*The Standing Committee of European Doctors (CPME) represents national medical associations across Europe. We are committed to contributing the medical profession's point of view to EU and European policy-making through pro-active cooperation on a wide range of health and healthcare related issues.*

# Proposed amendments to the Commission's Proposals for the Directive on the Union code relating to medicinal products for human use and the Regulation lying down Union procedures for the authorization and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency

## Medicine shortages and security of supply

Shortages of medicines can have a serious negative impact on public health. Deteriorating availability of many medicines on the European market poses a risk to health of patients and creates burden for healthcare professionals. CPME welcomes the strong focus on addressing medicine shortages and strengthening security of supply in the revision. Earlier notifications of shortages and withdrawals are positive proposal, as well as strengthened cooperation and monitoring by the EMA and competent authorities. Introduction of clear definitions of shortages and critical shortages is also a positive development. Finally, CPME welcomes an obligation of having in place shortage prevention plans by marketing authorisation holders and a possibility to transfer marketing authorisation to another party in case of withdrawal.

To further improve provisions in the pharmaceutical legislation CPME calls for binding uptake of recommendations issued by the competent authorities and introduction of penalties in case of noncompliance. We also call for an extension of the obligation to offer a transfer of marketing authorisation to all medicines, not only critical products. Clear and timely recommendations for healthcare professionals and patients are also necessary, including on available alternatives. CPME considers provisions related to safety stocks insufficient and we call for introduction of mandatory stocks at the company level, examples of which already exist in some Member States. Finally, greater transparency shall be implemented regarding the publication of information on shortages and their causes.

| Amendment 1 | |
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| **Article 56.3 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| The marketing authorisation holder of a medicinal product placed on the market in a Member State shall, within the limits of its responsibility, ensure appropriate and continued supplies of that medicinal product to wholesale distributors, pharmacies or persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered.<br>The arrangements for implementing the first subparagraph should, moreover, be justified on grounds of public health protection and be proportionate in relation to the objective of such protection, in compliance with the Treaty rules, particularly those concerning the free movement of goods and competition. | The marketing authorisation holder of a medicinal product placed on the market in a Member State shall~~,~~ ***~~within the limits of its responsibility,~~*** ensure appropriate and continued supplies of that medicinal product to wholesale distributors, pharmacies or persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered.<br>The arrangements for implementing the first subparagraph should***~~, moreover, be justified on grounds of public~~ be based on the high level of human*** health protection ***~~and be proportionate in relation to the objective of such protection, and~~*** in compliance with the Treaty rules***~~, particularly those concerning the free movement of goods and competition~~***. |
| **Justification** | |
| The term "within the limits of its responsibility" is not clear and does not provide sufficient accountability of the marketing authorisation holders. It is common knowledge that many reasons for medicine shortages lay on the side of the marketing authorisation holder. It is therefore essential to either clarify those limits or to remove them from the legislation. Additionally, as proposed in the second subparagraph, a clear reference to the Treaty-based high level of human health protection would help in guiding the arrangements for this obligation. | |

| Amendment 2 | |
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| **Recital 24.1 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| The marketing authorisation holder shall declare if such action is based on the following grounds:<br>(a) the medicinal product is harmful;<br>(b) it lacks therapeutic efficacy;<br>(c) the benefit-risk balance is not favourable;<br>(d) its qualitative and quantitative composition is not as declared;<br>(e) the controls on the medicinal product or on the ingredients and the controls at an intermediate stage of the manufacturing process have not been carried out or if some other requirement or obligation relating to the grant of the manufacturing authorisation has not been fulfilled; | The marketing authorisation holder shall declare if such action is based on the following grounds:<br>(a) the medicinal product is harmful;<br>(b) it lacks therapeutic efficacy;<br>(c) the benefit-risk balance is not favourable;<br>(d) its qualitative and quantitative composition is not as declared;<br>(e) the controls on the medicinal product or on the ingredients and the controls at an intermediate stage of the manufacturing process have not been carried out or if some other requirement or obligation relating to the grant of the manufacturing authorisation has not been fulfilled; |

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| or<br>(f) a serious risk to the environment or to public health via the environment has been identified and not sufficiently addressed by the marketing authorisation holder. | or<br>(f) a serious risk to the environment or to public health via the environment has been identified and not sufficiently addressed by the marketing authorisation holder;<br>***(g) a decision based on commercial reason, without prejudice to any information of a commercially confidential nature.*** |
| **Justification** | |
| Many withdrawals from the market happen due to commercial reasons. This information shall be made available to the regulators and the public. | |

| **Amendment 3** | |
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| **Article 24.4 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 4. Where the marketing authorisation holder intends to permanently withdraw the marketing authorisation for a critical medicinal product, the marketing authorisation holder shall, prior to the notification referred to in paragraph 1, offer, on reasonable terms, to transfer the marketing authorisation to a third party that has declared its intention to place that critical medicinal product on the market, or to use the pharmaceutical non-clinical and clinical documentation contained in the file of the medicinal product for the purposes of submitting an application in accordance with Article 14 of [revised Directive 2001/83/EC]. | 4. Where the marketing authorisation holder intends to permanently withdraw the marketing authorisation for a ***~~critical~~*** medicinal product, the marketing authorisation holder shall, prior to the notification referred to in paragraph 1, offer, on ***fair and*** reasonable terms, to transfer the marketing authorisation to a third party that has declared its intention to place that ***~~critical~~*** medicinal product on the market, or to use the pharmaceutical non-clinical and clinical documentation contained in the file of the medicinal product for the purposes of submitting an application in accordance with Article 14 of [revised Directive 2001/83/EC].<br><br>***A marketing authorisation holder to whom a marketing authorisation is transferred shall notify the Agency of the transfer within 30 days, stating the value of the transaction between the two parties. The Agency shall make this information publicly available.*** |
| **Justification** | |
| A problem particularly affecting less profitable Member States' markets is discontinuation or withdrawal of effective medicines. As there is a lack of transparency regarding their reasons, they are at least partly due to commercially motivated decisions by the pharmaceutical companies. Such practices can not only hinder equal access to medicines for all EU citizens and lead to medicine shortages, but also place Member States in different positions regarding prices. If the availability of a specific product cannot be guaranteed, healthcare systems may be forced to introduce more expensive medicines or less effective alternatives. As observed by the Council of the European Union, the management of uncontrolled withdrawals is critical for continuity of care. The possibility of continuing production and supply should cover all medicines, not only those that have been recognised as critical within the meaning of the Regulation. Additional transparency | |

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| requirements should be attached to transfer of marketing authorisation. |

| Amendment 4 | |
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| **Article 116.1 point (d) (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| d) a temporary disruption in supply of a medicinal product in a given Member State, of an expected duration of in excess of two weeks or, based on the demand forecast of the marketing authorisation holder no less than six months before the start of such temporary disruption of supply or, if this is not possible and where duly justified, as soon as they become aware of such temporary disruption, to allow the Member State to monitor any potential or actual shortage in accordance with Article 118(1). | d) a temporary disruption in supply of a medicinal product in a given Member State, of an expected duration of in excess of two weeks or, based on the demand forecast of the marketing authorisation holder ***and public authorities*** no less than six months before the start of such temporary disruption of supply or, if this is not possible and where duly justified, as soon as they become aware of such temporary disruption, to allow the Member State to monitor any potential or actual shortage in accordance with Article 118(1). |
| **Justification** | |
| Demand forecasts of the pharmaceutical companies should not be the only warning sign of an expected shortage. Often, the pharmaceutical companies use their internal forecasts to prove they are prepared for changing demand. In reality, no one can check their internal documents and forecasting quality. | |

| Amendment 5 | |
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| **Article 118.2 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| For the purposes of paragraph 1, the competent authority concerned as defined in Article 116(1) may request any additional information from the marketing authorisation holder as defined in Article 116(1). In particular, it may request the marketing authorisation holder to submit a shortage mitigation plan in accordance with Article 119(2), a risk assessment of impact of suspension, cessation or withdrawal in accordance with Article 119(3), or the shortage prevention plan referred to in Article 117. The competent authority concerned may set a deadline for the submission of the information requested. | For the purposes of paragraph 1, the competent authority concerned as defined in Article 116(1) may request any additional information from the marketing authorisation holder as defined in Article 116(1). In particular, it may request the marketing authorisation holder to submit a shortage mitigation plan in accordance with Article 119(2), a risk assessment of impact of suspension, cessation or withdrawal in accordance with Article 119(3), or the shortage prevention plan referred to in Article 117. The competent authority concerned ***shall*** set a deadline for the submission of the information requested. |
| **Justification** | |

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| When dealing with medicine shortages, the marketing authorisation holders shall be provided with a clear deadline to submit the requested information. It is known that without the proposed framework, regulators struggle with obtaining information on time or at all. |

| Amendment 6 | |
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| **Article 121.1 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 1. The competent authority of the Member State shall:<br>a) assess the merits of each confidentiality claim made by the marketing authorisation holder as defined in Article 116(1) in accordance with Article 119(1), point (e), and shall protect information which that competent authority considers to be commercially confidential against unjustified disclosure;<br>b) publish information on actual shortages of medicinal products, in cases in which that competent authority has assessed the shortage, on a publicly available website;<br>c) report to the Agency, through the single point of contact working party referred to in Article 3(6) of Regulation (EU) 2022/123, any shortage of a medicinal product that it identifies as a critical shortage in that Member State to the Agency without undue delay. | 1. The competent authority of the Member State shall:<br>a) assess the merits of each confidentiality claim made by the marketing authorisation holder as defined in Article 116(1) in accordance with Article 119(1), point (e), and shall protect information which that competent authority considers to be commercially confidential against unjustified disclosure;<br>b) publish information on actual shortages of medicinal products, ***including known reasons, where applicable in accordance with Article 24.1 second subparagraph points (a) to (e)***, in cases in which that competent authority has assessed the shortage and ***has provided recommendations to healthcare professionals and patients, including on available alternatives,*** on a publicly available website;<br>c) report to the Agency, through the single point of contact working party referred to in Article 3(6) of Regulation (EU) 2022/123, any shortage of a medicinal product that it identifies as a critical shortage in that Member State to the Agency without undue delay. |
| **Justification** | |
| Many withdrawals from the market happen due to commercial reasons. This information shall be made available to the regulators and the public.<br>Additionally, competent authority shall be obliged to provide recommendations to healthcare professionals and patients, not only on a critical shortage, but on any actual shortage. Prescribers must be informed about available alternatives to medicine in shortage. | |

| Amendment 7 |
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| **Article 123.4 (Regulation)** |

| Text Proposed by the Commission | CPME Proposed Amendment |
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| The MSSG may provide recommendations on measures to resolve or to mitigate the critical shortage, in accordance with the methods referred to in Article 122(4), point (d), to relevant marketing authorisation holders, the Member States, the Commission, the representatives of healthcare professionals or other entities. | The MSSG ***shall*** provide recommendations on measures to resolve or to mitigate the critical shortage, in accordance with the methods referred to in Article 122(4), point (d), to relevant marketing authorisation holders, the Member States, the Commission, the representatives of healthcare professionals, ***including on available alternatives***, or other entities. |
| **Justification** | |
| MSSG plays a crucial role in the management of medicine shortages at EU level and its recommendations should be a standard procedure. Information and recommendations are necessary for healthcare professionals.<br>Prescribers must be informed about available alternatives to medicine in shortage. | |

| Amendment 8 | |
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| **Article 124.3 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| The Agency shall establish within its web-portal referred to in Article 104 a publicly available webpage that provides information on actual critical shortages of medicinal products in cases in which the Agency has assessed the shortage and has provided recommendations to healthcare professionals and patients. This webpage shall also provide references to the lists of actual shortages published by the competent authorities of the Member State pursuant to Article 121(1), point (b). | The Agency shall establish within its web-portal referred to in Article 104 a publicly available webpage that provides information on actual critical shortages of medicinal products, ***including known reasons, where applicable in accordance with Article 24.1 second subparagraph points (a) to (e)***, in cases in which the Agency has assessed the shortage and has provided recommendations to healthcare professionals and patients. This webpage shall also provide references to the lists of actual shortages published by the competent authorities of the Member State pursuant to Article 121(1), point (b). |
| **Justification** | |
| Many withdrawals from the market happen due to commercial reasons. This information shall be made available to the regulators and the public. | |

| Amendment 9 | |
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| **Article 125.1 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| Following the addition of a medicinal product to the list of critical shortages of medicinal products in accordance with Article 123, paragraphs 1 and 2, or recommendations provided in accordance with Article 123(4), the marketing authorisation holder as | Following the addition of a medicinal product to the list of critical shortages of medicinal products in accordance with Article 123, paragraphs 1 and 2, or recommendations provided in accordance with Article 123(4), the marketing authorisation holder as defined in |

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| defined in Article 116(1) and subject to those recommendations shall:<br>a) provide any additional information that the Agency may request;<br>b) provide additional relevant information to the Agency;<br>c) take into account the recommendations referred to in Article 123(4);<br>d) comply with any measures taken by the Commission pursuant to Article 126(1), point (a), or actions taken by the Member State pursuant to Article 121(5), point (d);<br>e) inform the Agency of any measures taken pursuant to points (c) and (d) and the report on results of such measures;<br>f) inform the Agency of the end date of the critical shortage. | Article 116(1) and subject to those recommendations shall:<br>a) provide any additional information that the Agency may request;<br>b) provide additional relevant information to the Agency;<br>c) ***comply with*** the recommendations referred to in Article 123(4);<br>d) comply with any measures taken by the Commission pursuant to Article 126(1), point (a), or actions taken by the Member State pursuant to Article 121(5), point (d);<br>e) inform the Agency of any measures taken pursuant to points (c) and (d) and the report on results of such measures;<br>f) inform the Agency of the end date of the critical shortage. |
| **Justification** | |
| When dealing with critical medicine shortages, the marketing authorisation holders shall be provided with clear recommendations and be obliged to implement them to improve the situation. MSSG plays a crucial role in the management of medicine shortages at EU level and its recommendations must be taken up, not only considered. | |

| **Amendment 10** | |
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| **Article 128.3 (new) (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| | ***The marketing authorisation as defined in Article 116(1) authorisation shall be responsible for setting up and maintaining minimal safety stocks of critical medicinal products referred to in Article 131.***<br><br>***Minimal safety stocks of critical medicinal products shall be sufficient to meet the two-month demand for that critical medicinal product in Member States where the medicinal product has been placed on the market.***<br><br>***The marketing authorisation holder may submit a request to the competent authority concerned for an exemption from maintaining minimal safety stocks on the following grounds:***<br><br>***(a) the manufacturing process or shelf life of the*** |

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| | ***critical medicinal product is not compatible with the duration of the minimal safety stocks;***<br>***(b) other valid reasons agreed with the competent authority concerned.*** |
| **Justification** | |
| Following the good example of some Member States, it is highly recommended to introduce an obligation for marketing authorisation holders to establish and maintain safety stock of finished medicinal product sufficient to meet two-month long demand in a Member State. The obligation should apply to critical medicinal products selected in accordance with this Regulation. | |

**Amendment 10 shall be considered together with amendment 11.**

| **Amendment 11** | |
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| **Article 134.2 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| The Commission, taking into consideration the information or the opinion, referred to in paragraph 1, or MSSG recommendations, may decide to adopt an implementing act to improve security of supply. The implementing act may impose contingency stock requirements of active pharmaceutical ingredient or finished dosage forms, or other relevant measures required to improve security of supply, on marketing authorisation holders, wholesale distributors or other relevant entities. | The Commission, taking into consideration the information or the opinion, referred to in paragraph 1, or MSSG recommendations, may decide to adopt an implementing act to improve security of supply. The implementing act may impose contingency stock requirements of active pharmaceutical ingredient ***~~or finished dosage forms,~~*** or other relevant measures required to improve security of supply, on marketing authorisation holders, wholesale distributors or other relevant entities. |
| **Justification** | |
| If above safety stocks are introduced, there is no need for the European Commission to impose contingency stock requirements in an implementing act. | |

| **Amendment 12** | |
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| **Article 130.1 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| Role of the Agency<br>1. The Agency shall, in collaboration with the working party referred to in Article 121(1), point (c), ensure the following:<br>(a) develop a common methodology to identify critical medicinal products, including the evaluation of vulnerabilities with respect to the supply chain of those medicines, in consultation, where appropriate, with relevant stakeholders;<br>(b) specify the procedures and criteria for establishing and reviewing the Union list of critical | Role of the Agency<br>1. The Agency shall, in collaboration with the working party referred to in Article 121(1), point (c), ensure the following:<br>(a) develop a common methodology to identify critical medicinal products, including the evaluation of vulnerabilities with respect to the supply chain of those medicines, in consultation, ***~~where appropriate,~~*** with relevant stakeholders;<br>(b) specify the procedures and criteria for establishing and reviewing the Union list of critical |

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| medicinal products referred to in Article 131;<br>(c) specify the tools, methods of and criteria for the monitoring and reporting provided for in Articles 127(6), point (a), and 128(1), point (a);<br>(d) specify the methods for the provision and review of MSSG recommendations referred to in Article 132, paragraphs 1 and 3.<br>The Agency shall publish the information referred to in points (b), (c) and (d) on a dedicated webpage on its web-portal. | medicinal products referred to in Article 131;<br>(c) specify the tools, methods of and criteria for the monitoring and reporting provided for in Articles 127(6), point (a), and 128(1), point (a);<br>(d) specify the methods for the provision and review of MSSG recommendations referred to in Article 132, paragraphs 1 and 3.<br>The Agency shall publish the information referred to in points ***(a) to (d)*** on a dedicated webpage on its web-portal. |
| **Justification** | |
| Inclusion of HCPs and other relevant stakeholders in the development of a common methodology to identify critical medicinal products cannot be optional. Methodology should be transparent and elaborated in a collaborative way.<br>The methodology to identify critical medicinal products (Article 130.1 (a)) shall be published on Agency's web-portal. Transparent selection of critical medicinal products is necessary, as well as involvement of relevant stakeholders in the decision-making. | |

| **Amendment 13** | |
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| **Article 133 point (c) (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| Obligations on the marketing authorisation holder after the MSSG recommendations Following the addition of a medicinal product to the Union list of critical medicinal products in accordance with Article 131(3) or any recommendations provided in accordance with Article 132(1), the marketing authorisation holder as defined in Article 116(1) of a medicinal product on that list or subject to those recommendations shall:<br>a) provide any additional information that the Agency may request;<br>b) provide additional relevant information to the Agency;<br>c) take into account the recommendations referred to in Article 132(1);<br>d) comply with any measures taken by the Commission in accordance with Article 134(1), point (a), or by the Member State pursuant to Article 127(7), point (e);<br>e) inform the Agency of any measures taken and report on the results of such measures. | Obligations on the marketing authorisation holder after the MSSG recommendations Following the addition of a medicinal product to the Union list of critical medicinal products in accordance with Article 131(3) or any recommendations provided in accordance with Article 132(1), the marketing authorisation holder as defined in Article 116(1) of a medicinal product on that list or subject to those recommendations shall:<br>a) provide any additional information that the Agency may request;<br>b) provide additional relevant information to the Agency;<br>c) ***comply with*** the recommendations referred to in Article 132(1);<br>d) comply with any measures taken by the Commission in accordance with Article 134(1), point (a), or by the Member State pursuant to Article 127(7), point (e);<br>e) inform the Agency of any measures taken and report on the results of such measures. |
| **Justification** | |

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| When dealing with critical medicinal products, the marketing authorisation holders shall be provided with clear recommendations and be obliged to implement them to improve security of supply. MSSG plays a crucial role in the management of medicine shortages at EU level and its recommendations must be taken up, not only considered. |

| Amendment 14 | |
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| **Annex II (Regulation)**<br>**LIST OF THE OBLIGATIONS REFERRED TO IN ARTICLE 172 [sanctions]** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| | ***(26) the obligation to notify the competent authority of the Member State and, where relevant, the Agency about cessation, withdrawal, or suspension in accordance with indicated timing as provided for in Article 116;***<br>***(27) the obligation to have in place and keep up to date a shortage prevention plan as provided for in Article 117;***<br>***(29) the obligation to comply with the recommendations and measures taken in case of a critical shortage as provided for in Article 125;***<br>***(30) the obligation to comply with the recommendations and measures taken in relation to critical medicinal products as provided for in Article 133.*** |
| **Justification** | |
| For the most important measures related to medicine shortages and security of supply, the Regulation should impose sanctions in case of noncompliance. | |

## Incentives for innovation and unmet medical needs

CPME welcomes the proposed system of incentives that will limit the granting of regulatory protection and provide tailored and proportionate rewards for relevant innovation.

CPME strongly calls for a definition of an "innovative medicine" as one that meets a previously unmet or inadequately met, substantive health need and offers enhanced effectiveness or other incremental benefit relative to existing therapeutic alternatives and for further improvements in the proposed definition of "unmet medical need" to consider quality of life.

| Amendment 15 | |
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| **Recital 4 a (new) (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| | ***In the interest of public health and for the well-*** |

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| | ***functioning EU regulatory framework, the innovative medicinal product should be understood as one that meets a previously unmet or inadequately met, substantive health need and offers enhanced effectiveness or other incremental benefit relative to existing therapeutic alternatives.*** |
| **Justification** | |
| A number of terms and concepts require common definitions. One of them is "innovative medicine". "Innovative" and "innovation" are widely used terms but are rarely defined explicitly. There is evidence that not all "innovative" medicines bring a real added value to patients.[1,2,3] There is a clear need to better define what constitutes "innovation" for the benefit of patients and health systems. This definition is also needed for the optimisation of the incentive system and for the improved access to affordable medicinal products. | |

| **Amendment 16** | |
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| **Recital 3 a (new) (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| | ***In the interest of public health and for the well-functioning EU regulatory framework, the innovative medicinal product should be understood as one that meets a previously unmet or inadequately met, substantive health need and offers enhanced effectiveness or other incremental benefit relative to existing therapeutic alternatives.*** |
| **Justification** | |
| A number of terms and concepts require common definitions. One of them is "innovative medicine". "Innovative" and "innovation" are widely used terms but are rarely defined explicitly. There is evidence that not all "innovative" medicines bring a real added value to patients.[4,5,6] There is a clear need to better define what constitutes "innovation" for the benefit of patients and health systems. This definition is also needed for the optimisation of the incentive system and for the improved access to affordable medicinal products. | |

[1] Neyt Mattias, Devos Carl, Thiry Nancy, Silversmit Geert, De Gendt Cindy, Van Damme Nancy, Castanares-Zapatero Diego, Fairon Nicolas, Hulstaert Frank, Verleye Leen. Do innovative medicines against cancer always have a real added value?. Health Technology Assessment (HTA). Brussels. Belgian Health Care Knowledge Centre (KCE). 2021. KCE Reports 343

[2] Vokinger K N, Glaus C E G, Kesselheim A S, Serra-Burriel M, Ross J S, Hwang T J et al. Therapeutic value of first versus supplemental indications of drugs in US and Europe (2011-20): retrospective cohort study BMJ 2023

[3] Chapman, S., V. Paris et R. Lopert (2020), « Challenges in access to oncology medicines : Policies and practices across the OECD and the EU », Documents de travail de l'OCDE sur la santé, n° 123, Éditions OCDE, Paris

[4] Neyt Mattias, Devos Carl, Thiry Nancy, Silversmit Geert, De Gendt Cindy, Van Damme Nancy, Castanares-Zapatero Diego, Fairon Nicolas, Hulstaert Frank, Verleye Leen. Do innovative medicines against cancer always have a real added value?. Health Technology Assessment (HTA). Brussels. Belgian Health Care Knowledge Centre (KCE). 2021. KCE Reports 343

[5] Vokinger K N, Glaus C E G, Kesselheim A S, Serra-Burriel M, Ross J S, Hwang T J et al. Therapeutic value of first versus supplemental indications of drugs in US and Europe (2011-20): retrospective cohort study BMJ 2023

[6] Chapman, S., V. Paris et R. Lopert (2020), « Challenges in access to oncology medicines : Policies and practices across the OECD and the EU », Documents de travail de l'OCDE sur la santé, n° 123, Éditions OCDE, Paris

| Amendment 17 | |
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| **Article 83.1 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| A medicinal product shall be considered as addressing an unmet medical need if at least one of its therapeutic indications relates to a life threatening or severely debilitating disease and the following conditions are met:<br>b) there is no medicinal product authorised in the Union for such disease, or, where despite medicinal products being authorised for such disease in the Union, the disease is associated with a remaining high morbidity or mortality;<br>c) the use of the medicinal product results in a meaningful reduction in disease morbidity or mortality for the relevant patient population. | A medicinal product shall be considered as addressing an unmet medical need if at least one of its therapeutic indications relates to a life threatening or severely debilitating disease and both following ***cumulative*** conditions are met:<br>a) there is no medicinal product authorised in the Union for such disease, or, where despite medicinal products being authorised for such disease in the Union, the disease is associated with a remaining high morbidity or mortality;<br>b) the use of the medicinal product results in a meaningful reduction in disease morbidity or mortality ***or significant increase in quality of life as measured with validated tools*** for the relevant patient population. |
| **Justification** | |
| Unmet medical need exists when no disease-specific therapy is available and only supportive care is possible or when an established treatment does not significantly improve quality of life or provide significant or substantial additional benefit. | |

## Availability and affordability of medicines

Available and affordable medicines are the priority for this revision of the pharmaceutical legislation. CPME supports the reduction of the default regulatory protection and other measures such as introduction of reporting obligation on public support to research and development of medicines, as well as incentivizing comparative clinical trials.

Further improvements are necessary to ensure that available and affordable medicines become a reality in the EU. CPME appreciates the proposal to introduce an incentive for the launch of medicines in all Member States, however we believe that pharmaceutical companies should be obliged to file for pricing and reimbursement in a timely manner instead. We also call for further clarification of the Bolar exemption that will allow for a day one availability of the generic and biosimilar medicines. We also believe that the scope of R&D costs reporting should be enlarged to include indirect benefits and basic information on overall development costs.

| Amendment 18 | |
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| **Article 56.1 point (a) (new) (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| | ***The marketing authorisation holder shall, in good faith, file for pricing and reimbursement in the Member States in which the marketing authorisation is valid within 4 months months after the marketing authorisation was granted. The marketing authorisation holder shall be exempt from this obligation provided the competent authority of the Member State grants a product specific waiver.***<br><br>***The obligation referred to in the first subparagraph shall exclude medicinal products defined in Article 4.1 (13), Article 10, Article 11, Article 12.***<br><br>***Member States representatives may request the Commission to discuss issues related to this obligation in the Committee established by Council Decision 75/320/EEC ("Pharmaceutical Committee). The Commission might invite bodies responsible for health technology assessment as referred to in Regulation (EU) 2021/2282 or national bodies responsible for pricing and reimbursement, as required, to participate in the deliberations of the Pharmaceutical Committee.*** |
| **Justification** | |
| Proposed incentive for launch in all Member States concerned does focus on the end results – availability of medicines – but at the same time the extension of regulatory data protection applies only to approx. 30% of medicines (where the RDP is the last period of regulatory protection). CPME welcomes this attempt to improve availability of medicines, however we believe that an obligation for all marketing authorisation holders to file for pricing and reimbursement, in good faith, will result in broader coverage of medicines and will push manufacturers and the Member States to negotiate fair prices and ensure availability of medicines. Proposed obligation does not cover generic and biosimilar medicinal products. This amendment results in deleting provisions related to 24 months extension of regulatory data protection. | |

**Amendment 18 shall be considered together with amendments 19 and 20.**

| Amendment 19 | |
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| **Article 81.2 (a) (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 24 months, where the marketing authorisation holder demonstrates that the conditions referred to in Article 82(1) are fulfilled within two years, from the date when the marketing authorisation was granted or, within three years from that date for any of the following entities:<br>(i) SMEs within the meaning of Commission Recommendation 2003/361/EC;<br>(ii) entities not engaged in an economic activity ('not-for-profit entity'); and<br>(iii) undertakings that, by the time of granting of a marketing authorisation, have received not more than five centralised marketing authorisations for the undertaking concerned or, in the case of an undertaking belonging to a group, for the group of which it is part, since the establishment of the undertaking or the group, whichever is earliest. | ~~*24 months, where the marketing authorisation holder demonstrates that the conditions referred to in Article 82(1) are fulfilled within two years, from the date when the marketing authorisation was granted or, within three years from that date for any of the following entities:*~~<br>~~*(i) SMEs within the meaning of Commission Recommendation 2003/361/EC;*~~<br>~~*(ii) entities not engaged in an economic activity ('not-for-profit entity'); and*~~<br>~~*(iii) undertakings that, by the time of granting of a marketing authorisation, have received not more than five centralised marketing authorisations for the undertaking concerned or, in the case of an undertaking belonging to a group, for the group of which it is part, since the establishment of the undertaking or the group, whichever is earliest.*~~ |
| **Justification** | |
| With reference to amendment 18. | |

| Amendment 20 | |
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| **Article 82 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| Prolongation of the data protection period for medicinal products supplied in Member States<br><br>1. The prolongation of the data protection period referred to in Article 81(2), first subparagraph, point (a), shall only be granted to medicinal products if they are released and continuously supplied into the supply chain in a sufficient quantity and in the presentations necessary to cover the needs of the patients in the Member States in which the marketing authorisation is valid. | ~~*Prolongation of the data protection period for medicinal products supplied in Member States*~~<br><br>~~*1. The prolongation of the data protection period referred to in Article 81(2), first subparagraph, point (a), shall only be granted to medicinal products if they are released and continuously supplied into the supply chain in a sufficient quantity and in the presentations necessary to cover the needs of the patients in the Member States in which the marketing authorisation is valid.*~~ |

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| The prolongation referred to in the first subparagraph shall apply to medicinal products that have been granted a centralised marketing authorisation, as referred to in Article 5 or that have been granted a national marketing authorisation through the decentralised procedure, as referred to in Chapter III, Section 3. | ~~*The prolongation referred to in the first subparagraph shall apply to medicinal products that have been granted a centralised marketing authorisation, as referred to in Article 5 or that have been granted a national marketing authorisation through the decentralised procedure, as referred to in Chapter III, Section 3.*~~ |
| 2. To receive a prolongation referred to in Article 81(2), first subparagraph, point (a), the marketing authorisation holder shall apply for a variation of the relevant marketing authorisation.<br>The application for a variation shall be submitted between 34 and 36 months after the date when the initial marketing authorisation was granted, or for entities referred to in Article 81(2), first subparagraph, point (a), between 46 and 48 months, after that date.<br>The application for a variation shall contain documentation from the Member States in which the marketing authorisation is valid. Such documentation shall:<br>(a) confirm that the conditions set out in paragraph 1 have been satisfied in their territory; or<br>(b) (b)waive the conditions set out in paragraph 1 in their territory for the purpose of the prolongation.<br>Positive decisions adopted in accordance with Articles 2 and 6 of Council Directive 89/105/EEC 74 shall be considered equivalent to a confirmation referred to in the third subparagraph, point (a). | ~~*2. To receive a prolongation referred to in Article 81(2), first subparagraph, point (a), the marketing authorisation holder shall apply for a variation of the relevant marketing authorisation.*~~<br>~~*The application for a variation shall be submitted between 34 and 36 months after the date when the initial marketing authorisation was granted, or for entities referred to in Article 81(2), first subparagraph, point (a), between 46 and 48 months, after that date.*~~<br>~~*The application for a variation shall contain documentation from the Member States in which the marketing authorisation is valid. Such documentation shall:*~~<br>~~*(a) confirm that the conditions set out in paragraph 1 have been satisfied in their territory; or*~~<br>~~*(b) (b)waive the conditions set out in paragraph 1 in their territory for the purpose of the prolongation.*~~<br>~~*Positive decisions adopted in accordance with Articles 2 and 6 of Council Directive 89/105/EEC 74 shall be considered equivalent to a confirmation referred to in the third subparagraph, point (a).*~~ |
| 3. To receive the documentation referred to in paragraph 2, third subparagraph, the marketing authorisation holder shall make a request to the relevant Member State. Within 60 days from the request of the marketing authorisation holder, the Member State shall issue a confirmation of compliance or, a reasoned statement of non-compliance or alternatively provide a statement of non-objection to prolong the period of regulatory data protection pursuant to this | ~~*3. To receive the documentation referred to in paragraph 2, third subparagraph, the marketing authorisation holder shall make a request to the relevant Member State. Within 60 days from the request of the marketing authorisation holder, the Member State shall issue a confirmation of compliance or, a reasoned statement of non-compliance or alternatively provide a statement of non-objection to prolong the period of regulatory data protection pursuant to this*~~ |

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| Article.<br>4. In cases where a Member State has not replied to the application of the marketing authorisation holder within the deadline referred to in paragraph 3, it shall be considered that a statement of non-objection has been provided.<br>For medicinal products granted a centralised marketing authorisation the Commission shall vary the marketing authorisation pursuant to Article 47 of [revised Regulation (EC) No 726/2004] to prolong the data protection period. For medicinal products granted a marketing authorisation in accordance with the decentralised procedure, the competent authorities of the Member States shall vary the marketing authorisation pursuant to Article 92 to prolong the data protection period.<br>5. Member States representatives may request the Commission to discuss issues related to the practical application of this Article in the Committee established by Council Decision 75/320/EEC 75 ('Pharmaceutical Committee'). The Commission may invite bodies responsible for health technology assessment as referred to in Regulation (EU) 2021/2282 or national bodies responsible for pricing and reimbursement, as required, to participate in the deliberations of the Pharmaceutical Committee.<br>6. The Commission, based on the experience of Member States and relevant stakeholders, may adopt implementing measures relating to the procedural aspects outlined in this Article and regarding the conditions mentioned in paragraph 1. Those implementing acts shall be adopted in accordance with the procedure referred to in Article 214(2). | ~~*Article.*~~<br>~~*4. In cases where a Member State has not replied to the application of the marketing authorisation holder within the deadline referred to in paragraph 3, it shall be considered that a statement of non-objection has been provided.*~~<br>~~*For medicinal products granted a centralised marketing authorisation the Commission shall vary the marketing authorisation pursuant to Article 47 of [revised Regulation (EC) No 726/2004] to prolong the data protection period. For medicinal products granted a marketing authorisation in accordance with the decentralised procedure, the competent authorities of the Member States shall vary the marketing authorisation pursuant to Article 92 to prolong the data protection period.*~~<br>~~*5. Member States representatives may request the Commission to discuss issues related to the practical application of this Article in the Committee established by Council Decision 75/320/EEC 75 ('Pharmaceutical Committee'). The Commission may invite bodies responsible for health technology assessment as referred to in Regulation (EU) 2021/2282 or national bodies responsible for pricing and reimbursement, as required, to participate in the deliberations of the Pharmaceutical Committee.*~~<br>~~*6. The Commission, based on the experience of Member States and relevant stakeholders, may adopt implementing measures relating to the procedural aspects outlined in this Article and regarding the conditions mentioned in paragraph 1. Those implementing acts shall be adopted in accordance with the procedure referred to in Article 214(2).*~~ |
| **Justification** | |
| With reference to amendment 18. | |

| Amendment 21 | |
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| **Article 57 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 1. The marketing authorisation holder shall declare to the public any direct financial support received from any public authority or publicly funded body, in relation to any activities for the research and development of the medicinal product covered by a national or a centralised marketing authorisation, irrespective of the legal entity that received that support. | 1. The marketing authorisation holder shall declare to the public any direct financial support ***and indirect financial benefits*** received from any public authority or publicly funded body, in relation to any activities for the research and development of the medicinal product covered by a national or a centralised marketing authorisation, irrespective of the legal entity that received that support. |
| Within 30 days after the marketing authorisation is granted the marketing authorisation holder shall:<br><br>(a) draw up an electronic report listing:<br><br>(i) the amount of financial support received and the date thereof;<br>(ii) the public authority or publicly funded body that provided the financial support referred to in point (i);<br>(iii) the legal entity that received the support referred to in point (i). | Within 30 days after the marketing authorisation is granted the marketing authorisation holder shall:<br><br>(a) draw up an electronic report listing:<br><br>(i) the amount of financial support received and the date thereof;<br>(ii) the public authority or publicly funded body that provided the financial support referred to in point (i);<br>(iii) the legal entity that received the support referred to in point (i);<br>**(iv)** ***the percentage of total research and development costs of the medicinal product covered by the support referred to in point (i).*** |
| **Justification** | |
| It should be a requirement that the R&D costs of medicinal products that have benefited from public funding are transparent and include minimum information on the breakdown between private and public investment. This would empower national authorities by reducing information asymmetry in pricing negotiations, enable informed discussion on what constitutes a fair price for these medicines and allow public accountability for the use of public resources. It is important to know the ratio of the public and private investments, to know the scale of public support, which often is higher than claimed. | |

| Amendment 22 | |
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| **Article 85 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| Patent rights, or supplementary protection certificates under the [Regulation (EC) No 469/2009 - OP please replace reference by new instrument when adopted] shall not be regarded as infringed when a reference medicinal product is used for the purposes of:<br>(a) studies, trials and other activities conducted to generate data for an application, for:<br>(i) a marketing authorisation of generic, biosimilar, hybrid or bio-hybrid medicinal products and for subsequent variations;<br>(ii) health technology assessment as defined in Regulation (EU) 2021/2282;<br>(iii) pricing and reimbursement.<br>(b) the activities conducted exclusively for the purposes set out in point (a), may cover the submission of the application for a marketing authorisation and the offer, manufacture, sale, supply, storage, import, use and purchase of patented medicinal products or processes, including by third party suppliers and service providers.<br>This exception shall not cover the placing on the market of the medicinal products resulting from such activities. | Patent rights, or supplementary protection certificates under the [Regulation (EC) No 469/2009 - OP please replace reference by new instrument when adopted] shall not be regarded as infringed when ~~***a reference medicinal product is used for the purposes of***~~:<br>(a) studies, trials and other activities ***are*** conducted ~~***to generate data for an application***~~, for ***the purpose of***:<br>(i) ***applying for*** a marketing authorisation of generic, biosimilar, hybrid or bio-hybrid medicinal products and for subsequent variations;<br>(ii) ***conducting*** health technology assessment as defined in Regulation (EU) 2021/2282;<br>(iii) ***filing for*** pricing and reimbursement;<br>(iv) ***participating in a procurement to enable market entry of a generic or biosimilar product as soon as the relevant patents or supplementary protection certificates expire.***<br>(b) the activities ~~***conducted exclusively for the purposes set out in point (a), may cover***~~ ***falling under the first subparagraph include*** the submission of the application for a marketing authorisation and the offer***ing***, manufacture, sale, supply, storage, import, ***export***, use and purchase of patented medicinal products or processes, including by third party suppliers and service providers.<br>This exception shall not cover the placing on the market of the medicinal products resulting from such activities. |
| **Justification** | |
| All obstacles that prevent generic and biosimilar medicines from entering the market on the first day after the protection expires should be removed. This amendment proposes clarifications needed for the Bolar | |

exemption to be effectively implemented. There should be no doubt about the application for authorization and filing for pricing and reimbursement, as well as conducting health technology assessment. Applying for supply is also needed to effectively achieve a day-one launch.

## Incentives for new antimicrobials

A new comprehensive alternative market model is needed to ensure sustainable and equitable access to antibiotics. Due to the nature of the use of antibiotics (the less the better), the current market model is not appropriate and is not in line with public health objectives.

The proposal foresees a creation of a new incentive – transferable exclusivity extension voucher. This incentive is based on a broader framework for regulating the pharmaceutical market and the protection awarded to registered and marketed medicines existing in the European Union. The vouchers do not require direct funding from national governments and often are pictured as effective and sufficient tool. However, indirect costs for health systems and ethical considerations seem to outweigh its potential benefits.

Firstly, the funding of this incentive is based on a significant extension of the protection period for other medicines. This may mean a disproportionate level of subsidising one area of healthcare at the expense of another. This would also have the effect of delaying generic market entry, which undermines competition and takes away market predictability. The total cost of this incentive, from both a social and health perspective, may be too high. Secondly, vouchers do not contribute to the rational consumption of antibiotics, because they still make additional profit conditional on the quantity of the product sold.

Therefore, CPME recommends deleting the voucher from the pharmaceutical legislation, and instead focusing on investing EU and Member States efforts in non-legislative tools, such as incentives under development within the Health Emergency Preparedness and Response Authority (HERA) and payment models successfully tested in some EU countries. Should the EU legislators decide to adopt the provisions related to the voucher, CPME recommends safeguarding it from abusive practices and improving supply obligations to avoid shortages.

## Antimicrobial resistance

The proposal foresees several promising measures to tackle the growing threat of AMR, including obligatory Environmental Risk Assessment. CPME welcomes the general direction taken by the Commission. However, we believe that most of the measures can be further improved.

We believe that antimicrobial stewardship should be reserved to system-wide approach to promoting rational use of antimicrobials, therefore using this term in relation to a single pharmaceutical company action is not justified. In line with the EU Guidelines on prudent use of antimicrobials, the revision of the EU legislation should be used to introduce per unit

disposal of antimicrobial, instead of just adjusting packaging sizes. Finally, we call for further specifications of subjecting antimicrobials to medical prescription.

| Amendment 23 | |
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| **Article 17 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 1. Where the application for a marketing authorisation concerns an antimicrobial, the application shall, in addition to the information referred to in Article 6, contain the following:<br>(a) an antimicrobial stewardship plan as referred to in Annex I;<br>(b) a description of the special information requirements outlined in Article 69 and listed in Annex I.<br>2. The competent authority may impose obligations on the marketing authorisation holder if it finds the risk mitigation measures contained in the antimicrobial stewardship plan unsatisfactory. | 1. Where the application for a marketing authorisation concerns an antimicrobial, the application shall, in addition to the information referred to in Article 6, contain the following:<br>(a) an ***antimicrobial resistance mitigation*** plan as referred to in Annex I;<br>(b) a description of the special information requirements outlined in Article 69 and listed in Annex I.<br>2. The competent authority may impose obligations on the marketing authorisation holder if it finds the risk mitigation measures contained in the ***antimicrobial resistance mitigation*** plan unsatisfactory. |
| **Justification** | |
| Antibiotic stewardship is not the right term for what is expected from the marketing authorization holders in relation to approved antimicrobials. As defined in the European Commission's guidelines of prudent use of antimicrobials, antimicrobial stewardship is an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness. Activities to be taken solely by the pharmaceutical company should not be called antimicrobial stewardship, as this term is reserved for a broader and systemic actions to be taken by health systems and healthcare professionals. | |

| Amendment 24 | |
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| **Article 17.3 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 3. The marketing authorisation holder shall ensure that the pack size of the antimicrobial corresponds to the usual posology and duration of treatment. | 3. ***The marketing authorisation holder shall ensure, wherever possible, that the antimicrobial may be dispensed per unit in a number corresponding to the quantities described on the prescription.***<br>***If an antimicrobial can not be dispensed per unit,*** the marketing authorization holder shall ensure that the pack size of the antimicrobial corresponds to the usual posology and duration of treatment. |

| Justification |
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| Per unit dispensing of antimicrobials has been listed as a core component of prudent use of antimicrobials in the EU guidelines. As the actual size of packaging of antimicrobials is difficult to adjust to all clinical guidelines, which may also change over time, the best way to dispense the needed quantity and to avoid stocking and waste is to dispense the exact number of units needed. The proposed provision on adjusting the package size to the usual posology and duration of the treatment is a step in the right direction, however per unit dispensing is more ambitious measure to limit the spread of AMR. |

| Amendment 25 | |
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| **Article 51.1 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 1. A medicinal product shall be subject to medical prescription where it:<br>(a) is likely to present a danger either directly or indirectly, even when used correctly, if used without medical supervision;<br>(b) is frequently and to a very wide extent used incorrectly, and as a result is likely to present a direct or indirect danger to human health;<br>(c) contains substances or preparations thereof, the activity or adverse reactions of which require further investigation;<br>(d) is normally prescribed by a doctor to be administered parenterally;<br>(e) is an antimicrobial; or<br>(f) contains an active substance which are persistent, bioaccumulative and toxic, or very persistent and very bioaccumulative, or persistent, mobile and toxic, or very persistent and very mobile for which medical prescription is required as risk minimisation measure with regard to the environment, unless the use of the medicinal product and the patient safety require otherwise. | 1. A medicinal product shall be subject to medical prescription where it:<br>(a) is likely to present a danger either directly or indirectly, even when used correctly, if used without medical supervision;<br>(b) is frequently and to a very wide extent used incorrectly, and as a result is likely to present a direct or indirect danger to human health;<br>(c) contains substances or preparations thereof, the activity or adverse reactions of which require further investigation;<br>(d) is normally prescribed by a doctor to be administered parenterally;<br>(e) is an ***antibiotic or systemic antiviral or systemic antifungal;***<br>***(f) is an antiparasitic; or***<br>(g) contains an active substance which are persistent, bioaccumulative and toxic, or very persistent and very bioaccumulative, or persistent, mobile and toxic, or very persistent and very mobile for which medical prescription is required as risk minimisation measure with regard to the environment, unless the use of the medicinal product and the patient safety require otherwise. |
| **Justification** | |
| Restricting availability of all antimicrobials to prescription may result in unnecessary burden on health systems and on delays in care, while evidence suggests that medicines are more effective when applied earlier. Also, the potential to create resistance of topical antivirals and antifungals is very low. Antiparasitic medicines should also be subject to prescription as they can contribute to the spread of AMR. | |

| Amendment 26 |
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| **Article 51.2 (Directive)** |

| Text Proposed by the Commission | CPME Proposed Amendment |
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| 3. Member States may set additional conditions on the prescription of antimicrobials, restrict the validity of medical prescription and limit the quantities prescribed to the amount required for the treatment or therapy concerned or submitting certain antimicrobial medicinal products to special medical prescription or restricted prescription. | 2. Member States may set additional conditions on the prescription of antimicrobials, restrict the validity of medical prescription ~~***and limit the quantities prescribed to the amount required for the treatment or therapy concerned or submitting***~~ or ***submit*** certain antimicrobial medicinal products to special medical prescription or restricted prescription. |
| | 2a. (new) ***Wherever possible, Member States shall provide that prescriptions and dispensation shall be aligned with the number of units required for the treatment or therapy concerned.*** |
| **Justification** | |
| Per-unit dispensing of antimicrobials has been listed as a core component of prudent use of antimicrobials in the EU guidelines. As the actual size of packaging of antimicrobials is difficult to adjust to all clinical guidelines, which may also change over time, the best way to dispense the needed quantity and to avoid stocking and waste is to dispense the exact number of units needed. The proposed provision on adjusting the package size to the usual posology and duration of the treatment is a step in the right direction, however per-unit dispensing is more ambitious measure to limit the spread of AMR. | |

| Amendment 27 | |
|---|---|
| **Article 69 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| The marketing authorisation holder shall ensure availability of educational material to healthcare professionals, including through medical sales representatives as referred to in Article 175(1), point (c), regarding the appropriate use of diagnostic tools, testing or other diagnostic approaches related to antimicrobial-resistant pathogens, that may inform on the use of the antimicrobial. | ***In case of absence of appropriate guidelines, t***he marketing authorisation holder ***may*** ensure availability of ***informational*** material to healthcare professionals, ~~***including through medical sales representatives as referred to in Article 175(1), point (c),***~~ regarding the appropriate use of diagnostic tools, testing or other diagnostic approaches related to antimicrobial-resistant pathogens, that may inform on the use of the antimicrobial.<br><br>***The informational material referred to in the first paragraph shall be compatible with the summary of product characteristics.***<br><br>***Materials referred to in the first subparagraph shall not constitute advertising referred to in Chapter XIII.*** |
| **Justification** | |

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| The best source of information on the use of diagnostics tools are the official guidelines. Only in cases, where such guidelines do not exist, marketing authorisation holders may provide information to healthcare professionals. The medical sales representatives are not the right way to provide this information to healthcare professionals. It must be ensured that the information on appropriate use of the diagnostic tools is compatible with the summary of products characteristics and does not involve advertising. |

| Amendment 28 | |
|---|---|
| **Article 69.2 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 2. The marketing authorisation holder shall include in the packaging of antimicrobials a document that contains specific information about the medicinal product concerned and that is made available to the patient in addition to the product leaflet ("awareness card") with information on antimicrobial resistance and the appropriate use and disposal of antimicrobials.<br>Member States may decide that the awareness card shall be made available in paper format or electronically, or both. In the absence of such specific rules in a Member State, an awareness card in paper format shall be included in the packaging of an antimicrobial. | 2. The marketing authorisation holder shall include in the packaging of antimicrobials a document that contains specific information about the medicinal product concerned and that is made available to the patient in addition to the product leaflet ("awareness card") with information on antimicrobial resistance and the appropriate use and disposal of antimicrobials.<br>~~***Member States may decide that***~~ The awareness card shall be made available in paper format ***and*** electronically~~***, or both***~~. In the absence of such specific rules in a Member State, an awareness card in paper format shall be included in the packaging of an antimicrobial. |
| **Justification** | |
| Ensuring that AMR awareness information is accessible to all, and in particular to patients/consumers with diverse abilities, is essential, and therefore the AMR awareness card with information on antimicrobial resistance and disposal shall be accessible in paper format as well. Same rule should apply to package leaflet (Article 63 Directive). | |

| Amendment 29 | |
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| **Annex I (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| (21) Where the application concerns an antimicrobial medicinal product, the application shall also contain:<br>a) an antimicrobial stewardship plan which shall in particular outline:<br>(I) information about risk mitigation measures to limit antimicrobial resistance development related to the use, prescription and administration of the medicinal product;<br>(II) how the marketing authorisation holder intends to monitor and report to the competent authority the resistance to the antimicrobial medicinal product. | (21) Where the application concerns an antimicrobial medicinal product, the application shall also contain:<br>a) an ***antimicrobial resistance mitigation*** plan which shall in particular outline:<br>(I) information about risk mitigation measures to limit antimicrobial resistance development related to the use, prescription and administration of the medicinal product;<br>(II) how the marketing authorisation holder intends to monitor and report to the competent authority the resistance to the antimicrobial medicinal product. |
| **Justification** | |

Antibiotic stewardship is not the right term for what is expected from the marketing authorization holders in relation to approved antimicrobials. As defined in the European Commission's guidelines of prudent use of antimicrobials, antimicrobial stewardship is an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness. Activities to be taken solely by the pharmaceutical company should not be called antimicrobial stewardship, as this term is reserved for a broader and systemic actions to be taken by health systems and healthcare professionals.

## Authorisation of medicinal products

CPME welcomes the fact that regulatory framework for authorisation of new medicines has been thoroughly revised to improve efficiency and European competitiveness.

However, we would like to draw attention to the increasing number of advanced medicinal products entering the market with limited information on safety issues and effectiveness. A strictly regulated framework is indispensable to safeguard patient safety and healthcare systems. Therefore, we call for strengthening the language regarding requirements of evidence for authorisation of new medicines. Real-world data can provide useful supplementary information in the context of marketing authorisation processes and post-approval surveillance activities. However, it should only be considered as complementary to randomised clinical trials and should under no circumstances be promoted as a replacement for these. Post marketing evidence generation is key to assess medicines already present on the market. The legislation should strengthen the obligations and requirements for market authorisation holders to conduct necessary study introducing penalties in case of noncompliance.

| Amendment 30 | |
|---|---|
| **Article 19.3 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 3. Conditional marketing authorisations or a new conditional therapeutic indication granted pursuant to this Article shall be subject to specific obligations. Those specific obligations and, where appropriate, the time limit for compliance shall be specified in the conditions to the marketing authorisation. Those specific obligations shall be reviewed annually by the Agency for the first three years after granting the authorisation and every two years thereafter. | 3. Conditional marketing authorisations or a new conditional therapeutic indication granted pursuant to this Article shall be subject to specific obligations. Those specific obligations and~~***, where appropriate,***~~ the time limit for compliance shall be specified in the conditions to the marketing authorisation. Those specific obligations shall be reviewed annually by the Agency for the first three years after granting the authorisation and every two years thereafter. |
| **Justification** | |
| The specific obligations related to the conditional marketing authorisation shall be subject to a specific and mandatory deadline. As the conditional marketing authorisation is granted prior to the submission of comprehensive clinical data, it is essential to confirm in a reasonable timeframe that the benefit-risk balance is favourable. The same applies to possible post-authorisation studies that might be imposed on the marketing authorisation holder and might constitute an obligation as a condition of a marketing authorisation (such as safety and efficacy studies, as well as environmental risk assessment). Patient safety and high-quality of approved medicinal products shall be ensured by an ambitious regulatory framework. | |

| Amendment 31 | |
|---|---|
| **Article 56 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| Where the Agency concludes that a holder of a marketing authorisation granted in accordance with Article 19, including a new therapeutic indication granted referred to Article 19, failed to comply with the obligations laid down in the marketing authorisation, the Agency shall inform the Commission accordingly. The Commission shall adopt a decision to vary, suspend or revoke that marketing authorisation in accordance with the procedure set out in Article 13. | Where the Agency concludes that a holder of a marketing authorisation granted in accordance with Article 19, including a new therapeutic indication granted referred to Article 19, failed to comply with the obligations laid down in the marketing authorisation, ***including in accordance with Article 20***, the Agency shall inform the Commission accordingly. The Commission shall adopt a decision to vary, suspend or revoke that marketing authorisation in accordance with the procedure set out in Article 13. |
| **Justification** | |
| Marketing authorisation shall be revoked when the post-authorisation studies imposed on the marketing authorisation holder are not delivered on time. | |

| Amendment 32 | |
|---|---|
| **Article 104.1 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| (i) conclusions of assessments, recommendations, opinions, approvals and decisions taken by the Agency and its Committees under this Regulation and [revised Directive 2001/83/EC], unless it is required that this information is made public by the Agency by other means; | (i) conclusions of assessments, recommendations, opinions, approvals, ***obligations under conditional marketing authorisation*** and decisions taken by the Agency and its Committees under this Regulation and [revised Directive 2001/83/EC], unless it is required that this information is made public by the Agency by other means; |
| **Justification** | |
| To ensure full transparency and scrutiny, information on obligations under the conditional marketing authorisation shall be made public not only in the summary of the product characteristics and the package leaflet (Article 19), but as well in the web-portal run by the European Medicines Agency. Information on conditions and time limits shall be made public. | |

| Amendment 33 | |
|---|---|
| **Article 44.2 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 2. The marketing authorisation shall lay down deadlines for the fulfilment of the conditions referred to in paragraph 1, first subparagraph, where necessary. | 2. The marketing authorisation shall lay down deadlines for the fulfilment of the conditions referred to in paragraph 1, first subparagraph. ~~***where necessary.***~~ |
| **Justification** | |
| The specific obligations related to the conditional marketing authorisation shall be subject to a specific and mandatory deadline. As the conditional marketing authorisation is granted prior to the submission of comprehensive clinical data, it is essential to confirm in a reasonable timeframe that the benefit-risk balance is favourable. The same applies to possible post-authorisation studies that might be imposed on the marketing authorisation holder and might constitute an obligation as a condition of a marketing authorisation (such as safety and efficacy studies, as well as environmental risk assessment). Patient safety and high-quality of approved medicinal products shall be ensured by an ambitious regulatory framework. | |

| Amendment 34 | |
|---|---|
| **Annex II (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 5.2.5.1. Study Reports of Controlled Clinical Studies Pertinent to the Claimed indication<br>In general, clinical trials shall be done as 'controlled clinical trials' if possible, randomised and as appropriate versus placebo and versus an established medicinal product of proven therapeutic value; any other design shall be justified. The treatment of the control groups will vary from case to case and also will depend on ethical considerations and therapeutic area; thus it may, in some instances, be more pertinent to compare the efficacy of a new medicinal product with that of an established medicinal product of proven therapeutic value rather than with the effect of a placebo. | 5.2.5.1. Study Reports of Controlled Clinical Studies Pertinent to the Claimed indication<br>~~***In general,***~~ Clinical trials shall be done as 'controlled clinical trials' ~~***if possible***~~, randomised and as appropriate versus placebo and versus an established medicinal product of proven therapeutic value; any other design shall be ***duly*** justified ***providing ethical and clinical reasons***. The treatment of the control groups will vary from case to case and also will depend on ethical considerations and therapeutic area; thus it may, in some instances, be more pertinent to compare the efficacy of a new medicinal product with that of an established medicinal product of proven therapeutic value rather than with the effect of a placebo. |
| **Justification** | |
| The revised legislation should improve evidence requirements for the approval of new medicinal products. The acceleration of science and innovation can never compromise patient safety. EU regulatory framework shall therefore require submission of randomized clinical trials assuring quality, efficacy and safety, and any | |

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| other design shall be duly justified. |

## Paediatric medicinal products

| Amendment 35 | |
|---|---|
| **Article 91.3 (Regulation)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 3. When products are authorised in accordance with the provisions of this Regulation, the Commission may update the summary of product characteristics and package leaflet, and may vary the marketing authorisation accordingly. | 3. When products are authorised in accordance with the provisions of this Regulation, the Commission may update the summary of product characteristics and package leaflet, ***including dosage accuracy***, and may vary the marketing authorisation accordingly. |
| **Justification** | |
| Paediatric medicines should be marketed with a packaging suitable for paediatric use, offered in a safe and suitable form and with adapted package leaflets, with particular attention to dosage accuracy to avoid medication errors. | |

## Information to patients

While digitalisation offers opportunities to enhance information delivered to patients, CPME strongly believes that the electronic product information (ePI) should never replace the paper version included in medicine packets but remain complementary.

| Amendment 36 | |
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| **Article 63 (Directive)** | |
| **Text Proposed by the Commission** | **CPME Proposed Amendment** |
| 4. Member States may decide that the package leaflet shall be made available in paper format or electronically, or both. In the absence of such specific rules in a Member State, a package leaflet in paper format shall be included in the packaging of a medicinal product. If the package leaflet is only made available electronically, the patient's right to a printed copy of the package leaflet should be guaranteed upon request and free of charge and it should be ensured that the information in digital format is easily accessible | 3. ~~***Member States may decide that***~~ The package leaflet shall be made available in paper format and electronically, ~~***or both. In the absence of such specific rules in a Member State, a***~~ A package leaflet in paper format shall be included in the packaging of a medicinal product~~***. If the package leaflet is only made available electronically, the patient's right to a printed copy of the package leaflet should be guaranteed upon request and free of charge and***~~ It should be ensured that the information in digital format is easily accessible to |

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| to all patients. | all patients. |
| | ***4a. (new) A package leaflet shall include a key information section summarising benefit and harm data for each authorised indication.*** |
| 5. The Commission is empowered to adopt delegated acts in accordance with Article 215 to amend paragraph 3 by making mandatory the electronic version of the package leaflet. That delegated act shall also establish the patient's right to a printed copy of the package leaflet upon request and free of charge. The delegation of powers shall apply as of [OP please insert the date = five years following 18 months after the date of entering into force of this Directive]. | ~~***5. The Commission is empowered to adopt delegated acts in accordance with Article 215 to amend paragraph 3 by making mandatory the electronic version of the package leaflet. That delegated act shall also establish the patient's right to a printed copy of the package leaflet upon request and free of charge. The delegation of powers shall apply as of [OP please insert the date = five years following 18 months after the date of entering into force of this Directive].***~~ |
| 7. Where the package leaflet is made available electronically, the individual right to privacy shall be ensured. Any technology giving access to the information shall not allow the identification or tracking of individuals, nor shall it be used for commercial purposes. | 7. ***Utilisation of the electronic package leaflet shall ensure the individual right to privacy.*** Any technology giving access to the information shall not allow the identification or tracking of individuals, nor shall it be used for commercial purposes. |
| **Justification** | |
| Ensuring that product information is accessible to all, and in particular to patients/consumers with diverse abilities, is essential, and therefore the electronic product information (ePI) should never replace the paper version included in medicine packets but remain complementary. If used, ePI must meet standards of objectivity, be transparent, independent, and free of any advertising or commercial interests. Same rule should apply to AMR awareness card (Article 69 Directive). | |