CDDF SPRING CONFERENCE 2021
08 - 10 February 2021
Virtual Conference
Current and future challenges of innovative oncology drug development

Possible avenues to speed up patient access

Industry perspective

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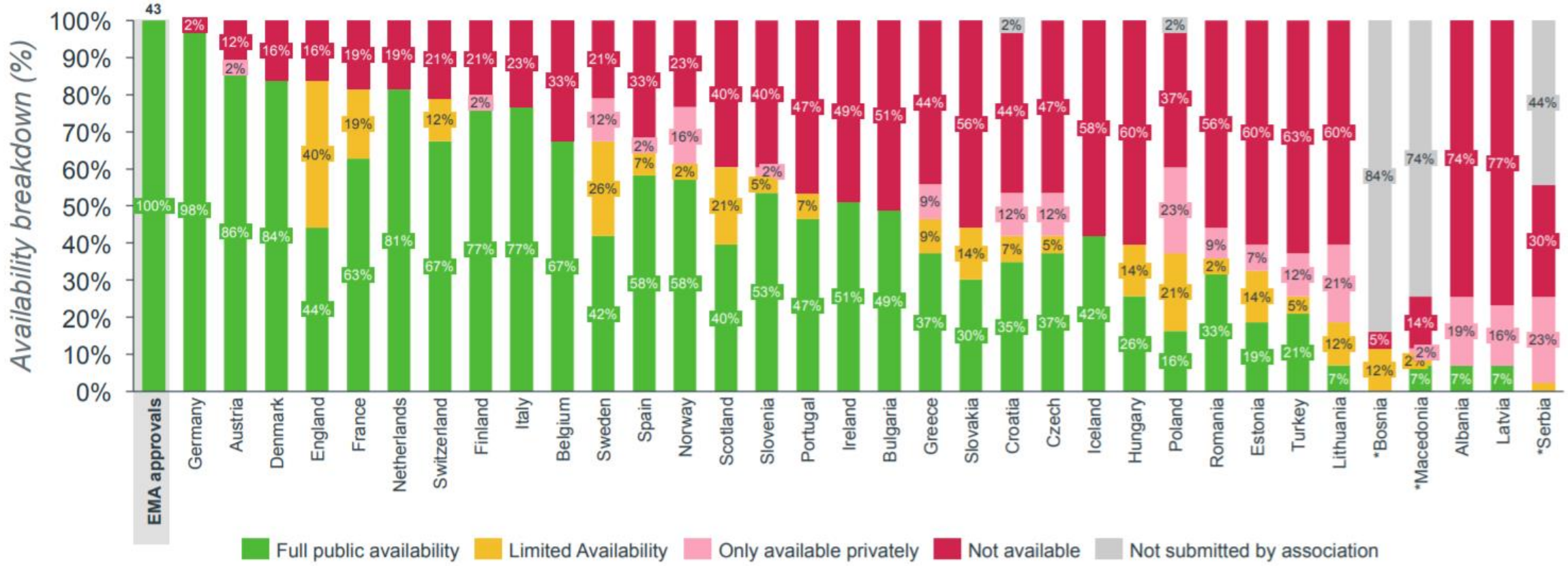
The Challenge

EFPIA W.A.I.T. Indicator for oncology medicines

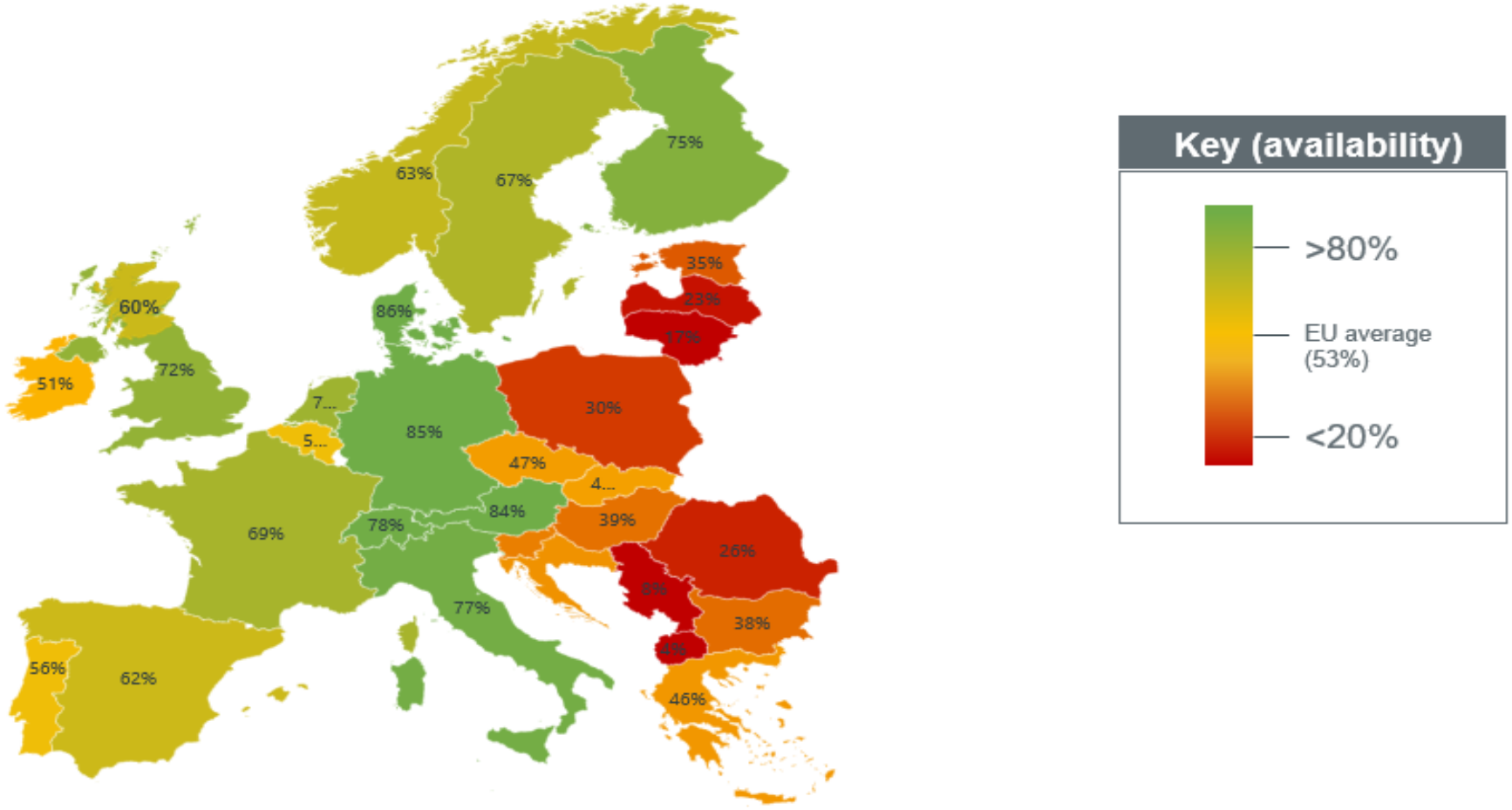
Rate of availability (2015-2018)

The **rate of availability** is the number of medicines available to patients in European countries (for most countries this is the point at which the product gains access to the reimbursement list*). This includes all medicines status to provide a complete picture of the availability of the cohort of medicines studied.



Unequal access to innovative medicines

Geographical variation (EMA approved NMEs 2015-2018)



Source: IQVIA, CRA. Root causes unavailability. July 2020

EFPIA W.A.I.T Indicator for oncology medicines

Key observations (IQVIA)

- Patient access to new Oncology medicines is highly varied across Europe, with the greatest rate of availability in Northern and Western European countries.
- In 88% of the countries, the rate of availability is **higher for Oncology products** compared to all products approved between 2015-2018
- In Germany, France, England, Netherlands, Belgium, Bulgaria, and Romania, the availability of oncology medicines in more than 10% above the rate of all medicines approvals.
- Limited availability is prevalent within the oncology medicines with over 20% of oncology medicines having a restriction placed upon them after SmPC in England (40%), Sweden (26%), Scotland, (21%), and Poland (21%)
- The average delay between market authorisation and patient access for Oncology products varies 2.5 months to over 2.5 years

Challenge 2: the changing face of biomedical innovation

A lot needs to be explained, new approaches for HTA and decision making are needed

- Smaller, focused RCTs, adaptive trial designs, expanded use of single-arm trials, surrogate- and intermediate endpoints
- Rare disease innovation with more limited information at the time of (initial) marketing authorization
- Increasing number of biomarker-specific therapies with co-depencies with diagnostic technologies (“precision medicine”)
- Lifecycle approach to medicine development, substantially increased development activity after initial launch
- Faster evolution of clinical «standards of care»
- Innovation to support personalised prescribing of medicines (“clinical decision support”)

Root causes of non-availability and delayed patient access

10 interrelated factors contributing to access delays

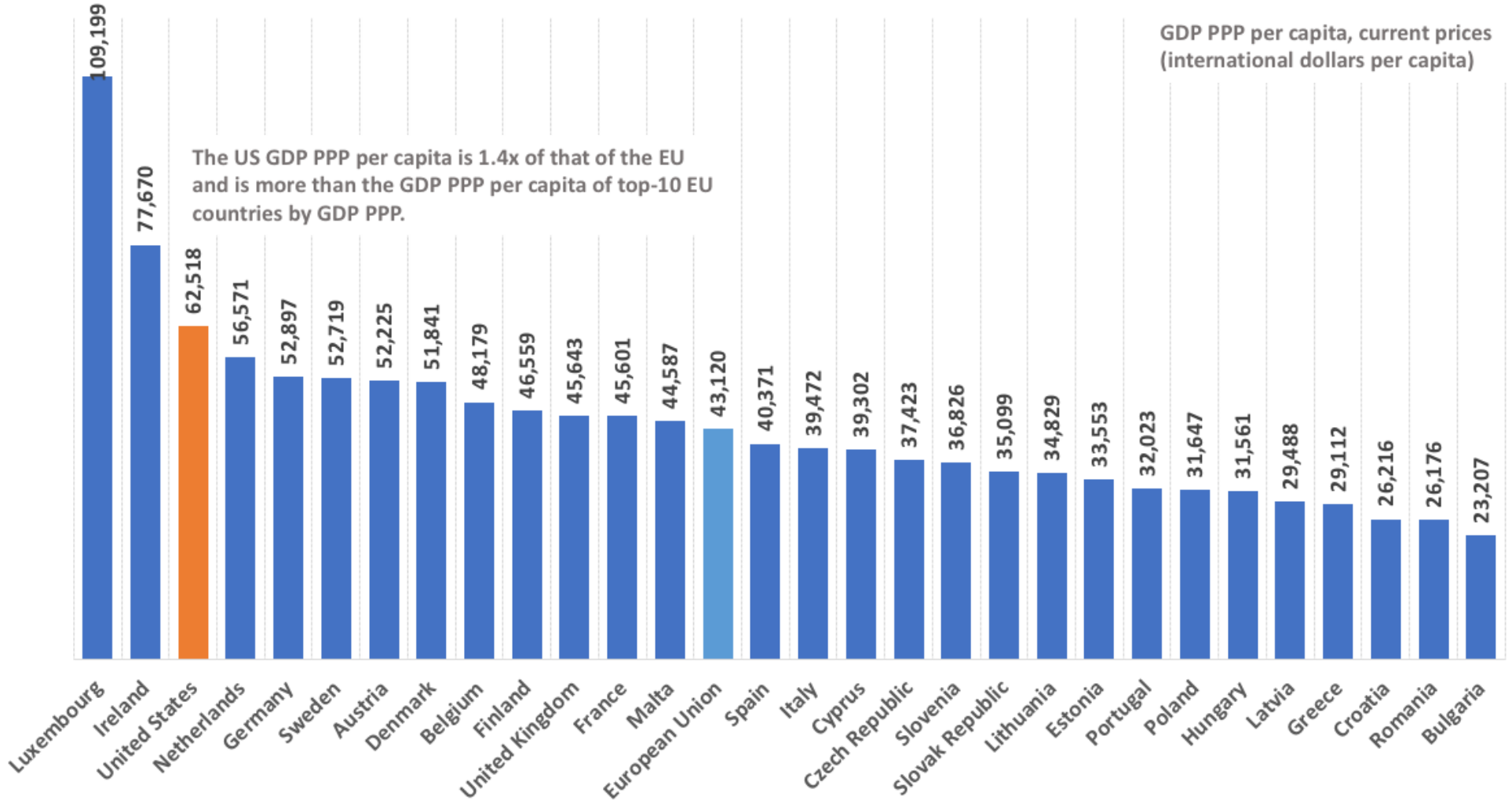
Category	Potential root causes
The time prior to market authorisation	1. The speed of the regulatory process 2. Accessibility of medicines prior to marketing authorisation
The price and reimbursement process	3. Initiation of the process 4. The speed of the national timelines and adherence
The value assessment process	5. Misalignment on evidence requirement 6. Misalignment on value and price 7. The value assigned to product differentiation and choice
Health system readiness	8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure and relevance to patients
Delay from national to regional approval	10. Multiple layers of decision-making processes

CRA/EFPIA 2020

- Many interrelated factors can explain unavailability and access delay.
- Is not possible to untangle their impact with perfect precision
- Factors are rooted in the access systems and processes of EU Member States and the corresponding impact on commercial decision making of companies

Large economic differences between countries

Major implictions for health and health systems



Data Source: IMF World Economic Outlook, October 2018

Data Analysis by: MGM Research

Together we can do better!

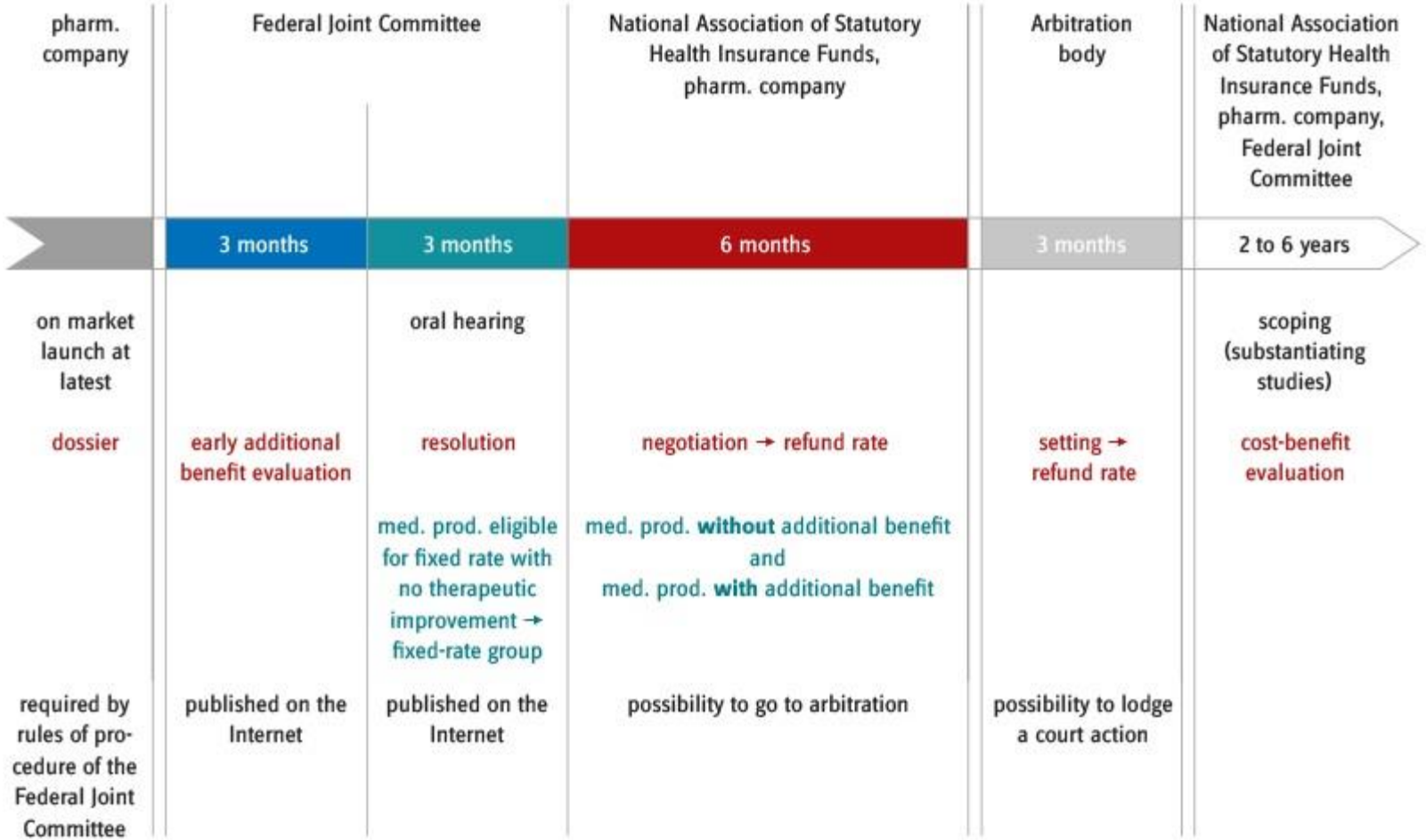
Publication just ahead of #WorldCancerDay with press conference from @MargSchinas and @SKyriakidesEU

📅 3 February 2021, +/- 12.00
🎥 Follow LIVE here:
europa.eu/!Jw63DJ

#EUCancerPlan #HealthUnion

No doubt, fast and broad patient access is achievable!

Example Germany: Reimbursed patient access from day 1

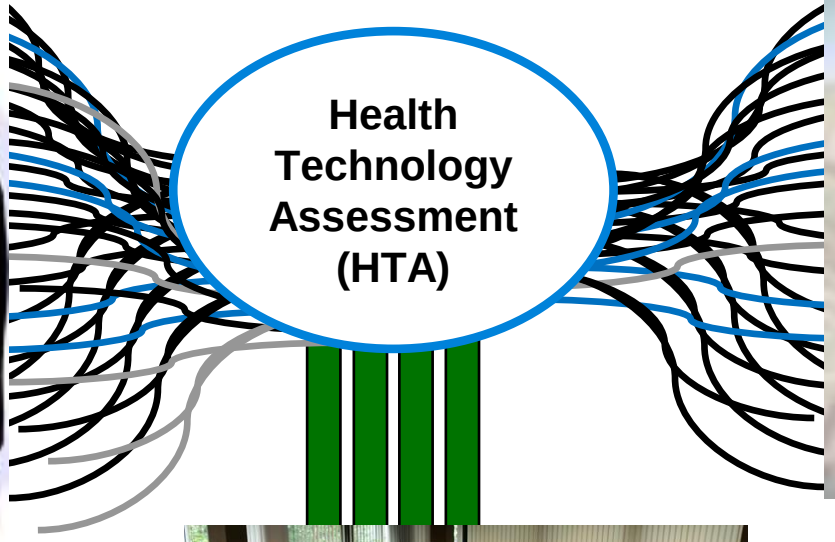


GKV Spitzenverband 2016

Politically accountable HTA and decision making

Understanding, not overriding citizen and patient preferences

Assess the impact of technology in light of social preferences



Investigate and understand citizen/patient preferences

Deliberative appraisal, there are no simple decision making algorithm

Quality of Life (QoL) assessments and HTA

We are getting better, but more needs to be done

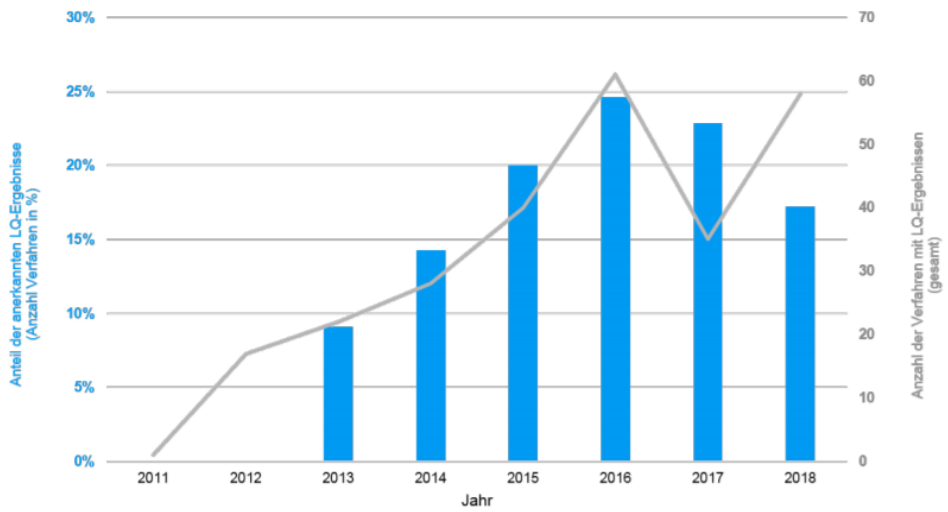


Abbildung 2: Übersicht der Verfahren mit LQ-Erhebungen im Zeitverlauf

A Validität der LQ-Fragebögen muss nachgewiesen sein.

B Rücklaufquote sollte ≥ 70% sein bzw. < 15%-Punkte Unterschied zwischen den Gruppen.

C Begründung für fehlende Werte anführen, geeignete Imputation nutzen.

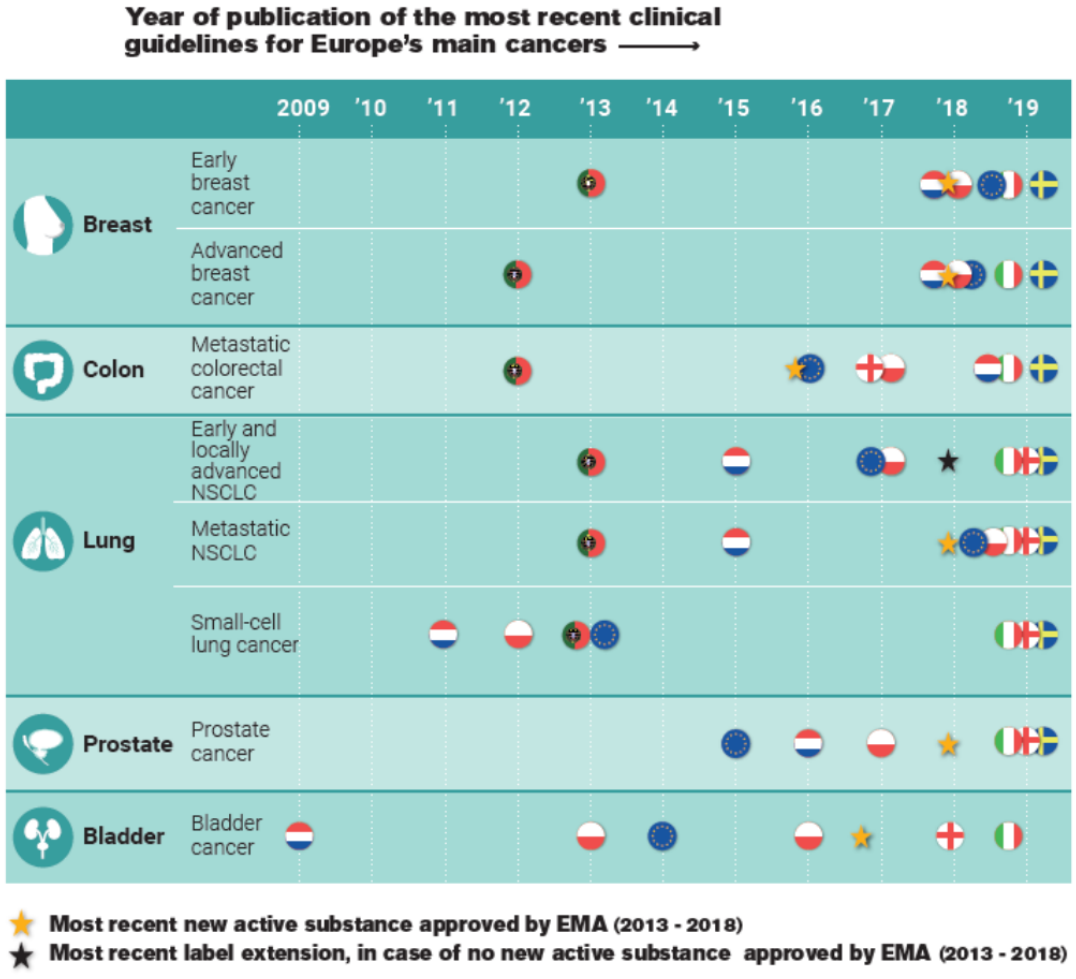
D Irrelevanzschwelle darf nicht unterschritten werden.

Abbildung 3: Anforderungen des G-BA an LQ-Erhebungen

Schmidt/Pütz, DAK AMNOG Report 2019

- How will accelerated clinical development pathways impact the ability to systematically collect HRQoL data?
- Are we effective in communicating HRQoL findings?

Are clinical guidelines coming too late to inform decision making?



Source NICE, 2020, Associazione Italiana di Oncologia Medica, 2020, Integraal Kankercentrum Nederland, 2020, Serviço Nacional de Saúde , 2020, Regionala Cancercertrum, 2020, European Society for Medical Oncology, 2020.

- Can oncologists be more systematically engage in HTA and Decision Making processes?
- Can instruments like the ESMO Magnitude of Clinical Benefit Scale (MCBS) close the gap?

Acceptance of clinical evidence by decision makers

Acceptance of evidence characteristics by EMA

and six national HTA bodies, based on self-assessment by agency representatives

Legend

Accepted | **Often accepted** | **Case-dependent** | **Often not accepted** | **Not accepted**

Evidence characteristics (for the clinical or cost effectiveness assessment)		Autho-rization	Health technology assesment						Level of align-ment among HTA bodies
		EMA	UK-ENG	IT	NL	PL	PT	SE	
Population	• Target population as authorized by EMA	[N/A]							50%
	• Use of biomarkers								100%
	• Extrapolation to other populations								33%
Comparator	• Selected comparator								100%
	• Class effects								33%
	• Indirect comparisons								50%
Clinical end points	• PFS as endpoint								50%
	• Other surrogate endpoints (non PFS)								0%
	• Absence of QoL data								50%
Trial design and data sources	• Real-world evidence								100%
	• Network Meta-Analysis								50%
	• Single armed trials								50%
	• Novel trial designs								50%
	• Cross over in trial								33%
	• Evidence from small population								67%
	• Short time period								50%
Statistical analysis	• Absence of statistical significance								67%
	• Post-hoc subgroup analyses								83%
	• Clinical relevance of effect acc. to EMA								67%
Level of acceptance per agency (HTA bodies and EMA)		**79%**	**68%**	**42%**	**47%**	**79%**	**37%**	**58%**	

Sources ASC Academics and Vintura, 2020 (see Annex C).

EU HTA Regulation: > 5 years in the making

Proofpoint for Member States' commitment to EU collaboration?

European Commission

More than 10 years of cooperation: projects, joint actions

ACHIEVEMENTS

- **Trust** between HTA bodies
- **Capacity building**
- Development of **joint tools** (e.g. EUnetHTA Core Model, POP EVIDENT databases)
- Piloting **joint work** (e.g. early dialogues, joint assessments)

LIMITATIONS

- **Low uptake of joint work** ⇒ duplication of work
- Differences in the **procedural framework** and administrative capacities of Member States
- Differences in national **methodologies**
- **No sustainability** of current cooperation model

Commission legislative proposal

MEMBER STATE-DRIVEN JOINT WORK	**Member States role** • In charge of the scientific work and the decisions • Organised in a member state-led "Member State Coordination Group on HTA" (the coordination group) **Commission role** • Adoption of tertiary (implementing) legislation • Obligation to verify joint reports before their publication • Monitor implementation of common rules **and use of joint work**
JOINT WORK BASED ON 4 PILLARS	Joint clinical assessments; Joint scientific consultations; Identification of emerging health technologies *(horizon scanning)*; Voluntary coordination *(other areas of HTA)*
SCOPE: MEDICINAL PRODUCTS SUBJECT TO CENTRALISED PROCEDURE	New active substances New therapeutic indications for existing active substances Certain medical devices
TIMING	Align timing to regulatory process to ensure timely availability of the joint assessment : • at time of Commission decision for MA • but both remaining within appropriate remits

Source: Sanofi

efpia

www.efpia.eu

Risk, that poor legislative compromize will add new layer of complexity to current patient access pathways.

“Value” is a moving target!

Only “learning”health care systems” capture value

- Value of a technology in a specific indication changes over time due to many reasons
  - Introduction of new technology with similar or improved outcomes
  - Clinicians and patients gather experience with the new technology, use it more efficiently or effectively
  - Price changes of technology or relevant alternative technologies
- Value can be actively influenced by healthcare policy decision makers through utilization management

→ It is more important to know how to influence costs and benefits of a technology over time than to exactly measure them at a single time point in its lifecycle e.g. at launch before it has actually been used

It can be done: AIFA's post marketing registries

Focus on drug utilization and outcomes

153 registries: all drug based

31 registries: disease approach data collection

48 MAH

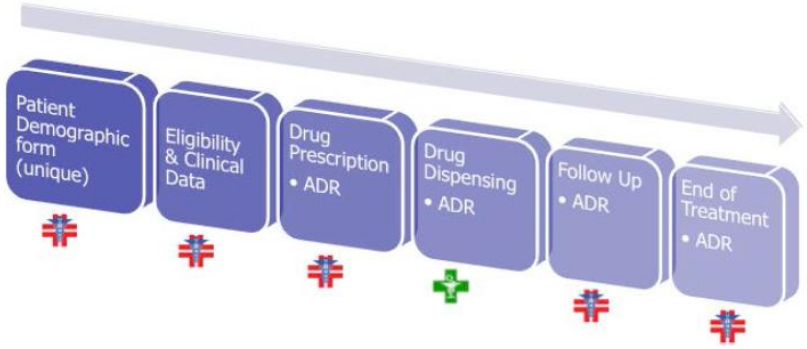
≈888,000 patients

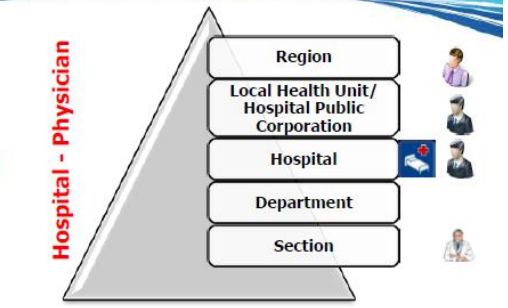
≈29,000 physicians

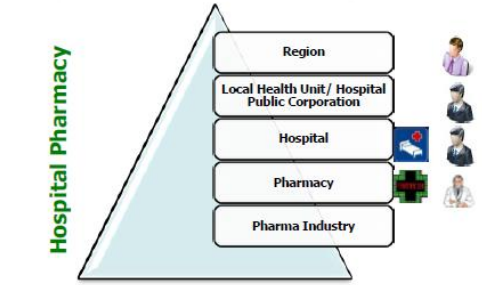
≈2,000 pharmacists

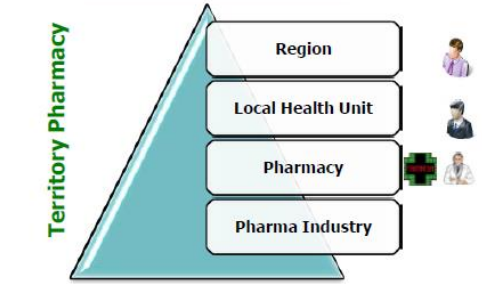
≈1,700 Health managers

49 Regional referees



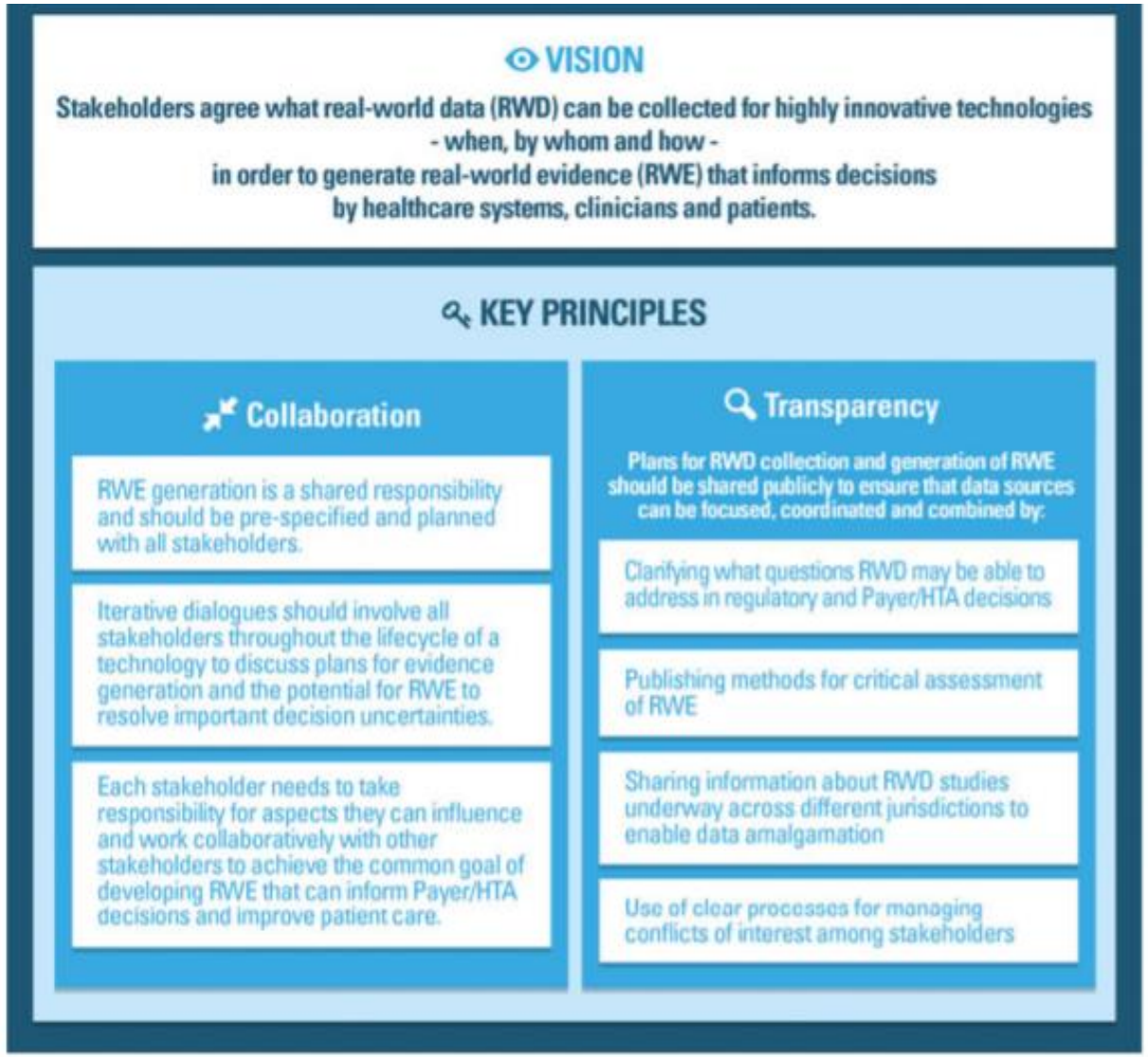






Xoxi CDDF (2016)

RWE4Decisions - Towards a multi-stakeholder EU Learning Network for the use of RWE in decision making

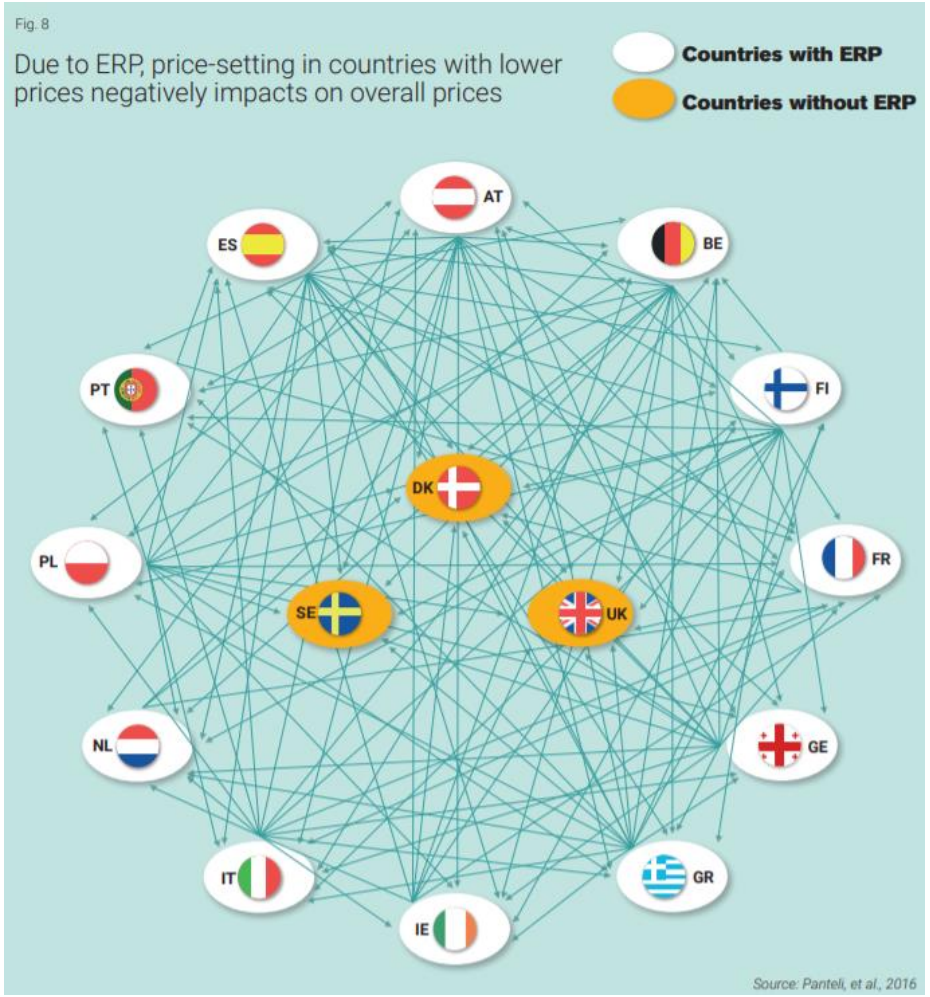


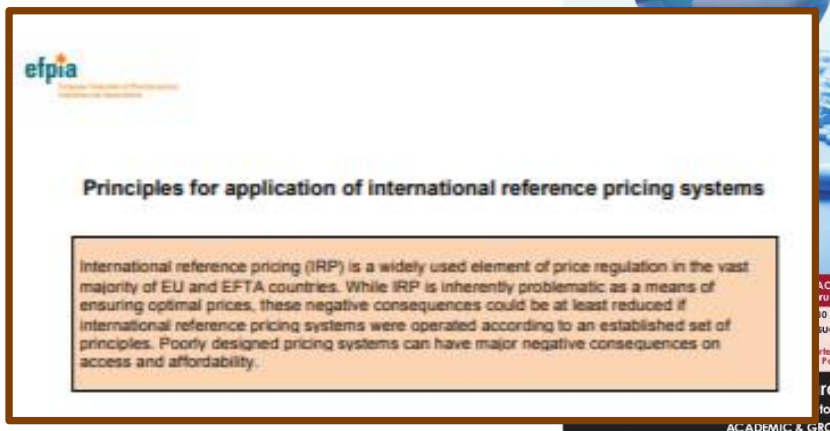
Facey, Rannanheimo, Batchelor, Borchardt, de Cock 2020

www.rwe4decisions.com

Solidarity between countries beyond COVID-19

Can we finally overcome the unintended consequences of international reference pricing and parallel trade?





Short term opportunities

The time is now!

Major EU initiatives with opportunities for improved patient access and outcomes across the EU

EU4Health

Emerged as a result to COVID-19 crisis and pushes for a stronger EU role on health issues. EU will invest financial resources to EU Member States, health organisations and NGOs with impact on healthcare staff, patients and health systems in Europe. Focus on creating reserves of medical supplies and staff and boost the cross-border health crisis response, but also on issues such as combatting the antimicrobial resistance.

Europe's Beating Cancer Plan

The current Commission's flagship initiative in health aims to improve the way we prevent, diagnose and treat cancer, in addition to the follow-up care. Special groupings across the EU institutions are evaluating opportunities for the EU to take concrete action, identifying legislation and other measures that can help prevent and fight cancer, and looking into the best ways to support research.

Pharmaceuticals Strategy

Aims to ensure equal access to safe, state-of-the-art and affordable therapies for all Europeans while taking advantage of digitalization and reducing environmental burden. The strategy will also tackle the issue of the EU's reliance on importing active pharmaceutical ingredients from third countries by incentivizing production to return to the EU, while pushing for third countries to adopt harmonized international standards on quality and safety. Linkage with Horizon Europe is anticipated.

Health Technology Assessment legislation

Assessment of the added value of new or existing health technologies – medicines, medical devices and diagnostic tools, surgical procedures, as well as measures for disease prevention, diagnosis or treatment – compared with other health technologies. Renewed interest in passing legislation post-COVID-19 by several EU Member States to gain a powerful tool in dealing with access to medicines.

@VNemecEU, 15.09.2020

EU Pharmaceutical Strategy and unequal access

Tangible progress requires a dedicated forum

- More equal access to innovative medicines across the EU is a declared key priority for the EU Pharmaceutical Strategy.
- Tangible progress requires that root causes of unequal access are identified and addressed.
- Key barriers can only be removed in multilateral engagement involving all Member States and stakeholders

ESTABLISH A FORUM FOR BETTER ACCESS TO HEALTH INNOVATION

A multi-stakeholder Forum for Better Access to Health Innovation, covering all aspects of innovation, from disease prevention, therapies, technologies, and supply chains, to improvements in care pathways and healthcare services, should be established to enhance progress towards equal access across the EU. The Forum should discuss all drivers and barriers to access innovation, including economic, budgetary, organisational, and regulatory.

The European Commission should facilitate a multi-stakeholder Forum for Better Access to Health Innovation, involving all stakeholders – from Member States and regional authorities to patients and civil society, from healthcare professionals to industry.

https://www.euhealthcoalition.eu/recommendations/

More equal access to innovative (oncology) medicines
A call to action for all stakeholders

- Establish and aligned understanding of the root caused of non-availability and patient access delays
- Patient access solutions that ensure
  - incentives for future valuable biopharmaceutical innovation are in place
  - patients have access from day 1 (EU Marketing Authorization)
  - patients have access to the full new indication as per EMA regulatory label
  - Sustainable health care systems´ funding is available, relevant infrastructure is in place
- Required will be upgrades to HTA, pricing, and funding mechanisms plus relevant health system strengthening initiatives

Doing now what patients need next