CALL TO ACTION TO IMPROVE CANCER PATIENTS' ACCESS TO THE BEST TREATMENTS AVAILABLE ACROSS THE EUROPEAN UNION (EU)

ECL position on the proposal for a new Directive on the Union code relating to medicinal products for human use

Representing national and regional cancer societies across Europe, the Association of European Cancer Leagues (ECL) welcomes a new proposal for the Directive on the Union code relating to medicinal products for human use (COM (2023) 192) (henceforth Directive), published by the European Commission on 26 April 2023. The draft legislation is an opportunity to make the pharmaceutical system patient-centred and fit for purpose by addressing unmet medical needs and ensuring availability and timely access to safe, effective, and affordable medicines for all patients in need. To that end, we share our views on key elements of the proposed Directive that we support and those that we are concerned about and suggest amending.

1. Development of medicines and new uses for existing medicines to address unmet medical needs

In Europe, around 2.7 million people are diagnosed with cancer every year – and this number is expected to grow. Despite the increased provision of cancer medicines on the market due to medical and technological developments, many of these cancer patients have unmet medical needs, meaning that there are no targeted or only limited treatment options for them. For example, there is no standard post-remission therapy to prevent relapse of acute myeloid leukemia. There is also a lack of approved pharmaceuticals to treat glioblastoma multiforme, mainly because of the inability to bypass the blood-brain barrier. In addition, fewer than half of patients diagnosed with mesothelioma survive the first year after diagnosis. Other cancers with low survival rates include metastatic non-small cell lung cancer and diffuse intrinsic pontine glioma, which primarily affects children and pancreatic cancer[1].

While the new Directive alone cannot solve the issue of unmet medical needs, it is key in addressing some of its root causes.

As current investments in developing medicines do not always prioritise the greatest unmet medical needs, we applaud the establishment of a criteria-based definition of "unmet medical need" in **Article 83** to incentivise the development of medicinal products in therapeutic areas that are

[1] Coppens D, Rommel W. (2023). The potential for academic development of medicines in Europe: case study of advanced therapy medicinal products. The Association of European Cancer Leagues. Available at: https://www.cancer.eu/wp-content/uploads/2023-03-23-Policy-paper_The-potential-for-academic-development-of-medicines-in-Europe.pdf.

currently underserved. The European Commission correctly identified key criteria for such definition, and we welcome its further specification in implementing acts, considering scientific input by the European Medicines Agency (EMA).

We welcome **Article 2** on the application of the hospital exemption (HE), which allows for the use of the advanced therapy medicinal products (ATMPs) without a marketing authorisation under certain circumstances. Proposed measures for collection and reporting of data, as well as a yearly review of these data by the competent authorities and their publication by the EMA in a repository are vital to ensure patient safety and appropriate use of the HE. The authorised ATMPs under the HE should be made public to provide insight into the available treatments across the EU.

Moreover, the harmonisation of the HE is needed as the current divergent national laws hinder export and equitable patient access to innovative medicines across Europe. Efforts to harmonise should include a uniform definition of "non-routine basis" concept referred to in Article 2(1) and its application should be limited to targeting unmet medical needs. In addition, holders of a hospital exemption that exceed preparation on a non-routine basis should be granted a transition period to obtain a centralised marketing authorisation. This non-commercial academic pathway to the patient, leading to an authorisation by the EMA, should include an academic registration trajectory, with lower or no regulatory fees, some regulatory flexibility to take into account the very small patient populations and the intricate complexity of niche and personalised treatments, as well as support to academics to fulfil the procedures and requirements[2].

For-profit companies should not be eligible for the HE. Instead, they should be encouraged to obtain a centralised marketing authorisation for commercially viable products that are produced on an industrial scale, and to aim for equitable patient access among Member States. The divergent national laws also create an unlevel playing field among academic and not-for-profit entities from different Member States and impose a threat to EU-wide patient access.

Acknowledging that harmonisation efforts may be challenging, we suggest including provisions that allow one Member State to adopt or to acknowledge the HE from another Member State, allowing cross-border exchange based on unmet medical needs. Separate provisions for established ATMPs under the HE with low risk profiles are encouraged as part of the implementing acts referred to in Article 2(7)(a).

[2] Coppens D, Rommel W. (2023). The potential for academic development of medicines in Europe: case study of advanced therapy medicinal products. The Association of European Cancer Leagues. Available at: https://www.cancer.eu/wp-content/uploads/2023-03-23-Policy-paper_The-potential-for-academic-development-of-medicines-in-Europe.pdf.

Article 2 - paragraph 1		
Text proposed by the Commission	**Amendment**	**Justification**
1. By way of derogation from Article 1(1), only this Article shall apply to advanced therapy medicinal products prepared on a non-routine basis in accordance with the requirements set in paragraph 3 and used ***within the same Member State*** in a hospital under the exclusive professional responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient ('advanced therapy medicinal products prepared under hospital exemption').	1. By way of derogation from Article 1(1), only this Article shall apply to advanced therapy medicinal products prepared on a non-routine basis in accordance with the requirements set in paragraph 3 and used in a hospital under the exclusive professional responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient ('advanced therapy medicinal products prepared under hospital exemption'). ***A non-routine basis entails a treatment scale that does not exceed the treatment capacity of a hospital. Member States shall ensure that only hospitals are granted hospital exemption approvals. A transition period of 5 years is granted to holders of a hospital exemption (public and private) that exceed preparation on a non-routine basis to obtain a centralised marketing authorisation. During the transition period, deviations from a non-routine basis guarantee patient access. Member States shall ensure that the scope for use is centred around targeting unmet medical need, in situations when similar treatment is not available and/or affordable.***	Approvals should be granted per hospital where treatment occurs. The definition of non-routine should be centred around a treatment scale that is limited to the treatment capacity of the hospital. If the treatment scale exceeds the capacity of a hospital, or multiple hospitals provide one treatment under several licences, a transition period should be offered to enable centralised marketing authorisation and possible decentralised manufacturing. Furthermore, Member States should take unmet medical needs as the main use case to grant HE licences, taking accessibility and affordability into account in their decision-making. Companies should not be eligible for the hospital exemption, a scheme for treatment on a non-routine scale in case of unmet medical need. Instead they should aim for product development and production on an industrial scale.

Article 2 - paragraph 6		
Text proposed by the Commission	**Amendment**	**Justification**
6. The competent authority of the Member State shall transmit the data related to the use, safety and efficacy of an advanced therapy medicinal product prepared under the hospital exemption approval to the Agency annually. The Agency shall, in collaboration with the competent authorities of Member States and the Commission, set up and maintain a repository of that data.	6. The competent authority of the Member State shall transmit the data related to the use, safety and efficacy of an advanced therapy medicinal product prepared under the hospital exemption approval to the Agency annually. The Agency shall, in collaboration with the competent authorities of Member States and the Commission, set up and maintain a repository of that data. ***The Agency shall ensure that an overview of approved advanced therapy medicinal products prepared under hospital exemption is made public.***	Transparency and insight into available treatments is vital to ensure equitable access across the EU, in particular for ultra rare conditions.

Article 2 - paragraph 9 (New)		
Text proposed by the Commission	**Amendment**	**Justification**
	9. Member States may allow for cross-border exchange of advanced therapy medicinal products prepared under hospital exemption in case of unmet medical needs, if preparation on a non-routine basis is maintained. Competent authorities should share with each other information on hospital exemption approvals and the evidence used for such approvals	It is critical to allow cross-border exchange to improve all patients' access to the therapies they need regardless of where they live, in particular for ultra rare conditions.

	upon request. In case of deviations between national laws, the authorities of the importing country should indicate that these deviations are acceptable. Requirements in Article 2(3-6) should be maintained.	

2. Access and affordability

Patient access to oncology medicines varies considerably across the EU. While in Germany 45 out of 46 (98%) new cancer medicines authorised between 2018 and 2021 at EU level were accessible to patients, countries with comparatively low prices or with low GDP, like Romania, had only 14 cancer drugs available. Moreover, small Member States such as the Baltic ones had less than 10 available (e.g., Latvia and Estonia - 8, Lithuania - 4)[3]. The time to patient access is also significantly longer for most of these latter countries, e.g. approximately 991 days after marketing authorisation in Romania compared to 102 days in Germany[4].

In addition to unequal access across the EU, the prices of cancer medicines also differ significantly between Member States. One study showed that official or list prices differ substantially between countries (up to 92% lower than the highest), and actual prices also differ between countries (up to 58% lower) and some medicines are more expensive in countries with lower GDP[5].

The new Directive can improve the conditions for generic and biosimilar authorisation and competition, therefore improving access and affordability.

We support **Articles 9 – 12** on requirements for abridged applications for marketing authorisation as regards generic, hybrid, biosimilar, and bio-hybrid medicinal products. We also welcome broadening the scope and harmonising the application of the 'Bolar exemption' in **Article 85.** To improve access to medicines and their affordability across the EU, generics and biosimilars should enter the market at day-1 of the expiry of the market exclusivity period.

[3] Newton et al. (2023). EFPIA Patients W.A.I.T. Indicator 2022 Survey. Available at: https://www.efpia.eu/media/s4qf1eqo/efpia_patient_wait_indicator_final_report.pdf.
[4] Newton et al. (2023). EFPIA Patients W.A.I.T. Indicator 2022 Survey. Available at: https://www.efpia.eu/media/s4qf1eqo/efpia_patient_wait_indicator_final_report.pdf.
[5] van Harten, W. H., Wind, A., de Paoli, P., Saghatchian, M., & Oberst, S. (2016). Actual costs of cancer drugs in 15 European countries. Lancet oncology, 17(1), 18-20. https://doi.org/10.1016/S1470-2045(15)00486-6

We strongly support **Article 81** which redesigns the regulatory protection system from 'one size fits all' to a modulated one that promotes patient access to affordable medicines across the EU and addresses the problem of unmet medical needs. We applaud the reduction of basic regulatory data protection period and provision for additional periods of data protection if a medicinal product is placed on the market within 2 years in all Member States where market authorisation is valid, it addresses an unmet medical need, comparative clinical trials are conducted, or if a new therapeutic indication is developed.

While we support the European Commission's efforts to increase transparency around public funding for medicinal products development in **Article 57** in order to help national authorities in the price negotiations, it is important to clarify that funding received from charities needs to be disclosed as well as in some cases they play a key role in the development of medicines[6]. However, to truly incentivise fair pricing and improve access to affordable medicinal products, transparency on all R&D costs and tax breaks is necessary.

Article 57 - paragraph 1		
Text proposed by the Commission	**Amendment**	**Justification**
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 ***or indirect*** financial support received***, including tax breaks,*** from any public authority or publicly funded body, ***as well as any charity,*** 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.	Besides the direct financial support provided by 'public money', an indirect one can be provided by tax deductions or exemptions - this also needs to be reported for full transparency of public financial support. Also, charities, such as cancer societies, often play an important role in development of new drugs by funding the research (e.g. Zolgensma). Not all charities are publicly funded bodies, therefore it should be clarified that financial support provided by them must also be reported.

[6] https://www.afm-telethon.fr/fr/la-therapie-genique-zolgensma-precision-sur-son-prix-et-role-joue-par-genethon.

Article 57 - paragraph 2 - point a		
Text proposed by the Commission	**Amendment**	**Justification**
(a) draw up an electronic report listing: (i) the amount of financial support received and the date thereof; (ii) the public authority or publicly funded body that provided the financial support referred to in point (i);	(a) draw up an electronic report listing: (i) the amount of financial support ***and tax breaks*** received and the date thereof; (ii) the public authority or publicly funded body ***as well as the charity*** that provided the financial support referred to in point (i);	Besides the direct financial support provided by 'public money', an indirect one can be provided by tax deductions or exemptions - this also needs to be reported for full transparency of public financial support. Also, charities, such as cancer societies, often play an important role in development of new drugs by funding the research (e.g. Zolgensma). Not all charities are publicly funded bodies, therefore it should be clarified that financial support provided by them must also be reported.

About the Association of European Cancer Leagues (ECL)

The Association of European Cancer Leagues (ECL) is a non-profit, pan-European umbrella organisation connecting 32 national and regional cancer societies in 27 European countries. Its Access to Medicines Task Force (A2M TF) aims to make safe and effective medicines available to all cancer patients in Europe by insisting on accessibility, availability, affordability, and increased transparency related to medicine prices, which will make healthcare systems more sustainable. Contact ECL:

- Toma Mikalauskaitė, Senior Policy Officer
- Ward Rommel, Chair of Access to Medicines Task Force

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