ECL ACCESS TO MEDICINE TASK FORCE

CROSS-BORDER COLLABORATION INITIATIVES IN THE HEALTHCARE SPACE

Facilitating access to innovative treatments at fairer prices

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ABOUT THE ECL ACCESS TO MEDICINES TASK FORCE

Established in 2016, the ECL Access to Medicines Task Force connects 29 national and regional cancer societies in 25 European countries, representing over 500 million Europeans. It 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, ultimately leading to sustainability of health-care systems. The Task Force strongly believes in the power of constructive dialogue. We urge all stakeholders to push for access to high-quality, affordable treatments, improving both survival and the quality of life of cancer patients and survivors.

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Opinions expressed in this paper reflect the position of the ECL Access to Medicines Task Force collectively and it may not reflect the opinion of individual Task Force's members, nor the views of their respective organisations.

FOREWORD

The cancer oncology drug pipeline confronts governments and patients with huge challenges: disparities in access, daunting prices, lack of clear data about patient benefits, and weak systematic involvement of patients in research.

No single country can confront these challenges on its own.

European countries have shown an increased willingness to work together on access to medicines. These initiatives such as BeNeLuxA, the Nordic collaborations and the Valletta Declaration, aim to improve the management of financial resources and/or enhance timely and efficient patient access to innovative therapies.

Existing cross-border collaborations have shown the potential of pooling resources to facilitate access to new drugs for patients at a fair price. These initiatives can lay the foundations of robust joint health technology assessments and horizon scanning processes and foster more transparency in the pharmaceutical market.

EU-level negotiations and purchasing of treatments can restore the balance of power between public health authorities and pharmaceutical companies. At the same time, we need to thoroughly examine the EU-level COVID-19 vaccine procurement, by learning from its shortcomings and building on its achievements.

The ECL Access to Medicines Task Force supports policies and initiatives that deliver the timeliest access to (innovative) affordable treatments for patients, whilst ensuring the financial sustainability of our healthcare systems.

We strongly believe that national governments should systematically consider cross-border collaborations for the sake of patients and national health budgets.

Steering Committee of the ECL Access to Medicines Task Force

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EXECUTIVE SUMMARY

The ageing populations and increasing incidence of cancer, coupled with the fast-growing prices of cancer treatments, threaten both the sustainability of healthcare budgets and patient outcomes across Europe. The launch prices of cancer drugs have more than doubled over the last 20 years[1] but the costs required to place a product on the market are still to a large extent unknown.

Despite efforts to achieve better coordination, fragmentation is an enduring feature of the European health landscape: the lack of cooperation, differences in the price and reimbursement systems, and differences in off-label and experimental drug usage.

While the European Commission is in the process of building a resilient European Health Union and the World Health Organization Regional Office for Europe (WHO/Europe) is developing a new social contract between the private and public sector via the Oslo Medicines Initiative, the pharmaceutical framework should be redesigned to truly ensure equal access affordable, safe, effective, and high-quality medicines for all patients across the European region and beyond. This can be facilitated through cross-country collaboration in the pharmaceutical market.

In this paper, the ECL Access to Medicines Task Force outlines the lessons learnt from (i) existing European cross-border initiatives in the field of medicines and (ii) from the cooperation and solidarity demonstrated by the EU Member States and EU institutions during the COVID-19 pandemic and in the aftermath of the outbreak.

"*Cross-border collaboration*" and "*cross-country collaboration*" are used interchangeably in this paper, as there are no set definitions of the two terms, and these terms seem to be used interchangeably in the sources that informed this paper.

The scope of this paper extends beyond the 27 Member States of the European Union, as the ECL Access to Medicines Task Force strongly encourages to keep open lines of communication with members of the European Free Trade Association (Iceland, Liechtenstein, Norway and Switzerland) and the United Kingdom.

The paper concludes that a clear political mandate is critical to establishing cross-country collaborations, which can be developed either through a bottom-up or a top-down approach. The paper also outlines the key ingredients needed to facilitate the success of intergovernmental initiatives in the healthcare space and recommends the following actions:

- **EU policymakers should seize the momentum** of solidarity coming from the COVID-19 pandemic and willingness to come together to face increasingly complex challenges. From a political and diplomatic perspective, acting as a single buyer in the pharmaceutical sector would be a powerful signal of unity. EU policymakers should build on the COVID-19 vaccine and treatment procurement experiences to guarantee equitable access to medicines for the benefit of all European citizens. The recent joint procurement agreement signed by the European Commission for the supply of a monoclonal antibody treatment for coronavirus patients is another step in the right direction.

- **National policymakers should seize the momentum** to share experiences, information, and best practices across Europe to streamline regulatory processes, avoid duplication of efforts, and align on principles and criteria that impact price policies. Collaborating with EU institutions and with national counterparts does not mean undermining the division of the competencies laid in the Treaty of the Functioning of the European Union but it rather means pooling resources to increase efficiency.

- **Civil society organisations should seize the momentum** and take the opportunity to call on national policymakers, EU policymakers and regulatory agencies for a fairer pharmaceutical system in Europe to overcome inequities and inequalities in affordability, accessibility, and availability of new health technologies.

RECOMMENDATIONS

Key recommendations for EU policymakers and WHO/Europe advisers:

- Build on the COVID-19 vaccine procurement experience and the EU Strategy on COVID-19 Therapeutics to centrally purchase effective, novel cancer treatments to guarantee equitable access to new drugs with proven added value in all European countries;
- Build on the lessons learnt from the latest European Commission's Joint Procurement Agreements to enhance transparency and perform a rigorous Health Technology Assessment (HTA) as part of the process;
- Organise and facilitate roundtables jointly coordinated by the World Health Organization Regional Office for Europe (WHO/Europe) and the European Commission to encourage cooperation and information sharing in relation to price-setting procedures;
- Financially support e-learning modules to allow national and regional authorities, where suitable, to map existing best practices, principles, and criteria that can facilitate cross-country initiatives and evaluate whether these can be applied and implemented in other comparable settings. These e-learning modules could be developed by WHO/Europe, with the aim of boosting the capacity of national and regional authorities and providing them with guidance and expertise in joint procurement;
- Continue to play a central role in overseeing ethical business behaviour in the use of incentives and, as for the Aspen case, focusing on medicines for rare cancers and diseases.
- Support and advance development of medicines by academia, non-profit research organisations and non-commercial entities.

Key recommendations for national and regional policymakers:

- Acknowledge and reward research funded by charities and non-profit research organisations;
- Apply the principles and guidance outlined in chapter 2 '*Ingredients for a successful cross-border collaboration*' to establish and/or reinforce collaboration initiatives aimed at enhancing medicine price transparency to, in turn, increase availability, affordability and accessibility to medicines;
- Share and take stock of success stories and lessons learnt from the implementation of existing cross-border initiatives;
- Build communication channels with EU Member States and regions that face similar challenges in terms of affordability, accessibility, and availability of unaffordable health technologies;
- Encourage the use of the European Integrated Price Information Database (EURIPID), which enables authorities to quickly access official prices of publicly reimbursed, mainly out-patient medicinal products;
- Facilitate cross-border collaborations:
    - to leverage and negotiate stronger agreements with industry and solve uncertainties about value (e.g. by making clear agreements with industry about post-marketing studies);
    - to establish joint horizon scanning initiatives so that countries are in a stronger position and can act as proactive buyers.

Key recommendations for civil society organisations:

- Team-up with like-minded organisations to advocate for equal access to medicines at the national and regional level and come up with a common vision and mission;
- Call on national policymakers to improve the national pharmaceutical market by presenting case studies where cross-border collaboration had an impact on, for instance, prices of health technologies (e.g. joint procurement activities in hospitals in the Nordic countries and the BeNeLuxA initiative);
- Call on the European Commission to foster close cooperation with national authorities building on the experience and lessons learnt from procurement during the COVID-19 crisis;
- Developing in-house skills to run communication and advocacy campaigns, and identify and act when windows of opportunity arise (e.g. during political campaigns).

CONTENTS

INTRODUCTION

One of the lessons that can be drawn from the Council conclusions on COVID-19 lessons learned in health (2020/C 450/01) was about improving access to and facilitating the sharing of information in relation to medicinal products. **More transparency, coordination, and participative approaches in the pharmaceutical sector are urgently needed in Europe, now and in the future.** The current misalignment of information and poor transparency are major barriers to a fair system when negotiating price and reimbursement issues. The generalised lack of transparency has led to justified criticism and eroded societal trust in medicine, governments, and EU institutions[2].

In addition, due to limited resources, several governments are struggling to anticipate and analyse the potential of new medicines coming into the market. This leads to information asymmetries when countries are at the negotiating table with the pharmaceutical industry[3]. Therefore, in the last 9 years, EU Member States have joined forces and launched several cross-country initiatives to foster timely and affordable access to medicines (see table below).

Overview of European cross-border collaborations in the field of medicines

NAME	COUNTRIES INVOLVED	SCOPE
Baltic Partnership Agreement (2012)	Latvia, Lithuania and Estonia	• Centralised joint purchasing (i.e. tenders, negotiation, payment and distribution) to reduce expenditures and ensure continuity of access to medicines, medical devices (lending) and vaccines (joint procurement)
BeNeLuxA (2015)	2015: Belgium, Luxembourg and The Netherlands 2016: Austria 2018: Ireland Interested Parties[1]: France, Italy, Switzerland, Czech Republic, Romania and Slovenia	• Health Technology Assessment (HTA) • Horizon scanning • Information sharing on prices and markets • Joint negotiation for purchasing to ensure affordability • Exchange of strategic information
Central Eastern European and South-Eastern European Countries Initiative (2016)	Bulgaria, Croatia, Latvia, Poland, Romania, Serbia, Slovakia, Slovenia, North Macedonia and Moldova	• Price negotiations for pharmaceuticals

Declaration of Sofia (2016)	Bulgaria, Croatia, Estonia, Hungary, Latvia, North Macedonia, Romania, Serbia, Slovakia and Slovenia	• Information sharing on prices and markets, with potential for joint purchasing in the future
Fair and Affordable Pricing (FaAP) Initiative (2019)	Czech Republic, Hungary, Lithuania, Poland and Slovakia	• Information sharing • HTA • Joint pilot negotiation
FINOSE Collaboration (2017)	Finland, Norway and Sweden	• Horizontal scanning • Price negotiations • Information sharing of old & new hospital medicines
International Horizon Scanning Initiative (2019)	Belgium, Denmark, Ireland, the Netherlands, Norway, Portugal, Sweden and Switzerland	• Horizon scanning • HTA
La Valletta Declaration (2017)	2017: Cyprus, Greece, Ireland, Italy, Malta, Portugal, Romania and Spain 2018: Slovenia, Croatia Interested Parties: France (Observer) and Estonia	• Information sharing • Best practice identification • Horizon scanning of innovative medicines and therapies • Exploration of mechanisms for price negotiations and joint procurement
Nordic Council Working Group on Exchange of information and Experience in the Medicines Area (WGEMA) Collaboration (2017)	Denmark, Finland, Iceland, Norway and Sweden	• Focus on availability and affordability of medical products. • Improving coordination, cooperation and research at the EU level
Nordic Pharmaceuticals Forum (2015)	Denmark, Iceland, Norway and Sweden	• Horizon scanning • Information sharing on prices and markets
Romanian and Bulgarian Initiative (2015)	Bulgaria and Romania	• Joint negotiations in purchasing to get lower prices for pharmaceuticals • Cross-border exchange of medicines in short supply to ensure continuity of access
Southern European Initiative (2016)	Bulgaria, Cyprus, Greece, Italy, Malta, Portugal and Spain	• Information sharing on prices and markets • Collaboration on R&D on innovative medicines
Spanish and Portuguese Initiative (2017)	Portugal and Spain	• Joint procurement to ensure affordability

Source: adapted from Espin et al. 2016

Despite the acknowledgement of the potential added value of cross-country collaboration to facilitate access to medicines across Europe and break down inequalities in the availability and affordability of medicines, there is little evidence of the effectiveness of joint procurement.

There is a growing interest in further developing cross-country collaboration in the field of health, both at a bilateral and a multilateral level[4] to ensure access to new medicines at a fair price that, according to European Cancer Leagues should be: *justifiable, predictable, and cost-effective within the aims and priorities of the healthcare systems and the available budget*[21].

The aim of this paper is to amplify the achievements of successful cross-border collaborations, as well as make tangible recommendations to re-energise existing initiatives, building on the lessons learnt from the EU Strategy on COVID-19 Therapeutics to explore potential new avenues for collaboration.

"COVID-19 illustrates and emphasizes the urgent need to further increase transparency in pharmaceuticals, and to strengthen collaboration amongst Member States."

Dr Milka Sokolović
Director General, European Public Health Alliance (EPHA)

1. EUROPEAN CANCER LEAGUES' VISION

Cancer patients and survivors continue to be treated and cured differently across Europe. The health divide and inequality in access to treatment and outcomes among EU member states are unacceptable. No one should lack access to treatment just because they live in a specific geographical area. It is high time to bring the right medicines, at the right time, to the right people.

The ECL Access to Medicines Task Force echoes the European Parliament resolution of 2 March 2017 on EU options for improving access to medicines in which the European Parliament:

"Calls on the Commission and the Council to develop measures that ensure affordable patient access to medicines, and benefit to society, whilst avoiding any unacceptable impact on healthcare budgets, to employ different measures, such as horizon scanning, early dialogue, innovative pricing models, voluntary joint procurements and voluntary cooperation in price negotiations, as is the case in the initiative between the Benelux countries and Austria [..];".

"Notes with concern that, owing to the lower negotiating power of small and lower-income countries, medicines are comparatively less affordable in such Member States, especially in the field of oncology; regrets, in the context of international reference pricing, the lack of transparency in list prices of medicines, as compared to actual prices, and the information asymmetry this brings to negotiations between industry and national health systems;".

In the context of cross-border collaborations, the Task Force believes that:

1. Different types of cross-border collaborations may be established depending on each country's needs. However, the overarching goal of each initiative should be the **empowerment of payers, national healthcare systems, and ultimately of patients**;
2. **National governments will be able, in the long-term, to overcome some of the barriers around pricing, reimbursement**, as well as lead the way to bring new health technologies with proven added value to patients whilst ensuring the sustainability of their healthcare systems;
3. **Joint activities have the potential to provide more evidence for decision making in both the policy and regulatory fields**. By working together, regulatory authorities and HTA bodies can streamline clinical research and become more efficient in generating evidence;
4. **National governments, as well as the European Commission, should be the primary actors deciding whether collaboration on pricing, reimbursement, and access is needed**. Once a need is identified, a small coordination group that would include patients and patient advocates should decide the price tag to propose to the pharmaceutical industry;
5. **Increased transparency** regarding studies and documentation reporting the value of the medicinal product, its actual price, and the cost of developing and bringing the product to market **is crucial for a level playing field for policy, regulatory, and financial decisions**. The European Commission and the EU Member States should also incorporate collective safeguards regarding public funding, such as transparency, accessibility, and affordability clauses, as per the European Parliament resolution of 10 July 2020 on the EU's public health strategy post-COVID-19.

1.1 THE FUTURE OF CANCER MEDICINES

Novel technologies are entering the health care systems at an unprecedented pace. In particular, in recent years, new high-priced cancer medicines with limited evidence of their added value have been authorised in various European markets. This raises immense challenges for all health stakeholders (including policymakers, regulatory authorities, payers, patients and physicians) and fuels the need for cross-country collaboration to better understand how to cope with pricing, reimbursement, and procurement of expensive new treatments. In fact, the willingness and need for greater expertise and information sharing among competent authorities have substantially increased over the last 9 years.

The number of new active substances approved by the European Medicine Agency (EMA) this year grew by ~80% as compared to 2019[2]. **The pharmaceutical industry has dozens of new health technologies in the pipeline, most of which are oncology drugs and a combination of cancer therapies, and many of those will be eligible for the centralised marketing authorisation.** This is the first step of a challenging path that EU countries would face following the marketing authorisation approval granted from the EMA.

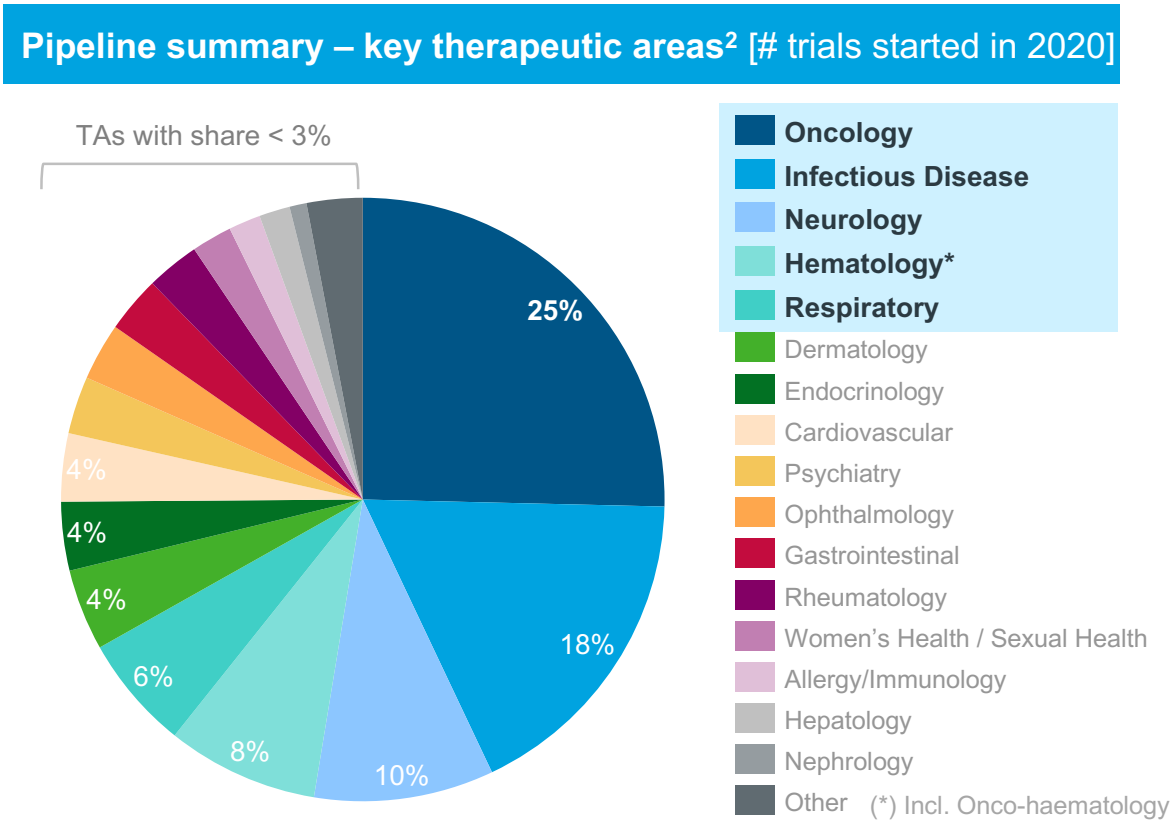

Figure 1. *The volume of initiated clinical trials has increased year on year since 2015 with oncology having the most extensive pipeline. Source:* IQVIA/EFPIA (2021) Pipeline Review 2021 Update

On the one hand, patients wish to have more and better treatments available to cure their diseases effectively and with limited impact on their quality of life. On the other hand, as reported in a European Commission's Staff Working Document published in 2020 in view of the revision of the orphan medicinal products regulation and previously by the World Health Organization in 2018, pharmaceutical companies are leveraging scientific developments to head towards the creation of artificial subsets of common diseases ('salami-slicing')[7]. Receiving ad hoc drug treatment leads to better clinical outcomes and improved quality of life compared to standard drug treatment, without considering the amount of money saved from administering ineffective drugs and treating side effects[22]. Nevertheless, better treatment does not justify the skyrocketing cost of new therapies and the misuse of incentives for the development of orphan drugs.

1.2 WHY IS JOINING FORCES NEEDED?

Considering the upward trend of cancer drugs centrally approved in Europe, European Cancer Leagues share some concerns:

1. OVERALL SUSTAINABILITY OF HEALTHCARE SYSTEMS

Cancer care and treatments have been dramatically improving and becoming more personalised and tailored to patients, as science advances. Collectively, rare cancers account for around 22% of new cases in Europe[3].

Evidence shows that growing expenditure on cancer medicines greatly exceeds the rate of growth of new cancer cases. Increased expenditure may be primarily due to increases in medicine prices coupled with the increasing number of people with cancer and multi-morbidity as populations age. This exacerbates inequalities, as people from deprived areas are more likely to experience co- or multi-morbidity and experience it earlier in their lives. In addition, the growth in prices of cancer medicines is set to exceed the growth in total cancer spending[4]. **Hence, the current pharmaceutical model is not sustainable in the long term**.

2. WIDENING OF UNEQUAL ACCESS TO NEW TREATMENTS

EU level actions to (i) reduce socioeconomic and geographical disparities, and (i) tackle differences in cancer prevalence, survival rates and access to new treatments, is urgently needed[5].

With the launch of the Pharmaceutical Strategy for Europe and other relevant initiatives, such as the Europe's Beating Cancer Plan and the European Industrial Strategy, **EU institutions are playing a critical role in shaping the next generation of medicines**. Yet, despite the great geopolitical ambitions, the EU currently lacks the means to fulfil them.

Many relatively small countries are not economically attractive and do not have the chance to opt for new treatments. This is widening the inequalities in availability and access to new treatments across Europe. Indeed, once the marketing authorisation under the centralised procedure is received, it is up to the pharmaceutical companies to launch those products at a national level and decide at which negotiation table to sit.

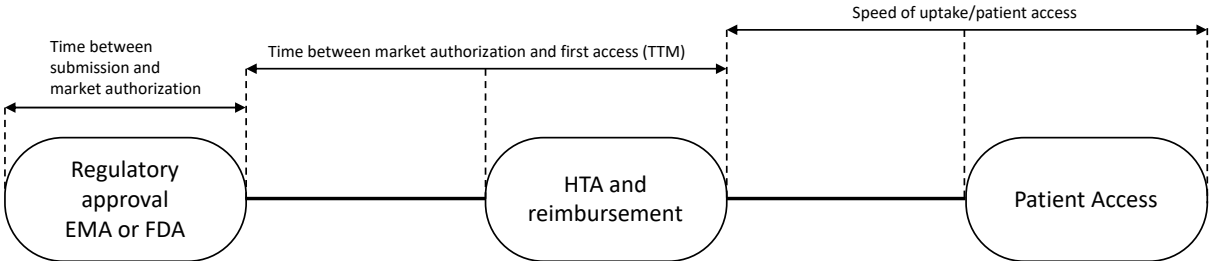

Figure 2. *Patient newly registered drug access pathway. EMA: European Medicines Agency; FDA: USA Food and Drug Association; HTA: health technology assessment; TTM: time to market. Source:* Uyl-de Groot C.A et al (2020) 'Unequal Access to Newly Registered Cancer Drugs Leads to Potential Loss of Life-Years in Europe'.

After regulatory approval, the pharmaceutical industry launches the product in high-income countries first and a reference pricing system is applied in other countries. This negatively impacts patient access across Europe. A study that analysed data on 12 cancer drugs in 28 European countries for the period 2011–2018, clearly shows that access widely varies among countries and the average time to market in Europe was 403 days with a range spanning from 17 to 1187 days[10].

Aside from gaps and discrepancies in access, there is also a paucity of information around the price data that can become available throughout the years and, as a result, does not mirror the situation in real-time.

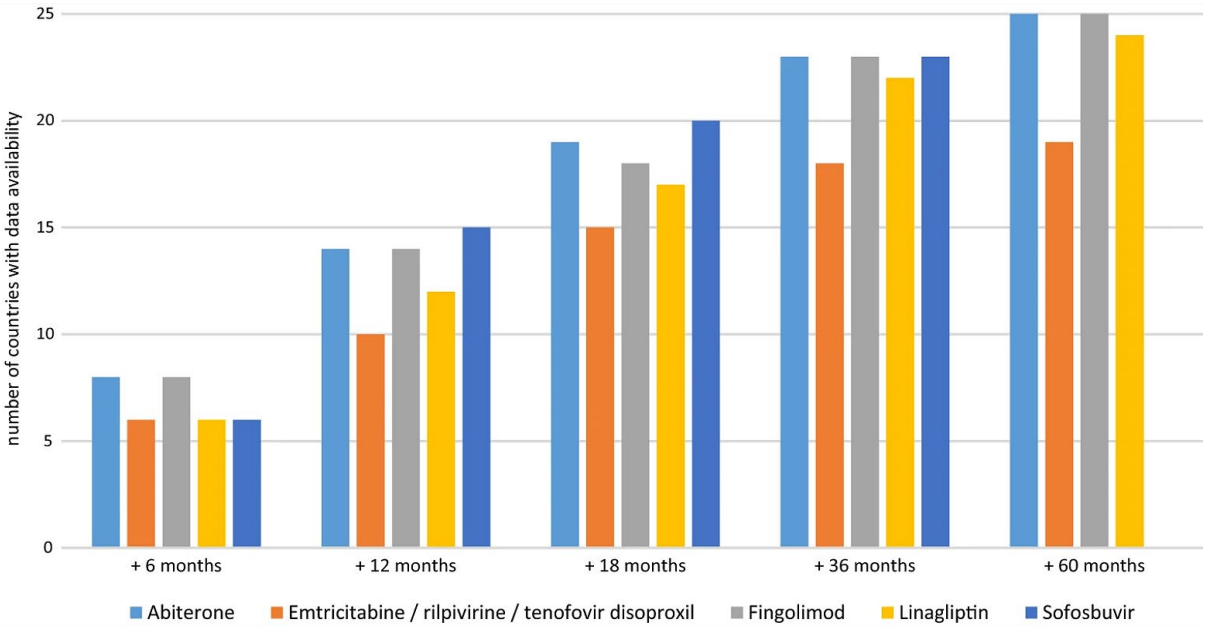

Figure 3. *Price data availability of the selected medicines in the EU Member States. No data for sofosbuvir were available for the '60 months' period as the product only received marketing authorisation in January 2014 (data surveyed in March 2017). In Portugal, no price data for fingolimod were available for 12 months because, since 2012, no price data for medicines used in hospitals have been published in Portugal; however, the national price list informs that the product is marketed. Source:* Vogler et al. (2019) 'Evolution of Average European Medicine Prices: Implications for the Methodology of External Price Referencing'

3. WEAK EVIDENCE ON THE VALUE OF INNOVATIVE MEDICINES

New health technologies often come to the market with high prices and limited evidence on their added value compared to existing or other health technologies[23]. There may be a lack of data demonstrating clear benefit at earlier time-points[11] and/or the post-marketing authorisation studies are not adequately followed up. Multinational trials are essential for recruiting the number of patients needed and improving access to medicines.

National competent authorities and the European Medicines Agency (EMA) should not rush to approve health technologies because of public or political pressure. New health technologies are welcome only if they are safe, demonstrate patient benefit, and do not pose a serious threat to the financial sustainability of national healthcare systems[24].

To address the knowledge gap behind the real added value of health technologies, the ECL Access to Medicines Task Force believes that the latest steps achieved with the proposal of an EU regulation on HTA can be a game-changer and improve equality in access and affordability of new medicines. **To address knowledge gaps, especially in disease areas that are not particularly attractive from a commercial point of view, academia and research institutes can play a critical role in the development of expensive cancer drugs.**

Repurposing may also be a valid strategy to (i) improve the accessibility and availability of medicines and (ii) address the issue of medicine shortages, especially where a lack of commercial interest may occur (e.g. repurposed generic and older medicines). Nevertheless, the regulatory process for repurposing led by the marketing authorization holder is different from the process that other actors (e.g. academia) need to go through.

It is more cumbersome for non-pharmaceutical companies to pursue repurposing with the current legal framework. These challenges have been highlighted also during the joint meeting of Directors for Pharmaceutical Policy of EU Member States and the Pharmaceutical Committee of the European Commission in July 2021. This challenge contributes to off-label use in the EU, which can consequently lead to access issues due to withdrawal of the medicine from the market and complex responsibility issues.

1.3 DIFFERENT TYPES OF CROSS-BORDER COLLABORATION

It has become increasingly challenging for governments to efficiently conduct activities, such as horizon scanning, HTA, or joint price negotiations when it comes to new health technologies[6] as their level of complexity increases[7].

Cross-border collaborations to steer access to human medicines can be of different types, take place at different levels and have different objectives (see Fig. 1) depending, to a large extent, on two main missions: (i) collection and sharing information and (i) purchasing and contracting. Sharing good practices will help make better use of the resources available in order to achieve the best possible health outcomes.

There is no single term that describes the action of several buyers pooling resources to buy medical goods and supplies at more favourable conditions than if this was done separately[8]. However, Espin et al. (2017) have identified four main levels:

1. INFORMED PROCUREMENT

Countries decide which information to share about prices and suppliers. This is the most flexible form of collaboration also in terms of time dedicated to this joint form of initiative.

2. COORDINATED INFORMED PROCUREMENT

This level of coordination allows countries to collaborate on market research, price monitoring, and sharing information on the performance of suppliers.

3. GROUP CONTRACTING / JOINT PRICING NEGOTIATION

This system is applied when countries jointly select the supplier and negotiate the prices. The participating Member States jointly negotiate with the supplier(s) and agree to purchase from the selected supplier(s) under common contracting conditions.

4. CENTRAL CONTRACTING / JOINT PROCUREMENT

This is the highest level of collaboration, and it is applied when a centralised body conducts the negotiation and establishes the contracts on behalf of the participating countries. Pooled procurement (also called joint procurement, central procurement, and group purchasing) has been defined as: '*purchasing done by one procurement office on behalf of a group of facilities, health systems or countries.*'[14].

"By joining our forces in knowledge and innovation, we can beat cancer in Europe if we make it happen together. We need to step up cross-border collaborations. We are stronger together."

MEP Sirpa Pietikäinen (EPP, Finland), Member, MEPs Against Cancer (MAC) Interest Group

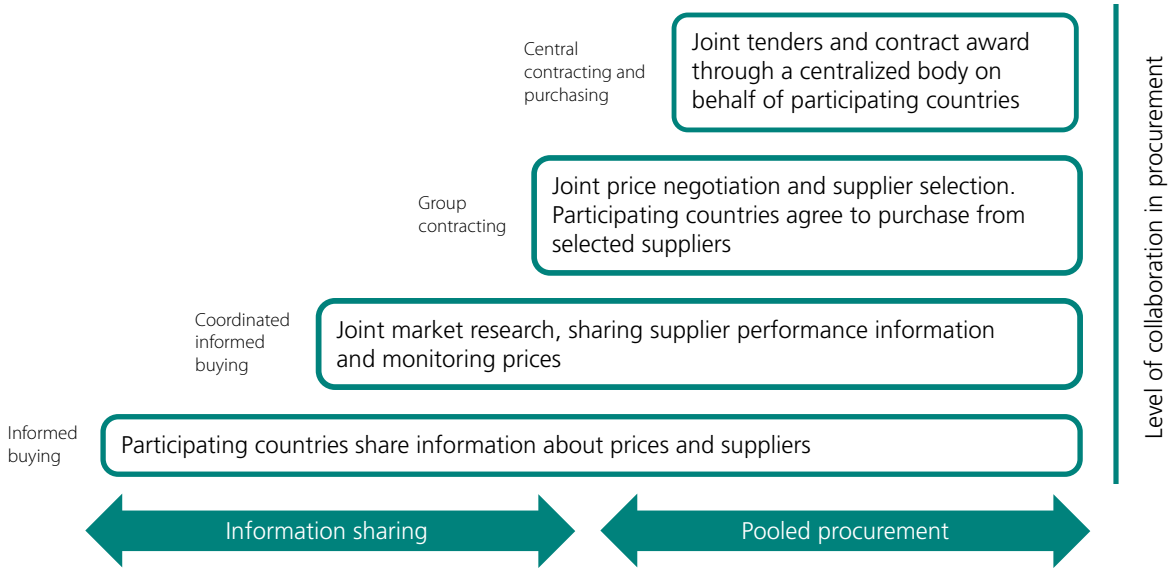

Figure 3. *Level of collaboration in procurement. Source:* Espín, J.et al. (2016) How can voluntary cross-border collaboration in public procurement improve access to health technologies in Europe?

2. INGREDIENTS FOR SUCCESSFUL CROSS-BORDER COLLABORATIONS

The ultimate goal of information and data sharing, and purchasing and joint pricing negotiations would not be limited to achieving short-term financial cost containment but also to (i) facilitating patient access to fairly priced medicines with a proved patient benefit, (ii) establishing healthcare system sustainability in the long term, (iii) enabling the pooling of different skills and expertise between the authorities[25].

The BeNeLuxA initiative, for instance, aims to leverage cooperation and the sharing of expertise on drug pricing and reimbursement between the governments of Belgium, The Netherlands, Luxembourg, Austria, and Ireland, with the aim of (i) giving smaller countries greater negotiating power in discussing drug pricing, (ii) sharing policy expertise, information on products and markets, and (iii) reducing unnecessary duplication[16].

2.1 OFF TO A GOOD START

A cross-border collaboration finds its purpose **when several countries face a common challenge,** and, in the case of innovative health technologies, this usually is high prices[9].

Aside from identifying challenges, it is of utmost importance that all the countries involved realise the **benefits they would gain from being part of a joint initiative. Before signing any agreement,** participating countries should share the **same priorities, expectations, and vision**.

1. POLITICAL COMMITMENT

Past experiences (e.g. BeNeLuxA and Nordic Council) showed that it is **better to start off with less risky arrangements and a lower level of commitment**. As soon as mutual trust and confidence are established and the pilots show promising results, participants become more committed to the initiative. Although cross-borders initiatives are often set up through bottom-up approaches, a strong political commitment is needed to further development of cooperation[10].

The signing of a partnership agreement is the starting point of collaboration. The launch of an initiative always creates enthusiasm, but different priorities may quickly slow things down and result in delays in starting the work. Therefore, the agreement must be flexible and gradually adapted, based on mutual learning and results.

2. GOVERNANCE

Finding the **right governance structure** for collaboration is probably the most complex task for cross-border innovation policy. Cross-border initiatives need to rely on **formal or informal governance arrangements or both**, depending on the number of collaborators and their organisational and legal framework. A formal framework enables countries to not accept non-disclosure agreements with the pharmaceutical industry and to share price information among member countries. An informal collaboration is in place when a network of technical experts working in public authorities responsible for pharmaceutical pricing and reimbursement, exchange information[11].

Above all, **trust is an essential ingredient** and takes time to build. As a matter of fact, an experience with a successful collaboration is surely a meaningful facilitating factor and lessons learnt during the first successful pilots can foster mutual trust and collaboration. Often, case studies serve as examples of why collaboration can be an opportunity[12].

As a first step, it is best to start with a **small group of public authorities willing to cooperate**. Since *governance* goes beyond *government*, **an inclusive approach involving all stakeholders is necessary for sustainability**[19]. It is vital to ensure industry stakeholders are interested and willing to participate and to respond to a call for tenders[18].

3. FINDING EXPERTS AND COLLABORATORS

Interested countries need to start the internal process of **anticipating the entry of new drugs on the market,** assessing their benefits, and market dynamics. Horizon scanning to identify, plan, and manage the entry of new technologies into the health system is certainly a way to lay the foundations of robust capacity building. Through cross-border collaboration and by collecting knowledge and information, countries can build strong systems to forecast future expenditure. Inspiration can be taken from existing systems in The Netherlands, Norway, and Sweden as well as from the International Horizon Scanning Initiative (IHSI) to inform pharmaceutical expenditure projections[13].

To efficiently support the collaboration, the **chosen experts** should have two main characteristics: (i) they must be **highly motivated** and (ii) able to bring a high level of **expertise to working groups**. Key players are not necessarily the most influential or recognised personalities in the debate[18]. As these initiatives are time consuming, a high level of commitment is crucial.

A **mapping of different stakeholders** (eg. national authorities, public health institutions, etc.) helps to identify the potential support that the initiative may benefit from. This should be accompanied by a robust internal and external communication strategy, including tailored messages for each stakeholder group.

After all of these have been done and defined, the **budget should be reassessed**. It must include the resources and the contribution foreseen (at least) for the following year.

4. FINDING COMMON GROUNDS

Individual countries should **investigate which other countries could face the same challenges and could benefit from collaborating** on horizon scanning, HTA, joint price negotiation, or joint procurement[17].

Finding a common ground also means defining a common vision, clear objectives and the scope of the collaboration. The partnership agreement should be unanimously approved and signed to mark the official beginning of the collaboration. The partnership agreement shall also state expected outcomes, progress indicators, as well as the monitoring and evaluation strategy. Hence, as raised by an expert during an interview European Cancer Leagues set up as part of the development of this paper, it is critical to start by pulling together the knowledge and skills that can successfully contribute to the cause and then tackle possible challenges along the way.

2.2 SMOOTH FUNCTIONING

Strong negotiation skills are an essential piece of the puzzle when creating a forum for strategic procurement. A supranational entity like the World Health Organization is well placed to organise meetings, webinars, training and boost the capacity of countries that are willing to start joint procurement activities[13].

1. KEEP IT SIMPLE

Procedures and documents should be concise but precise enough to avoid misunderstandings and different interpretations. Evidence shows that ownership, equity, transparency, stable central financing, standardisation, flexibility, and gradual development are important prerequisites[17].

2. WORKING STRUCTURE AND LEADERSHIP

Participating countries shall clarify from the very beginning what resources they are able to commit to support the collaboration. Targeted joint activities are time and staff consuming and come with financial implications for participating countries.

To support a smooth and efficient process, the duties of all stakeholders involved in the collaboration must be clearly defined. This includes applying project management principles and set timelines and milestones. Although the overall structure and hierarchy must be defined, rotation of responsibilities and leading roles has proven effective for the joint procurement of vaccines under the Baltic Procurement Initiative[18].

3. COMMUNICATION STRATEGY AND INTERNAL FLOW OF INFORMATION

Mapping stakeholders allows the establishment of a clear communication strategy. Messages should be tailored to different audiences (e.g. politicians, regulatory experts, media)[18].

Participating countries may not have the same level of expertise across the different aspects part of the collaboration. Therefore, interested countries should identify their strengths and weaknesses at an early stage. This assessment would support the development of the work plans and timelines for different activities.

Making use of available digital tools, such as teleconferencing and communications platforms, would save everyone's resources vis-à-vis interviews, information sharing. The chosen shared platform should also include a database on key factors such as prices, patent status, medicine registration[17].

Founding countries should develop and communicate their collaboration vision to all interested countries. This vision should be included in documents describing the implementation of the strategy[18].

"One of the key lessons from this pandemic is that the EU can work together to respond to health issues. We should use that power to fight against health crises but also to improve the health of our citizens, together as a union that we are."

MEP Sara Cerdas (S&D, Portugal), Vice-Chair, MEPs Against Cancer (MAC) Interest Group

2.3 BYPASSING HURDLES

Public procurement in the EU is regulated by Directive 2014/24/EU and, at the national level, by implementing laws. The Joint Procurement Agreement is, to date, valid for medical countermeasures for cross-border health threats (as per Decision No 1082/2013/EU).

It is well known that healthcare systems in the EU differ widely because of the economic context, willingness and possibility to pay, different reimbursement and price regulations, amongst other factors. In addition, the heterogeneity of treatment guidelines and traditions inevitably lead to different views on the added value of new medicines. This is a major hurdle that can be bypassed with joint HTA, even though it remains to be seen how much consideration Member States will give to centralised assessments.

Legislative changes are not necessarily needed before starting the collaboration, as the Baltic Procurement Initiative proved. In this agreement, members decided that the legal framework adopted during the negotiations was that of the leading country.

Language barrier is another challenge that can be overcome by deciding on a common language for all the documents. Nevertheless, translating a document into different languages requires resources, time and effort from the participating parties[18].

The abovementioned hurdles should not undermine mutual learning and best practice exchange in the field of procurement and payment policies, as proposed in the Pharmaceutical Strategy for Europe. More alignment in value assessments and cost-effectiveness analysis require intensified collaboration between countries[14].

"I fully support making a joint purchase procedure for medical products the standard. As far as negotiating with industry is concerned, the EU is stronger when it speaks with one voice, on behalf of all member states."

MEP Véronique Trillet-Lenoir (RE, France), Chair, MEPs Against Cancer (MAC) Interest Group

3. LEARNING FROM EXPERIENCE

3.1 BECAUSE IT WORKS (1/3): THE CASE SPINRAZA®

Positive results have been achieved by the BeNeLuxA Initiative which is paving the way towards a more balanced model for the pharmaceutical market.

The BeNeLuxA Initiative was started by Belgium and The Netherlands in April 2015 to share knowledge about medicine prices and negotiate together with more information at hand. After a few months, they were joined by Luxembourg and Austria and, in 2018, by Ireland. These countries decided to collaborate closely to ensure access to innovative drugs, initially orphan drugs, at affordable prices for the respective citizens. Their joint activities to date are: (i) HTA, (ii) horizon scanning, (iii) exchange of information on pharmaceutical markets, prices, and disease-specific cross-border registries, and (iv) pricing and reimbursement talks facilitation (including) joint negotiations.

The well-known agreement on the pricing of **Spinraza®**, a drug for Spinal Muscular Atrophy (SMA) developed by the biotechnology company Biogen, was the first positive outcome of a joint negotiation of the Beneluxa Initiative.

Belgium and The Netherlands successfully conducted a joint HTA, followed by a joint price negotiation. As a result of negotiations with Spinraza®, the two countries were able to increase their purchasing power and decrease substantially the price paid for this new drug. In December 2020, they planned to reimburse temporarily the drug and to assess the safety and efficacy of Spinraza® based on real-world evidence[18].

This success story for Belgium and The Netherlands was picked up across Europe and praised by all stakeholders, from Health Ministries to pharmaceutical companies. From that point onwards, national health ministers became aware of the positive impacts of collaborating at the international level; whereas the pharmaceutical company involved in the process received faster authorisation in Belgium and The Netherlands. Overall, this collaboration was a win-win and was praised by both parties[18].

The BeNeLuxA Initiative always approach joint price negotiations by carrying out a joint HTA first. Based on the outcome of the HTA assessment, countries decide whether they would like to proceed or not with a joint price negotiation. Hence, BeNeLuxA does not aim to only reduce the price of medicines, but also to prioritise the optimisation of the various preparatory building blocks before a possible joint price negotiation.

The Spinraza® case shows the potential that cross-country collaborations have to enable advantageous and faster access to new innovative drugs for patients.

3.2 BECAUSE IT WORKS (2/3): COVID-19 VACCINE PROCUREMENT

Dr Clemens Martin Auer, Special Envoy for Health for the Federal Ministry of Labour, Social Affairs, Health, Care and Consumer Protection of Austria and Co-chair of EU Steering Board in charge of negotiations until spring 2021, describes the legacy of the COVID-19 vaccine procurement as follows:

"What we have now is a best practice example in which the 27 and Commission were able to procure and negotiate contracts and fair prices. We should present this as best practice and continue doing this for high priced innovative medicines for European citizens. Because now there is no fair access in the club of EU when it comes to innovative medicines"[15].

A few countries signed a letter of intent at the beginning of the pandemic, and this attracted the attention of other countries that wanted to be included in the joint negotiation and purchasing under one mandate and mission to secure access to safe and quality vaccines to all EU citizens at the same time.

Considering the urgency of the situation caused by the new virus, the EU's regulatory flexibility was needed to accelerate the development, authorisation and availability of vaccines while maintaining the standards for vaccine quality, safety and efficacy.

In return for the right to buy a specified number of vaccine doses in a given timeframe and at a given price, part of the upfront costs faced by vaccines producers was financed from the Emergency Support Instrument (ESI), while the allocation of vaccines between Member States was population-based.

The European Commission also adopted the EU Strategy on COVID-19 Therapeutics in May 2021, supporting the development and availability of much-needed COVID-19 therapeutics, including for the treatment of 'long COVID'.

Cooperation on therapeutics is essential if we are to leave no one behind and guarantee timely access to new treatment to all patients. Actions taken in 2020 and 2021 during the COVID-19 emergency required an unprecedented collective effort in terms of energy, knowledge, and skills. Both private and public sectors soon realised that collaboration allows for optimal use of resources and fosters access to treatments.

All countries in the extended European region and beyond, in fact, face issues with access to medicines. One of the main causes is the broken pharmaceutical system that urges payers and governments to make decisions on the budget and sacrifice other aspects of health care. As exemplified by the BlueBird case, despite the disadvantages already faced by national authorities, the current broken model allows pharmaceutical companies to exit the market (of an entire continent) because of (i) confidential reasons and because (ii) the price they demand does not meet the price counter-negotiated by the authorities[16]. U.S. gene therapy company BlueBird Bio pulled out of the European market citing an unfavourable pricing environment. This came after the company was not able to come to an agreement with Germany over the reimbursement for Zynteglo, a therapy for a rare blood disease that had been cleared for use in the EU.

Advocates for the pharma and biotech industry say that the EU regulatory and pricing environment is not favourable for these therapies. European Cancer Leagues advance that Bluebird's decision is a failure for all the stakeholders especially patients that will not have the chance to benefit from a new treatment. This case demonstrates that adjustments to the EU regulatory framework are needed to facilitate the development of drugs by non-commercial entities. **The question we should therefore ask ourselves is: have we entered an era where pharmaceutical companies can deprive a whole continent of new therapies if payers do not accept their prices?**

3.3 BECAUSE IT WORKS (3/3): INTERNATIONAL HORIZON SCANNING INITIATIVE (IHSI)

The newly launched International Horizon Scanning Initiative (IHSI) is a successful spin-off from the BeNeLuxA initiative consisting of eight countries (Belgium, Denmark, Ireland, Netherlands, Norway, Portugal, Sweden, and Switzerland). The IHSI aims at creating a common database gathering available public information on drugs in the pipeline.

IHSI aims to advocate for fair and transparent prices by creating foresight about which drugs are coming to the market in the coming years. Participating countries will soon benefit from this initiative and carry out more efficient horizon scanning exercises. By creating awareness and knowledge about forthcoming pharmaceuticals, countries will be able to act as proactive buyers. Public authorities have time to transparently discuss which drugs they want to reimburse and how much they want to pay for them if the drug delivers on its promised value.

HOW DID IT TURN OUT[17]?

BENEFITS

- **Increased EU power in the global arena:** (i) a central procurement process with a single point of contact for pharmaceutical companies, (ii) limited competition between Member States to secure supplies of vaccines, and (iii) increased EU leverage in negotiations with industry.
- **Lowered prices:** *"For other drugs, a pharmaceutical company negotiates with EU governments. While the firm engages in up to 27 different sets of pricing talks, governments are bound to secrecy by a combination of confidentiality clauses and a fear that making their deals public will cause the company to insist on a higher price tag. This allows companies to play one country against another. When it came to vaccines, the Commission proposed doing something that would turn the tables."* (Excerpt from interview with an expert)
- **Preventing monopolies:** the COVID-19 vaccine procurement exercise highlighted the importance of creating a wide portfolio of new health technologies instead of investing in one. Preventing monopolies avoided unaffordable vaccines and increased competition, whilst rewarding innovation brought about by mRNA vaccines.
- **Liabilities:** the EU legal framework for consumer protection remained in place, despite indemnifications being transferred to the governments.

CHALLENGES

- Some tensions arose between EU Member States:
  - After the UK and the US ended up starting their vaccination campaigns much before the EU, politicians in several EU Member States wondered whether they could have moved faster on their own. They did also, however, consider the political repercussions that an individualistic decision would have had within their national political dynamics[18].
  - Tensions between countries with and without companies producing vaccines.
- Initial supply and production issues stemming from a lack of negotiation experience with the pharmaceutical industry[19];
- Lack of transparency regarding the contracts, which were not made publicly available. Prices were kept confidential, although a leaked price list suggests that the EU was able to negotiate a good deal[20].

CONCLUSIONS

The increasing calls from cancer leagues and multiple stakeholders about the unacceptability of the high prices of (new) medicines require **urgent action to guarantee patient access to drugs with proven clinical benefits.** In this context, increased **collaboration between countries** - in terms of sharing information relevant to making informed decisions on clinical value, price and reimbursement, and procurement practises - **is a step in the right direction.**

The COVID-19 pandemic turned the entire world upside down and continues to threaten the status quo of the pharmaceutical sector.

Respecting the principle of subsidiarity, EU Member States spoke and negotiated with a single voice after several months that the COVID-19 pandemic had started. Countries realised that overcoming the disruption caused by the pandemic could only be done through **collaboration and coordination**. For the first time ever, the European Commission had the mandate to negotiate and purchase a new health technology on behalf of its 27 EU Member States.

There are many lessons that can be learnt from this experience and **it is reasonable to question whether the** Treaty of the Functioning of the European Union, as it is written today**, is still fit for today's challenges and opportunities.**

The pandemic has acted as a wake-up call to move towards a robust European Health Union. With political support, the **European Union together with the European Free Trade Association (Iceland, Liechtenstein, Norway and Switzerland) and the United Kingdom can pool expertise and resources and solve common challenges related to both communicable and non-communicable diseases, including negotiating price policy and market access for novel cancer medicines[26].**

This approach would also benefit the pharmaceutical industry, as companies are then able to (i) market their products to larger patient populations and (ii) go through more streamlined market access pathways, reducing the burden on small and medium-sized companies.

We strongly believe that national governments should systematically consider cross-border collaborations for the sake of patients and national health budgets.

"A European Health Union cannot fully exist without joint EU solutions in health, like joint procurement, joint treatment facilities, for example for rare cancers, or EU public manufacturing capabilities."

Momir Radulović
Executive Director, Agency for Medicinal Products and Medical Devices of the Republic of Slovenia

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