



Workshop report: Managed entry in the context of adaptive pathways

(London, 5 July 2016)

The work leading to these results was conducted as part of the ADAPT SMART consortium (Accelerated Development of Appropriate Patient Therapies: a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes). For further information please refer to www.adaptsmart.eu. This paper is the result of the collective input from working group D3.05 and D3.07 and only reflects the views of the authors.

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115890. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.



- The workshop was held in London on the 5th July 2016 and around 30 attendees represented key European stakeholder groups: health technology assessment (HTA) bodies, payer organisations, or manufacturers. The workshop was also attended by several patient representatives, healthcare professionals, and academics. The workshop was convened to discuss the findings of a series of interviews with HTA bodies, payers and industry representatives. The interviews discussed experiences with managed entry agreements for products that were introduced with considerable uncertainty at licensing in recent years (conditional approval/approval under exceptional circumstances).
- More information on adaptive pathways can be found at the European Medicines Agency (EMA) website.
- A managed entry agreement is defined as an arrangement between a manufacturer and payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions. These arrangements can be simple financial arrangements or use a variety of mechanisms to address uncertainty about the performance of technologies.

Summary of main findings presented at workshop

- A series of interviews were performed with HTA bodies, payers and manufacturers from different European countries. The interviews focused on both experiences with arrangements for conditional approval and approval under exceptional circumstances products, as on general experiences with managed entry agreements (depending on the actual experience of the interviewee).
- The interviews confirmed that financial-based arrangements – such as confidential discounts, rebates, and price-volume agreements – are very common in European countries although not all countries use them. The use of outcomes-based managed entry agreements, where additional data is collected in clinical practice and that could take the form of conditional coverage, coverage with evidence development, pay-for-performance, or risk-sharing, were much less common.
- A key finding was that ‘market introduction with considerable uncertainty’ in itself does not automatically trigger the use of outcomes-based agreements. Out of the 48 products that received marketing authorisation under either exceptional or conditional circumstances in recent years, only a few were found to have managed entry agreements involving additional data collection.
- The interviews identified the following reasons for the lack of use of outcomes-based managed entry agreements: a lack of policies that allow the use of such arrangements in some countries,

uncertainty about the ability of outcomes-based arrangements to meet their objectives in practice, lack of administrative infrastructure that would enable an easy implementation, the need to align and appropriately incentivise all healthcare system stakeholders to enable consistent and high quality data collection, and a limited ability to collect meaningful (comparative) effectiveness data in clinical practice.

- The company interviews identified a bigger interest in exploring the use of outcomes based arrangements but during the interviews the HTA bodies and payers expressed reluctance because of high initial prices and the added complexity and lack of administrative infrastructure that would easily facilitate outcomes-based arrangements.

Additional data collection under adaptive pathways

- Most attendees agreed that more coordinated efforts with regard to the planning of data collection post- approval and exploring the extent to which aligning efforts between different countries would be possible might be beneficial. Early dialogue under adaptive pathways could facilitate such coordinated efforts.
- There was agreement among attendees that given the burden of additional data collection on healthcare systems, there needs to be sufficient reason for each parameter that needs to be collected. It was suggested that in many cases, only collecting a few but essential parameters might be preferable over more comprehensive data collection as each additional parameter might lower compliance with data collection, the amount of missing data, and thus effectively lowering the overall quality of data collection efforts. Many attendees agreed that a sensible data collection strategy would be needed.
- Successful coordination efforts during early dialogue involving HTA bodies, payers and regulators could enable the manufacturer to prepare a plan for additional data collection that would be available and in place the moment a marketing authorisation might be granted. A multi-country framework agreement whereby more than one country could agree on the parameters to be collected would be great progress as compared to current practices. Furthermore, coordinated efforts might improve the time it would take to answer research questions.
- It was discussed during the workshop that during recent years, progress was made in several countries with regard to the establishment of disease registries and most stakeholders agreed that ways to explore making better use of existing registries, especially in the context of adaptive pathways, might be beneficial.
- The suggestion was made to start exploring whether it would be possible if post-authorisation

data collection efforts performed to address HTA and payer related questions could be integrated. Such a comprehensive post-approval evidence generation plan could be agreed by all parties during a joint scientific advice process involving all relevant parties. During the breakout session of the payers and HTA bodies representatives it was proposed that data collection efforts could be included in the risk management plans (RMPs) for products under non-imposed studies. Although EMA cannot impose requirements for HTA bodies or payer commitments, manufacturers could provide payers and HTA bodies reassurance that there will be monitoring and periodic reporting of such studies by voluntarily including components in the RMP. However, the feasibility and stakeholder support for this suggestion would need to be further explored.

Adaptive pathways

- It was discussed during the workshop that from the HTA and payer perspective, the early dialogue component in the adaptive pathway approach offers the opportunity to influence clinical development programs for products. Products that are under development now might reach the market, be it using adaptive pathways or using a normal development pathway. Adaptive pathways could offer a better and enhanced prospectively planned coordination, including HTA bodies, payer and regulatory requests, than unplanned regulatory fast track/conditional authorization pathway which does not consider HTA bodies and payer downstream considerations.
- For manufacturers, ensuring commercially confidential information is respected was mentioned as a critical point.
- It was commented by several attendees that there still is little information available about adaptive pathways, especially the EMA pilot phase, and the exact approach it takes. As none of the pilot products have reached the market yet this makes it difficult for payers and HTA bodies to anticipate what models might work.
- HTA bodies and payers expressed interest during the workshop in establishing a 'platform for shared learning' on the design principles of managed entry agreement models and experiences with different models used by other countries.

Model proposed and initial discussion during workshop

- Considering affordability concerns and the inherent uncertainty regarding effectiveness, budget impact, and utilisation of products entering the market under adaptive pathways, a flexible pricing model with variable discounts might be acceptable for both payers and manufacturers.

In this scenario, payer and manufacturer would agree on a negotiated list price and conditions under which a discount would be modulated over time in light of reduced uncertainty and new evidence that would be generated and evaluated at set milestones. This way, payers might both have fewer concerns over affordability and possible value for money and manufacturers would be incentivised to ensure that additional evidence is indeed generated.

- It was however recognised that this particular model might not be feasible or acceptable in all countries and that other models could be proposed as well. In addition, it was agreed that payment models should be aligned with national processes as pricing and reimbursement is a national competence in the EU, need to be tailored to the product in question, preferences of payers, manufacturers, and the feasibility of implementing models that would require data collection.

Next steps

- A paper reporting the findings from the series of interviews will be developed.
- In parallel, proposals and recommendations/ways forward regarding managed entry in the context of adaptive pathways products will be developed in consultation with a broad group of stakeholders.