are most affected by delays	42-44
Spain	**NA** (budget-based system)		**Insufficient budgets**	• The lack of a national approach to CDx funding and limited budgets create an uneven landscape where access to CDx is determined by local economic capabilities	16, 19
UK	**NA** (budget-based system)		**Insufficient budgets**	• CDx–drug combinations approved by NICE do not come with additional funding; hospitals and laboratories must find funding from existing budgets	45-47

Green shading indicates a positive impact (eg, greater predictability or fewer resources required) and red shading indicates a negative impact (eg, less predictability or more time and resources required).
Abbreviations: CDx, companion diagnostic(s); IHC, immunohistochemistry; LDT, laboratory-developed test; NA, not applicable; NICE, National Institute for Health and Care Excellence; TARDOC, Quality and Cost Control System; TARMED, Swiss Tariff System; UK, United Kingdom.

Sponsorship for funding

- Full coverage of CDx is often lacking; therefore, alternative routes to fund CDx testing are required
- Pharmaceutical industry sponsorship of CDx testing is permitted as a funding bridge in Belgium, Canada, Italy, Spain, and the UK but not in France and Germany (**Table 4**)
  - In countries with sponsorship restrictions (France and Germany), laboratories must absorb costs or find alternative funding sources to maintain CDx testing access
- Findings on the permittance of pharmaceutical industry sponsorship of CDx were confirmed via qualitative interviews

Table 4. Pharmaceutical Company Sponsorship of CDx

Country	Permittance of CDx Sponsorship	Pharmaceutical Company Sponsorship of CDx	References
Belgium	**Allowed**	• Pharmaceutical company sponsorship can support access to CDx for an unlimited period until a reimbursement decision is reached	48, 49
Canada	**Allowed**	• Budget constraints typically prevent test implementation; pharmaceutical company sponsorship can support the implementation of new tests, typically until the test becomes standard of care or public funding becomes available	50, 51
Italy	**Allowed**	• Pharmaceutical company sponsorship temporarily supports CDx access and drug launches due to regional budget constraints and delayed reimbursement; test funding must be integrated into regional budgets once sponsorship ends	52-54
Spain	**Allowed**	• Pharmaceutical companies typically sponsor CDx in hospitals to overcome budget constraints and allow timely testing; once sponsorship ends, hospitals must fund tests	16, 55, 56
UK	**Allowed**	• Pharmaceutical company sponsorship removes short-term funding barriers and helps establish CDx in routine clinical practice, which helps facilitate the transition of funding to the NHS	57-60
Switzerland	**Not determined**	• Lack of transparency and awareness around pharmaceutical company sponsorship of CDx leads to the conclusion that it is not practiced or allowed; pharmaceutical companies support EQA programs and research grants as workarounds	
France	**Not allowed**	• Direct pharmaceutical company sponsorship of diagnostic testing is prohibited; limited sponsorship is permitted during early market access programs before formal reimbursement is established	61, 62
Germany	**Not allowed**	• Pharmaceutical companies face significant restrictions on directly supporting CDx due to strict antibribery regulations; laboratories must absorb costs	63

Green shading indicates a positive impact (eg, greater predictability or fewer resources required), yellow shading indicates a neutral impact (eg, comparable impact or moderate burden), and red shading indicates a negative impact (eg, less predictability or more time and resources required).
Abbreviations: CDx, companion diagnostic(s); EQA, external quality assessment; NHS, National Health Service; UK, United Kingdom.

CONCLUSIONS

- In some healthcare systems, discrepancies between drug and CDx reimbursement processes and timing can create challenges in timely access to diagnostics or access disparities within countries
- In all assessed healthcare systems, there is insufficient funding and reimbursement for CDx biomarker testing, leading to the need for laboratories, hospitals, or patients to close the funding gap or for short-, medium-, or longer-term sponsored testing by the pharmaceutical industry (where locally permitted)
- Healthcare systems need to work toward harmonizing drug and CDx reimbursement processes and timelines to ensure timely access for patients to drugs and CDx by aligning evidence assessments
  - It is important for stakeholders to understand that using CDx to identify patients most likely to respond to a treatment can lead to improved patient outcomes
- Additionally, healthcare systems should invest in biomarker testing (particularly given the low cost of testing vs treatment) to avoid the need for other stakeholders (eg, laboratories, hospitals, patients, and/or industry sponsorship) to close funding gaps, minimize patient exposure to treatments that are unlikely to be effective, and ultimately improve patient outcomes
  - This will be increasingly important with the introduction of IVDR and the criticality of CDx access and availability across all markets in Europe

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