

Cancer Leagues present their vision for the

EU PHARMACEUTICAL STRATEGY

Timely patient access to affordable medicines



POSITION PAPER

AIMS & SCOPE

The Association of European Cancer Leagues (ECL) welcomes the initiative of building a patient-centred Pharmaceutical Strategy with a strong emphasis on addressing unmet need, achieving greater medicines access, availability, affordability as well as building sustainable healthcare systems.

This paper sets out the key priorities of the ECL Access to Medicines Task Force for the Strategy and suggests concrete recommendations for national and European decision-makers on how to best use legislative and non-legislative tools in order to enable patient access to safe and effective medicines throughout the European Union.

This paper is based on the situation analysis and priority setting within the ECL Access to Medicines Task Force. The paper is not intended to be exhaustive but reflects the collective vision of ECL.

CONTENTS

Introduction	4
SECURING AVAILABILITY	5
I. Tackling Medicine Shortages	5
SUSTAINABLE INNOVATION	8
II. Research, Development & Intellectual Property	8
III. Clinical Trials as the Basis for Safe High-Quality Medicines Clinical Trials	11
IV. Robust Regulatory Environment for the Approval of Medicines	13
V. Review Regulatory Framework for Orphan and Paediatric Medicines	15
ACHIEVING AFFORDABILITY	17
VI. The Power of International Collaboration	18
VII. Striving for Fair Prices of Medicines	20
References	22



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INTRODUCTION

In recent years, prices of cancer medicines have become subject to an increasing concern among health policy-makers and payers in Europe, as well as in other parts of the world. The growing health needs of aging populations combined with growing prices of medicines and an increase in the societal cost of providing care cause budgetary and affordability constraints for most health systems. However, these concerns arising from the experienced growth of the healthcare expenditure on cancer medicines cannot be justified by the rising incidence of cancer alone.

All patients have the right to effective and optimal treatment, regardless of their financial means, gender, age or nationality. Nevertheless, at the current rate of healthcare spending, without real attention to ensuring treatments' value for money, societies may have to make difficult prioritising decisions in order to provide access to health care for the entire population in the near future. This situation, further amplified by the COVID-19 crisis, calls for strategies to obtain economically sustainable health care and healthcare systems.

Therefore, the EU *'Pharmaceutical Strategy - Timely patient access to affordable medicines'* provides the perfect opportunity to address the shortcomings in the current functioning of the pharmaceutical market, from R&D to patient access, and ensure access to essential medicines and new therapies that are clinically superior as well as cost-effective.

SECURING AVAILABILITY



I. TACKLING MEDICINE SHORTAGES IN EUROPE



Growing number of (oncology) medicine shortages throughout Europe

The increasing levels of medicine shortages across Europe pose severe threats to patient safety and adversely impact patient outcomes and the patient care continuum. In recent years, the prevalence of medicine shortages reported in most EU countries has increased exponentially. In France, there were 1,450 medicine shortages in 2019, compared to 868 in 2018 (and to 44 in 2008).¹ In the Netherlands, the number of drug shortages almost doubled in 2019 - 1,492 in 2019, compared to 769 in 2018.² In the Czech Republic, 2,208 products were affected by supply interruptions in 2019, compared to 1,630 in 2018 and 19 in 2008.³

A recent survey of the European Association of Hospitals Pharmacists (EAHP) pointed to the rising shortages of oncology medicines, with 47% of respondents stating that oncology products are among the medicines most commonly in shortage (compared to 39% in 2018).⁴

The EU Pharmaceutical Strategy should call for enhanced coordination at the EU level and the development of tools to prevent, manage and address medicine shortages.



Patients on the front line

A survey conducted by the French League Against Cancer shows that nearly 60% of oncologists claim that shortages have worsened over the past 10 years and 68% of them estimated that the shortage they experienced will have an impact on the chances of their patients surviving for another five years. The survey also showed that shortages lead to significant emotional distress for patients, with many of them expressing feelings of worry (51%), incomprehension (51%) and anger (39%) after having faced a situation of drug shortage.⁵

Medicine shortages can also impair the health of patients who are switched to an alternative therapy, other than a generic or a biosimilar, causing (i) an increased risk of medication or administrative errors; (ii) increased risk of adverse events, greater toxicity or development of drug resistance in some patients; and (iii) suboptimal treatment or therapeutic failures. Additionally, medicine shortages also cause higher costs for the social security system (including hospitals) and more out-of-pocket expenses for patients.



COVID-19 crisis highlights the need to find solutions

This critical situation was apparent long before the COVID-19 pandemic, but the crisis highlighted how the fragility of the medicines' production system directly impacts the quality of care of patients. The

supply issue of curare and sedatives medicines which occurred during the crisis had a devastating impact for cancer patients - as a number of non-essential surgeries had to be delayed putting patient at risk of disease progression.⁶

Lack of knowledge about the causes

In order to put suitable solutions in place, it is crucial to know what causes medicine shortages. Shortages are typically caused by manufacturing, production capacity, supply or commercial decisions issues. Currently, there is a lack of information on the specific causes and they differ from one country to another. Moreover, causes are reported unevenly throughout EU Member States and are typically described in a general way, making it impossible to get a clear picture and understanding of the situation.

European response to the problem

The lack of European coordination on the matter allowed for an inefficient allocation of stocks, legal uncertainty for Members States restricting parallel trade and limited enforcement of legal provisions and application of sanctions.

However, the COVID-19 crisis triggered numerous initiatives at the EU level, including:

- i. Own-initiative report of the European Parliament on medicine shortages;
- ii. European Commission study to (1) identify the root causes of shortages in the EU, (2) assess whether the current legislation provides the right tools to effectively prevent or mitigate the effects of shortages in the EEA countries/markets and (3) map possible solutions to address the problem of shortages in the EU;
- iii. Enhanced cooperation with the 'Single Point of Contact' (SPOC) network increasing communication between the Commission, the EMA the national authorities regarding shortages of all essential COVID-19 medicines.

Medicine shortages are a cross-border health threat and national measures need to be coordinated, complemented and supported by European efforts in order to achieve desirable results. ECL appreciates the enhanced activities at the EU level and presents the below recommendations to further address the situation:

1. Strengthen the existing EU pharmaceutical legislative framework to improve notification of medicines shortages and reinforce obligations of the market Authorisation Holders (MAHs) and wholesalers to supply the market;
2. Require that all medicines marketed in more than one EU Member State have accompanying concrete and legally binding European shortage management and prevention plans in order to switch from crisis management to an upstream approach;
3. Enhance transparency, traceability, oversight and security in the medicine supply chain by sharing information between companies and regulators about the roles of different actors, including raw material and API manufacturers, marketing authorisation holders, distributors, wholesalers etc.
4. Create early warning systems on medicine shortage at both the national and European level and set up a permanent system for monitoring medicine shortages in the EU by building on the SPOC system experience (ensuring that the system focuses on both prevention and crises management of shortages);
5. Ensure timely delivery of the European Commission's study on medicine shortages and include an assessment of the impact of shortages on patients (including health outcomes and associated costs) among its objectives;⁷
6. Publish new EU guidance elaborating on instances when free movement of medicines may be restricted in order to prevent and address medicine shortages;
7. Publish new EU guidance on prudent procurement practices to help prevent the occurrence of shortages of generic medicines;
8. Launch an EU Joint Action focusing on the prevention of, and solutions to, medicine shortages, allowing medicine agencies to exchange best practice and draw plans, as the EMA/HMA's agenda does not have the capacity to tackle the full spectrum of issues.⁸

SUSTAINABLE INNOVATION



II. RESEARCH, DEVELOPMENT & INTELLECTUAL PROPERTY

The patent system and additional mechanisms (e.g., supplementary protection certificate - SPC) protect medicines from generic competition and incentivise companies to do research and development. In the EU, a new medicine is protected from competition for 13 years on average.⁹ In this period, the absence of competition keeps the price at a high level¹⁰ and companies can gain high profit margins, which recover their R&D costs. This further allows them to continue investing in R&D and discover new treatments.¹¹ Although this system undeniably stimulates private R&D,¹² it also has disadvantages.



Mismatch between R&D investment and unmet needs

Commercial development is often inefficient, as it predominantly focuses on limited therapeutic areas. In 2016, 803 clinical studies on checkpoint immuno-therapy for cancer involving 166,000 patients took place. A lot of these studies were superfluous, as companies developed comparable studies in similar molecules but did not share their data. At the same time, other essential research questions were not being investigated, e.g., medicines targeting genetic mutations in cancer.¹³



Negative impact of IP protection on products' affordability

Patent protection prevents access to generics and biosimilars and keeps prices at a high level. Growing competition, particularly related to increased availability of biosimilars, significantly contributes to savings in medicine's budget, allowing for both greater availability of off-patent medicines and greater investments in innovative treatment options.



Lack of data transparency prevents additional research

Patents and incentives, such as data exclusivity, can slow down research. Researchers and companies who intend to patent an invention are not inclined to share information about their work. But sharing early research results gives an impetus to further research.¹⁴

As explained above, the current system of medicine development has limitations. To ensure sustainable innovation that brings real value to patients, decision-makers and stakeholders should focus their efforts on the priorities suggested below:

1. Fund pilot studies to find alternative ways to (i) incentivise and award medicine development and (ii) ensure R&D models result in affordable products.

Research should not be driven by the chase after IP, but rather by societal return where valuable solutions for patients are awarded. There is little evidence analysing alternative models which are designed to bring about innovative medicines at reduced and affordable prices.¹⁵ This uncertainty should lead to a cautious approach, particularly regarding initiatives such as delinkage (see details below), which are highly disruptive and require legal change and/or substantial change in the practice of medicine development.

Therefore, pilot studies financed at the EU level should be conducted to test the potential and feasibility of alternative models, particularly the impact on (i) innovation and price, (ii) the success factors, (iii) the necessary practical and legal changes, and (iv) the dysfunctions of the proposed solutions. Pilot projects should be steered by multi-stakeholder groups which include patient and consumer organisations, healthcare professionals, academia, industry, governmental bodies and health insurance funds. These projects should be financed by European funds, national governments and philanthropic organisations that pool resources from the business world or voluntary partnerships between countries.

All pilot projects must meet the following conditions: (i) transparency about research data; (ii) disclosure of related R&D costs; (iii) focus on needs-driven development; (iv) ensured accessibility and affordability of developed products; and (v) financial and scientific independence.

Examples of Alternative R&D & Reward Systems

Drugs for Neglected Diseases Initiative (DnDi) focuses on affordable medicines for neglected diseases. DnDi is a collaboration of partners in the public and private sector. DnDi works according to the following principles: (i) Research is needs-driven: it is directed at diseases with a high need for a (better) treatment; (ii) Medicines should be accessible and affordable for people who need them; (iii) Research and medicines are public goods. Thus, when DnDi licenses developed products, it negotiates conditions guaranteeing an affordable price and no limitations for further research; and (iv) financial and scientific independence.¹⁶ Since 2003 DnDi has developed eight treatments for five deadly diseases.¹⁷ **Fair Medicine Foundation** is an initiative trying to apply comparable principles, but their scope is not limited to neglected diseases.¹⁸

Delinkage model suggests that costs and risks of R&D are rewarded not by the price of the product and the volume sold (as is currently the case)¹⁹, but by the level of R&D investment and the drug's added value. An example of delinkage is the '**health impact fund**'²⁰ which would directly reward medicine developers. A developer would be able to voluntarily register a product in the fund and agree to bring it to the market at the cost of production and distribution. Over the following ten years, the developer would receive a yearly compensation from the fund.

The compensation would be proportionate to the measured health impact of the medicine. A comparable proposal is the 'medical innovation prize fund'.²¹

Under pressure from the COVID-19 pandemic, the EU proved that it is capable to incentivise companies' product development in new ways. The European Commission established several 'Advance Purchase Agreements' (APAs) for promising vaccines against coronavirus. APAs guarantee that, in return for the right to buy a specified number of vaccine doses in a given timeframe at a given price, part of the upfront costs faced by vaccine producers will be financed by European funds.²² Of course, the success of this strategy remains to be seen and the context of a viral pandemic differs from the medical needs of cancer patients or other rare and chronic diseases.

2. Match R&D with unmet need.

Unmet need should be defined by authorities in close collaboration with stakeholders, namely patients, consumers, healthcare professionals and non-profit researchers, and be based on added patient/societal benefit taking into account the disease severity, burden and treatment alternatives. Both public and private R&D should be steered toward areas with no, limited or inadequate treatment options. Public research should additionally focus on areas with low commercial interest.

3. Increase competition for commercial development by extending the role of public, academic and non-profit research from basic research to market-ready products.²³

This approach might be particularly promising in the field of gene and cell therapy, where treatments are tailor-made to fit the genetic profile of an individual patient. To achieve success, legislation related to the marketing of products would need to include public research entities and non-profit organisations. In addition, the EMA and national medicines agencies should evaluate clinical evidence provided by public researchers and non-profit organisations, (e.g., related to new indications). Subsequently, it is necessary to work with sponsors to enable extension of the product to new indications based on additional data from public/non-profit research, and thus enabling off-label use to become on-label.



III. CLINICAL TRIALS AS THE BASIS FOR SAFE HIGH-QUALITY MEDICINES

Clinical trials are the gold standard for testing a treatment's efficacy and safety. Not only do they help drive progress in cancer research, but they also afford vital opportunities for patients who may have few other treatment options available. Europe is a global leader in clinical research, with around 5,000 cancer trials currently ongoing.²⁴ However, we still see a lack of trials in areas in need of better treatment options, both for rare and more prevalent diseases.²⁵



Delay in the implementation of Clinical Trials Regulation

The 2014 Clinical Trial Regulation (CTR), due to come into force in the coming years, will be a significant improvement on the current Clinical Trials Directive, harmonising the regulatory environment for clinical trials across the EU, to the benefit of both patients and researchers. It will allow for a more efficient setup of cross-border clinical trials, and provide new technological infrastructure, including a portal and database which will simplify trial application and approval procedures. The Regulation aims to significantly reduce assessment and approval times for proposed trials. However, the implementation of CTR has been considerably delayed. Given the noted shortcomings of the current Directive, implementation as soon as practically possible must remain a priority.



Integration of clinical trials data with rigorous real-world data is key

The randomised controlled trial (RCT) has been the golden standard for designing clinical trials for decades, noting of course its well-known limitations. However, the increasing costs of large-scale RCTs, the need for long follow-up periods, and large patient groups for diseases with rare events and personalised medicine, means that the use of RCTs has becoming increasingly less attractive to medical product developers. As a result, these developers are increasingly using real-world data (RWD) and real-world evidence (RWE) to support clinical trial designs (e.g., large simple trials, pragmatic clinical trials (trials in usual clinical practice)).

Though we recognise the value of studies using RWE, which often consist of multiple RWD sources, it is important that their growing use does not lead to these studies being designed with less rigour than their RCT counterparts. These studies should be conducted with the most rigorous possible design, without bias and using appropriate analytic approaches. It is important to note that such studies should serve as additional data sources and should not fully substitute RTC.



Post-marketing research and additional data collection

In addition, further studies in medicines' safety and efficacy after they enter the market should be encouraged. Data from such studies should be used for the re-evaluation and potentially for the extension of indication of marketed products. Therefore, it is necessary to support studies where there is limited private investment (e.g., repurposing trials of off-patent medicines, research optimisation or combination research).



Uncertain outcomes of personalised treatments

The uptake of personalised medicine is currently hampered by uncertainty about its outcomes connected to added value of such treatments to patients in terms of prolonging survival and quality of life.²⁶ Personalised medicine requires large datasets for advanced statistical analysis and learning and large-scale collaborations. Therefore, advancements in the methodology and set up of trials in the area of personalised medicine is needed and must be developed in close collaboration with decision-makers. Further support for research into personalised medicine would provide insights into their outcomes and reduce uncertainty over their use.

In collaboration with the planned European Research Area, Horizon Europe's Cancer Mission, and Europe's Beating Cancer Plan, the new pharmaceutical strategy for Europe should develop more opportunities for clinical research and trials across the Union by:

- 1. Ensuring the full implementation of the Clinical Trial Regulation as soon as possible;**
- 2. Ensuring that the EU-UK Future Relationship sustains collaboration on clinical research, as the UK is currently involved in 28% of all EU trials and leads on more paediatric and rare disease trials than any EU Member State;²⁷**
- 3. Supporting independent (non-profit) clinical research that ultimately demonstrates the added therapeutic value for patients (i.e., overall survival and quality of life);**
- 4. Incentivising novel clinical trial designs and research on treatments that are neglected by the pharmaceutical industry, such as:**
 - i. Treatment optimisation research to identify the optimal dosage and duration of existing treatments, both for the benefit of patients and to guarantee the sustainability of healthcare systems;
 - ii. Drug re-purposing research to find new applications of well-established, effective and widely available generic medicines;
 - iii. Multimodality combination treatments.
- 5. Making research results and data sets from all clinical trials submitted to the EMA for marketing authorisation publicly available, in order to build trust in the EU's regulatory framework and foster further research concerning a product's efficacy and safety;**
- 6. Compelling public and private research entities to abide by the WHO Joint statement on public disclosure of results from clinical trials, as timely disclosure increases value and efficiency in the use of funds and reduces reporting bias, which ultimately leads to better decision-making in health;**
- 7. Setting up rigorous design of clinical trials using real world data, with appropriate analytic approaches, to minimise the inherent risk of bias in such studies to avoid decision making based on flawed results;**

8. **Advancing the methodology and setting up trials in the area of personalised medicine in close collaboration with decision-makers, and further support for research into personalised medicine, to provide insights into their outcomes and reduce uncertainty over their use.**



IV. ROBUST REGULATORY ENVIRONMENT FOR THE APPROVAL OF MEDICINES

The European Medicines Agency (EMA) aims to ensure timely access to safe and efficacious new treatment possibilities. This entails a delicate balance where the need for timely access to new innovative medicines without unnecessary delay is met without compromising decision making based on robust evidence.



Questionable use of accelerated schemes

In order to support both fast access to new treatment options and to stimulate medicine development in areas of unmet need, the EMA introduced accelerated access schemes with lower regulatory requirements (e.g., adaptive pathways, use of surrogate end points in conditional marketing authorisation, enhanced communication with developers in the PRIME Scheme and enhanced post-marketing surveillance). This means that certain new medicines or new indications can obtain faster marketing authorisation in Europe based on relatively small clinical studies with a short observation period (e.g., phase II trials, single arm trials).

Cancer medicines are the single largest group of new active substances receiving a positive opinion from the EMA under accelerated approval schemes, which are primarily intended to accelerate access in areas of high unmet medical need. However, it is not clear whether early access schemes are used as intended or whether they result in patients being exposed to new medicines where the benefits are uncertain and safety issues unknown.



Not all new treatments are innovative in terms of added patient benefit

Patients in particular and society in general expect new therapies to be clinically better than existing alternatives as well as cost-effective. However, several studies have demonstrated that cancer medicines do not meet the clinical benefit threshold when measured using the validated frameworks of the American Society of Clinical Oncology (ASCO) and the European Society of Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). A recent study of the EMA's decisions found that out of the 48 cancer drugs approved for 68 indications between 2009 and 2013, only 24 (35%) of the indications demonstrated an extended survival (median 2.7 months) and only 10% demonstrated improvement related to patients' quality-of-life.²⁸



The need for generation and uptake of real-world evidence

It is crucial to align patient and public health needs with the development of new medicines, as well as to maintain high regulatory standards. However, as data from clinical trials used for EMA assessments are often based on surrogate measures and the evaluation rarely reflects how the treatment will perform under real-life conditions, clinical trial data are often insufficient to demonstrate clear benefits for patients.

Real-world data (RWD) and real-world evidence (RWE) are playing an increasing role in medicines development and healthcare decision-making. Regulatory authorities use RWD to monitor safety and to verify effectiveness post-marketing, particularly after granting marketing authorisation based on surrogate measures. It is therefore concerning that post-marketing evidence generation is often not available. In addition, health systems use RWE to develop guidelines for clinical practice. It is of utmost importance that RWD are delivered systematically to EMA throughout the medicine life-cycle and are made available for further research and decision-making.



Alignment between personalised medicines and accompanying diagnostic tools is crucial

Personalised medicines offer promising results in maximising the effects of therapies and diminishing adverse reactions. However, they pose a great challenge to regulatory bodies, as they consist of both a pharmaceutical and a companion diagnostic measure which undergo different EU regulatory pathways. Clinical use of personalised medicines will require prescription of both the drug and the diagnostic tool, and the effect of the treatment will largely depend on the diagnostic measure. Differences in the development and authorisation for medicines and in-vitro diagnostic tools (IVDs) make it difficult to synchronise timing. European guidelines for co-development of both products and co-ordination of approval procedures do not currently exist.

Since the uptake of new cancer medicines is currently hampered by uncertainty about their outcomes, close collaboration between developers, academia, health professionals, patients and decision-makers on setting up clinical trials and relevant outcomes are necessary. The Pharmaceutical Strategy, the EMA Regulatory Science Strategy 2025 and the EMA/HMA Joint Network Strategy 2025 should:

- 1. Ensure high quality benefit-risk assessments of patient-relevant endpoints before granting market access to medicines, stressing the need for surrogate endpoints in clinical trials to be accompanied by hard endpoints reflecting improvements in overall survival and quality-of-life measures;**
- 2. Grant market access via modified pathways and accelerated approval schemes only in cases of unmet medical need, as intended, and prevent their misuse in cases where sufficient evidence for market approval is lacking;**
- 3. Address challenges of pharmaceutical and diagnostic co-development in personalised medicines by developing transparent European guidelines on trial designs, statistical methodology, authorisation processes and clinical use;**

4. Demand systematic collection and submission of real-world evidence (including overall survival, adverse reactions and quality-of-life improvements) once medicines enter the market and their timely re-assessment, where appropriate;
5. Ensure that the quality of medicines and good manufacturing practice is not compromised by regulatory flexibility measures put in place by the European Commission during the COVID-19 pandemic and other public health emergencies.



V. REVIEW REGULATORY FRAMEWORK FOR ORPHAN AND PAEDIATRIC MEDICINES



Development of rare disease treatments while securing affordability of designated products

Orphan medicinal products (OMP) have become an attractive destination for investment and, thanks to the many incentives offered by the 2000 Orphan Regulation (e.g., scientific advice and protocol assistance with fee exemptions, orphan status and market exclusivity), many new orphan medicines (ranging from products providing symptom management to curative solutions) were introduced to the European market.

As the Pharmaceutical Strategy seeks to enable the Commission's ambitious agenda in combatting cancer, it is essential that it also recognises the unmet need for treatments of rare cancers – which comprise 20-30% of all cancer diagnoses²⁹ and often have notably poorer outcomes and fewer treatment options than more common cancers. As we seek to drive up survival, we must do more to foster new treatments, including through the orphan designation.

With the desired review of the Orphan Regulation, decision-makers need to ensure that its success will not be overshadowed by the negative side effects of the Regulation's IP protection and that medicines developed with the assistance of public incentives will be available to patients and affordable for health systems. Importantly, personalisation of treatments should not lead to orphanisation of disease areas (including cancer) and proliferation of granted incentives. Shortcomings flagged in the recently published study to support the evaluation of the EU Orphan Regulation³⁰ should be addressed by changes in the current regulatory framework.



The need for further investigation in paediatric populations

The Paediatric Medicines Regulation, introduced in 2007, seeks to drive licensing of medicines for children through a combination of incentives (such as 10 years of data and market exclusivity) and additional requirements for research into paediatric medicines (Paediatric Investigation Plan, PIP). It is widely acknowledged that there is a lack of new cancer medicines being developed specifically for children relative to adults and the development of paediatric treatments is driven by adult needs.

Therefore, promoting additional investment in paediatric treatment options remains critical. For instance, for childhood cancers, the Regulation failed to achieve its desired impact, with only three paediatric-use marketing authorisations granted between 2007 and 2016.

PIP waivers are granted too liberally, often on the grounds that the treatment is aimed at a cancer type which is not present in children, rather than based on the mechanism of action of the treatment which might turn out to be effective in childhood cancers. Therefore, only two innovative cancer medicines were approved via PIPs between 2007 and 2016.

In addition, the Regulation risks being overtaken by scientific advances, such as the increasing importance of biomarkers in determining which treatment to offer. One UK study suggests that around 50% of paediatric cancers have genetic mutations that can be targeted by existing drugs used in adults but found only 7% of paediatric patients were receiving these treatments. This suggests a gap in research into and access to these drugs for paediatric patients – although it's important to note new biomarker-driven treatments will not always be more appropriate than existing regimens.³¹

Confirmation that the Commission will review the Orphan and Paediatric Regulations as part of the Pharmaceutical Strategy is welcome. As it does so, priorities should include:

- 1. Setting clear and transparent criteria for sustaining orphan designation at the time of marketing authorisation by the EMA based on significant benefit and prevention of misuse and overuse of the orphan status (incl. evergreening and salami slicing);**
- 2. The Commission's recent move to provide free scientific advice to academics working on rare disease therapeutics is welcome. It should consider what other non-regulatory incentives might be offered to organisations under the Regulation;**
- 3. Ensuring the right balance between awarding incentives in orphan medicine development, particularly where there exist no treatment alternatives, and preventing unintended effects on affordability (e.g., by revoking market exclusivity when a medicine has generated sufficient return on investment; or evaluating the benefit-risk ratio of extended market and data exclusivity);**
- 4. Ensuring criteria for orphan designation exclude eligibility of personalised treatments for more prevalent diseases and prevent proliferation of market exclusivity and other incentives;**
- 5. All awarded incentives for orphan medicines (and other areas including paediatric medicines, antimicrobials etc.) should be evaluated periodically to assess whether they have reached the intended effect and not posed obstacles to patient access to these products;**
- 6. Introducing the 'mechanism of action principle' in the Paediatric Regulation, to prevent granting of PIP waivers when an adult cancer has no paediatric iteration**

(e.g., lung cancer treatments) but the drug's mechanism of action (such as targeting a specific genetic variation) is plausibly beneficial for some paediatric cancers, thereby reducing the ratio of waivers to PIPs in the long-run;

7. Introducing regulatory requirements and rewards for early PIP completion that will establish an evidence base for the paediatric population, even if the adult development program is aborted. Currently, new medicines showing promise for children are not adequately researched after a medicine fails to show potential in an adult indication;
8. Allowing inclusion of adolescents in paediatric phase I, II and III trials where relevant (e.g., for adolescents with paediatric cancer type or biological targets);
9. Considering alignment and synergies with global initiatives on paediatric medicine development – including the recently introduced RACE for Children Act.

ACHIEVING AFFORDABILITY



Growth in healthcare spending

In recent years, prices of cancer medicines have become subject to an increasing concern among health policy-makers and payers in Europe, as well as in other parts of the world. The growing health needs of aging populations combined with growing prices of medicines and an increase in the societal cost of providing care cause budgetary and affordability constraints for most health systems. However, these concerns arising from the experienced growth of the health system expenditures on cancer medicines cannot be justified by the rising incidence of cancer alone.



The dilemma between unmet need, fast access, lacking evidence and budgetary constraints

All patients have the right to medical treatment, regardless of their financial means, gender, age or nationality. Nevertheless, at the current rate of healthcare spending, it may not be possible to provide access to health care for the entire population in the near future. Within cancer care there is a dilemma between the wish to address the unmet medical need with fast access to new cancer medicines, and the lack of robust evidence regarding the safety and efficacy of new treatments, and the increasing prices and impact on healthcare budgets of cancer medicines. This situation calls for strategies to obtain economically sustainable health care, including fairer, more transparent, justifiable and predictable input prices (e.g., the cost of personnel, buildings, equipment and medicines, including cancer medicines), better knowledge about the value for money of different treatment options and enhanced international collaboration about reimbursement criteria, documentation, and processes across Europe.



VI. THE POWER OF INTERNATIONAL COLLABORATION

Over the last decade, oncology treatments have become highly innovative and complex. Countries are faced with a lack of data to anticipate adequately the evolution of the market and to evaluate the clinical benefit of newly launched products.



Unequal capacity to support uptake of new treatment options

While collaboration and expertise in terms of regulatory approval of medicines significantly improved with the establishment and growth of the European Medicines Agency (EMA), not all EU Member States have equal resources to perform high quality Horizon Scanning (HS) and to identify emerging technologies which would enable them to prepare in terms of necessary structural changes and budget planning. In addition, not all countries have the same capacity to perform Health Technology Assessment (HTA) to evaluate cost-effectiveness of new medicines compared with existing treatments and the standard of care.



Information asymmetry related to medicines prices and pricing practices

Lack of information combined with the scarce transparency of the medicine market create an information asymmetry between national governments and often global pharmaceutical companies. Many solutions to achieve greater transparency, better regulation and enhanced international collaboration are already on the agenda of many decision-makers and stakeholders. Since 2015, Europe noted a wave of creation of voluntary inter-governmental initiatives, such as the Beneluxa and the Valletta Declaration, which contribute to knowledge-sharing on best practices and method harmonisation in horizon scanning, HTA, and medicines pricing and reimbursement. However, to be successful, they require strong political will and trust and between the decision-makers involved.

ECL strongly encourages decision-makers to commit to enhanced international collaboration. Joint price negotiations and purchasing should be the ultimate objective to be achieved and different levels of information-sharing and resource-pooling can serve as a basis to build the necessary trust between countries. This will allow countries to better define their own willingness to pay based on the most relevant information and try to obtain the best possible deals.

The Pharmaceutical Strategy should recognise international collaboration as the most effective way to face challenges related to sustainability of health systems. It should:

1. Provide resources to support collaboration in Horizon Scanning

Many international collaborations aim at performing HS, as it may be the easiest way to build trust between participants. Recently, the International Horizon Scanning Initiative (IHSI) was

created to pool resources from different countries. Currently, nine countries are participating in this initiative: The Netherlands, Belgium, Luxembourg, Ireland, Denmark, Norway, Portugal, Sweden and Switzerland.³² This promising initiative allows decision-makers to anticipate the launch and uptake of new products. It is also an essential first step that can lead to more complex collaborations, including HTA and joint negotiations and procurement.

2. Ensure sustainable European cooperation in Health Technology Assessment

ECL continues to support the European Commission's legislative proposal on health technology assessment published on 31 January 2018 and the amendments adopted by the European Parliament on 3 October 2018. ECL hopes that members of the Council of the European Union will be able to reach an agreement and adopt a regulation establishing European HTA cooperation, which will ultimately improve access to high-quality medicines for all patients in Europe.

To overcome the main challenge in unifying the different methods and selecting priorities for the cost-benefit analysis, supporting voluntary cooperation (e.g., under EUNetHTA or Beneluxa) can further contribute to necessary trust-, capacity- and capability-building among Member States.

Any cooperation should strive for the highest possible standards and involvement of patients, healthcare professionals, academia and public health entities to get a clearer understanding of societal needs and preferences.

3. Encourage cooperation on pricing and purchasing

Information exchange on prices and pricing practices is crucial to increase the bargaining power of public payers in pricing negotiations. The EURIPID database provides countries with list price information and has the potential to include more information for countries to share to support their pricing and reimbursement decisions at the national level (e.g., sharing information on real prices of products).

The possibility for a joint price negotiation requires a lot of trust among decision-makers and the willingness of the pharmaceutical industry. It has so far been achieved only in 2018 in the case of Spinraza under the Beneluxa initiative, which should be regarded as good practice. It is still not clear which factors are essential to succeed in a joint price negotiation, but this success demonstrates that it is possible to find a win-win situation where the industry can also benefit from direct and quick access and reimbursement of their products on several countries at once.

Untapping the potential of joint procurement in the area of medicines has been recently explored for the purchasing of vaccines for COVID-19. Decision-makers should evaluate this experience and seek opportunities for similar practice beyond public health emergencies.



VII. STRIVING FOR FAIR PRICES OF MEDICINES

The ECL Access to Medicines Task Force supports the establishment of a **High-Level Working Group on fair pricing**, facilitated by the European Commission, which would connect all relevant stakeholders, including public authorities, payers, patients, public health NGOs, academia and the industry in order to define a fair price and identify opportunities and challenges connected to different pricing models.

ECL recently published a new definition of a fair price, stating key principles that should be reflected in any pricing model used by pharmaceutical companies and payers. ECL believes that:

A 'fair price' is justifiable, predictable and cost-effective within the aims and priorities of the healthcare systems and the available budget.

At the same time, a fair pricing policy that takes into account the ethical and financial dimensions of patient access to care, affordability and sustainability of healthcare systems should be encouraged and rewarded.*

Whereas 'justifiable' means a price that reflects the documented and clinically relevant benefit of the medicine, and a reasonable relationship between the cost of bringing the product to market (including R&D, production, marketing) and the price.

Whereas 'predictable' relates to the need for health payers, policy makers and systems to be able to predict the total costs of investing in the treatment.

'Cost-effective'(ness) could be a common criterion for evaluating whether the price seems 'justifiable' as it links benefits with costs in a systematic way and provides a comparable decision-making tool across healthcare interventions.

Finally, 'affordability' addresses the financial side of the sustainability of health systems.

A prerequisite for obtaining fairer prices is a higher level of transparency and access to information about end-user prices, documentation of product value and the cost of developing and bringing the pharmaceutical product to market as well as reimbursement decision-making processes.

* The definition can only be interpreted in the context of the recitals.

All stakeholders have a role to play in achieving fair prices and payers, policy-makers, and legislators have a very large stake in fair pricing. However, without international collaboration and cultural changes within pharmaceutical companies, fairer prices and pricing approaches will not be achieved.

Policy-makers and payers should:

1. Strive towards the full implementation of the WHA Resolution on improving the transparency of markets for medicines, vaccines and other health products;
2. Pool resources and enhance collaboration throughout the entire medicines access pathway, to prepare health systems for (i) the arrival of new medicines and technologies, (ii) conducting high quality HTA and (iii) sharing information about prices and pricing and reimbursement strategies, in order to enhance countries' ability to (a) prioritise medicines with higher clinical value, (b) review and adjust prices based on new evidence, and (c) effectively negotiate the prices of medicines;
3. Provide structures, control systems and incentives to either reward socially responsible and highly ethical industrial behaviour or punish unethical behaviour;
4. Review regulatory incentives where they may lead to unaffordability of products (e.g., orphan medicines) and ensure that awards for innovation do not lead to a lack of competition and monopolistic prices;
5. Attach conditionalities to both national and European public funding (e.g., Horizon Europe, Innovative Medicines Initiative - IMI), and ensure that public investment in R&D is accounted for and that medicines resulting from publicly funded research are available for a fair and affordable price;
6. Ensure that criteria and processes for priority setting in health care are explicit, transparent and that there is a clear link between priorities, national pricing policies and practices, and the actual price of medicines. Furthermore, pricing and reimbursement authorities should be transparent about their decisions, how they are made, what criteria are used and who is involved in the process.

Pharmaceutical companies should:

1. Price new medicines fairly and responsibly to ensure that they are accessible and affordable. They should also incorporate responsibility for access and sustainability (CSR) of healthcare systems as part of their market access and pricing strategies for pharmaceuticals), as seen within other commercial areas;
2. Apply a higher degree of cost-consciousness (i.e., lowering the cost of bringing the product to market) throughout the product value chain;
3. Be transparent about the costs of bringing the product to market as well as end-user prices (by disclosing these figures to relevant stakeholders, e.g., public authorities);
4. Include HTA and payer considerations early on in the product development;
5. Incorporate an ethical charter and guidelines within product development and pricing processes;
6. Focus on steering R&D investments toward areas with higher unmet need and develop pharmaceutical products with added value for patients and public health.

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The Association of European Cancer Leagues (ECL) is a non-profit, European umbrella organisation of national and regional cancer societies. Located in Brussels, ECL provides an exclusive platform for members to collaborate with their international peers, primarily in the areas of cancer prevention, tobacco control, access to medicines and patient support, and creates opportunities to advocate for these issues at the EU level.

VISION: A Europe free of cancers

MISSION: To advocate for improved cancer control and care in Europe through facilitating collaboration between cancer leagues, and influencing EU and pan-European policies.



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Wish to further discuss ECL's vision for the Pharmaceutical Strategy?

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