



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

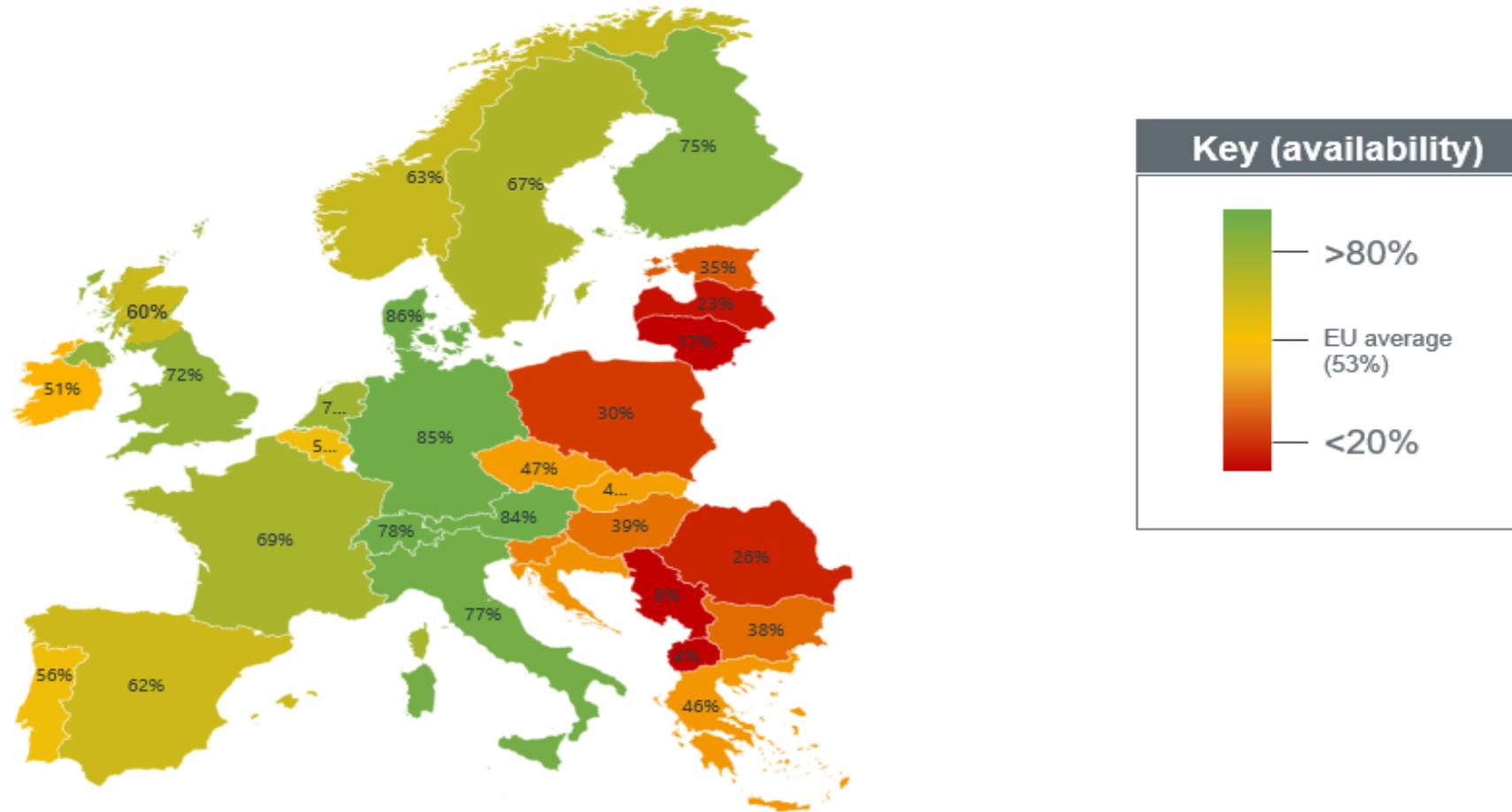
Rate of availability (2015-2018)

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 is 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-dependencies 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

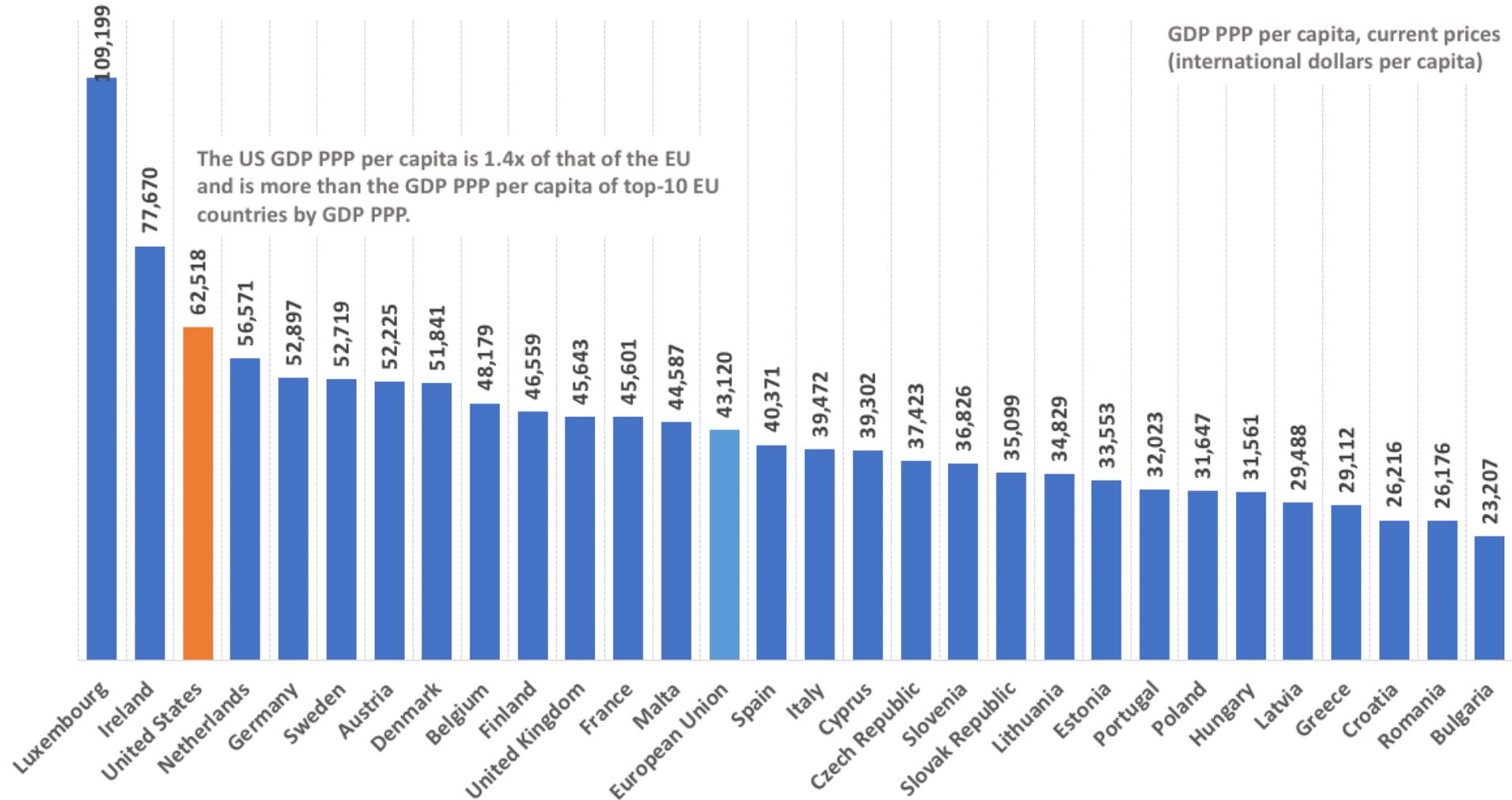
10 interrelated factors contributing to access delays

Category	Potential root causes
The time prior to market authorisation	<ol style="list-style-type: none"> 1. The speed of the regulatory process 2. Accessibility of medicines prior to marketing authorisation
The price and reimbursement process	<ol style="list-style-type: none"> 3. Initiation of the process 4. The speed of the national timelines and adherence
The value assessment process	<ol style="list-style-type: none"> 5. Misalignment on evidence requirement 6. Misalignment on value and price 7. The value assigned to product differentiation and choice
Health system readiness	<ol style="list-style-type: none"> 8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure and relevance to patients
Delay from national to regional approval	<ol style="list-style-type: none"> 10. Multiple layers of decision-making processes

- 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 implications for health and health systems



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

 17 3 February 2021, +/- 12.00

 Follow LIVE here:
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#EUCancerPlan #HealthUnion



Europe's beating cancer plan

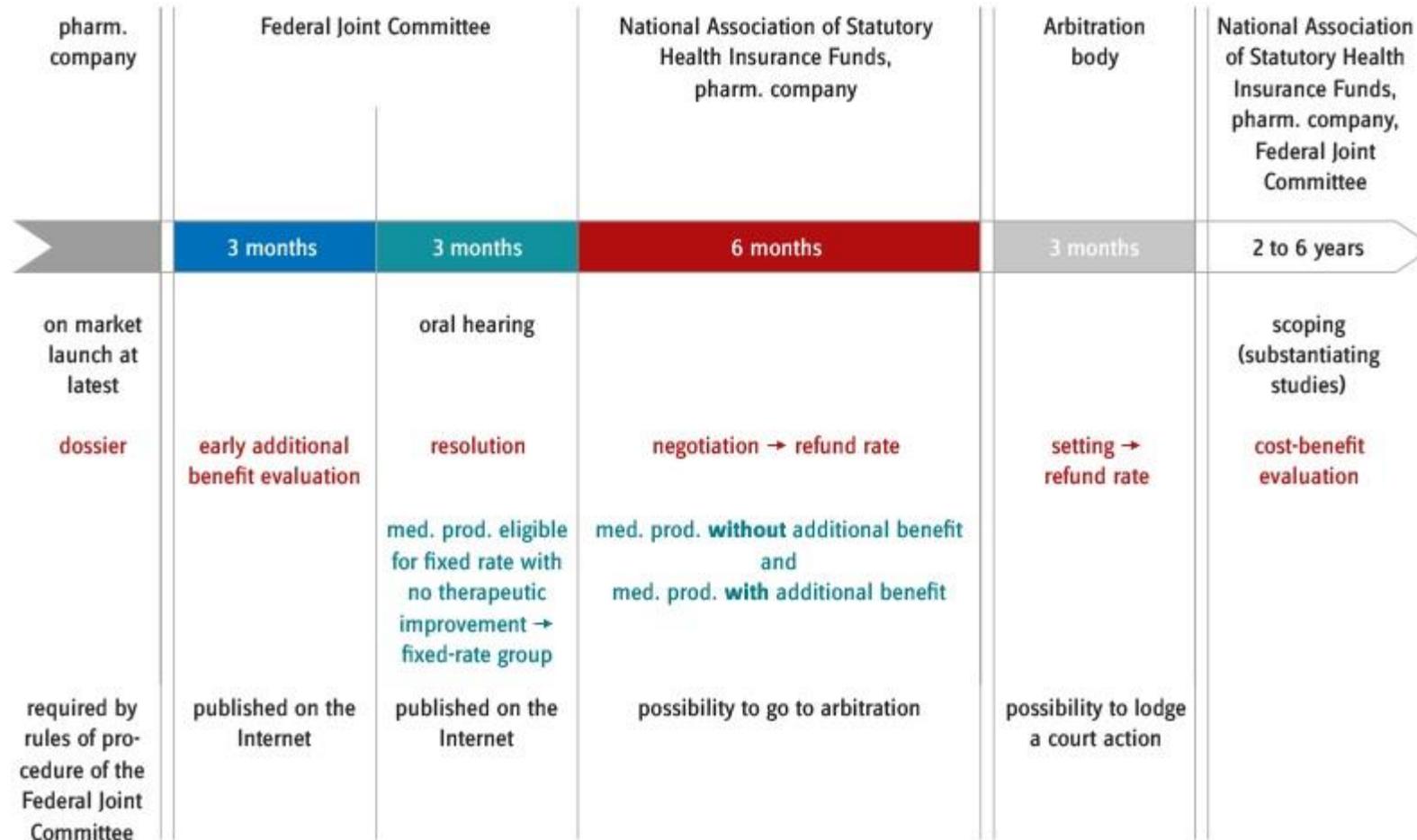
3 February 2021

#EUCancerPlan
#HealthUnion



No doubt, fast and broad patient access is achievable!

Example Germany: Reimbursed patient access from day 1

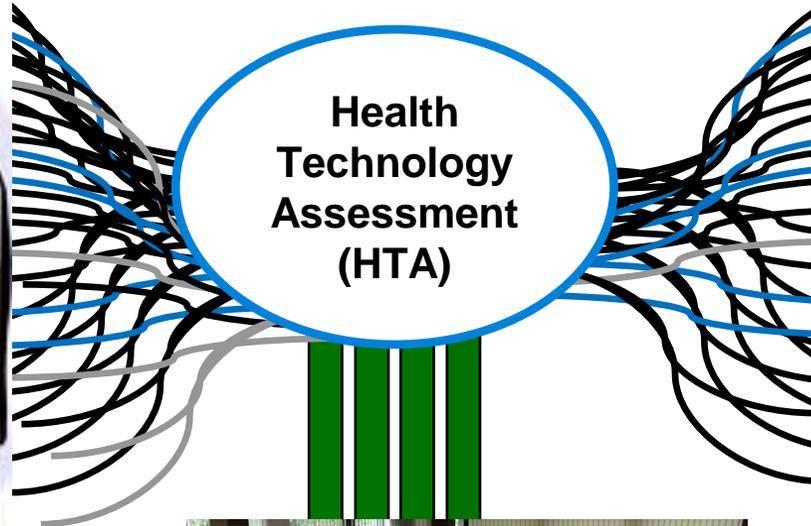


Politically accountable HTA and decision making

Understanding, not overriding citizen and patient preferences



Investigate and understand citizen/patient preferences



Assess the impact of technology in light of social 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

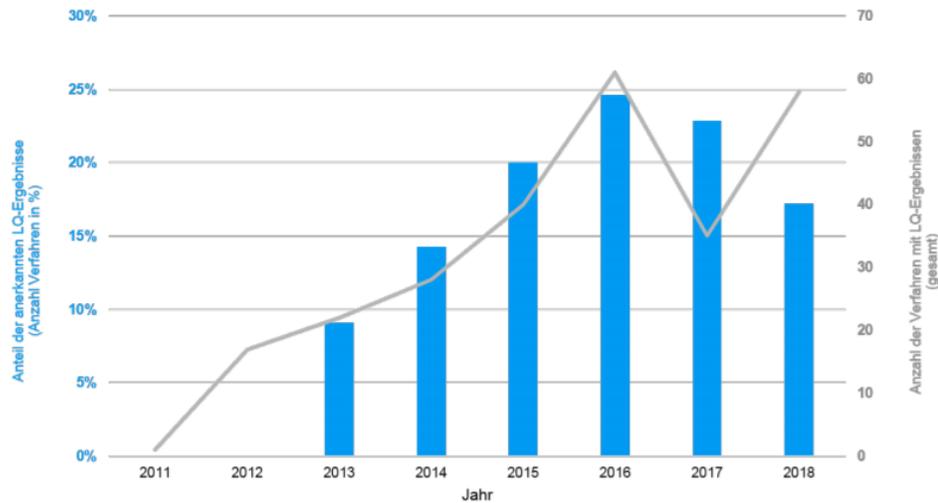


Abbildung 2: Übersicht der Verfahren mit LQ-Erhebungen im Zeitverlauf

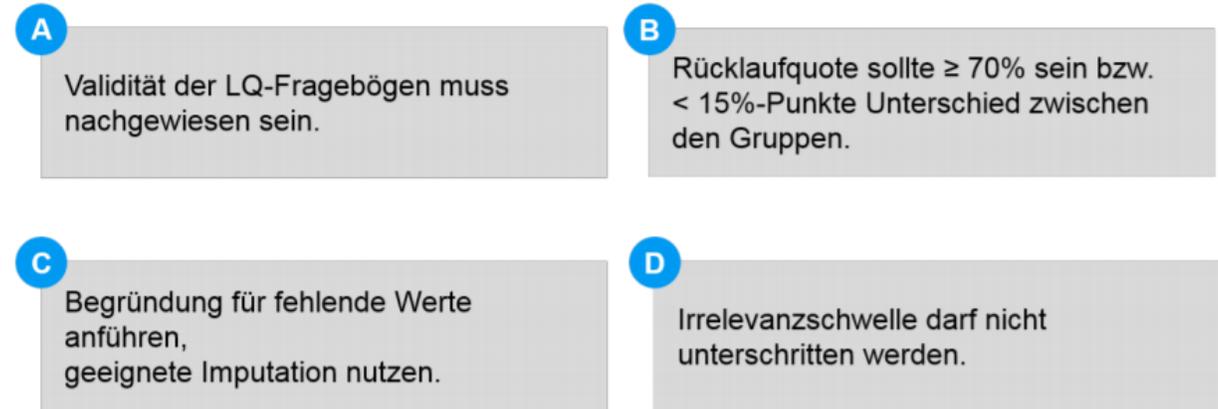
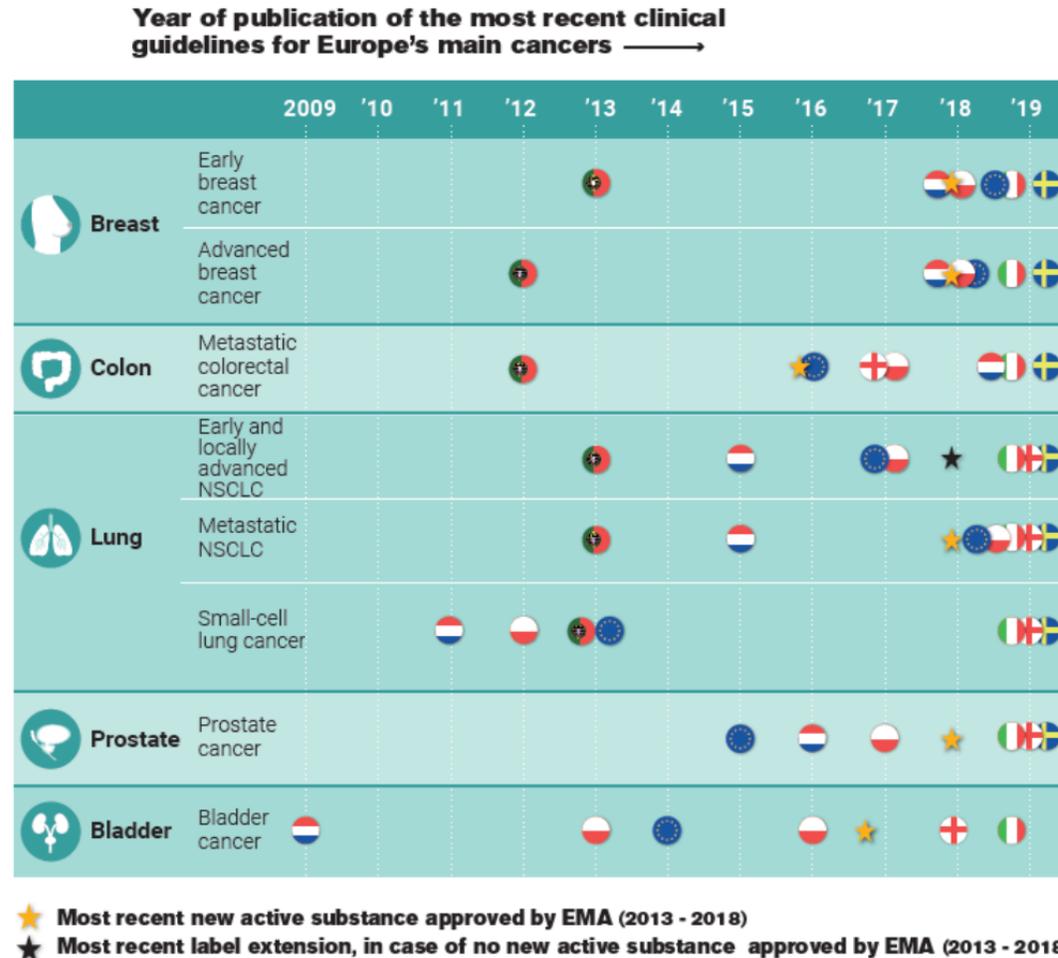


Abbildung 3: Anforderungen des G-BA an LQ-Erhebungen

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 Cancercentrum, 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



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]	Accepted	Often not accepted	Case-dependent	Often not accepted	Often not accepted	Often not accepted	50%
	• Use of biomarkers	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	100%
	• Extrapolation to other populations	Accepted	Accepted	Often not accepted	Case-dependent	Accepted	Often not accepted	Case-dependent	33%
Comparator	• Selected comparator	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	100%
	• Class effects	Accepted	Case-dependent	Not accepted	Case-dependent	Accepted	Not accepted	Case-dependent	33%
	• Indirect comparisons	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	50%
Clinical end points	• PFS as endpoint	Accepted	Accepted	Often not accepted	Accepted	Accepted	Often not accepted	Accepted	50%
	• Other surrogate endpoints (non PFS)	Often accepted	Case-dependent	Case-dependent	Not accepted	Accepted	Often not accepted	Accepted	0%
	• Absence of QoL data	Often not accepted	Not accepted	Often accepted	Often not accepted	Accepted	Accepted	Often not accepted	50%
Trial design and data sources	• Real-world evidence	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	100%
	• Network Meta-Analysis	Accepted	Accepted	Case-dependent	Accepted	Case-dependent	Accepted	Accepted	50%
	• Single armed trials	Accepted	Accepted	Accepted	Accepted	Accepted	Often not accepted	Accepted	50%
	• Novel trial designs	Accepted	Accepted	Accepted	Case-dependent	Accepted	Accepted	Accepted	50%
	• Cross over in trial	Accepted	Accepted	Accepted	Accepted	Accepted	Case-dependent	Case-dependent	33%
	• Evidence from small population	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	67%
	• Short time period	Accepted	Accepted	Case-dependent	Often not accepted	Accepted	Case-dependent	Accepted	50%
	• Absence of statistical significance	Often not accepted	Case-dependent	Not accepted	Case-dependent	Often not accepted	Not accepted	Not accepted	67%
Statistical analysis	• Post-hoc subgroup analyses	Often not accepted	Often not accepted	Often not accepted	Not accepted	Often not accepted	Often not accepted	Often not accepted	83%
	• Clinical relevance of effect acc. to EMA	Case-dependent	Case-dependent	Case-dependent	Often not accepted	Accepted	Case-dependent	Case-dependent	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?

More than 10 years of cooperation: projects, joint actions

ACHIEVEMENTS

LIMITATIONS

- **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)

- **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

JOINT WORK BASED ON 4 PILLARS

SCOPE: MEDICINAL PRODUCTS SUBJECT TO CENTRALISED PROCEDURE

TIMING

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 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

www.efpia.eu

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

“Value” is a moving target!

Only “learning”health care systems” capture value

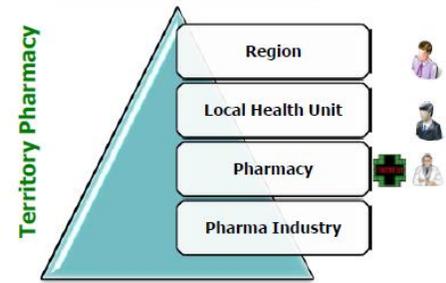
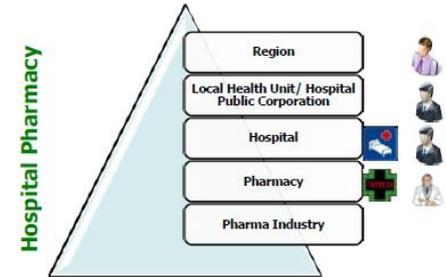
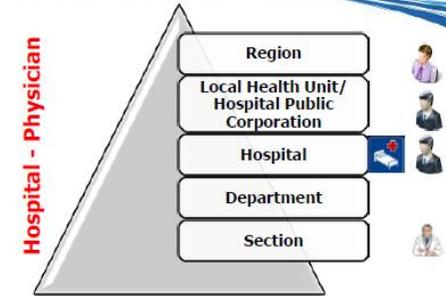
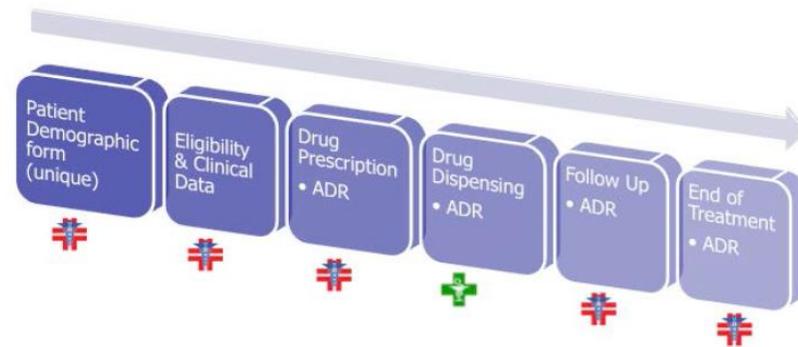
- Value of a technology in a specific indication changes over time due to many reasons
 - Introduction of new technology with similar or improved outcomes
 - Clinicians and patients gather experience with the new technology, use it more efficiently or effectively
 - Price changes of technology or relevant 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



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

 **VISION**

Stakeholders agree what real-world data (RWD) can be collected for highly innovative technologies
- when, by whom and how -
in order to generate real-world evidence (RWE) that informs decisions
by healthcare systems, clinicians and patients.

 **KEY PRINCIPLES**

 Collaboration	 Transparency
<p>RWE generation is a shared responsibility and should be pre-specified and planned with all stakeholders.</p>	<p>Plans for RWD collection and generation of RWE should be shared publicly to ensure that data sources can be focused, coordinated and combined by:</p>
<p>Iterative dialogues should involve all stakeholders throughout the lifecycle of a technology to discuss plans for evidence generation and the potential for RWE to resolve important decision uncertainties.</p>	<p>Clarifying what questions RWD may be able to address in regulatory and Payer/HTA decisions</p>
<p>Each stakeholder needs to take responsibility for aspects they can influence and work collaboratively with other stakeholders to achieve the common goal of developing RWE that can inform Payer/HTA decisions and improve patient care.</p>	<p>Publishing methods for critical assessment of RWE</p>
	<p>Sharing information about RWD studies underway across different jurisdictions to enable data amalgamation</p>
	<p>Use of clear processes for managing conflicts of interest among stakeholders</p>

RWE4Decisions
REAL WORLD EVIDENCE

Health Innovation – the European Health Data Space and Real-World Evidence

10
NOV
2020

14.00-17.30

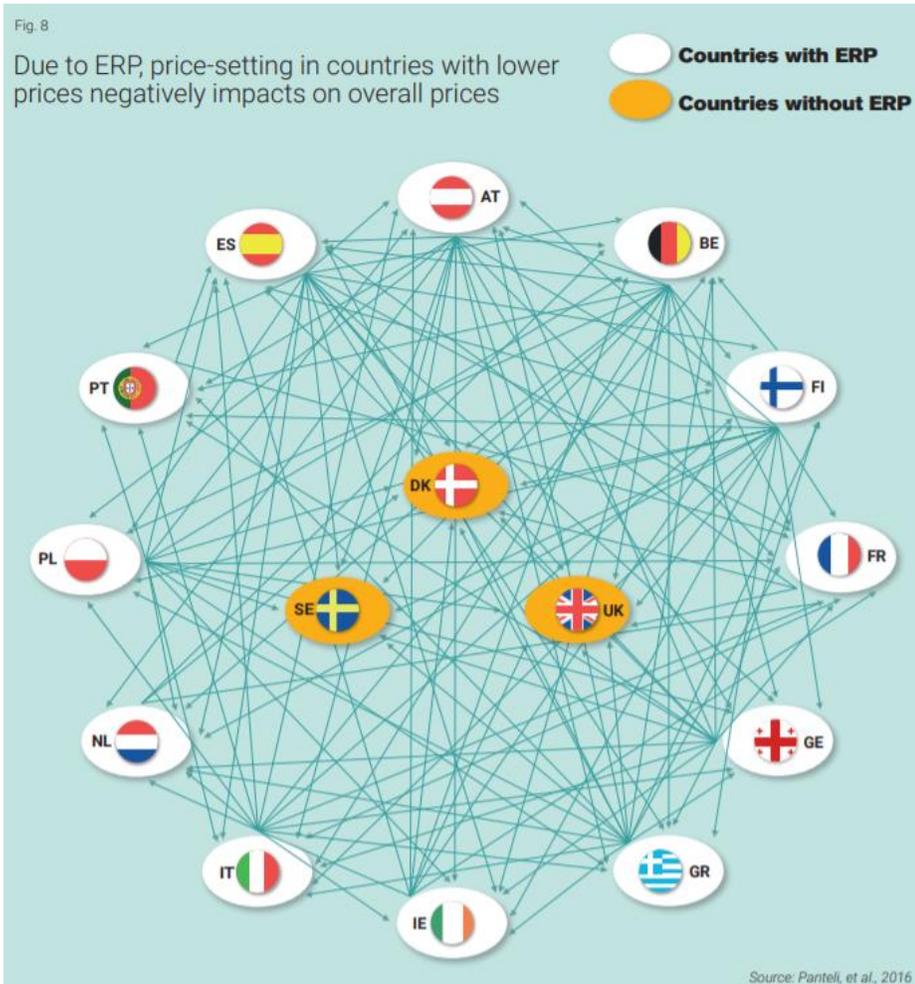
Virtual Conference



www.rwe4decisions.com

Solidarity between countries beyond COVID-19

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



efpia

Principles for application of international reference pricing systems

International reference pricing (IRP) is a widely used element of price regulation in the vast majority of EU and EFTA countries. While IRP is inherently problematic as a means of ensuring optimal prices, these negative consequences could be at least reduced if international reference pricing systems were operated according to an established set of principles. Poorly designed pricing systems can have major negative consequences on access and affordability.

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Parallel Trade

CONFERENCE: 6TH - 7TH
WORKSHOPS: 8TH
FEB 2017

The opportunities and challenges ahead – beyond FMD and Brexit

HOLIDAY INN KENSINGTON FORUM, LONDON, UK

CHAIRMAN:
Eric Noehrenberg, Director, Regional Market Access Lead, Latin America, Sire International GmbH

KEY SPEAKERS INCLUDE:

- Heinz Kobe, Director European Affairs, European Association of Euro-Pharmaceutical Companies
- Dr. Rik Greville, Director, Sales and Director, Distribution & Supply, The Association of the British Pharmaceutical Industry
- Tomasz Dziško, President, Delfama
- Dr. Shobham Hanasab, Senior Consultant, IMS Health
- Dermal Glynis, Senior Advisor, Europe Economics
- Katarzyna Kolasa, Science PhD, Warsaw Medical University
- Mike Islet, Executive Director, European Alliance for Access to Safe Medicines
- Dr. Andrew Blakshorpe, Director Market Access and Managed Entry, Research Health
- Karoline Zwierzynska, Associate, Arnold & Porter (UK) LLP
- Fermin Wagner, CEO, Abacus Medicine
- Maarten Kamp Nils, Business Development Director, Fisher Fajma
- Vladimir Zah, Health Economics Consultant, SPOR

With Brexit and the new EU Falsified Medicine Directive, what does the future hold for parallel trade? This event will discuss short term versus long term concerns of pharma manufacturers, regulators, as well as parallel traders. They will engage in an interactive debate and discuss how to keep ahead of the current trends and how to overcome all challenges. Discussion topics include:

- Parallel Trade 101 – Which factors determine the flow of pharmaceutical products in Europe?
- The European Commission's Falsified Medicines Directive – recent updates
- Falsified Debate – in the spotlight: Shortages
- Parallel traders panel – challenges and opportunities
- Beyond pharmaceutical products – parallel imports of medical devices
- Falsified Debate – in the spotlight: Technology and new trends
- Regional and country focus – Scandinavia, UK and Eurasia

ACTIVE HALF-DAY POST-CONFERENCE WORKSHOPS
February 2017, Holiday Inn Kensington Forum, London, UK

WORKSHOP B | 13.30 – 17.30

Issues in parallel trade

Parallel Trade – Management Strategies

Workshop Leader:
Janice Haigh, Practice Leader, Market Access, Quintiles

Parallel-trade.com
to +44 (0) 870 9090 712 or call +44 (0) 870 9090 711

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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.

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.

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