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Optimised drug-development: Integrating regulatory and HTA

To get a new drug to market, clinical drug development has traditionally focused on fulfilling the regulatory requirements put forward within agency guidelines or scientific advice procedures. This has concentrated on study design, selection of endpoints and comparators, with a European wish for inclusion of an appropriate active comparator. This process has worked well for many years and in most cases it has enabled pharmaceutical companies to reach the market by focusing on obtaining a marketing authorisation.

But the world has changed. Having a marketing authorisation is no longer enough to enable new drugs to gain access to patients. In recent years, many companies have realised that the payers now have the final say on whether or not your product will gain access to the market. We have seen products being refused reimbursement or prices being cut to meet payer's expectations, raising the question: Do the costs/prices of these new drugs match the value gained for the patient and society?

In many circumstances industry is not well-prepared to answer this question. Following the traditional route of focusing on regulatory approval first, clinical studies have been performed to meet these regulatory expectations, and as such do not necessarily meet the payer's expectations with regard to endpoints, comparator and duration.

In other words: There is a mismatch between the regulatory requirements and those expectations set by Health Technology Assessment (HTA) bodies.

So far industry has tried to fill this gap by setting up post-authorisation studies, either as randomised trials, cohort studies or more 'real life' studies. The result has been a further delay in patients getting access to new medicines, which is clearly unsatisfactory.

The process has to be revised - in everybody's interest

The systems challenge for biosimilars is to demonstrate that the benefit/risk is similar to the innovator. This implies the marketing authorisation holder MAH for a biosimilar manages a similar pharmacovigilance (PV) system to the innovator and operates to similar standards. As well as an educational programme, currently reliance has been placed on routine PV for biosimilars within a risk management plan for obtaining benefit/risk evidence, although in certain EU Member States (such as Norway), switching studies have been requested. Despite the EU requiring brand name and batch number reporting for individual cases with biologicals, there remain no international standardised definitions and agreed best practice for measurement and reporting of adverse events of interest and reactions. Indeed, evidence is emerging that some EU pharmacists are not always recording batch number and that pharmacy software does not routinely allow recording of batch number (2).

To improve the chances of good medicines reaching patients faster, we really need a more integrated approach, bringing payers' and regulators' needs together, where regulators and HTA bodies engage in a mutual discussion striving at consensus. This would benefit industry and ultimately patients by driving discussion and reaching agreement on the mutual requirements of both parties.

Additionally, to make this new approach a reality, we also need to address the structural set-up of industry. Life sciences companies need to look to break down the silos, where they currently have separate regulatory and HTA/market access departments, with different objectives, focus and incentives based on their individual achievements. Instead, they need to work in a more integrated fashion. Regulatory affairs, market access and HTA experts must be engaged at an early time-point during drug candidate development, not only to discuss labelling and claims, but to create an integrated drug development program encompassing both regulatory and HTA requirements.

Bringing regulatory and HTA requirements together will most certainly speed up the drug development process, reduce resource needs and costs, and could ultimately help to ensure that patients gain access to new medicines much faster.

The Adaptive Pathway

For some years now industry in Europe has had access to joint scientific and HTA advice offered in collaboration between the EU agency EMA/CHMP and EUNetHTA, a collaborative network of EU HTA bodies. The process has worked as a sequential consultation, starting with a regulatory review, followed by input from relevant HTA bodies. This process has now been taken one step further and been included in the current pilot of an Adaptive Pathway in EU. This is clearly a step in the right direction.

However, although regulators and HTA-experts may agree and guide the industry in the direction of a more aligned drug-development process, we still need to see payers accepting this approach. Payers may regard the Adaptive Pathway as less rigorous where new medicines become approved for a narrow indication, which then is supposed to finance further development into larger and perhaps more relevant indications from a payer and societal perspective. Moreover, the Adaptive Pathway is an EU centralised approach, whereas pricing and reimbursement is a purely national policy decision creating further potential for discrepant views. If these obstacles are not overcome the Adaptive Pathway in EU will not be able to succeed in gaining patients faster access to new medicines.