

Adaptive pathways: Why are we cautious?

In order to improve access to medicines, the European Medicines Agency (EMA) has recently been merrily pushing towards speeding up marketing authorisation for new medicines. Several projects have been launched: GetReal, ADAPTSMART or Adaptive Pathways. All of these pave the way for a possible new model for drug marketing authorisation. Without wanting to throw out the baby with the bath water, AIM's members express concerns and call for caution. Why are we cautious?

1. Because early access to the market does not guarantee benefit for the patients

Early access of a drug to the market can be beneficial for the patients, especially in case of rare diseases. However, because a new active component looks promising and is expected to bring serious added value doesn't mean (unfortunately) that that will actually be the case. The risk-benefit ratio, as well as, efficacy and side effects are crucial data to have in mind before authorising, prescribing, swallowing a pill or injecting a new substance.

To ensure that early access is beneficial for patients, we must clearly define what high unmet medical needs are and, as requested by the Council in its conclusions of June, we must clarify the exact conditions for the selection of innovative medicinal products in early marketing authorisation schemes.

2. Because the pre-marketing procedure is essential to ensure safety and demonstrate efficacy

Pre-marketing authorisation is a minimum standard that unfortunately still does not always prevent dangerous or ineffective drugs being put on the market. There are many examples of medicines which presented early data promising enough to be considered for approval, but were subsequently proven to be ineffective or unsafe in phase III trials and consequently never licensed. As an even worse example, the drug *Vioxx* was withdrawn from the market five years after marketing authorisation and successful clinical trials because of severe side effects causing heart attacks and strokes. That is why pre-marketing procedure should be reinforced and not weakened. Furthermore, early marketing schemes should only be used in case of high unmet medical need.

3. Because clinical trials are safe harbours for patients to test new drugs

Patients enrolled in clinical trials are monitored and taken care of. Experimental use and testing a drug on thousands of patients in real life first limits the possibilities of monitoring and assessing carefully the safety and efficacy. Secondly, in case of severe side effects, it is not yet clear who will be liable for the damages.

Furthermore, outside clinical trials, patients may not correspond to the inclusion criteria and therefore encounter additional risks of mortality and morbidity due to unknown interactions. Another concern is whether patients will be advised that they are prescribed a drug that hasn't proven efficacy and positive risk-benefit ratio yet.

4. Because it is difficult to withdraw or delist a drug that was offered to patients

Once a drug, as ineffective as it can turn out to be, is offered to a patient, we can expect that withdrawing it from the market won't be well received by patients. In such a situation, pressure will be put on authorities to continue granting access even with missing scientific evidence of efficacy.

5. Because there are already existing possibilities to speed up the marketing of promising drugs in case of high unmet medical needs

There are alternatives to the normal marketing authorisation procedure currently available. They must be further explored. These are: accelerated assessment, conditional marketing authorisation and compassionate use.

6. Because it has not been properly investigated if and how the current standard procedure unnecessarily delays market access of innovative pharmaceuticals

Before starting the discussion about how to shape a process of adaptive pathways, it is first important to investigate the functioning of the current mechanisms. So far, that investigation has not been properly completed.

7. Because post-marketing commitments might not be honoured by the different parties involved

A drug assessment system based on post-marketing evaluation raises many issues such as the quantity and reliability of voluntary and spontaneous reporting of adverse events, the poor quality of reports and underreporting and the lack of willingness of patients and doctors to participate in collection of "real world evidence".

8. Because early access to the market might not be the best solution to foster R&D in pharma

Early access to the market is expected to foster innovation. However, it doesn't mean that research will be directed towards public health priorities as it is desired. We think that other mechanisms could be better suited to foster R&D to address high unmet medical needs, such as directing public funding for R&D towards public health

priorities and ensuring that drugs that tackle high unmet medical needs are well rewarded.

9. Because dialogue about adaptive pathways requires political steering and not only dialogue between industry and the European Medicine Agency

The pharmaceutical industry is, together with the European Medicines Agency, highly involved in the development of the Adaptive Pathways approach, through projects like ADAPT SMART, GetReal, etc. More political guidance to this development is needed, with all stakeholders equally involved in the process.

10. Because access to medicines is not only about fast market authorisation, but more about pricing and reimbursement of drugs

A drug that is too expensive to be available to those in need is useless. Marketing of a multitude of new expensive drugs, whose added value remains to be proven, carries the risk of a heavy financial burden for Member States and reduced access to healthcare for patients. At EU level a discussion is needed about how to increase transparency of pricing, efficacy and effectiveness of a drug as well as transparency of clinical trials results. In addition, it is necessary to reflect on what a fair price is for new pharmaceuticals entering the market and how prices could be set under the adaptive pathways scheme considering that faster authorisations reduce the availability of data at the moment of market access.