The Consumer Voice in Europe

PUBLIC CONSULTATION ON THE REVISION OF PHARMACEUTICAL LEGISLATION

BEUC response

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Why it matters to consumers

Medicines are crucial when we are sick or suffer from a long-term condition, so we need to have easy access to them. Unfortunately, there might be medicine shortages, or medicines that are not reimbursed to consumers because of how expensive they are. Both of these problems challenge our healthcare system. In addition, new medicines don't always work better than existing treatments. These problems should be addressed by amending the EU pharmaceutical legislation and adopting new measures in relation to medicines' development, authorisation, availability and affordability.

Summary

The revision of the EU general pharmaceutical legislation must improve access to medicines across Member States. The EU must:

Improve medicine marketing authorisation by:

1. Requiring the submission of more robust evidence on medicines' safety and efficacy.
2. Keeping the scope of early approval schemes for medicines to limited and justified situations only, and strengthen these schemes.
3. Improving the readability of medicine packages and leaflets. The EU can promote electronic product information as a complement but under no circumstances as a substitution to the package leaflet.
4. Ensuring good governance in relation to scientific advice procedures.

Improve availability of medicines availability by:

5. Obliging pharma companies to develop and submit drug shortage prevention plans to competent authorities.
6. Obliging companies to keep safety stocks in order to avoid supply disruptions.
7. Requiring earlier notification of drug shortages by pharma companies.
8. Promoting that centrally authorised products are available across the EU.
9. Improving the monitoring of medicines' supply and demand.
10. Enabling patients and consumers to report on shortages.
11. Requiring Member States to lay down dissuasive penalties for non-compliance by companies with these new obligations.

Increase medicine affordability by:

12. Revisiting the intellectual property incentives system and putting in place safeguards to ensure drug affordability.
13. Facilitating the introduction of generics and biosimilars on the market.

1. Introduction

European consumers face longstanding challenges when it comes to accessing the medicines they need. The reasons are complex.

First, while some new medicines have clear, clinical benefits to consumers and are better than available treatments, others are not better, have uncertain benefits or are not even recommended.[1], [2]

For example, an independent assessment by a renowned French drug bulletin showed that, over a ten-year period, only 9 of 109 new medicines or uses constituted a notable therapeutic advance.[3] In 2016, BEUC member organisation Test Achats/Test Aankoop found that 11% of 6,500 medicines sold in Belgium were of questionable benefit and 2% were not recommended at all.[4] Likewise, in Germany Stiftung Warentest rated a quarter of 2,000 over-the-counter medicines as 'unsuitable', because their therapeutic efficacy was either insufficient or low compared to the side effects.[5]

Second, consumers cannot always get hold of their medicines due to shortages. Surveys by five BEUC members showed that between a fifth and almost half of households were unable to get the medicine they needed at least once in the last two years.[6] There were shortages for all sorts of conditions, from cardiovascular problems to bacterial infections. This had consequences on people's health and on their pockets as they sometimes had to pay more for alternative treatments. Shortages mean that across the EU some people struggle to access medicines they need.

Third, the prices of new medicines can go through the roof. Increasingly, the treatments for some serious diseases cost up to hundreds of thousands of euros per year.[7] As a result, in some countries the state is unable to reimburse them. High prices and a late market entry of generics and biosimilars threaten to the ability of consumers to receive the medicines they need.

The revision of the legislation announced in the Commission's Pharmaceutical Strategy for Europe brings an opportunity to address these challenges by adopting new measures in relation to medicines' development, authorisation, availability, and affordability.

BEUC welcomes the opportunity to respond to the Commission's public consultation on the revision of the EU general pharmaceutical legislation. This paper develops further some of our answers to the questionnaire and lists other measures that are necessary to ensure that the legislation is fully aligned with consumers' needs and expectations.

1 Prescrire. Drugs in 2020: a brief review, 1 April 2021 [online, accessed 15 November].
2 KCE. 'Do innovative cancer medicines against cancer always have a real added value?', 2021.
3 See reference 1.
4 Test Santé. 'Médicaments à foison près de 900 sont du gaspillage'. num. 132, 2016.
5 See Spiegel online. Stiftung Warentest: Jedes vierte rezeptfreie Medikament fällt durch, June 2019.
6 Surveys carried out in 2019 and 2020 by the Spanish consumer organisation Organización de Consumidores y Usuarios (OCU), Test Achats/Test Aankoop (Belgium), Altroconsumo (Italy) and Forbrukerrådet, the Norwegian Consumer Council.
7 BEUC. Position paper 'Time to lift the blindfold. Abolishing price secrecy to help make medicines affordable'. 2021.

2. BEUC recommendations

In this section we outline key measures that are necessary to promote medicine research and development (R&D) and consumers' access to safe, effective and affordable medicines. In doing so, we develop further some of the options put forward by the Commission in the public consultation's questionnaire.

2.1. Medicines' marketing authorisation

The public consultation barely addresses the need to *reinforce* standards for medicine approval. However, stronger scientific requirements for marketing authorisation are necessary to ensure that drug developers generate the type of evidence that is most useful for patients and consumers, health technology assessments and decisions on reimbursement.

In addition, the EU must improve the readability of medicines' packages and paper package leaflets, and boost transparency of regulatory processes. This will reinforce the safe use of medicines, as well as legitimacy and accountability in regulatory decision-making.

For these reasons, we call on the EU to ensure that the revised legislation leads to:

2.1.1. More robust evidence on medicine safety and efficacy

To improve health outcomes, new medicines should be more effective and/or safer than current treatments.

However, this is not always the case. Companies do not even generate more systematically the type of studies that allow the measuring directly of the comparative benefits and harms of treatments.[8] [9] [10] The revised legislation should lead to better evidence generation on medicines' safety and efficacy. This will, in turn, enhance public trust in the regulatory framework.

BEUC recommendations:

- Annex I point 5.2.5.1 in Directive 2001/83 should be strengthened. Marketing authorisation applicants must submit evidence from randomised controlled clinical trials versus standard treatment, unless exceptionally where justified and in line with the principles laid down in the Declaration of Helsinki. Regulation 726/2004 should include the same language or be bound to the previous article.

- In addition, these pieces of legislation should explicitly require that full marketing authorisation is granted upon demonstration of benefit based on clinically relevant outcomes, including adequately validated surrogate endpoints.[11]

[8] Estellat C., Revaud P. Lack of Head-to-head Trials and Fair Control ArmsRandomized Controlled Trials of Biologic Treatment for Rheumatoid Arthritis. *Arch Intern Med,* 2012;172(3):237-244. doi:10.1001/archinternmed.2011.1209.

[9] Gerardi C., et. al. Preapproval and postapproval evidence on drugs for multiple sclerosis. *Neurology*, 2018;0:1-10. doi:10.1212/ WNL.0000000000005561.

[10] Joppi R., et.al. A disease looking for innovative drugs: The case of pulmonary arterial hypertension. *Eur J Intern Med*. 2018 Sep;55:47-51.

[11] Directive 2001/83 only includes language on ''clinically meaningful endpoints'' in the section on advanced therapy medicinal products, 5.1.6.

2.1.3. Early drug approvals only in justified situations

When medicines receive early authorisation, there is greater uncertainty about their safety and efficacy. As such, fast-track procedures should only be used in specific and well-justified circumstances.

In principle, the scope for conditional marketing authorisation should remain limited to:

- Emergency situations in response to public health threats, life-threatening or seriously debilitating diseases including orphan products, and
- Conditions for which there exists no authorised satisfactory method of diagnosis, prevention, or treatment, or even if such a method exists, in relation to which the medicine concerned will be of major therapeutic advantage to those affected.[12]

At the same time, the revised legislation should strengthen the framework on conditional marketing authorisation.[13] [14] [15]

BEUC recommendations:

- Regulation 726/2004 should be amended to require holders of a conditional marketing authorisation to provide conclusive evidence on benefits based on clinically relevant outcomes for full marketing authorisation in a timely manner.

- The EMA should set up a public, user-friendly and electronic database that centralises information about conditionally authorised products, specific obligations to be fulfilled by companies, the timeframe for completion of studies and any deviations from it and applicable penalties if delays are unjustified.

2.1.4. Improved readibility of packages and package leaflets

Safe use of medicines requires that consumers can read easily and understand the information in medicines' packages and on leaflets.

Whilst Directive 2001/83 (title V) requires that packages and leaflets are 'legible, clear and easy to use', a 2014 study for the European Commission found that the language on package leaflets, their design and lay-out are not always user-friendly.[16] Likewise, BEUC member organisations have received some consumer complaints about poor readability of medicines packages such as expiry dates not being engraved with ink and the size of the letters being too small.

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12 As laid down in Regulation 507/2006. In relation to Q3 of the questionnaire, we find interesting the proposed option to include in the definition of 'unmet medical need' a situation of ''lack of access for patients across the EU to an authorised treatment.'' At the same time, we consider that any proposal to link conditional marketing authorisation with such criteria would require further discussion.

13 A study on cancer drugs approvals by the EMA between 2009-2013, some of which conditionally authorised, shows that most drugs entered the market without evidence of benefit on survival or quality of life. At a minimum of 3.3 years after market entry, there was still no conclusive evidence that these drugs either extended or improved life for most cancer indications. When there were survival gains, they were often marginal. In Davis C. et.al. 'Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13'. *BMJ, 2017;359:j4530.*

14 Banzi R. et.al. Approvals of drugs with uncertain benefit-risk profiles in Europe. *European Journal of Internal Medicine,* 2015 DOI:https://doi.org/10.1016/j.ejim.2015.08.008.

15 KCE. 'Evidence gaps for drugs and medical devices at market entry in Europe and potential solutions'. 2021.

16 van Dijk L. et.al. 'Study on the package leaflets and the Summaries of Product Characteristics of Medicinal Products for Human Use', 2014.

The 2014 study concludes that most of the identified problems could be addressed by improving guidelines, rather than changing the legislation. However, we call on the Commission to take stock of the revision of the pharma legislation and propose additional measures in the law that improve the readability and comprehension of labelling and packaging.

BEUC recommendations:

- The revised legislation should establish clear legibility criteria for packages and package leaflets, for example in relation to minimum font size, letter spacing and material surface and text/background contrast. Inspiration could come from the requirements for hazard pictograms in Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation).

- At the same time, Article 65 of Directive 2001/83 should be amended so it requires the Commission to update existing guidelines in consultation with consumer and patient groups and draw up new ones, such as on best ways to communication on the benefit-risk balance of approved medicines in regulatory information materials.

In addition, we strongly disagree with the questionnaire's proposal (option 8.7) to replace the paper leaflet with electronic product information (ePI). The paper package leaflet is essential and should remain mandatory, as it is the easiest option and to some consumers, the only option, to get information on the safe use of medicines. In fact, there are many people without internet at home or a smartphone. Thus, we recommend that the legislation promote ePIs as a complementary tool for medicines that are given to consumers and patients, but not as a substitute.[17] [18]

BEUC recommendations:

- The revised legislation should promote the development of ePIs as a complementary tool to mandatory paper package leaflets in the national language(s). An exception being situations where Member States need to import urgently medicines' packages that are in another language to respond to a shortage.

- The legislation should be amended so it requires the Commission to develop guidance documents to ensure that electronic product information is fully aligned with EU data protection requirements, to ensure the highest level of data privacy and security.

- In addition, it must include the following safeguards: medicines agencies are the bodies entrusted to manage a single portal for ePIs as well as any apps developed to facilitate the provision of ePIs; it is not possible to track personal data of people accessing the ePI; ePIs are not used to deliver promotional information.[19]

2.1.5. More transparent and independent scientific advice procedures

Scientific advice procedures can facilitate the development of new medicines to the benefit of patients and consumers. However, these processes must be more transparent for accountability purposes and independent from conflicts of interest to avoid biases.

[17] If healthcare professionals agree to replace the paper package leaflet by the ePI for those medicines that are 'only' administered at the hospital, patients should at least be able to receive a QR code or link, and those who prefer so a printout of the package leaflet.

[18] BEUC. Position paper 'Why moving essential product information online is a no-go', 2021.

[19] BEUC. Letter 'Subject: EU key principles for electronic product information for medicines – a consumer perspective. 2019'.

Following some civil society concerns about poor transparency of EMA's early interactions with drug developers, in 2017 the European Ombudsman initiated a strategic inquiry into the matter. Two years later, the Ombudsman called on the EMA to report better in European Public Assessment Reports about pre-submission interactions with companies and to ensure a separation between those experts responsible for providing scientific advice and those assessing marketing authorisation applications.[20]

The revised EU legislation should at the very minimum include the suggestions of the European Ombudsman to enhance public trust in regulatory processes.

These are:

- Regulation 726/2004 should, at the very minimum, embed the recommendations made by the European Ombudsman to enhance transparency and avoid conflicts of interest in scientific advice procedures at the EU level:
    - To the greatest extent possible, ensure that there is a separation between those responsible for providing scientific advice to a medicine developer and those subsequently involved in evaluating a marketing authorisation application for the same medicine.
    - Document the reasons for exceptions and publish the information in the European Public Assessment Report (EPAR), together with a detailed log of all relevant pre-submission activities.

- Directive 2001/83 should be amended to include the same requirements for scientific advice provided at the national level.

BEUC recommendation:

- Our preference is for the European Commission to take stock of the revision process to consider alternative models for the provision of scientific advice that would bring further transparency.[21]

2.2. Medicines' availability

We very much agree with the options outlined in the public consultation's section ''Security of supply of medicines'', as they would help mitigate the problem of drug shortages. In addition, we support some of the options in the section ''Rewards and obligations related to improved access to medicines'' (in particular, the notification of market launches and allowing early introduction of generics on the market in case of delayed market launch)

To improve medicines' availability, the revised EU legislation must ensure:

2.2.1 Obligation for companies to develop drug shortage prevention plans

To reduce the incidence of medicine shortages, companies should adopt strong preventive measures.

At present, whilst EU legislation requires pharmaceutical companies to ensure continued supplies of medicines, it does not require developing drug shortage prevention plans. If competent authorities everywhere would receive and review such plans, they could identify risks in supply chains early on and promote mitigation measures, for example, by calling on manufacturers to diversify the number of suppliers of active pharmaceutical ingredients.

[20] European Ombudsman. 'Decision in strategic inquiry OI/7/2017/KR on how the European Medicines Agency engages with medicine developers in the period leading up to applications for authorisations to market new medicines in the EU', 2019.

[21] Joint civil society stakeholder statement. 'Recommendations on a new model for the provision of scientific advice', 2017.

In recent years, France started requiring that pharma companies develop and share shortage prevention and management plans with regulators.[22] This measure should apply across the EU.

BEUC recommendation:

- The revised EU legislation should require companies to submit drug shortage prevention and management plans to national competent authorities, following a common EU template, and to the EMA for centrally authorised products.

2.2.2 Mandatory safety stocks

Pharmaceutical companies should maintain adequate levels of safety stocks to mitigate the impact of supply disruptions on the healthcare system and consumers.

To ensure that they do so, this requirement should be embedded in law as France did.[23] By adding a new obligation on safety stocks in the revised pharmaceutical legislation, patients and consumers across the EU would be better protected against supply disruptions. At the same time, a coordinated EU approach on safety stocks would ensure that measures in one Member State do not have unintended consequences in others.

BEUC recommendation:

- Directive 2001/83 should require that companies maintain safety stocks according to some common criteria that builds on existing best practices and considering the global dimension of drug supply chains.[24]

2.2.3 Earlier notification of drug shortages

Pharmaceutical companies should notify the authorities about drug shortages in a timely manner so they can apply mitigation measures as soon as possible.

Today, EU legislation requires pharma companies to notify Member States no less than two months if a medicine ceases to be placed on the market either temporarily or permanently.

But some countries require earlier notification periods. For example, in Italy companies should in principle notify shortages four months in advance. In Belgium and Spain, the notice period is six months if a medicine (reimbursed in Belgium) is withdrawn from the market. Whilst in France, there is a one-year notification period for the withdrawal of medicine of 'major therapeutic interest'. At the same time, the EMA and HMA recommend that companies notify the authorities as soon as the shortage or the impending/anticipated shortage is confirmed.[25] The revised pharmaceutical legislation should build on these developments.

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[22] In France, marketing authorisation holders have had to do this progressively since 2017 at least for medicines of 'major therapeutic interest'. For more information on BEUC position on prevention plans, see 'Addressing medicines shortages during the COVID-19 pandemic and beyond: the consumer check-list', 2020.

[23] A 2021 French Decree mandates companies to hold safety stocks from two to four months for medicines of 'major therapeutic interest'. For other types of medicines, companies could be required to stockpile medicines for up to a month. More information here

[24] The EU should also call for initiatives on safety stocks by third parties to take into account the global dimension of drug supply chains and global demand.

[25] EMA. 'Guidance on detection and notification of shortages of medicinal products for marketing authorisation holders in the Union', 2019.

BEUC recommendations:

- Article 23 (a) in Directive 2001/83 should be amended and require companies to:
  1. notify Member States about anticipated shortages as soon possible, and in any case no less than a pre-defined notification period;
  2. provide a justification if exceptionally they cannot comply with the pre-notification period whilst ensuring that the shortage or impending/anticipated shortage was reported as soon as confirmed.

- The new and earlier notification period should be established according to best practices identified among Member States. The notification of product withdrawals should have a notification period that is even longer.

- The Directive should outline in a new article the type of information that companies must submit to competent authorities. The HMA and EMA guideline on the notification of shortages should be used as a reference for that purpose.[26] However, the scope of the article should cover also withdrawals due to commercial reasons.

2.2.4 Placing of medicines across the EU market

To ensure equitable access to medicines across the EU, pharmaceutical companies should place centrally authorised medicines in all Member States.

However, at present some medicines approved by the EMA do not reach patients in all countries specially in the smaller ones. This is partly due to the fact that there is no obligation for companies to enter all EU markets nor are there measures to promote it. This should be reversed.

BEUC recommendations:

- The legislation should be amended and require originator companies that obtained a market authorisation by the EMA to inform regulators about their market launch plans.

- The revised legislation should foresee measures to ensure that holders of an EMA marketing authorisation place the product across Member States. There could be a requirement for companies that do not intend to place the product in some countries or to do it at considerable later stage, to allow generic companies to enter earlier in those markets under fair and reasonable licensing conditions.

2.2.5 Dissuassive penalties for non-compliance by companies

Dissuasive penalties are necessary to promote companies' compliance with their legal obligations in relation to drug supply security.

However, at present penalties are not dissuasive enough and/or enforced systematically.[27] This does not help improve medicines' availability.

BEUC recommendation:

- The revised pharma legislation should require Member States, and the Commission where applicable, to lay down dissuasive penalties for new established obligations and report publicly about any applied penalties.

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[26] See reference 25.

[27] OCU. 'OCU alerta del desabastecimiento de medicamentos', 13 Feburary 2020; and France Assos Santé 'Renforcer et rendre publiques les sanctions : France Assos Santé salue les propositions d'une mission de l'Assemblée nationale', 24 June 2021.

2.2.6 Improved monitoring of medicines' supply and demand

Competent authorities should have a good overview of available stocks and demand volume to be able to assess the risk of shortages and how supply disruptions evolve.

However, well-established monitoring and early warning system are generally lacking at national level.

BEUC recommendations:

- Directive 2001/83 should be amended to require Member States to set up electronic monitoring and early warning systems on drug shortages.

- These systems should be interoperable with the European Shortages Monitoring Platform (ESMP) that will be set up by the EMA for the prevention and management of shortages in public health emergencies and major situations as required in the new Regulation on a reinforced role for the Agency. In addition, the scope of the ESMP should be expanded progressively.

2.2.7 Better public communication on drug shortages

Competent authorities must ensure good public communication on drug shortages so healthcare professionals, patients and consumers can take action to minimise the impact on care.

Although most Member States have online registers on drug shortages, they are not always user-friendly and/or critical information is not systematically reported.[28] In addition, the scope of the EMA catalogue on drug shortages is limited to situations that have been assessed by one of its scientific committees.[29]

Building on the EMA and HMA's 'Good practice guidance for communication to the public on medicines availability issues', the EU pharma legislation should include specific measures to ensure good public communication on drug shortages.

BEUC recommendations:

- Directive 2001/83 should be amended to require that all EU Member States set up a public online and user-friendly database on drug shortages. These databases should contain critical information such as the start and end dates of the shortage, a detailed description of the causes including commercial reasons, and recommendations for healthcare professionals and patients/consumers.

- Regulation 726/2004 should be amended to mandate the EMA to set up a public European database that collates information about drug shortages reported at the national level for all reasons.

[28] BEUC. 'Addressing medicine shortages during the COVID-19 pandemic and beyond: the consumer check list', 2020.

[29] https://www.ema.europa.eu/en/documents/other/decision-tree-escalation-national-european-level_en.pdf

2.2.8 Enabled consumer reporting on drug shortages

Competent authorities should enable consumer reporting on drug shortages. This would lead to a better understanding about the societal impact of supply disruptions, and improve drug shortage management.

However, as it stands the general EU pharmaceutical legislation does not mandate Member States to set up such a system. The upcoming revision brings an opportunity to reverse this and allow consumer reporting across the EU.

BEUC recommendation:

- Directive 2001/83 should be amended to require that Member States facilitate patient and consumer reporting of medicine shortages.

For additional recommendations, including the need to adopt a common definition on drug shortages that includes the question of commercial withdrawals, and criteria see BEUC paper: Addressing Medicines Shortages during the COVID-19 pandemic and beyond: The Consumer Check list

2.3. Medicines' affordability

In relation to the IP incentives system and the competitive functioning of the market to ensure affordable medicines, there are some interesting options in the questionnaire: providing different and shorter periods of data and market protection depending on the product (Q4.2 and Q3) and stimulating earlier market entry of generics and biosimilars through the Bolar exemption (Q9.2).

In addition, we recommend introducing in Directive 2001/83 a waiver on data and market protection if a Member State decides to trigger compulsory licensing.

2.3.1 Targeted provisions on data and market protection and waiver

The revised legislation should ensure that whilst it promotes innovation in drug development, medicines remain affordable and generics and biosimilars can enter the market as soon as possible.

Today, between patents, supplementary protection certificates, data and market protection the EU provides originator companies with long periods of intellectual property protection. At the same time, there are increasing concerns about high drug prices. The EU should revisit the IP incentives system.

BEUC recommendations:

- Article 10 in Directive 2001/83 should be amended and lay down different data and market protection periods, with the longest protection for medicines for serious diseases/health threats for which there is less commercial interest (e.g., novel antibiotics). Protection periods beyond the current maximum period should only be granted if:
    - Companies share data on R&D costs for these products with competent authorities and justify the need for additional protection.
    - The legislation includes possibilities for reducing the protection period if necessary to prevent excessive profits (e.g., 'revision clause').

- At the same time, for other types of products the current protection period of 10-years could either be reduced slightly or maintained but then with the possibility to reduce it if necessary to prevent abuses.

- A new article should be introduced in the Directive allowing Member States to waive data and market protection at any time if they trigger compulsory licensing.

2.3.1. Facilitate market entry of generics and biosimilars

To ensure timely access to generics and biosimilars, generic companies must be able to use patented pharmaceutical products when they conduct pre-marketing authorisation studies.

Whilst the EU allows this through the so-called 'Bolar exemption', application across Member Sates varies and some of them have adopted a more restrictive approach.[30] The revised pharmaceutical legislation should fix this.

BEUC recommendations:

- Article 10(6) in Directive 2001/83 should be amended so it clearly requires that the exemption applies across the EU to finished medicinal products and active pharmaceutical ingredients for R&D and marketing authorisation. The Directive should also clarify that originator companies can benefit from this exemption so they can do studies that compare an investigational product with other on-patent medicines.

- In addition, the Directive should outline some criteria in relation to the application of the Bolar exemption to ensure more harmonisation across the EU.

END

[30] European Commission. 'Commission Staff Working document: A Single Market Strategy for Europe - Analysis and Evidence', 2015.

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