REAL WORLD EVIDENCE & ADAPTIVE PATHWAYS

ARE WE NOW BEGINNING TO SEE THE FUTURE OF THE PHARMACEUTICAL INDUSTRY?

Adaptive Pathways with Real World Evidence could bring forward market authorisation by 8 years.

Read on to find out how.

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Introduction

We all want safe and effective medicines to reach patients as soon as possible, but as we know, drug development, market authorisation and payor assessment are all slow sections of a long and drawn out journey for a drug.

But what if patients could have access to medicines not just months earlier, but potentially 8 years earlier?

Surely this is not practical, or even possible?

Would this not require a major overhaul of the entire process?

This is exactly what the European Medicines Agency (EMA) have in mind, as they lead a broad and diverse group of key stakeholders towards a root-and-branch upheaval of current practice.

We are talking about Adaptive Pathways (AP), an ambitious and evolving new initiative which incorporates Real World Evidence (RWE): clinical data collected outside of a conventional randomised controlled trial.

What is Adaptive Pathways and how does it work?

AP reforms the existing regulatory approach. In fact, it goes beyond changes to market authorisation, instead taking a ‘lifespan’ approach that incorporates drug development and health technology appraisal.

Traditionally the product lifecycle of a drug can be divided into two distinct phases (pre- and post-authorisation). AP replaces this single (go/ no-go) market authorisation event with a process of ‘reduction of uncertainty’ alongside iterative periods of data collection and regulatory assessment. AP views drug development as a continuum with stages of regulatory approval and evidence development running parallel with marketing. 1, 2

Could Adaptive Pathways really bring forward access to a drug by 8 years?

The EMA’s primary goal for AP is ‘ensuring timely patient access to drugs’ and they refer to an in-depth case study published by the Massachusetts Institute of Technology (MIT) NEWDIGS program using a hypothetical dyslipidaemia drug. In the traditional model this drug would obtain market authorisation 13 years after phase I studies, whilst in the AP model, the drug receives initial authorisation in year 5. This case study has been tested with and can be applied to other drugs (see figure). 3

Aren’t there safety concerns with speeding up patient access to drugs?

AP is accompanied by ‘an acknowledged level of uncertainty’ and there must be a balance between hastening access to new drugs for patients with the need for adequate risk-benefit data (an example of ‘access versus evidence’). The EMA is keen to stress the difference between risk and uncertainty which is ‘often conflated in public debate’. The benefit-risk trade-off does not change with AP, only the level of uncertainty. 1
So who has signed up for Adaptive Pathways?
AP is a collaborative approach with a diverse range of participating stakeholders from across Europe and beyond. This includes academia, advisory bodies, pharmaceutical companies, and regulators. The stakeholders are ‘almost universally enthusiastic’ about AP, but some have expressed concerns about how AP would be implemented as understandably there can be a reluctance to step out of traditional roles.  

Wait, this sounds familiar, isn’t this the same as Adaptive Licensing?
You may well have heard of Adaptive Licensing since its announcement in 2012. In fact, we are talking about the same programme, the name was changed to Adaptive Pathways last year to reflect the evolution of the project through 2-3 years of discussion and feedback. The new proposals for AP include some notable changes with an increased emphasis on real-world data collection.  

What role does Real World Evidence play?
RWE has been presented as a key component of AP. The EMA propose moving away from Randomised Controlled Trials (RCTs) being used exclusively as the basis for regulatory decisions, instead using the ‘entire toolbox of knowledge generation’. This includes RWE data collection and studies in addition to conventional RCTs, pragmatic RCTs and observational trials. 

AP is part of a changing attitude to the perceived lack of ‘robustness’ of RWE and the EMA highlights how year-on-year advancements in RWE studies are seeing them become more systematic, generate increasingly reliable data, and undergo improvements in methodology.  

What are the benefits?
Discussion around AP has delivered a consensus amongst the stakeholders on its benefits. This is centred around an improved ability to meet patient expectations and satisfy unmet medical need by expediting the current process. Additionally, AP enables innovative, flexible, and patient-centred studies to thrive and take centre-stage. RWE data collection within AP has the potential to improve our understanding of disease processes, epidemiological factors, and difficult issues such as adherence, which will in turn allow RCTs to become more efficient. Another major commercial benefit of AP for pharmaceutical companies is that their products will have a longer patent lifecycle increasing their revenue potential.

What is happening at the moment?
Stage 1 of the pilot project ran from March to December 2014 and pharmaceutical companies were invited to submit their product for consideration if they met three criteria: 1) an iterative development plan which could either involve gradual expansion of the target population, or a progressive reduction of uncertainty based on surrogate endpoints, 2) the ability to engage with HTA and other downstream stakeholders and 3) monitoring, collection and use of real-world data to complement RCTs. Out of 34 applicants, 10 products were successful in meeting the criteria of iteration, acquisition of real world data, and HTA interaction, of which 6 have advanced to the next stage which is currently in-progress through to 2016.  

But what does it mean for me?
The EMA are leading a diverse group of stakeholders, who between them cover every aspect of the pharmaceutical industry, in planning an overhaul of the regulatory process.

This will impact not only market authorisation but the full development and product lifecycle of a drug.

This initiative has given us a clear idea of the direction that decision makers wish to take in the future. It is apparent that Real World Evidence will play an important part in what is to come, but are you prepared?

References & Further Reading
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