

The Consumer Voice in Europe

A FAST-TRACK APPROVAL FOR NEW MEDICINES – PATIENT SAFETY AT RISK?

BEUC position on adaptive pathways



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Why it matters to consumers

It is essential for consumers to have timely access to safe treatments. Regulators are now exploring a new approach called “adaptive pathways” to accelerate the approval of some new medicines. We are concerned that this new fast-track procedure can expose patients to unnecessary health risks. That is because these medicines would be put on the market before there is complete information about their safety.

Summary

In January 2014 the European Medicines Agency (EMA) launched a pilot project called “adaptive pathways”. The goal of the project was to improve timely access for patients to new medicines, by gathering evidence through real-life use to supplement clinical trials data. The eligible medicines would be put on the market for a subgroup of patients suffering from a disease for which there is no existing treatment. The use of such medicines would gradually be expanded based on additional data generated after the product has been placed on the market.

It is key for patients to have timely access to medicines, however BEUC considers that **sidestepping the standard benefit-risk assessment for licensing a medicine should only be done for a very limited range of medicines and only when there is no other available alternative.**

In particular we are concerned about the following:

1. The scope of the project is not clear

Originally, “adaptive pathways” was presented as a pilot project whose objective was to give patients timely access to treatments in the case of an unmet medical need. However, its scope and the criteria to select the products that can fall under the scheme remain unclear. Moreover no definition of unmet and of high medical needs has been provided yet.

2. The monitoring of medicines’ safety and efficacy is difficult and not fully operational

Medicines approved through expedited programmes are difficult to monitor once they enter the market. Despite the fact that post-marketing studies are required by law, pharmaceutical companies’ compliance with post-marketing obligations is very poor. The concept of adaptive pathways builds on the use of registries to gather real life data, while at present patients registries are not fully operational and it is still not possible to guarantee that they are an effective tool to monitor the use of medicines.

3. The information provided to patients needs to be adapted

Consumers implicitly trust the regulatory system to ensure that benefits of licensed medicines prevail over their risks. The majority of them overestimate the benefits of treatments while underestimating their harm. It can then prove very difficult to ensure that patients receive appropriate information about the higher risks associated with medicines approved through faster procedures.

4. The safeguards for patients in case of harm need to be upgraded

Due to greater uncertainty about the safety of medicines approved under an early access scheme, patients will take health risks comparable to participants in clinical trials, but without the same level of guarantee in case of harm.

5. Cost and reimbursement conditions are not clear

There is no evidence that adaptive pathways will help lower the price of new medicines. Similar concerns exist for the 'managed entry agreements'. They are being explored at national level but more evidence is needed to understand whether these schemes actually improve access to medicines and at what cost.

6. The lack of a transparent public debate

Since the launch of the project in 2014, little and contrasting information has been available and the public health community has not been sufficiently involved in the debate.

7. The rationale of adaptive pathways needs to put patients first

Faster revenues for pharmaceutical companies cannot be the driver of any early access scheme. Patients' safety should never be undermined because of commercial considerations.

8. The added value of adaptive pathways compared to other schemes is unclear

The EU pharmaceutical legislation already includes several provisions that allow patients to get medicines through faster approvals. Therefore, the added value of this additional early access scheme is unclear.

Introduction

In January 2014 the European Medicines Agency (hereafter EMA or Agency) launched a pilot project on adaptive licensing, subsequently renamed as “adaptive pathways”¹. The project is intended to improve timely access to medicines for a selected number of patients suffering from diseases for which there is no available treatment² (so called “unmet medical need”). The use of these medicines would gradually be expanded based on additional data generated after the products are placed on the market.

Over the last two years, very little information has been available on this pilot project. The Agency was expected to publish an interim report in the first quarter of 2016 but the publication has been delayed. Therefore, to date, **most of the concerns and questions** we raised in the [position paper](#) published in December 2015 **remain unanswered**, namely:

1. What is the scope of the pilot project?

Originally, adaptive pathways aimed to give patients timely access to treatments that “*promise to address serious conditions where there is an unmet medical need, especially when there are no satisfactory alternative therapies*”³. However, since its launch, EMA communications on the scope of the project have been vague and contradictory, and it is not clear if “unmet medical need” is a key criterion for the selection of medicines that can undergo this fast-track procedure. In its documents the Agency also refers to the similar concept of “high medical needs” but does not provide a clear definition of any of the two, despite they both constitute the basis for adaptive pathways⁴.

BEUC considers that sidestepping the standard benefit-risk assessment for licensing a medicine should only be done for a very limited range of medicines, in duly justified circumstances and only when there is no other available alternative. In other words, adaptive pathways, as any other faster approval procedure⁵, should be the exception rather than the rule.

Fast track approval procedures for new medicines should only be used for a very limited range of medicines and only when there is no other available alternative.

¹ For your information, the terms ‘staggered approval’, ‘progressive licensing’, and ‘adaptive licensing’ have been used, often interchangeably, to describe the same broad concept. More recently, the term ‘Medicines Adaptive Pathways’ (MAPs) or ‘Medicines Adaptive Pathways to Patients’ (MAPPs) is discussed as potentially more appropriate terminology.

² http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/03/WC500163409.pdf

³ See ref 2.

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http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp&mid=W00b01ac05807d58ce

⁵ Such as conditional marketing authorization and compassionate use.

Also EU health ministers have indicated in the “Council Conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States”⁶ adopted on 17 June 2016 that *“the exact conditions for the inclusion of innovative and specialised medicinal products in the existing schemes of early marketing authorisation could be further clarified in order to improve transparency, to ensure a continuous positive benefit risk balance of medicinal products put on the market under special conditions and to focus on medicinal products of major therapeutic interest for public health or to meet unmet medical needs of patients”*.

Some regulators alluded to the fact that adaptive pathways could go beyond its initial explorative goal and might introduce a new paradigm applicable to all new medicines⁷. Questions also arise as to whether such approach is in line with the existing EU legislation⁸.

2. How will medicines safety and efficacy be monitored?

2.1. Poor compliance with post-marketing studies

Some studies indicate that the current system does not promptly react to ineffective medicines, not even when the use of a drug is associated with increased mortality⁹. Withdrawal of products suspected of adverse reactions has not improved over the last 60 years¹⁰. This is of particular concern taking into account that adverse drug reactions (ADRs) cause a considerable amount of morbidity and mortality. According to the European Commission, approximately 5 % of all hospital admissions are caused by ADRs and ADRs are the fifth most common cause of hospital death¹¹.

In case of medicines approved through expedited programmes, **post-marketing controls raise even more concerns** because shifting the burden of the proof from pre-marketing to post-marketing authorisation means that regulators will have to rely on pharmaceutical companies to submit additional data in order to complete the profile of the medicines.

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http://dsms.consilium.europa.eu/952/Actions/Newsletter.aspx?messageid=5902&customerid=31372&password=enc_3167363863553131746E5932_enc

7 - H-G Eichler et al. 2012, Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval, Volume 91 n. 3. www.nature.com/cpt

- <http://efpiamapps.eu/adaptive-licensing-is-a-new-paradigm-for-everyone/>

- http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/03/WC500163409.pdf

8 Namely the pharmaceutical Directive 2001/83/EC, the EU Regulation on clinical trials n. 536/2014, the EMA Regulation n.726/2004 and the EU pharmacovigilance Directive 2010/84/EU

9 Darrow et al. New FDA Breakthrough-Drug Category —Implications for Patients. *New England Journal of Medicine* 2014;370:1252-8. - Fain et al. The food and Drug Administration Amendments Act and Post-marketing Commitments. *JAMA* 2013; 310 (2): 202-4.- Moore and Furberg. “Electronic Health Data for Post-marketing surveillance: a vision not realized” *Drug Saf* 2015; 38:601–610. - Onakpoya et al. Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature. *BMC Medicine* (2016) 14:10. - Seife. Research misconduct Identified by the US Food and Drug Administration. Out of sight, out of mind, out of the Peer Reviewed Literature. *JAMA Intern Med.* 2015; 175(4):567-577.

10 Onakpoya IJ, Heneghan CJ, Aronson JK. Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature. *BMC Medicine.* 2016;14:10. doi:10.1186/s12916-016-0553-2. ; Moore and Furberg. “Electronic Health Data for Postmarketing surveillance: a vision not realized” *Drug Saf* 2015; 38:601–610.

11 European Commission. Proposal for a regulation amending, as regards pharmacovigilance of medicinal products for human use. Regulation (EC) No 726/2004. Impact assessment. 2008. Available at: http://ec.europa.eu/health/files/pharmacos/pharmpack_12_2008/pharmacovigilance-ia-vol1_en.pdf.

Evidence from Canada's early access policy shows that there is little oversight of manufacturers' duties to confirm medicines' clinical benefits in post-marketing studies. Studies are conducted for some medicines in as early as 1.4 years after authorisation, while for other medicines these commitments were still unfulfilled after seven years¹².

In the United States, the General Accountability Office (GAO) was asked to provide information about the Food and Drugs Administration (FDA) expedited programmes and the post-market monitoring of the medicines approved through these procedures during 2006-2014. The report¹³ portrays quite an alarming picture where FDA lacks reliable and readily accessible data on tracked safety issues and post-market studies. In practice, once a product enters the market, pharmaceutical companies fail to provide data over its use and therefore prevent regulators from assessing its real safety and effectiveness.

In the EU, the average time to conduct post-marketing studies attached to conditional marketing authorization is 4 years. There are delays or discrepancies in the fulfilment of these obligations in more than one third of the authorization procedures.

The EU is not an exception in this respect and also EU Health ministers recently noted that "*the post-market compliance with certain obligations for marketing authorization holders is not always optimal, which may cause that independent research data and information from patient registries are*

not structurally generated, collected and made available for research and proof of effectiveness and safety" ¹⁴. Two recent analyses¹⁵ looked into the follow-up of post marketing studies of all medicines that were conditionally authorised in Europe and found out that the average time to address the specific obligations indicated in the conditional marketing authorisation was four years. In addition, there were delays or discrepancies in the fulfilment of these obligations in more than one third of the authorisation procedures, which allowed medicines with limited efficacy and safety information to be marketed for several years, for almost as long as their patents lasted¹⁶.

Against this background we are particularly concerned because a key component of the adaptive pathways concept is precisely to replace part of the data gathering during clinical trials with the collection of "real world evidence data" after the product has been placed on the market. In other words, it aims at collecting information on the safety/efficacy of a medicine through the response that patients will progressively provide by taking it.

¹² Lexchin, J. (2007). Notice of compliance with conditions: a policy in limbo. *Healthcare policy*, 2(4), 114.

¹³ United States Government Accountability Office, DRUG SAFETY, FDA Expedites Many Applications, But Data for Postapproval Oversight Need Improvement, December 2015, <http://gao.gov/assets/680/674183.pdf>

¹⁴

http://dsms.consilium.europa.eu/952/Actions/Newsletter.aspx?messageid=5902&customerid=31372&passwd=enc_3167363863553131746E5932_enc

¹⁵ Banzi R, Gerardi C, Bertele' V, Garattini S. Approvals of medicines with uncertain benefit-risk profiles in Europe. *Eur J Intern Med* 2015; 26: 572-84; and Hoekman, J., Klamer, T. T., Mantel-Teeuwisse, A. K., Leufkens, H. G. M., and De Bruin, M. L. (2016) Characteristics and follow-up of postmarketing studies of conditionally authorized medicines in the EU. *Br J Clin Pharmacol*, doi: 10.1111/bcp.12940.

¹⁶ Banzi R, Gerardi C, Bertele' V, Garattini S. Approvals of medicines with uncertain benefit-risk profiles in Europe. *Eur J Intern Med* 2015; 26: 572-84

2.2. Reliance on patients' registries that, in reality, are not yet fully operational

The concept of adaptive pathways builds on the use of registries to collect real life data and monitor the small group of patients for which the medicine has been authorised.

Registries are expected to contain information such as the natural history of the disease, the adherence to treatment, its effectiveness, long-term outcomes, drug utilisation, the time to treatment failure and many others.

However, patient's registries are not fully operational yet. EMA launched a pilot in 2015 since pharmaceutical companies and regulators were found to face many challenges in using existing registries or establishing new ones. These included a lack of coordination between initiatives at national and international levels, harmonised protocols, scientific methods and data structures, data sharing and transparency and sustainability. EMA is still collecting information and therefore we believe that relying on registries to get real data would be risky and the Agency might not obtain the data they need for the assessment of medicines safety¹⁷. Moreover the possibility to sustain the costs of registries in the short and long term remains uncertain. This means that at present **it is not possible to guarantee that medicines approved under adaptive pathways are used only in the small group of patients they have been authorised for and are appropriately monitored.**

2.3. Difficult withdrawal of unsafe and ineffective medicines

Another important consideration arises when fast-track approved medicines turn to be ineffective or unsafe. In the current system, it is much more difficult for regulators to remove a drug from the market than to prevent its marketing in the first place. Even when evidence proves a medicine's high risks or doubtful efficacy, withdrawing it from the market can be a lengthy and complicated process, often faced with opposition from patients groups¹⁸.

Although the pharmacovigilance legislation explicitly allows regulatory authorities to withdraw marketing authorisations when companies fail to conduct post-marketing studies¹⁹, this has never happened. Therefore, we call on **regulators to better monitor and address the deficiencies of the current system rather than considering further early access schemes.**

¹⁷

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000658.jsp&mid=Wc0b01ac0580961211

¹⁸ "Adaptive licensing" or "adaptive pathways": Deregulation under the guise of earlier access, Prescire, October 2015, http://english.prescire.org/Docu/DOCSEUROPE/20151019_AdaptiveLicensing.pdf

¹⁹ Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012 amending Directive 2001/83/EC as regards pharmacovigilance". Official Journal of the European Union, 27 October 2012; L299/1-L299/4. "Regulation (EU) No 1027/2012 of the European Parliament and of the Council of 25 October 2012 amending Regulation (EC) No 726/2004 as regards pharmacovigilance" Official Journal of the European Union, 27 October 2012; L299/1-L299/4.

3. How will patients be informed?

Consumers trust the current regulatory system to ensure that the benefits of medicines they use prevail over their risks. A recent analysis reviewing all studies that have assessed patients' expectations of the benefits and/or harms of any treatment, found that the majority of people overestimate the treatments' benefits and underestimate their potential harm²⁰.

Another research has also revealed important decision-making deficiencies in patients affected by serious diseases when compared with healthier patients. The former are less likely to retain information discussed during the informed-consent process²¹.

In general - as confirmed by the very limited people understanding²² of the black symbol to identify medicines under additional monitoring which was introduced with the new pharmacovigilance legislation in 2010 - increasing patients awareness of the higher risks associated with certain medicines is proven to be very difficult. This puts greater responsibility on the prescriber physicians who are considered the most reliable source of information about medicines²³.

Accordingly, adaptive pathways raises concerns about effective patients' awareness of the higher risks associated with medicines approved under this approach. Patients might

Patients suffering from severe diseases are less likely to retain information about the risks they are going through.

believe that medicines approved through adaptive pathways have their benefits and risks assessed the same way as medicines approved with standard procedures. They might not be

aware that further data will be needed to confirm or inform their safety and efficacy. If the information is not adequately provided, patients could end up being exposed to health risks they did not understand they were taking. Furthermore, we discard the idea that patients should become "*more sanguine with level of uncertainty*"²⁴ especially considering their vulnerable situation and the level of expectations they naturally have with regard to medicines.

4. How will patients be protected in case of harm?

Due to less testing and greater uncertainty, patients using medicines approved under the framework of adaptive pathways will take health risks comparable to participants in clinical trials. However, they are not guaranteed that they will be afforded the same safeguards, such as damage compensation.

²⁰ Hoffmann TC, Del Mar C. Patients' Expectations of the Benefits and Harms of Treatments, Screening, and Tests: A Systematic Review. JAMA Intern Med. 2015;175(2):274-286. doi:10.1001/jamainternmed.2014.6016.

²¹ Schaeffer, Monica H.; Krantz, David S.; Wichman, Alison; Masur, Henry; Reed, Eddie; Vinicky, Janicemarie K. The Impact of Disease Severity on the Informed Consent Process in Clinical Research. American Journal of Medicine. 1996 Mar; 100(3): 261-268.

²² EU Survey Report conducted within the framework of the pharmacovigilance legislation. SCOPE WP6, Survey Report, Patient and Consumer Consultation, 2016

²³ See above

²⁴ Eichler H-G et al. "From Adaptive Licensing to Adaptive Pathways: Delivering a Flexible Life-Span Approach to Bring New Medicines to Patients" Clinical Pharmacology & Therapeutics 2015; 97 (3): 234-246

In fact, under the adaptive pathways scenario, communication “*may lead to more participation of patients in defining acceptable thresholds of risk-tolerance as well as acceptable levels of uncertainty for each drug*” (...) that “*may reduce liability litigation in some circumstances*”²⁵. In

Consumers will be deprived from the possibility to seek for compensation in case of harm

addition, “*a prohibition on product liability suits, except for gross negligence, during the initial marketing period*” might apply to some ‘early access’ medicines²⁶. In other words, consumers will be deprived from the possibility to seek for compensation in case of harm, as the higher risk will be communicated to him/her beforehand. We believe adaptive pathways patients should not be considered as guinea pigs and should benefit from the same safeguards as clinical trial participants.

5. How will these medicines be financed?

Unaffordable medicines are one of the most problematic issues consumers²⁷ and Member States are facing in the pharmaceuticals area. Some expect this faster access scheme will contribute to lowering the price of new medicines²⁸. However, there is no concrete evidence to back this assertion. The main regulators supporting this approach acknowledge that price-setting for medicines approved through adaptive pathways will not be easily to determine. Indeed, in the adaptive phase payers will likely be reluctant to pay for a medicine whose safety and efficacy have not been fully demonstrated²⁹.

There is no concrete evidence that faster will mean cheaper.

Unsurprisingly, both some payers³⁰ and some Health Technology Assessment bodies³¹ have expressed many concerns and called for a cautious approach with regard to adaptive pathways, in that without data to assess the effectiveness of a medicine, they would not

be in the position to help Member States setting the right price. A similar pattern could be seen in the so-called “managed entry agreements” or risk sharing schemes. They are deals between public funders and drug companies to finance medicines that hold promise for treating certain conditions. These deals can entail agreements for public authorities to pay the drug manufacturer depending on the amount purchased or how well the medicine worked.

²⁵ Eichler, H. G., Oye, K., Baird, L. G., Abadie, E., Brown, J., Drum, C. L., & Hirsch, G. (2012). Adaptive licensing: taking the next step in the evolution of drug approval. *Clinical Pharmacology & Therapeutics*, 91(3), 426-437.

²⁶ See ref 24

²⁷ [Spanish households now pay 58% more for their medicines in than in 2010, according to a consumer survey in 2015 by BEUC's member OCU.15 39% of Portuguese consumers could not afford a medicine they needed in 2014, shown in a survey by BEUC's member DECO Proteste.](#)

²⁸ See ref. 24 and 3

²⁹ Transcript of interview with Professor Luca Pani, Director General of the Italian Medicines Agency (Agenzia Italiana del Farmaco – AIFA), April 2015, available at <http://vitaltransformation.com/wp-content/uploads/2015/04/Luca-Pani-Full-Interview-Transcript-April-2015.pdf>

³⁰ <http://aim-mutual.org/wp-content/uploads/2016/06/Adaptive-pathways-why-is-AIM-cautious.pdf>

³¹ Real world data – an asset for benefit assessments? How can registries and routine data contribute? Introductory and closing speeches by Jürgen Windeler, IQWiG*, 27-28 November 2015 available at https://www.iqwig.de/download/Introductory_and_closing_speeches_by%20Juergen_Windeler.pdf

Concerns have been raised about the potential high administrative costs, lack of transparency, conflicts of interest, the danger that public payers end up funding part of private drug development³² and the misleading effect these schemes have on the external reference pricing (ERP) system³³. Currently, there is little evidence about whether these schemes actually improve access to medicines and at what cost³⁴.

6. Has the public health community been sufficiently involved in the debate on adaptive pathways?

Since the launch of the pilot project in January 2014, little and patchy information has been available. Some discussions around it have been carried out with the Member States in the European Commission' Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) and in other meetings organized at the EMA, where only a selected range of stakeholders was invited³⁵. According to EMA the project has also been discussed in scientific conferences and in scientific publications however, given the significant implications of adaptive pathways on public health, we regret that the wider public health community, including consumers' organizations, public health NGOs and health care professional organizations have not been actively involved. In particular, we wished that the EMA platforms for exchange with patients and consumers organisation (Patients' and Consumers' Working Party-PCWP) and with health care professionals organisations (HCPWP) could have been consulted more extensively since the very beginning. We are however glad that after reiterated requests for a public debate, EMA is now planning to host a conference on this topic in autumn.

All parties have to be involved in the project and this can only be achieved through an open and transparent dialogue.

7. Adaptive pathways – which added value and for whose benefit?

The pharmaceutical industry and some regulators claim that adaptive pathways “*may help companies stagger clinical development costs, generate revenue earlier and remove some risk from Research and Development*”³⁶. In their views this is because this approach is expected to go beyond the “*elaborate super-structure*”³⁷ of the clinical trials, which in their views drives much of the current Research and Development (R&D) spending.

³² Adamski, J., Godman, B., Ofierska-Sujkowska, G., Osińska, B., Herholz, H., Wendykowska, K., ... & Gustafsson, L. (2010). Risk sharing arrangements for pharmaceuticals: potential considerations and recommendations for European payers. *BMC health services research*, 10(1), 153. <http://www.biomedcentral.com/content/pdf/1472-6963-10-153.pdf>

³³ The Eternal Price Referencing (EPR) is defined as « the practice of using prices of a medicine in one or several countries to derive a benchmark or a reference price of a medicine in a given country ». http://ec.europa.eu/health/systems_performance_assessment/docs/pharmaproductpricing_frep_en.pdf
Espín, J., Rovira, J., & García, L. (2011). Experiences and impact of European risk-sharing schemes focusing on oncology medicines. *Brussels: Commissioned by the European Commission, Directorate-General Enterprise*.
<http://whocc.goeg.at/Literaturliste/Dokumente/FurtherReading/Experiences%20and%20impact%20of%20European%20risk-sharing%20schemes.pdf>

³⁴ Espín et al.

³⁵

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2016/04/event_detail_001_281.jsp&mid=WC0b01ac058004d5c3 _Registration by invitation only

³⁶ See ref. 3

³⁷ See ref. 3

We believe that these inappropriate assertions fail to acknowledge the importance of clinical trials in assessing the safety and efficacy of medicines.

Ensuring that patients have timely access to safe and innovative medicines has always been a core objective for BEUC and its Members. **Patients need to receive the treatments they need on time, with the highest possible degree of safety and efficacy.** However, in some cases cures do not yet exist, or the disease has reached a life-threatening stage which leaves no hope to patients. For these exceptional cases, the EU pharmaceutical legislation already foresees several provisions to foster patients' early access to new medicines³⁸. These are:

- a) **Accelerated assessment:** reduces the timeframe for the review of an application for marketing authorisation for medicines of major interest for public health and therapeutic innovation.
- b) **Conditional marketing authorisation:** this scheme grants marketing authorisation before complete data are available. The benefit of immediate availability outweighs the risk of less comprehensive data than normally required. The authorisation is granted conditional to further data that the industry has to provide afterwards. This procedure is available for medicines aimed at treating, preventing or diagnosing seriously debilitating or life-threatening diseases.
- c) **Compassionate use:** allows the use of an unauthorized medicine for patients. Under strict conditions, products in development can be made available to groups of patients who have a disease with no satisfactory authorised therapies and who cannot enter clinical trials. The EMA provides recommendations for these products, but these do not create a legal framework, since compassionate use programmes are coordinated and implemented by Member States, which set their own rules and procedures.

Overall, the added value of adaptive pathways in relation to the current early access schemes remains unclear and we question the ultimate goal of this project.

Moreover, in March 2016 EMA also launched the Priority Medicines (PrIME) scheme "to enhance support for the development of medicines that target an unmet medical need"³⁹. The difference and interactions between PRIME and adaptive pathways remain unclear.

BEUC believes that "early access schemes" should always be the exception rather than the rule. **Programmes should be limited to subsets of medicines to treat genuine unmet medical needs.** Such limitation is essential as patients using 'early access' medicines are exposed to higher health risks with less safety and efficacy data when the medicines enter the market.

³⁸

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000856.jsp&mid=WCOB01ac058096f643

³⁹

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000660.jsp&mid=WCOB01ac058096f643

In 2008-2010, in the context of the revision of the EU pharmacovigilance legislation, a proposal put forward by the Commission tried to expand the “conditional marketing authorization” to all new medicines, not just for those that treated unmet medical needs. At the time, the aim of such proposal was to reduce R&D costs and provide pharmaceutical companies with a faster return on investment. Thanks to the opposition of the European Parliament and of the Member States the proposal was rejected. **Any attempt to deregulate the current legal framework needs to be carried out in a transparent manner and not through initiatives aimed at circumventing democratic processes.**

Conclusions

Adaptive pathways and other early marketing authorization procedures must remain the exception rather than the rule and they should be used only when there is no other available alternative. Accordingly, adaptive pathways should be used only for medicines that respond to unmet medical needs. This concept must be clearly defined, along with the extent to which the products fulfill an unmet need and the strength of the evidence.

A proper post-marketing surveillance must be guaranteed. Today, pharmaceutical companies poorly provide the post-marketing studies requested after the medicines have entered the market. This portion gets higher for medicines approved under conditional marketing authorisations. Additionally, not all Member States have registries to follow up the group of patients taking the medicines. Putting them in place might require additional financial efforts.

There is no evidence that adaptive pathways will contribute to lowering drug prices. We believe that any new initiative in this field should address the challenge of the affordability of medicines in Europe.

Finally, **a more transparent debate** on this sensitive issue should be assured. All actors have to be involved in an open dialogue before any further step is made.

ENDS