



Making the Difference: Pharmaceutical Access and Value

ACTION REPORT



Contents

Acknowledgements	3
Executive Summary	5
Introduction	7
Upcoming Revisions to the EU Pharmaceutical Regulations and What They Mean for Cancer Care	8
Unmet Medical Need	11
Opportunities for Addressing Medicines Shortages in 2023	14
The Application of the EU's HTA Regulation and its Relevance to Cancer Care	18
References	22

Acknowledgements

This report summarises discussions at the European Cancer Organisation (ECO) Community 365^a Roundtable Meeting: 2023 – Year of Opportunities on Pharmaceutical Access and Value^b, which was convened by ECO in February 2023, facilitated by the co-chairing of Matti Aapro, ECO Past-President, and Mirjam Crul, ECO Board Member.

We thank all speaker participants in the roundtable event who contributed their perspectives and expertise in respect of upcoming regulations, sharing their views on the opportunities to make these more beneficial for cancer patient care, now, and in the future. We also thank all those who provided views during the roundtable meeting via the chat function, as well as after the meeting. Finally, we thank those who contributed to the review of this report as part of ECO's Policy Approval Pathway^c.

Authors

Matti Aapro, Past-President, European Cancer Organisation, Member of the Board of Directors of the Union for International Cancer Control, Member of the Board of Directors of the Genolier Cancer Center, Genolier, Switzerland

Mirjam Crul, Board Member, European Cancer Organisation, Co-Chair, European Cancer Organisation's Special Network on the Impact of Covid-19 on Cancer and the Workforce Network; Vice-President of the European Society of Oncology Pharmacy (ESOP) and hospital pharmacist, Amsterdam UMC.

Contributors

Norbert Couespel, Senior Coordinator – Policy Research and EU Projects, European Cancer Organisation

Tomislav Sokol MEP, Member, Special Committee on the COVID-19 Pandemic (COVI), and Member, Parliamentarians for Cancer Action, Croatia

Richard Price, Head of Policy, European Cancer Organisation

Kostas Stamatopoulos, Member, Research and European Affairs Committees, European Hematology Association

Jean-Pierre Delord, Head Clinical Research Unit, Medical Oncology Dept, Toulouse-Oncopole

Antonella Cardone, Patient Advocacy Expert and Advisor, Board Member of Pancreatic Cancer Europe

Marcus Hollenbach, Councillor of Clinical Science, European Pancreatic Club

Lydie Meheus, Managing Director, Anticancer Fund

Nicholas Cosenza, Senior Manager Government Affairs, Amgen

Monica Dias, Head of Supply and Availability of Medicines and Medical Devices, European Medicines Agency

Despoina Makridaki, Director of Professional Development, European Association of Hospital Pharmacists

Romilda Baldacchino Zarb MP, Pharmacist, and Member, Parliamentarians for Cancer Action, Malta

- a. Community 365 is a group of charity, philanthropy, and industry contributors to the Focused Topic Networks of the European Cancer Organisation. Community 365 provide ideas, guidance, practical support, and resources for our work in convening stakeholders and building consensus in the European cancer community. Community 365 contributors do not have a decision-making role in our policy work. Rather, policies of the European Cancer Organisation, such as those represented in this document, are agreed by our Board after consultation with our Member Societies and Patient Advisory Committee, via our Policy Pathway process. More information here: <https://www.europeancancer.org/community-365>
- b. More information here: <https://www.europeancancer.org/events/230:community-365-roundtable-meeting-a-year-of-opportunities-on-pharmaceutical-access-and-value.html>
- c. European Cancer Organisation's Policy Decision Making Process: <https://www.europeancancer.org/2-uncategorised/24-policy-decision-making>

François Houÿez, Information and Access to Therapies Director, Health Policy Advisor, Eurordis

Charles Faid, Director, Global Trade Policy and Public Affairs, Pfizer

Roisin Adams, Head of HTA Strategy and Chair of the HTA Regulation Coordination Group, National Centre for Pharmacoeconomics, Ireland

Robin Doeswijk, Head of European Affairs, European Hematology Association

Claudia Furtado, Head of the Health Technology Assessment, Pricing and Reimbursement Division (DATS) as well of the Information and Strategic Planning Division (DIPE), INFARMED

Anne-Pierre Pickaert, Specialist on HTA and Patient Access, Patvocates

Brian Cuffel, Vice-President and Market Access Head, Oncology, Bayer

Suggested Citation

Apró M, Crul M (2023). Making the Difference: Pharmaceutical Access and Value. European Cancer Organisation; Brussels.

Coordinators

Jackie Partarrieu, Strategic Health Communications

Richard Price, Head of Policy, European Cancer Organisation

Agnese Konusevska, Head of Communication, European Cancer Organisation

Silvia Romeo, Policy Officer, European Cancer Organisation

Giuseppe Filiti, Communication Officer, European Cancer Organisation

Elena Garvi, Community and Governance Assistant, European Cancer Organisation



Executive Summary

The ECO Community 365 Roundtable Meeting: **2023 – A Year of opportunities on pharmaceutical access and value**, brought together policymakers, patient advocates, healthcare professionals, industry representatives, and other experts, to analyse the political and regulator landscape for the coming year, and, from the multi-stakeholder perspectives gathered, to identify potential consensus recommendations for the consideration of the European Cancer Organisation's Policy Approval Pathway.

Discussions centred around upcoming revisions to EU Pharmaceutical Regulations; further ways to address Europe's commonly experienced difficulties with medicines shortages; and, the application of the EU's Health Technology Assessment (HTA) Regulation to cancer medicines.

Summary of Recommendations from the Roundtable

On the new EU Pharmaceutical Regulations:

- The application of too narrow a definition of unmet medical need in EU pharmaceutical legislation could have unintended consequences**, such as disincentivising development of medicines that would otherwise meet what stakeholders would commonly consider to be unmet medical need. Examples mentioned during the roundtable include making treatment more tolerable, reducing side effects, and improving safety
 - There is a strong societal component to be taken into consideration when thinking about unmet medical needs. This includes how burden of treatment on patients, their families and carers can be reduced, as well as reducing burden on health systems by, for example, making therapies simpler and easier to administer. **There should be place for societal considerations within the definition structure of unmet medical need**
 - As a core principle, any application of a definition of unmet medical need should be
- sure that it commands **the confidence of patient communities** as representing what is most important to them.
- In the context of reshaping structures and procedures for medicines development and regulatory approval mechanisms, it will be important to secure improvements in the ways in which third parties are enabled to suggest to regulatory bodies potential new indications for patent and off patent medications. **Third parties, including not-for-profit entities, should be able to submit data to the European Medicines Agency and Competent Authorities of Member States, for indication extensions of already authorised medicines.**

On medicines shortages:

- Among the potential solutions to medicines shortages that were discussed at the roundtable were:
 - The stronger **maintenance of buffer stocks by manufacturers** in contingency for any unforeseen problems in production at manufacturing sites;
 - Better supporting the production of medicines within the EU;**
 - Including **supply obligations as part of procurement** arrangements;
 - Supporting **the ability of pharmacies to compound medicines in scenarios of acute shortage**
- Improving European coordination on medicines shortages also entails achieving improvements in the interoperability of IT platforms for understanding pan European medicines stock scenarios.
- The role of the European Centre for Disease Prevention and Control (ECDC), in terms of its contribution of epidemiological expertise**, could be heightened in respect to forecasting of medicines supply needs.

4. The scope to reform current requirements that medicines be dispensed with the inclusion of printed patient information leaflets in the language of the country market should be investigated. For example, **a universal patient information QR code could bring the patient to the same information, or even more up to date information, and in any language of their preference.** Such a change could make it simpler and faster to redirect medicines from one country to another country experiencing a shortage of that medicine.
5. Ongoing attention should be provided to ensuring all stakeholders are operating **to a common understanding and set of definitions in respect to medicines shortages**

On the new EU Health Technology Assessment Regulations:

1. **There is a risk inherent in the EU HTA Regulation that even after the production of Joint Clinical Assessments there then follows a significant divergence in the way Member States make use of the Assessments.** This would set back the attainment of the EU HTA Regulation's original purpose and should therefore be guarded

against via the guidance, Implementing Acts and other preparatory actions currently under development.

2. During this preparatory period, **patient involvement should be secured in all 3 main domains of the EU HTA Regulation:** Joint Clinical Assessments, Joint Scientific Consultation and Horizon Scanning.
3. **Conflict of interest procedures utilised in the implementation of the EU HTA Regulation must be pragmatic and proportionate,** taking due account of the reality that in many highly specialised areas there will inherently be only a limited pool of highly relevant expertise.

Introduction



Matti Aapro, Past-President, European Cancer Organisation



Mirjam Crul, Board Member, European Cancer Organisation

“What are the opportunities in 2023 to secure improved pharmaceutical access and value for Europe’s cancer patients?”

Matti Aapro, ECO Past-President and Mirjam Crul, ECO Board Member, co-chaired the February 2023 ECO Community 365 Roundtable Meeting on this subject in order to collate and better understand the perspectives of many impacted stakeholders.

A major awaited milestone at the time of the roundtable was the expected publication by the European Commission of a proposed revision to the current EU Pharmaceutical Regulations¹. The new legislation is intended by the European Commission

to support improved access to affordable medicines, whilst also fostering greater levels of innovation in areas of unmet medical need.

Further areas of opportunity include identifying and tackling medicines shortages especially in the aftermath of the Covid-19 pandemic during which the problems created by such shortages achieved a higher political awareness and recognition. The roundtable also aimed to give stakeholders a stronger preview and sense of understanding about the implications of the implementation of the EU Health Technology Assessment Regulation², which will result in Joint Clinical Assessments of cancer medicines from January 2025.

The European Cancer Organisation invited healthcare professionals, patient advocates, industry representatives and other experts to discuss how the proposed new pharmaceutical regulations could affect cancer care in Europe.

WHY THIS ROUNDTABLE?

- Address the upcoming revisions to the EU Pharmaceutical Regulations and what it means for cancer.
- Hear the views of experts and relevant stakeholders on the impact of the EU Pharmaceutical Regulations update on the EU healthcare environment.
- Gather opinions and discuss the topic of Unmet Medical Needs in relation to cancer and beyond.
- Explore opportunities and solutions for addressing medicines shortages across Europe.
- Discuss the application of the EU’s HTA Regulation and its relevance to cancer.

Upcoming Revisions to the EU Pharmaceutical Regulations and Implications for Cancer Care

SUMMARY

- A major revision of EU pharmaceutical legislation is currently underway, and is typically a once-in-a-generation opportunity to implement regulatory fixes to known issues in areas such as incentive structures for new pharmaceutical product development, as well as other matters such as mechanisms for preventing medicines shortage, or requirements associated to the supply of medicines (e.g. printed information leaflets).
- European Parliamentarians are predicting a lengthy scrutiny process of the new legislative file, providing opportunity for impacted stakeholder communities to form and convey opinions and suggestions about the Commission proposals. It was in this context that ECO convened the Community 365 Roundtable ‘2023 – A Year of Opportunities on Pharmaceutical Access and Value’ in February of the same year.



Norbert Couespel, Senior Coordinator – Policy Research and EU Projects, European Cancer Organisation

Tomislav Sokol MEP, Member, Special Committee on the COVID-19 Pandemic (COVI), and Member, Parliamentarians for Cancer Action, Croatia

Richard Price, Head of Policy, European Cancer Organisation

Setting the Scene: the Political Context

The proposal for revisions to EU pharmaceutical regulations do not come in isolation. Helping to set the scene, **Senior Coordinator – Policy Research and EU Projects, European Cancer Organisation**, presented key data from the European Cancer Pulse that indicate towards some of access issues requiring attention in respect to EU cancer patients and availability of pharmaceutical treatment. This includes important disparities in approach to matters such as reimbursement of new oncology medicines, uptake of medicines for key tumour types as well as uptake of immunotherapy.

In order to help ensure that such evidence of inequality in access is acted upon politically across Europe, the European Cancer Organisation has been delighted to work with many leading politicians with a passion for policy solutions to create a new

network of change-makers called ‘**National and European Parliamentarians for Cancer Action**’. A key figure in bringing this grouping to life has been **Tomislav Sokol MEP, Member, Special Committee on the COVID-19 Pandemic (COVI), and Member, Parliamentarians for Cancer Action, Croatia**, who joined the meeting to express thoughts from the perspective of the European Parliament on what might be achieved through legislative reform at the EU level.

Mr Sokol emphasised:

- National reimbursement processes for medicines are not straight forward to influence via EU level legislation as this activity is known as a ‘reserved competence of Member States’ and there is often strong opposition from Member States to initiatives that even touch close to this area. Evidence of this reluctance includes the failure of a previous proposal by the European Commission to improve the transparency requirements by which EU member states make decisions on reimbursement of medicines.
- The political challenge of getting alignment in the European Parliament on the topics raised by the forthcoming legal proposal, making it unlikely that the legislative reform will be concluded before the 2024 European Parliament elections.
- There is a need to put in place, via the new regulation, a strong system of incentives for bringing new pharmaceutical products to

market, whilst also ensuring that system is well calibrated in serving actual needs for healthcare systems. In particular, incentives need to better distinguish towards products delivering clear and inarguable added value and benefit

- The potential to build upon the Covid-19 joint procurement approach for vaccines as a means to make access to pharmaceuticals across Europe more equitable.

Richard Price, Head of Policy, European Cancer Organisation, then gave an overview summary of an internal version of the new regulations that was leaked towards the end of January 2023 and published by the Brussels based news outlet Politico³.

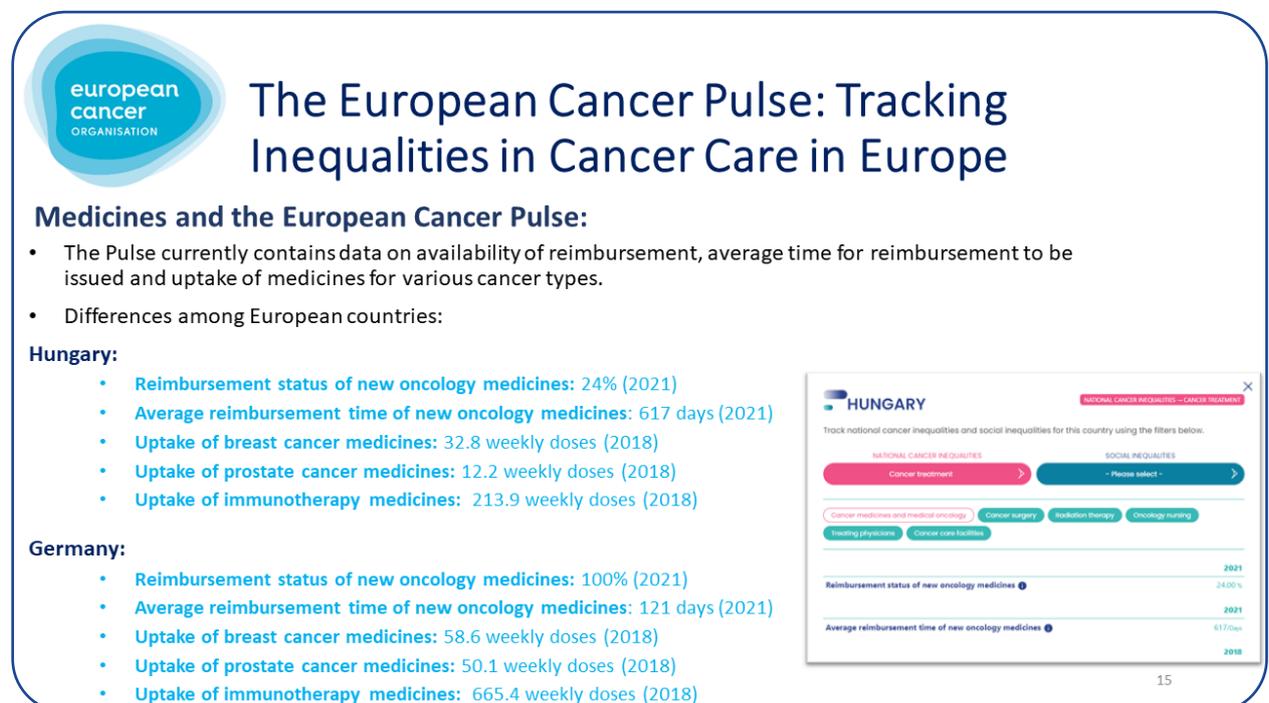
Eight highlights from the leak included:

1. **Incentive reform:** A proposal that the current standard of ten years market exclusivity for a new pharmaceutical product will be reduced

to a standard of eight years, with extensions available in certain circumstances, such as achieving launch of the product across all EU markets within a timeframe, or meeting a definition of addressing high unmet medical need.

2. **Exclusivity vouchers:** Developers of new antimicrobials being given the ability to apply 'exclusivity vouchers' which would grant an additional year of regulatory data protection to either use for a product in their own portfolio, or sell to another market authorisation holder.
3. **Medicines shortages:** The European Medicines Agency's (EMA) role in shortage monitoring to be further strengthened. This would include confirming a role of the EMA's Medicines Shortage Steering Group to provide recommendations to the European Commission for actions needed to mitigate or resolve critical shortages. Market authorisation holders would face stronger requirements to provide Shortage Prevention Plans. The concept

Figure 1. The European Cancer Pulse



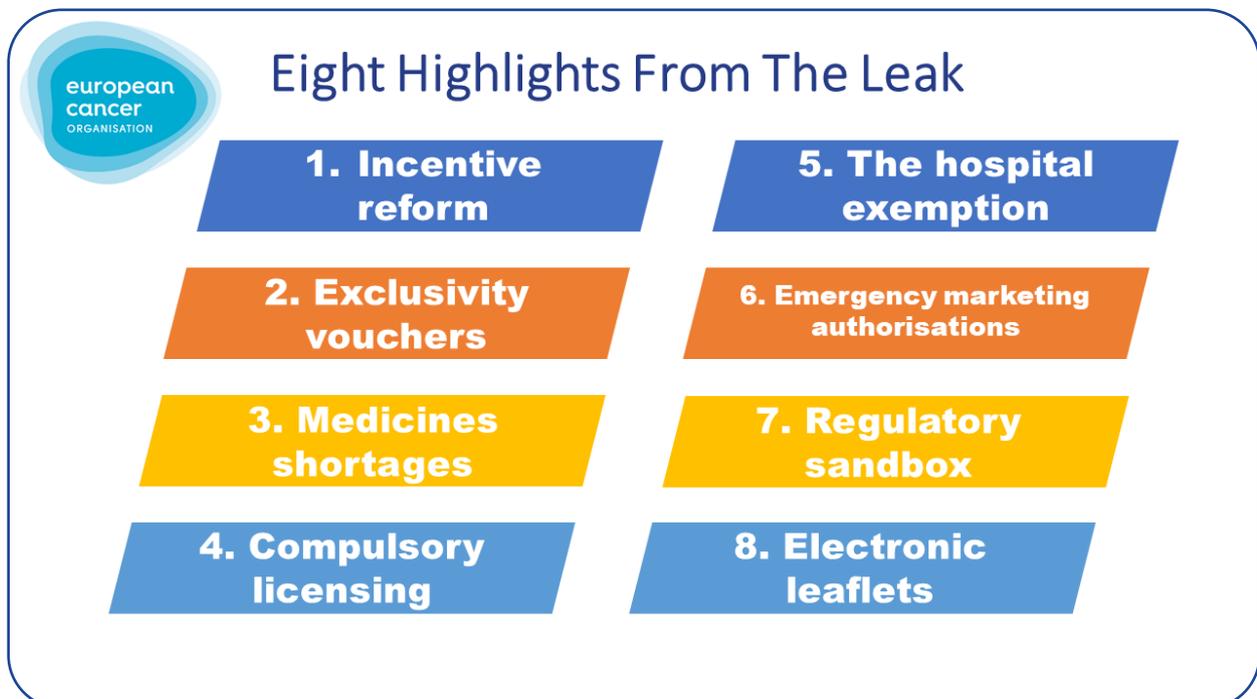
of critical medicinal products is clarified.

4. **Compulsory licencing:** The leaked proposal suggests the possibility of greater flexibility in the field of patent protection, with a potential for data and market protection to be suspended when a compulsory licence has been issued to tackle a public health emergency.
5. **Hospital exemption:** Presently, there is a legal exemption allowing hospitals to manufacture Advanced Therapy Medicinal Products (ATMPs) for human use that are based on genes, tissues, or cells. The proposal would clarify requirements for hospital exemption, including the safety and reporting standards to be maintained.
6. **Emergency market authorisations:** the proposal suggests a new procedure of Temporary Emergency Marketing Authorisation

when the regulator is satisfied that the benefit of *immediate availability outweighs the risk of* less comprehensive efficacy and safety data.

7. **Regulatory sandboxes:** scientific and technological progress today allows access to real world health data that can support the development, authorisation, and monitoring of medicinal products. The proposal suggests that the EMA could create “regulatory sandboxes” (controlled environments for testing innovative regulatory solutions). These would be limited in duration.
8. **Electronic leaflets:** the leaked proposal indicates towards a phased process that would enable medicine leaflets to be made available to patients in electronic formats in EU Member States, where presently all medicines made available to patients must be accompanied by written patient information leaflets.

Figure 2. Eight Highlights from The Leak



Unmet Medical Need

SUMMARY

With the European Commission proposing to reorientate the incentive structures within EU pharmaceutical legislation towards encouraging greater levels of medicines development in areas of unmet medical need, the way in which the definition of unmet medical need is framed and applied will require high levels of stakeholder scrutiny during the legislative passage of the new legal proposals.



Kostas Stamatopoulos, Member, Research and European Affairs Committees, European Hematology Association

Jean-Pierre Delord, Head Clinical Research Unit, Medical Oncology Dept, Toulouse-Oncopole

Antonella Cardone, Patient Advocacy Expert and Advisor, Board Member of Pancreatic Cancer Europe

Nicholas Cosenza, Senior Manager Government Affairs, Amgen

Lydie Meheus, Managing Director, Anticancer Fund

Marcus Hollenbach, Councillor of Clinical Science, European Pancreatic Club

ARTICLE 83

MEDICINAL PRODUCTS ADDRESSING AN UNMET MEDICAL NEED⁴

1. A medicinal product shall be considered as addressing an unmet medical need if at least one of its therapeutic indications relates to a life threatening or severely debilitating disease and the following conditions are met:

- a. there is no medicinal product authorised in the Union for such disease, or, where despite medicinal products being authorised for such disease in the Union, the disease is associated with a remaining high morbidity or mortality;
- b. a satisfactory diagnosis, prevention or treatment method exists and it has been demonstrated by the applicant that such a product will bring exceptional therapeutic advancement.

2. Designated orphan medicinal products referred to in Article 67 of revised Regulation (EC) No 726/2004 shall be considered as addressing an unmet medical need. population.

3. Where the Agency adopts scientific guidelines for the application of this Article it shall consult the Commission and the authorities or bodies referred to in Article 162 of revised Regulation (EC) No 726/2004.

Defining Unmet Medical Need

The meeting then moved to a panel discussion on the concept of unmet medical need (UMN) and its prospective use within the revised EU pharmaceutical legislation.

Kostas Stamatopoulos, Member, Research and European Affairs Committees, European Hematology Association, highlighted the lack of consensus at present among stakeholders about such matters as how to define the term unmet medical need. More than 15 different operational definitions of the term can be pointed to since 2016. The term evidently is understood differently dependent on perspective: patients, healthcare professionals, regulators, HTA experts, payers and the pharmaceutical industry. He advised avoiding rigid and restrictive definitions in this sense – “there must be adaptability to the unexpected” – and emphasised the need for patient centricity and the engagement of all relevant stakeholders.

Jean-Pierre Delord, Head Clinical Research Unit, Medical Oncology Dept, Toulouse-Oncopole remarked on the enormous progresses in science and understanding since he began his professional training in the 1990s. “It has been a revolution”. Cure of patients from cancer continues to become more

possible. However it has also been accompanied by some greater complexities in clinical decision-making, alongside a sense of non alignment between the clinician's perspective on treatment choices, and those that are being reimbursed by relevant authorities. A gap is growing as well between the USA and Europe in respect to the capacity to invest in treatment innovation. Better definitions about unmet medical need, agreed at European level and employed by all could certainly bring about improvement in this respect.

Antonella Cardone, Patient Advocacy Expert and Advisor, Board Member of Pancreatic Cancer Europe,

highlighted the very particular needs of pancreatic cancer patients. As a poor prognosis tumour often the best hopes for patients rely on being enrolled to a clinical trial. Therefore reports that Europe is losing its attractiveness as a clinical trial destination is a source for alarm. The perspective of Pancreatic Cancer Europe so far is that any definition of unmet medical need that is deployed in new EU pharmaceutical legislation must be of a flexible nature or else risk further diminishing Europe as a trial destination. A definition of Unmet Medical Need should also take account of societal need, such as where a treatment innovation can reduce the societal burden of a disease. Furthermore, the experience in pancreatic cancer in recent years suggest that progress often comes as a result of combinations of treatment advances, not from a single new cure. In this respect, Pancreatic Cancer Europe find the definition proposed within a leaked version of the Commission's proposal appears too rigid and restrictive.

Nicholas Cosenza, Senior Manager Government Affairs, Amgen, considered that a greater focus on unmet medical need in general could be a positive development. However it was necessary to express elements of concern at the direction of travel indicated by the leaked proposal, in respect to a narrow and rigid definition of what unmet medical need should be understood to be. A criteria based approach, focusing on outcomes important to patients, caregivers and families would seem a more preferable approach. This could include

considerations of such matters as improving compliance, for example, as an unmet medical need. Unintended consequences could also occur, such as driving research investments away from the major non communicable conditions such as cancer, or risky areas of research investment like rare diseases and rare cancers.

Lydie Meheus, Managing Director, Anticancer Fund (ACF),

conveyed the need for Market Authorisation Holders to improve transparency and information about indications for their products. Other evident weaknesses in the current regulatory and incentive landscape include the lack of incentives available for trial activity in respect of off-patent medications. Even for patented medicines there can be an almost systemic reluctance for new indications to be added to the label. Examples in this respect can be brought forward from the blood cancer field, where solutions for additional indication are available via connection to organisations such as the National Comprehensive Cancer Network (NCCN) which are not mirrored in Europe. A clear recommendation of ACF is that third parties should be able to submit clinical data to the European Medicines Agency for additional indication if there is clear unmet medical need that could be potentially addressed. Article 46 of the leaked proposal appears to open the door for such procedures to occur as part of a section on the repurposing of medicines. This could be especially relevant for the paediatric community, and offer prospective new options for rare and ultra rare cancers. "Solutions to how we address unmet medical need should not only be coming from companies."

Marcus Hollenbach, Councillor of Clinical Science, European Pancreatic Club

emphasised the urgency of securing more successful treatment strategies for patients with poor prognosis tumours such as pancreatic cancer. Continual improvement of infrastructures for the conduct of multi-national trials is one area for clear attention in this respect. Another area where improvement has been seen is in respect to treatment strategies with genomic components, but access across Europe to such treatments is presently deeply inequitable.

KEY RECOMMENDATIONS

- The application of too narrow a definition of unmet medical need in EU pharmaceutical legislation could have unintended consequences, such as disincentivising development of medicines that would otherwise meet what stakeholders would commonly consider to be unmet medical need. Examples mentioned during the roundtable include making treatment more tolerable, reducing side effects, and improving safety.
- There is a strong societal component to be taken into consideration when thinking about unmet medical needs. This includes how burden of treatment on patients, their families and carers can be reduced and made more convenient, as well as reducing burden on health systems by, for example, making therapies simpler and easier to administer. There should be place for societal considerations within the definition structure of unmet medical need.
- As a core principle, any application of a definition of unmet medical need should be sure that it commands the confidence of patient communities as representing what is most important to them.
- In the context of reshaping structures and procedures for medicines development and regulatory approval mechanisms, it will be important to secure improvements in the ways in which third parties are enabled to explore potential new indications for patent and off patent medications. Third parties, including not-for-profit entities, should be able to submit data to the European Medicines Agency and Competent Authorities of Member States, for indication extensions of already authorised medicines.

Opportunities for Addressing Medical Shortages in 2023

SUMMARY

- The European Medicines Agency (EMA) is currently operating a new legal mandate on medicines shortages in the wake of the Covid-19 pandemic. This has included the creation of a new EMA Medicines Shortages Steering Group to help bring about stronger coordination of response to pan-European medicines shortages.
- A further action to be undertaken by the EMA is the creation of a European Shortages Monitoring Platform. This will be operational by February 2025 and will help to foresee potential medicines shortages before they become acute and enable prompter enactment of remediating and preventing measures.
- Cited causation of medicines shortages raised during the meeting included single manufacturers of Active Pharmaceutical Ingredients and final products, and low prices for generic medication leading to low market participation in their production.
- The costs to health systems created by medicines shortages are high, with as much as 75M Euro a year suggested to be the cost to the Dutch health system.
- The human and patient impacts of medicines shortages include delays to treatment, avoidable worsening or regression of condition, and anxiety and distress for patients and their carers.



Mirjam Crul, ECO Board Member
Monica Dias, Head of Supply and Availability of Medicines and Medical Devices, European Medicines Agency
François Houÿez, Information and Access to Therapies Director, Health Policy Advisor, Eurordis
Despoina Makridaki, Director of Professional Development, European Association of Hospital Pharmacists
Charles Faid, Director, Global Trade Policy and Public Affairs, Pfizer
Romilda Baldacchino Zarb MP, Pharmacist, and Member, Parliamentarians for Cancer Action, Malta

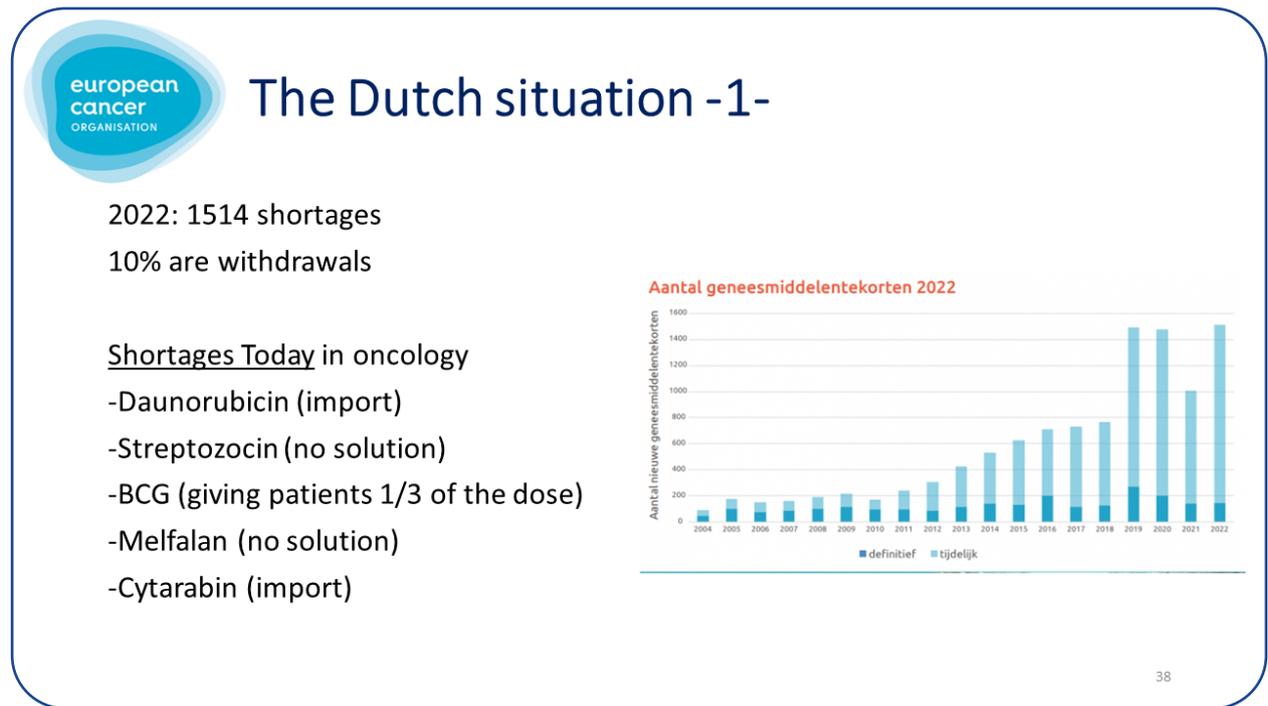
Medicines Shortages in Europe: The Dutch Situation

Mirjam Crul, ECO Board Member, gave an overview on Europe's present challenges with medicines shortages, drawing on her own experiences in her hospital pharmacy. European countries are currently facing growing shortages. This situation predates the Covid-19 pandemic which only aggravated the trend⁵.

The roundtable heard from Crul that the situation in the Netherlands today is worrying. There are currently 1,214 shortages, many of them affecting oncology, including lack of antibiotics and antiepileptic drugs used in cancer care. 10% are definite shortages (medicines have been withdrawn from the market), the rest are temporary.

Causes of medicines shortages often relate to production issues such as single manufacturers of Active Pharmaceutical Ingredients (APIs). Another notable factor is the low prices that authorities demand of generic medicinal products which can consequently lead to limited market participation in their production. The cost to health systems of mitigating medicines shortages can be substantial. In the Netherlands, this is suggested to amount to 75M € every year. As an indication on this, the

Figure 3. Dutch Medicines Shortages



Amsterdam Medical Centre needs to employ a pharmacist working full-time to help resolve the daily experience of medicines shortages.

Potential solutions suggested by Mirjam Crul could include:

- The stronger maintenance of buffer stocks by medicines manufacturers as a regular contingency in case of unforeseen production problems at manufacturing sites.
- Greater support towards the production of medicines within the EU.
- Including supply obligations as part of the arrangements underpinning government procurement of medicines.
- Support for the contingency capacity for pharmacists to compound and produce medicines in cases of critical shortage.

EMA’s New Role on Medicines Shortages

Monica Dias, Head of Supply and Availability of Medicines and Medical Devices, European Medicines Agency, presented an overview of the EMA’s new roles in the area of medicines shortages prevention and management. The Agency’s refreshed legal mandate in the policy area has, in large part, been brought about from the shared experiences and challenges that EU countries

faced on this matter during the Covid-19 pandemic. However, pan European structures and support mechanisms on the topic of shortages had been evolving and developing for a number of years prior to the pandemic in response to an identified growing need.

Regulation 2022/123⁶ establishes the Medicines Shortage Steering Group (MDSSG). The MDSSG is supported by the Working Party of Single Points of Contacts in the Member States (SPOC WP) and a Network of contact points from marketing authorisation holders (i-SPOC system). Together they:

- Provide recommendations on all matters relating to monitoring and management of shortages and availability during a crisis.
- Provide guidance to companies on the industry SPOC (i-SPOC) network.
- Update EMA’s plan for Emerging Health Threats.
- Establish a list of the main therapeutic groups of medicines necessary for emergency care, surgeries, and intensive care, to help prepare the lists of critical medicines to respond to public health emergencies or major events.

EMA is also creating new tools to coordinate responses of EU Member States to shortages of vital medicines in critical situations. Article 13 of

Regulation (EU) 2022/123 foresees the setting up of a centralised IT platform to facilitate the collection of information on shortages, supply, and demand for medicinal products, including information on marketing status and marketing cessations in the EU. The European Shortages Monitoring Platform (ESMP) should be implemented by February 2025 and aims to help foresee potential shortage problems before they occur and enable earlier mitigating actions as a result

A new EU funded 'Joint Action', bringing together Member State authorities for longer term strategic consideration about the topic of medicines shortages is also being established.

In the new post Covid-19 regulatory landscape, and the introduction of new cross-border health threat legislation, EMA is now also in closer and more systematic collaboration with the ECDC for epidemiological data, and with European Commission's DG for Health Emergency Preparedness and Response (DG HERA) and DG for Health and Food Safety (DG SANTE) for data collection and analysis of supply and demand information. Together, these bodies, actions and tools should allow better coordination within the EU to prevent and mitigate medicines shortages during emergency situations⁷.

Perspectives from Stakeholders

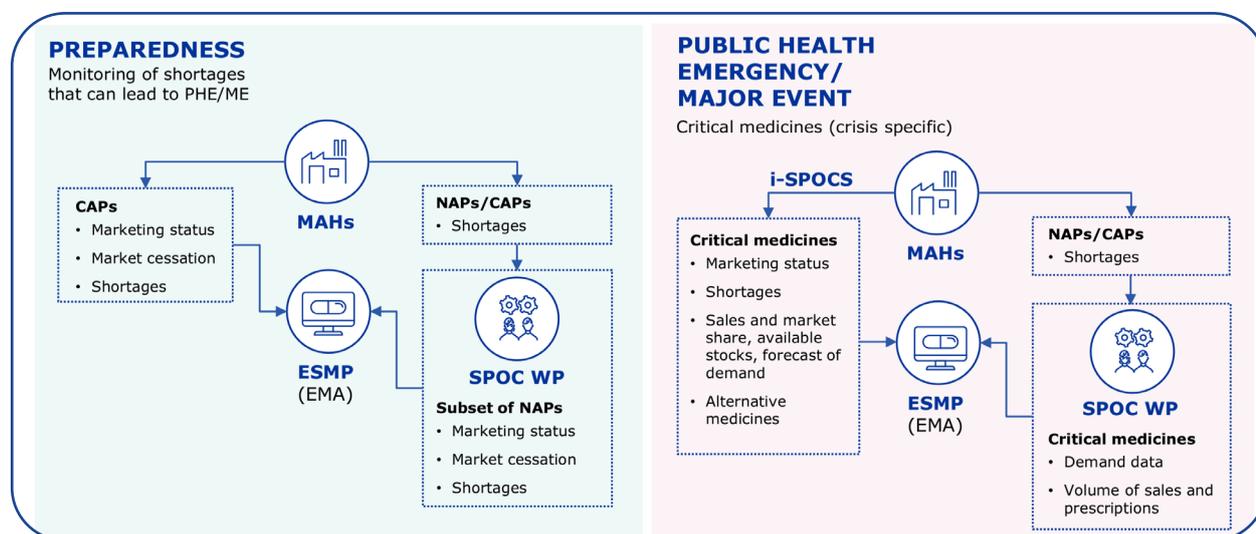
François Houÿez, Information and Access to Therapies Director, Health Policy Advisor, Eurordis, set out real life impacts of shortages, including delays to treatment, avoidable worsening or regression of disease condition, and anxiety and distress for patients and their carers. An aspect of the medicines shortages issue requiring awareness

and response is that the opportunities to import and export medicines between countries can often fuel shortage in some countries as lower priced medicines are moved to markets where a higher price can be obtained. Hospital production of medicines in scenarios of shortage appeared an important avenue for consideration in terms of remedying actions, including in considering what is legally permissible in the context of new EU pharmaceutical legislation and lesson learning from the Covid-19 pandemic.

Despoina Makridaki, Director of Professional Development, European Association of Hospital Pharmacists, drew attention to the regular EAHP pan European surveys on medicines shortages which consistently highlight oncology medicines as a top area of reported shortage. Proposals to amend EU pharmaceutical legislation to improve obligations on manufacturers to report production and supply issues with a potential to create shortage would be highly welcomed. Without good information on supply pharmacists too often have to operate in the dark in resolving a shortage and ensuring supply of a medicine to the patient.

Charles Faid, Director, Global Trade Policy and Public Affairs, Pfizer described the issue of medicines shortages as a sobering subject. Pfizer, as a global company with an expansive product portfolio across many therapeutic areas, is as impacted by, and as involved in seeking to resolve, medicines shortages as any other company. Needs still remain in respect to gaining clear and universally understood and deployed definitions in respect to medicines shortages. Any new EU level harmonised legal framework for preventing medicines shortages and mitigating impact when

Figure 4. The European Shortages Monitoring Platform



they do occur, needs to be underpinned by such clarity, or else risk partners in the process speaking different languages about shortages. Harmonised reporting requirements and interoperable IT platforms are other essential elements to achieving the ambitions of the EU in this area. Good levels of dialogue between supply chain stakeholders, and access to the kind of demand data that can help achieve stronger and more reliable forecasting, and responses to supply chain need, are other aspects for attention. On the latter point, there could be a potential role for the ECDC in supplying some of the required epidemiological data and expertise to support that task. The newly created European Medicines Verification System⁷ may also have a role in achieving greater real time level data about medicines in circulation across the European Union. Regulatory change, such as in respect to amending

existing requirements mandating medication supply be accompanied by printed patient information leaflets (e.g. to enable use of patient information available by QR code) could assist in enabling medicines in one country to be made available in another in cases of shortage.

Romilda Baldacchino Zarb, Member of the Maltese Parliament and pharmacist, emphasised the global nature of the medicines shortage problem with the real consequences felt by patients at the end of the supply chain. Malta has needed to be very active in monitoring and responding to medicines supply chain disruptions, at national, European and global level. The case study of various antibiotic shortage experiences was raised in this context.

KEY RECOMMENDATIONS

- Among the potential solutions to medicines shortages that were discussed at the roundtable were:
 - a. The stronger maintenance of buffer stocks by manufacturers in contingency for any unforeseen problems in production at manufacturing sites;
 - b. Better supporting the production of medicines within the EU;
 - c. Including supply obligations as part of procurement arrangements;
 - d. Supporting the ability of pharmacies to compound medicines in scenarios of acute shortage
- Improving European coordination on medicines shortages also entails achieving improvements in the interoperability of IT platforms for understanding pan European medicines stock scenarios.
- The role of the ECDC in terms of its contribution of epidemiological expertise, could be heightened in respect to forecasting of medicines supply needs.
- The scope to reform current requirements that medicines be dispensed with the inclusion of printed patient information leaflets in the language of the country market should be investigated. For example, a universal QR code could bring the patient to the same information, or even more up to date information, and in any language of their preference. Such a change could make it simpler and faster to redirect medicines from one country to another country experiencing a shortage of that medicine.
- Ongoing attention should be provided to ensuring all stakeholders are operating to a common understanding and set of definitions in respect to medicines shortages.

Application of the EU Health Technology Assessment Regulation in Relation to Cancer Care

SUMMARY

- In 2021 the EU adopted a new Regulation to harmonise the Health Technology Assessment (HTA) procedures applied by Member States when making reimbursement decisions for newly approved medicines. Currently, Member States have separate procedures and different standards that sometimes yield divergent conclusions for the same product.
- It is hoped the new Regulation can help to reduce duplication of procedures, speed up HTA decision-making timescales and, in so doing, reduce disparities across Europe in the time to access new treatments.
- Under the new HTA regulation, Joint Clinical Assessments will be conducted at the EU level. Currently governance procedures and the methodological approaches for this to take place are being established. This will include the development of secondary legislation known as 'Implementing Acts'.
- Cancer therapies will be the first therapies to which Joint Clinical Assessments will be applied, starting from 2025.
- While use of the Joint Clinical Assessments by EU Member States will be mandatory, the manner and extent to which they will be used was a matter of concern raised by stakeholders at the roundtable. Limited utilisation of the Joint Clinical Assessment would significantly undermine the objectives and original purpose of the HTA Regulation.



Roisin Adams, Head of HTA Strategy and Chair of the HTA Regulation Coordination Group, National Centre for Pharmacoeconomics, Ireland, provided the meeting with an overview of the EU Health Technology Assessment regulation. Among its original purposes is the reduction of duplication by Member States in this area of activity by providing one single report that national authorities can refer to when making reimbursement decisions about new medicines. In so doing, it is hoped that disparities in the time to access for patients across Europe might be reduced.

The new environment created by the EU HTA Regulation has three main constituent components:

1. **Joint clinical assessments (JCA):** Joint Clinical Assessments will provide comparator effectiveness reports (benefits provided over what is used in current practice). However, national level authorities will retain the right to independent decision-making on reimbursement. Cancer medicines will be the first therapies to which the HTA regulation's joint clinical assessments will be applied, starting 2025. Orphan medicinal products will follow thereafter, and by 2030 joint clinical reviews

Roisin Adams, Head of HTA Strategy and Chair of the HTA Regulation Coordination Group, National Centre for Pharmacoeconomics, Ireland

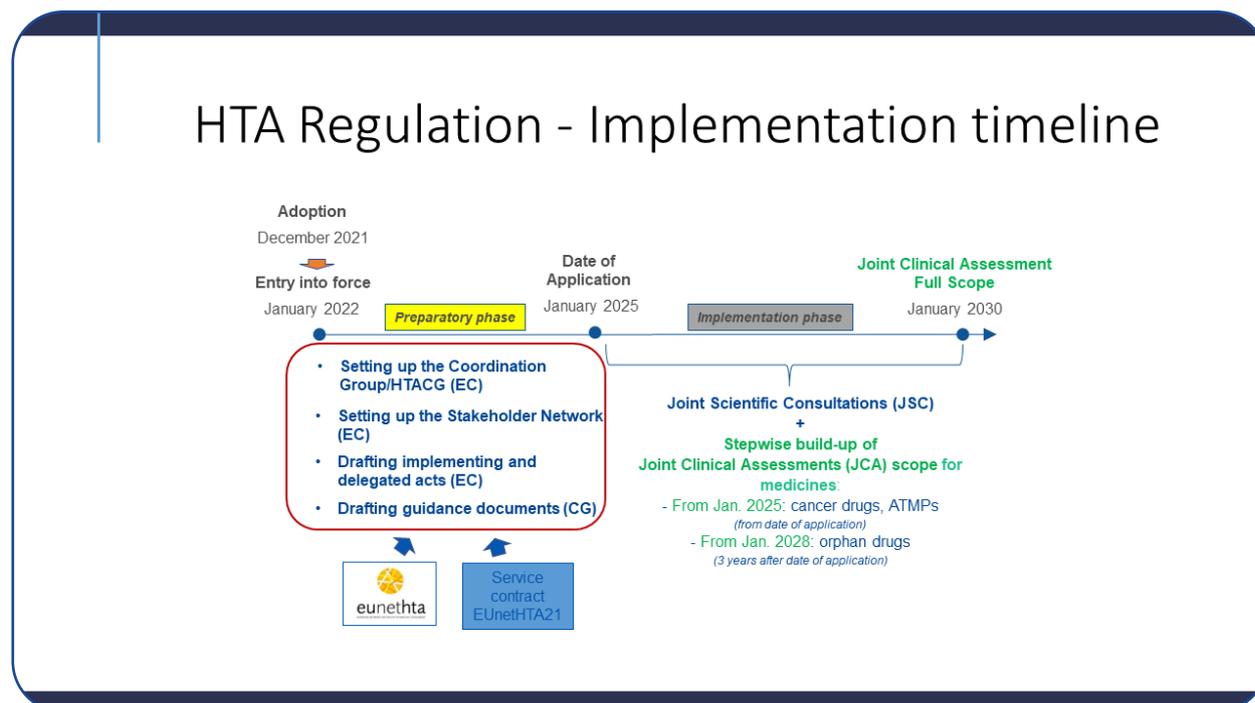
Anne-Pierre Pickaert, Specialist on HTA and Patient Access, Patvocates

Claudia Furtado, Head of the Health Technology Assessment, Pricing and Reimbursement Division (DATS) as well of the Information and Strategic Planning Division (DIPE), INFARMED

Brian Cuffel, Vice-President and Market Access Head, Oncology, Bayer

Robin Doeswijk, Head of European Affairs, European Hematology Association

Figure 5. HTA Regulation - Implementation Timeline



will apply to all new medicines. Timelines will be challenging as reports should be issued no later than 30 days after market authorisation is granted. Once reports are published, their use will be mandatory in national systems. However, the manner in which they will be used remains a subject of ongoing discussion.

2. **Joint scientific consultations (JSC):** Joint Scientific Consultations will provide early scientific advice by HTA bodies to health technology developers ahead of their submission of evidence to the European Medicines Agency for marketing authorisation approval, and sometimes before the start of clinical trials. Joint Scientific Consultations aim to improve the quality and appropriateness of data produced by the health technology developer in view of future HTA assessment. The Joint Scientific Consultations also intend to identify important questions that decision-makers will ask to decide on reimbursement of new products. Joint Scientific Consultations will be carried out from January 2025. The three-year delay application period aims to ensure that there is enough time to set up the organisational framework of the HTA Regulation.
3. **Horizon scanning/Emerging technologies:** The new HTA regulation provides new tools to help member states monitor the development

of health technologies and share results of this observation. Data collected will support prioritisation for HTA and provide healthcare decision-makers with relevant information on new and emerging technologies.

Challenges remain to be met before full implementation of the HTA Regulation in the EU can be achieved. These include: setting up the governing structures and frameworks; identifying methodology and procedures for Joint Clinical Assessments and Joint Scientific Consultations; creating guidelines and reporting templates, as well as constructing European PICO (Population, Intervention, Comparator, Outcome) frameworks for use in the joint work. PICO, as a tool, helps set out the key HTA questions for answer:

- What is the population this medicine will be used in?
- Can we obtain a clear description of the intervention
- What is the comparator - the added benefit compared to what is already used in practice?
- What is the measurable outcome of the treatment?

A key issue before the Member State coordinating group is securing consensus on the forms evidence accepted in indicating treatment effectiveness. A range of methodological guidelines and practical

guidelines are being brought forward to help articulate and confirm this.

A series of 'Implementing Acts' (five in total) must also be brought forward to bring about the full realisation of the EU HTA regulation.

Roundtable Perspectives

Anne-Pierre Pickaert, Specialist on HTA and Patient Access, Patvocates, gave a broad welcome for the introduction of the EU HTA regulation, calling it 'a big step forwards'. In particular she remained hopeful for its potential to increase the speed of access for patients to new treatments and reducing disparities between EU countries in this respect as well. Patient representatives are especially interested in the rules for patient involvement in Joint HTA processes that are expected to be set out in some of the Implementing Acts mentioned by Roisin. Patient involvement in all of the three main domains referred to in Roisin's presentation will be key: Joint Clinical Assessments, Joint Scientific Consultation, and horizon scanning. However, it must be recognised that patient involvement as a culture within decision-making is not fully mature in all EU countries. Enabling patient involvement within the tight deadlines the legislation sets will likely create further challenge too. This could raise a risk of more organised and well established patient communities being able to input meaningfully, while disease areas with smaller patient numbers being less able to. Allied to this, training to patient representatives to help ensure their understanding of regulatory processes and methodology will be important to support their fullest input.

Claudia Furtado, Head of the Health Technology Assessment, Pricing and Reimbursement Division (DATS) as well of the Information and Strategic Planning Division (DIPE), INFARMED, gave an impression of what the HTA regulation will mean for her country. The agency supports the Regulation as a means of delivering efficiency in decision-making processes for all participating countries. Efficiencies can be achieved by speeding up the decision-making process, but also by meeting together some of the growing complexities in decision-making associated to some innovations in treatment coming forward. The alignment anticipated by the EU HTA regulation should be reasonably achievable for Portugal it is anticipated, and this process has

already been assisted by pre-existing work of the EUNETHA collaboration.

Brian Cuffel, Vice-President and Market Access Head, Oncology, Bayer, raised a question as to whether the reality of the implementation of the HTA regulation implementation will match the reality of its original promise for true harmonisation of procedures. Some of the major areas of divergence presently between countries in HTA procedures include the questions raised following submission of evidence and the endpoints from trials that are considered relevant. The result is that the same sets of trials can end up being interpreted quite differently by different HTA bodies. A test of the EU HTA regulation will be whether it helps to solve this issue. The harmonisation of PICO statements within the HTA regulation will therefore be an important factor. Standards for clinical assessment need to reflect disease specific realities and cancer specific realities. Examples to consider in this respect include: accelerated regulatory pathways for genomically driven cancer treatments the possibilities for providing access for patients to these treatments alongside post approval evidence generation. The European HTA processes need to understand this scientific scenario, and to facilitate patient access while post marketing evidence accumulates. The expertise present and made use of in HTA processes requires attention as well. Expertise not only in HTA processes per se, but the patient expertise and that of other stakeholders in the process.

Robin Doeswijk, Head of European Affairs, European Haematology Association, emphasised the importance of how experts in the HTA process are identified, selected and also trained. As an example, and similar to concerns expressed by others, an overly rigorous approach to conflict of interest procedures could unintentionally exclude some of the best experts from the decision-making process. This would especially be the case in highly specialist fields. In any rare disease area, for example, often the pool of actual experts will necessarily be very confined. Robin also identified a risk that, even when EU level Joint Clinical Assessments are in place, national bodies may continue to retain significant licence to interpret the assessments differently. If this were the case, the result would be a failure to solve the problem the EU regulation was initially intended to correct.

KEY RECOMMENDATIONS

- There is a risk inherent in the EU HTA Regulation that even after the production of Joint Clinical Assessments there then follows a significant divergence in the way Member States make use of the Assessments. This would set back the attainment of the EU HTA Regulation's original purpose and should therefore be guarded against via the guidance, Implementing Acts and other preparatory actions currently under development.
- During this preparatory period, patient involvement should be secured in all three main domains of the EU HTA Regulation: Joint Clinical Assessments, Joint Scientific Consultation and Horizon Scanning.
- Conflict of interest procedures utilised in the implementation of the EU HTA Regulation must be pragmatic and proportionate, taking due account of the reality that in many highly specialised areas there will inherently be only a limited pool of highly relevant expertise.

FIND OUT MORE

- Roundtable recording
www.europecancer.org/events/230:community-365-roundtable-meeting-a-year-of-opportunities-on-pharmaceutical-access-and-value
- European Cancer Pulse
www.europecancer.org/pulse
- Parliamentarians for Cancer Action
www.europecancer.org/National-and-European-Parliamentarians-for-Cancer-Action

References

1. Revision of the EU General Pharmaceutical Legislation: https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12963-Revision-of-the-EU-general-pharmaceuticals-legislation_en
2. Health Technology Assessment Regulation: https://health.ec.europa.eu/health-technology-assessment/regulation-health-technology-assessment_en
3. Document: Draft Revision of the Pharmaceutical Legislation: <https://pro.politico.eu/news/159278>
4. Proposal for a Directive of the European Parliament and of the Council on the Union Code Relating to Medicinal Products for Human Use, and Repealing Directive 2001/83/EC and Directive 2009/35/EC: <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52023PC0192>
5. Europe is Running Out of Medicines. Politico, 29 Jan 2023: <https://www.politico.eu/article/health-care-pharma-why-is-europe-running-out-of-medicines-and-whats-being-done-about-it/>
5. Regulation (EU) 2022/123 of the European Parliament and of the Council of 25 January 2022 on a Reinforced Role for the European Medicines Agency in Crisis Preparedness and Management for Medicinal Products and Medical Devices: <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32022R0123>
6. European Medicines Agency - Monitoring and Mitigating Shortages of Medicines and Services: https://www.european-cancer.org/index.php?option=com_attachments&task=download&id=1144:presentation-session-1-monitoring-mitigating-shortages-medicines-devices-j-ferreira-ema_en
7. European Medicines Verification System: <https://emvo-medicines.eu/>

As the not-for-profit federation of member organisations working in cancer at a European level, the European Cancer Organisation convenes oncology professionals and patients to agree policy, advocate for positive change and speak up for the European cancer community.

Publication: May 2023



Rue de la Science 41
1040 Brussels, Belgium

+32 2 775 02 00

europeancancer.org

FOLLOW US:

[@EuropeanCancer](https://www.instagram.com/EuropeanCancer)

