How are Companion Diagnostics Evaluated and Reimbursed in Europe? Comparative Analysis of the EU-4 and UK

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Background

With the rise in genetic screening in recent years, there is a paradigm shift in healthcare from a disease-focused, non-patient-specific model of care to a precision medicine approach. The patient-tailored precision medicine approach is driven by the identification of predictive genetic biomarkers, providing an opportunity to target patients who are most likely to benefit from treatment (and consequently spare patients who are unlikely to respond from undergoing futile treatment approaches). Therefore, precision medicine has the potential to improve clinical outcomes while also reducing healthcare expenditure.[1]

In vitro diagnostic (IVD) tests are performed on samples such as blood or tissue to identify biomarkers of disease. Companion diagnostics (CDx) are a specific group of IVDs that are essential to identify patients for whom a particular treatment (Tx) is indicated. CDx provide healthcare practitioners and payers with critical information for decision making and are a fundamental tool to propel the shift towards precision medicine. As the utilisation of CDx increases, it is critical for countries to have established pathways for the health technology assessment (HTA) and reimbursement of CDx, to ensure timely access and adoption alongside their companion medicines.[2]

Objectives

The goal of this study is to compare HTA and reimbursement processes for CDx in the EU-4 and UK to understand country-specific challenges and opportunities for access.

Methods

Publicly available guidance documents on HTA and reimbursement processes for CDx in the EU-4 and UK were reviewed and supplemented with insights from interviews with local experts.[3-10] Key methodological elements were extracted and compared, including the responsible body, coordination of therapy/CDx processes, evidence requirements, source of reimbursement and timelines.

Results

- Evaluation of CDx in France and the UK is a transparent, standardised and centralised process, with published guidance available from all three major reimbursement agencies[3-8]
- NICE and SMC assess the value of CDx as part of their appraisal of the associated Tx[3-6]
- In contrast, the Tx and CDx are assessed by two different bodies in France (CT and CNEDiMTS, respectively)[7,8]
  - Ahead of HTA, CDx can be conditionally and temporarily reimbursed under the coverage with evidence development programme and registered with the nomenclature for innovative tests (RIHN)
- CDx do not undergo HTA in Germany, though reimbursement requirements and structures are well defined. CDx reimbursement is provided at the national level for patients with statutory health insurance, but reimbursement pathways differ for tests used in the outpatient vs. inpatient setting[9]
  - In the outpatient setting, a CDx is reimbursable under the doctor's fee scale (EBM) if the associated Tx makes prior testing mandatory
  - In the hospital setting, CDx are reimbursed via diagnosis-related group (DRG) codes
- There are no established assessment pathways for CDx in Italy and Spain, and reimbursement is determined at the regional/local level
  - In Italy, CDx are purchased directly from the NHS through tenders at regional and local level after receiving marketing authorisation from the Ministry of Health (MoH) which has put in place a specific regulatory framework for medical devices. Reimbursement of CDx happens through DRG tariffs if used in the inpatient setting or through ambulatory tariffs if outpatient[10]
  - In Spain, the MoH introduced a legal framework for the assessment of CDx, similar to that for Tx, but it has not been implemented as of Q4 2023; currently, companies notify the MoH of the marketing of the CDx and subsequently negotiate at the hospital or regional level

Table 1. Summary of CDx reimbursement process by country[3-10]

	England	Scotland	France	Germany	Italy	Spain
Responsible agency	NICE	SMC	HAS	G-BA	Ministry of Health	N/A
Joint pathway with Tx?	Joint	Joint	Separate	Separate	Separate	N/A
Evaluation pathway(s)	• STA/MTA • Diagnostics assessment • Early value assessment	Standard SMC appraisal processes for new medicines	Evaluation by CNEDiMTS	N/A (CDx do not undergo HTA)	• LEAs • Regional assessment	No standardised reimbursement pathways established
Timeline	• 7 months • 15 months • Not reported	4 months	Not reported	6 months	Not reported	N/A
Source of reimbursement	National (NHS)	National (NHS)	National	National (SHI)	Regional	Regional or hospital
Published guidance?	Yes	Yes	Yes	No	No	No

REIMBURSEMENT PROCESS TRANSPARENCY

CDx = companion diagnostic; CNEDiMTS = Commission Nationale d'évaluation des Dispositifs Médicaux et des Technologies de Santé; G-BA = Gemeinsamer Bundesausschuss; HAS = Haute Authorité de Santé; HTA = health technology assessment; LEA = Essential Levels of Assistance; MTA =multiple technology appraisal; N/A = not applicable; NHS = National Health Service; NICE = National Institute for Health and Care Excellence; SHI = statutory health insurance; SMC = Scottish Medicines Consortium; STA = single technology appraisal; Tx = therapeutic drug

Table 2. Summary of evidence requirements for CDx by country[3-10]

	England	Scotland	France	Germany	Italy	Spain
CDx sensitivity/specificity	✓	✓	✓	N/A	✓	N/A
Clinical utility*	✗	✗	✓	N/A	✓	N/A
CEA to include CDx	✓	✓	✓	N/A	✗	N/A
Sensitivity analysis without CDx cost	✓	✓	✗	N/A	N/A	N/A

CDx = companion diagnostic; CEA = cost-effectiveness analysis; N/A = not applicable. * Demonstration of the clinical utility of the CDx was not mentioned in guidance documents published by NICE and the SMC.

- In the UK and France, the cost of the CDx must be included in the cost-effectiveness analysis and evidence of the sensitivity and specificity of the CDx must be submitted[3-8]
- Evidence of the clinical utility of the test is a prerequisite in France to be evaluated as a CDx (rather than a standard diagnostic test), but is not required in the UK[3-8]
- Germany, Italy and Spain have not published guidance on evidence requirements for reimbursement of CDx (other than obtaining the CE mark); however, budget impact analysis and clinical documentation are likely required for regional formularies

Conclusions

- HTA and reimbursement processes for CDx vary widely across the EU-4 and UK, including differences in the availability of standardised pathways for assessment, evidence requirements, the source of reimbursement and transparency regarding the process
- As the healthcare industry evolves towards precision medicine, understanding country-specific HTA and reimbursement processes for CDx will be essential to facilitate successful and timely access to innovative targeted therapies

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