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EMA hosts workshop on adaptive pathways

Broad range of stakeholder questions addressed

The European Medicines Agency (EMA) has hosted a workshop with stakeholders to discuss adaptive pathways, an approach to medicines development that aims to facilitate access to medicines that address patients' unmet needs.

The adaptive pathways approach is not a new regulatory route but rather one that makes use of existing legislative and regulatory tools in a more efficient way.

- The adaptive pathways approach is intended only for medicines expected to have a significant clinical impact in patient populations with high unmet needs.
- It involves working with the full range of relevant stakeholders from very early in the development process to proactively plan the most appropriate ways of obtaining evidence.
- It identifies the appropriate tools to generate that evidence. This may mean making more use of observational (real world) data in addition to randomised controlled trials, especially where these trials are not adequate.
- It uses a stepwise approach, permitting approval of medicines in small, tightly defined populations until more data are available.
- The standards of regulatory approval remain unchanged.

In July 2016, EMA published a report on a pilot project to explore how the adaptive pathways concept can be applied in practice and developed guidance for companies considering using the adaptive pathways approach. While some stakeholders have supported adaptive pathways for its potential benefits to patients, others have voiced concerns about the possible impact on standards of evidence for medicines approval in the EU.

EMA's Executive Director, Professor Guido Rasi, who opened the workshop, recognized the considerable interest the adaptive pathways concept has generated among key stakeholders and civil society at large.

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“EMA welcomes the contributions of stakeholders in these discussions,” Professor Rasi said. “We will continue to listen and learn from you to make best use of the regulatory tools we have in the interest of patients.”

The workshop, organised by EMA and the European Commission (EC), tackled important questions arising from the adaptive pathways pilot, including how best to address patients’ needs and expectations; how to generate appropriate data to aid medicines evaluation; and how to ensure that high standards for approval in the EU continue to be met.

Managing uncertainty

All stakeholders – regulators, health technology assessment (HTA) bodies, payers, healthcare professionals and patients – live with some uncertainty, and regulatory decisions routinely take account of the uncertainty in the evaluation of the benefits and risks of medicines.

The adaptive pathway approach aims to better manage the uncertainties for medicines intended for patients with high unmet needs. For this group of patients, the need for treatment must be considered alongside the available evidence and the possibility of obtaining further data after approval in cases where full data are not yet available.

The adaptive pathways approach offers an opportunity to reduce uncertainty over the product life-cycle by planning better from the very beginning. Better planning and appropriate study design will allow medicines to be provided faster and more efficiently to a suitably restricted patient group.

Early collaboration between companies, regulators and HTAs is essential to achieve these objectives. Involvement of patient representatives and healthcare professionals can also help manage expectations of what a medicine can achieve and ensure that outcomes are relevant to end users.

It is also important that uncertainties and the evidence in the approval of medicines continue to be communicated to patients and healthcare professionals.

The real world data challenge

The use of real world data in the evaluation of medicines was a main point of discussion at the workshop. Real world data, including observational data, are collected outside the controlled environments of randomised clinical trials, often for purposes other than evaluating a particular product (e.g. electronic health records).

Randomised clinical trials remain central to the evaluation of medicines. The question with respect to adaptive pathways is how real world data can best support clinical trial data in cases when further information is necessary and cannot be obtained from clinical trials or when the trials themselves are difficult to run, or cannot fully answer the questions raised.

Concerns were raised about how real world data will be used in practice, with some attendees questioning the reliability or usefulness of these data, particularly in evaluating treatment effects.

The workshop discussed both the limitations (e.g. bias and problems with design) and strengths of observational studies (e.g. patient populations that reflect real world use). A commitment to transparency about the results – an area where EMA has led the way – is key to building trust in these techniques.

Collaboration with stakeholders

The workshop also discussed the role of organisations, such as HTA bodies and payers, which traditionally evaluated medicines post-authorisation in order to make decisions about price and reimbursement, thus determining the real uptake of any medicinal product. Experience to date with conditional marketing authorisations show that HTA bodies need to be involved early in development if more medicines are to meet HTA criteria and be made available to patients in a timely fashion. All stakeholders involved in the adaptive pathways pilot project stressed the value of the 'safe harbour' dialogue, in which participants can freely raise concerns at the start, in shaping the development process.

While views of payers differ on the potential benefits of adaptive pathways, there is broad agreement that adaptive pathways will apply only to limited number of products and that there is a need for appropriate exit strategies (i.e. to stop use of medicines when confirmatory data are not forthcoming) and measures to be put in place to control costs.

Patients' representatives have been involved in the adaptive pathways pilot, and workshop participants agreed on the importance of continued early input for this key stakeholder group.

Dr Andrzej Rys of the EC's Directorate-General for Health and Food Safety (DG SANTE) praised the open and constructive way in which workshop was conducted.

"Collaboration is key," he said. "We all want to make sure that patients in the EU get access to safe, effective and affordable medicines."

EMA and the EC will take stock of the different views expressed at the workshop to determine what actions need to be taken over the coming months. EMA will continue to build on the experience gained from the adaptive pathways pilot and will provide updates regularly and continue dialogue with all of stakeholders through various forums.

A full report of the workshop is currently being prepared and will be published on EMA's website.

The workshop was attended by representatives from patients' and healthcare professionals' organisations, pharmaceutical companies, HTA bodies and payers, national competent authorities (NCAs), the European Ombudsman, the European Commission and staff from EMA.

The list of participants, slide presentations and a video recording of the workshop will be made available on EMA's website.