ADAPTIVE LICENSING AND REAL WORLD EVIDENCE

INTRODUCTION

Traditional drug licensing approaches are based on binary decisions, i.e. to go and not to go, when an experimental therapy is prescriptively transformed into a fully vetted, safe and efficacious therapy.1

On the other hand, adaptive licensing (AL) is an ambitious and evolving initiative of drug licensing based on the adaptive pathway (AP) that incorporates Real World Evidence (RWE).2 Fig. 1.

AP is based on stop-by-stop learning under the conditions of acknowledged uncertainty with iterative phases of data collection and regulatory evaluation.3

The AP approach allows patient-specific approvals for timely access to new technologies and generates near real-time data for appropriate medical decisions.4

Adaptive approaches connect decision-making to an emerging evidence base, rather than a conventional single-point-in-time evaluation.5

It promotes patient access to innovation, reduces clinical uncertainty, ensures effectiveness, and improves the health technology development process.6

Nowadays, the collection programs of observational information are speeding up at much higher rates than ever, creating a huge volume of data. However, the accessibility of the healthcare evidence from the real world experiences is limited. In such scenarios, the generation and collection of RWE become necessity.

The aim of AP approach is to introduce flexibility in the decision-making by the regulators through enforcement of AL and emphasizing on generation of RWE.

Fig. 1 (a) The treatment population grows rapidly post-licensing and treatment experience does not contribute to evidence generation

Adaptive Licensing

Implementation of RWE in AL

• RWE is the planned and systematic recollection of clinical data generated outside a conventional RCT.

• It derives results from a larger dataset gathered through the analysis of observational data from various sources such as electronic medical records, registries or administrative databases, and medical claims databases.

• The healthcare evidence minimizes the time for a drug to reach a market, and reduce the costs and time of clinical trials.

• A growing number of regulators, payers and Healthcare Technology Assessment (HTA) organizations involves patients in their decision-making processes. This generates the patient-specific RWE to support the licensing authorities to take appropriate decisions on-marketing of an intervention.

• Additionally, the regulators have begun to explicitly address and communicate “uncertainty” in their benefit-risk assessment models that would need to step wise iterative learning before full licensing.

• RWE data collection within AL has the potential to improve the understanding of disease processes and epidemiological factors, which, in turn, would allow RCTs to become more efficient.

• National Institute for Health and Care Excellence (NICE), UK is on the way to setting up and standardizing the guidelines for evidence generation.

Fig. 1 (b) After an initial license, number of treated patients grow slowly due to restrictions and patient experience is captured to contribute to real-world information

Drivers of AL 3

• Patient expectations
• Demand for timely access to new technology with emphasis on unmet medical need

• Emerging science
• Fragmentation of treatment populations and early disease interception

• Healthcare systems under pressure
• Rise of payer influence

• Pharma investors under pressure
• Sustainability of drug development

Enablers of AL 3

• Improved understanding of diseases and medical conditions
• Better knowledge management
• Innovative clinical trial designs
• Rapid learning systems in the healthcare environment
• Feedback from patients: understanding acceptability and uncertainty
• Prediction, monitoring and targeted prescribing

Pilot project on APs approach

• European Medicines Agencies (EMA) launched a pilot project to explore the APs approach in 2014.4

• This project explored a scientific concept of medicines development and data generation intended for medicines that address unmet medical needs.

• Under the programme, EMA invited companies to submit ongoing medicine development programmes (MDPs) that met the pre-defined criteria (Fig. 2).

Outcomes of AP pilot project

• The AP pilot project focused on a flexible life-cycle development of medicines that can plausibly address an unmet medical need of a defined population.

• AP would encourage the multi-stakeholder dialogue, regulators, interested HTAs, healthcare professionals and patients to discuss a product development strategy for such medicines.

• An agreement between stakeholders can be reached on a prospective approach to evidence generation throughout the lifespan of these medicines, with a view to optimize and align their requirements as much as possible.

• AP can support MDPs in therapeutic areas where evidence generation is challenging, such as infectious diseases, Alzheimer’s disease, degenerative diseases, and rare cancers.

• The project suggests the creation of common evidence base to address both regulators and HTA needs while consulting all the concerned decision-makers on their respective requirements.

• An appropriate and prospective planning incorporates the intended multiple stakeholder’s requirements to avoid the need for additional studies later in the development stage.

• AL-based regulatory framework would offer robust mechanisms to ensure close monitoring of a medicine’s benefits and risks, once it is in the market, and a prompt regulatory reassessment and action can be taken if needed.

• AP concept is not applicable to all the medicines but applies to the medicines that would possibly be useful to a patient population with an unmet medical need and where the criteria for AP fits in (Fig. 3).

CHALLENGES AND FUTURE ASPECTS

• The participation of patients needs to be increased to accelerate the APs, support enrolment in trials and registries and provide insights on feasibility and ethical aspects.

• Inputs from healthcare professionals should be sought on the feasibility of implementing patient registries in clinical practice by having controls on prescription.

• The lack of commonly accepted and methodologically sound strategies of RWE generation and collection remains a challenge to support the successful implementation of AP approaches.

• The participation of decision making organizations that are responsible for pricing and reimbursement on the basis of HTA recommendations is essential.

• The decision makers input on design, acceptability and feasibility of adaptive pricing strategies, and payers input on the principles and feasibility of such schemes would be important.

• The life-span approach to licensing, coverage and learning from real-world experience as supported by APs.

Fig. 2 EMA’s pre-defined criteria for selection of participating companies for ongoing MDPs

Fig. 3 Criteria of AL approach for a product

References


