Understanding Drug-Companion Diagnostic Reimbursement Across the Key EU States

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Companion Diagnostics – One Element Towards Personalized Medicines

«[…] it is widely understood that personalised medicine refers to a medical model using characterisation of individuals’ phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.»

CDx Leading To Efficiency Gains in Clinical Research and Health Care

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<th>«Traditional treatment»</th>
<th>Personalized Medicines</th>
<th>Implications</th>
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<td><strong>Effectiveness of the test/marker</strong></td>
<td>Average health outcome, high # of non-responders</td>
<td>Targeted health outcome, high # of responders</td>
<td>Better (cost-) effectiveness, «minimizing waste»</td>
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<td><strong>Safety</strong></td>
<td>AE and subsequent cost implications</td>
<td>Fewer/ less AE (target)</td>
<td>Less secondary cost (hospitalization), better adherence, «maximising number needed to harm»</td>
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<td><strong>R&amp;D</strong></td>
<td>Large clinical trials</td>
<td>Smaller clinical trials</td>
<td>Less cost, shorter time to market; time to include the right patients</td>
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<td><strong>Business model</strong></td>
<td>«Blockbuster» model, i.e. higher volume</td>
<td>Targeted approach which leads to lower volume</td>
<td>Higher price/ lower budget impact</td>
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<td>Higher value for a specific # of patients</td>
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Source: Godman B et al. (2013), Personalizing health care: feasibility and future implications; BMC Medicine 11:179; EC (2013), Use of ‘omics’ technologies in the development of personalised medicine
Access to Personalized Medicines – Concern Noted By the Council of Ministers

«NOTES WITH CONCERN that not all patients have access to innovative methods of better-targeted prevention, diagnosis and treatments, and that a significant challenge for Member States consists in promoting appropriate uptake in healthcare systems, in order to ensure integration into clinical practice in line with the principles of solidarity and universal and equal access to high quality of care, while fully respecting Member States’ competences, and ensuring the sustainability of their national health systems»

Reimbursement For CDx and Rx Follow Different Pathways May Impede Access

In many cases reimbursement of CDx in a hospital depends on
- Reimbursement of the treatment as such
- DRGs (e.g. inclusion of the pathologist/ CDx)

Legislative Framework at EU Level Has Implications For Pricing and Reimbursement

- Management and financing of healthcare is in the remit of individual Member States: «The responsibilities of the Member States shall include the management of health services and medical care and the allocation of the resources assigned to them.» [1]

- The Transparency Directive’s fundamental principles include (1) timeliness of proceedings, (2) transparency, (3) objectivity, and (4) due process [2]

- CDx not expressly mentioned by the wording of the Transparency Directive («medicinal product»), however, does this mean that the Directive’s scope exclude CDx?
  - For personalised medicine, the diagnostic element is indivisibly linked to the medical compounds involved. It therefore would make no sense to apply the principles of the Transparency Directive to pricing and reimbursement of the medical compounds, but not applying the same principles to the pricing and reimbursement of the diagnostic elements.
  - The Court of Justice case law has made abundantly clear that the Directive’s scope is not limited by its wording (e.g. C-471/07 and 472/07).

Interaction Between Industry and Stakeholders Has Always Been Complex
... And Is Becoming More Complex With Personalized Medicine
## Country Examples

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<thead>
<tr>
<th>Country</th>
<th>Assessment</th>
<th>P&amp;R</th>
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| France  | Separate HTA for CDx and Rx; risk of mismatch and access delays | • While ambulatory setting provides a process for reimbursement of CDx, hospitals operate with a DRG system with retrospective calculation  
• Mechanism in place that facilitates access to CDx and Rx (Institut National du Cancer); however, limited to oncology and temporary in nature |
| Germany | Partly separate HTA for CDx and Rx | • Ambulatory: generic code ("Einheitlicher Bewertungsmassstab", EBM), can be an impediment for new CDx if new code has to be created  
• Hospital: covered by DRG; however, DRG calculations are retrospective so that new CDx won’t be reflected |

## Country Examples

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<td>Italy</td>
<td>While national HTA for Rx (AIFA) no common path for CDx</td>
<td>▪ Rx at national level (AIFA) with potential regional co-pay, and risk-sharing schemes; no formal process for reimbursement of CDx but generic codes allow coverage to some extent Hospital: DRG system in place which provides coverage for Rx and CDx</td>
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<td>Spain</td>
<td>Assessment: national for Rx but some regions have additional HTA agencies in place; for CDx at hospital level</td>
<td>▪ Rx reimbursement in principle decided at national level, followed by regional negotiations; CDx however supposed to be funded at hospital level, sometimes purchased via tenders but most often financed by pharmaceutical companies</td>
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<td>UK</td>
<td>NICE assessment covering both, CDx and Rx; however, uncertainty about funding of Rx assessment is negative but funded through Cancer Drug Fund</td>
<td>▪ However, general uncertainty about funding (despite NICE recommendation, budget decided by local budget holders)</td>
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General Considerations and Further Challenges That Impede Access

- Assessments such as HTA could be suitable tools to assess PM (CDx and Rx); however, this requires coordinated approach. CDx are assessed differently:
  - UK: central, joint assessment
  - FR, DE: central but independent assessment
  - ES, IT: regionally or locally
- Reimbursement schemes for CDx varies considerably, by the health system, pharmaceutical companies or patients
- Main problem: inconsistent funding of Rx and CDx
- Healthcare infrastructure: testing sometimes only provided in a few hospitals
- Education of physicians and patients: physicians’ understanding critical for access due to their “gatekeeper” role; patient education critical for the acceptance and effectiveness of PM

Personalized Medicine Changes Doctor-Patient Relationship and Healthcare

- Shift from «treatment-centered» to «patient-centred» care management requires:
  - Ensure greater patient empowerment and shared decision-making (“plain language”, listening skills)
  - Schedule time dedicated to patients, e.g. management of genomic information and its consequences
  - Ensure own (healthcare professional) training on genomics including health literacy among providers

- Better informed decision-making, reducing uncertainty about the value of a treatment

- Less uncertainty leading to better value for money

P&R For Personalized Medicines – The Way Forward

- Personalized medicines bears potential for better health outcomes for patients and efficiency gains for the health system

- Current assessment and P&R processes need to be improved to ensure access to personalized medicines

- Elements that foster personalized medicines
  - Coordinate assessment, e.g. HTA, and reimbursement of CDx and Rx
  - Ensure testing infrastructure is available
  - Education of healthcare professionals and patients
Annex
Market Access Hurdles for CDx and Rx – Access to Market and Pricing

- CDx and Rx have different MA pathways (EMA/ «Notified bodies»)
- Reimbursement of CDx differs from market to market
- Also differences between in- and outpatient reimbursement …