INNOVATE FOR LIFE

Oireachtas briefing

6th December 2023

#MedicinesMatter

Director of Commercial Policy – Jim McGrath

Irish Pharmaceutical Healthcare Association

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Who are IPHA?

- ✓ 45 innovative biopharmaceutical companies
- ✓ The IPHA Agreement has already delivered €400m in savings over its first two-years.

Why invest in medicines?

Sláintecare.
Right Care. Right Place. Right Time.

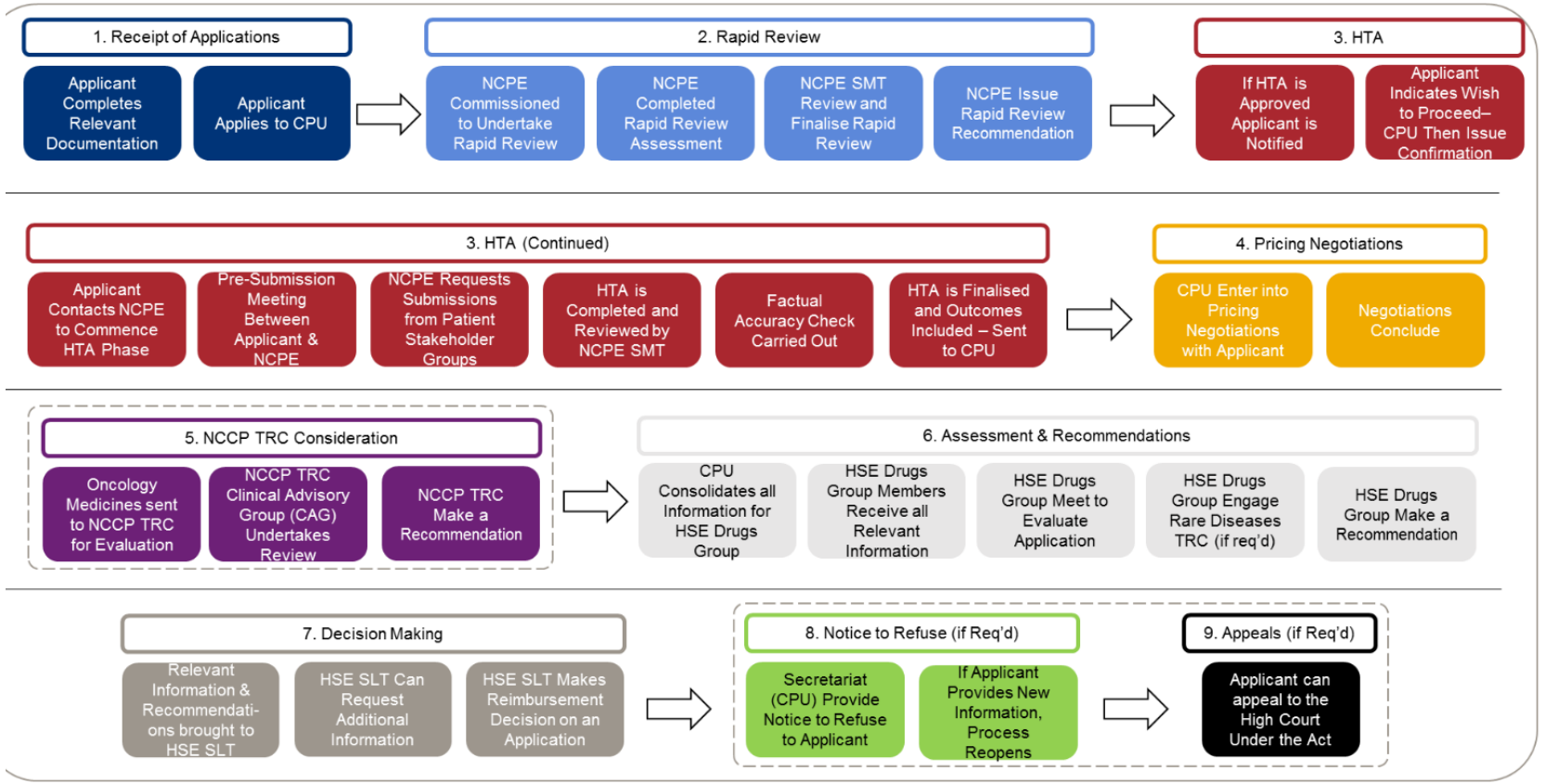
- Universal access to the latest medicines via the public health system is a major health enabler
- Living longer, Healthy aging and Preventing chronic illnesses (cervical cancer)
- Caring for people in their home and community and Freeing up acute care settings
- Improving cancer/cardiovascular and respiratory survival rates (Three largest causes of death)
- Combatting depression and improving society's mental health
- Preventing obesity and diabetes, assisting infertility etc.
- ***Rare disease sufferers are often highly if not wholly dependent on medicines (300K Irish ppl)***

Assessment Process: Pharma Companies must demonstrate a cost-effective health improvement

Criteria set out a decade ago under the 2013 Health Act

Multiple steps (20-30) from start to finish for innovative medicine

One of the most robust pre-assessment of investment in the Irish health service.



Who suffers from a no funding scenario?

4,000 patients equates to Irish towns like:

Town	Population
Saggart, Co Dublin	4573
Kilcoole, Co Wicklow	4569
Courtown, Co Wexford	4365
Macroom, Co Cork	4096
Castleblayney, Co Monaghan	3926
Claremorris, Co Mayo	3857
Kilcullen, Co Kildare	3815
Mitchelstown, Co Cork	3744
Cahir, Co Tipperary	3679
Enfield, Co Meath	3663

Health

At least 4,000 seriously ill patients may not get vital drugs due to Budget 2024 decision

PAUL CULLEN
Health Editor

At least 4,000 seriously ill patients may be unable to access potentially life-saving medicines next year due to the Government's decision not to provide funding for new drugs in last week's budget.

They include about 1,000 cancer patients hoping to access 23 new medicines going through a funding approval process, and 3,300 patients with other conditions that could be treated by 11 new medicines in ing for clinical programmes will result in a "significant slowdown" in their further development, HSE chief executive Bernard Gloster warned.

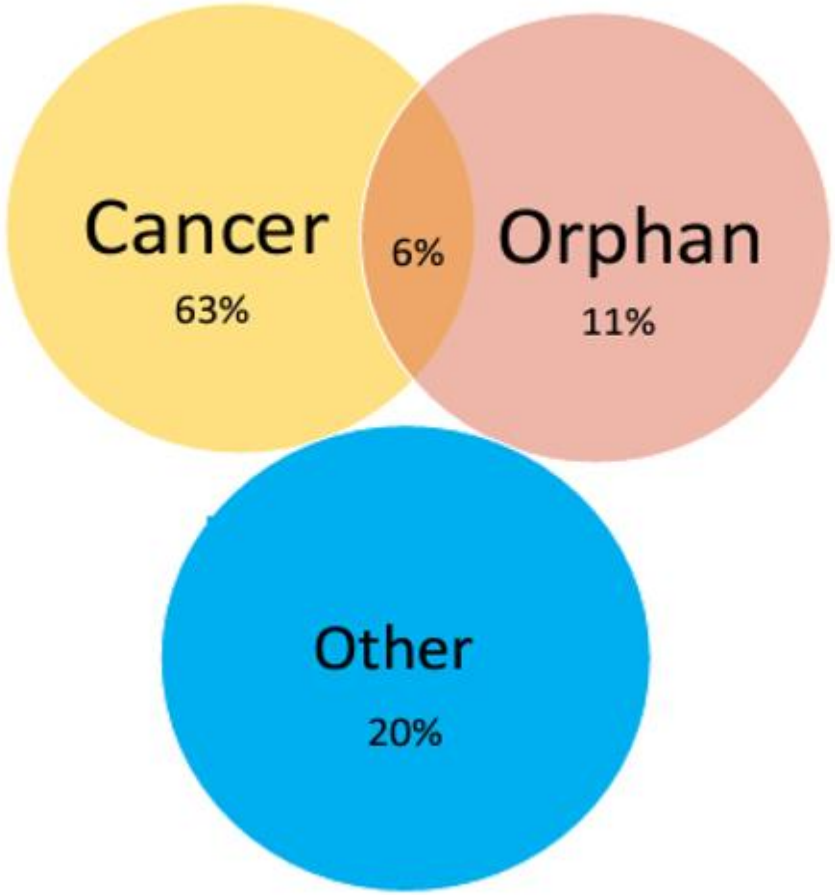
According to the Irish Pharmaceutical Healthcare Association (IPHA), before the budget decision, 322 cancer patients were set to benefit from eight medicines that have completed a health technology assessment, provided a price could be agreed with the HSE.

Over 4,000 patients could be denied critical new medicines

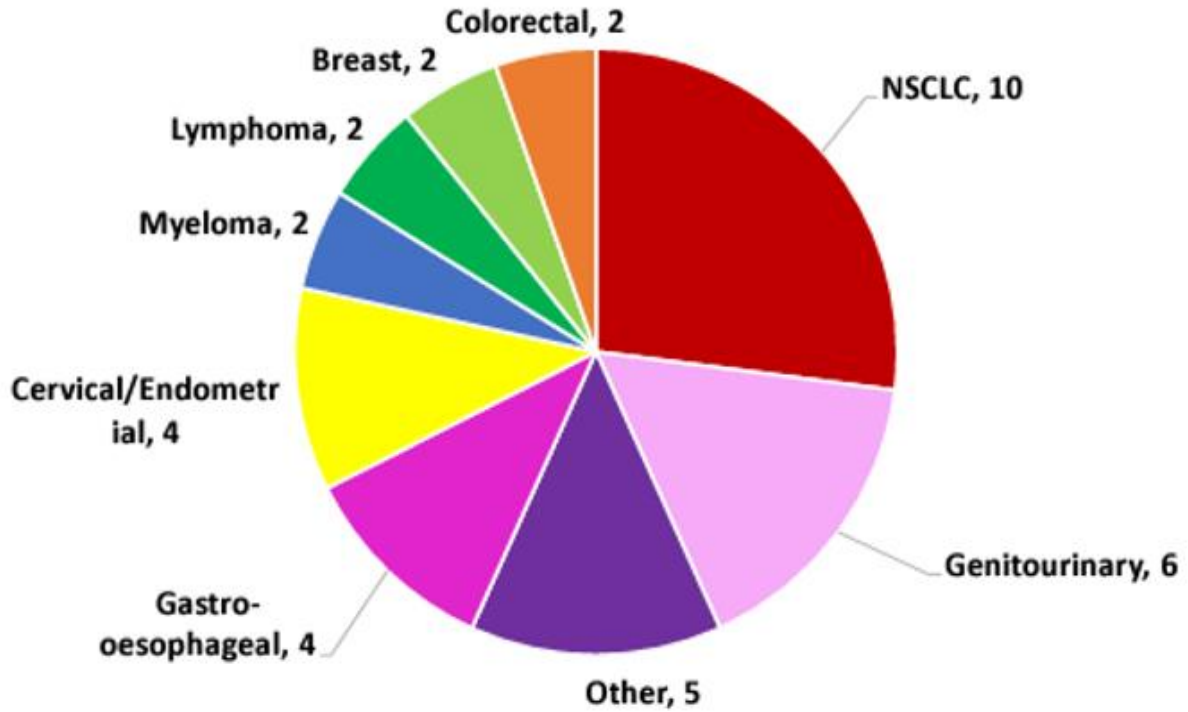
John Drennan
15/10/2023

More than 4,000 patients – including many with cancer – will miss out on critical new medicines unless more health funding is provided, the **Irish Pharmaceutical Healthcare Association (IPHA)** has said.

National Horizon Scanning July 2023: Applications for Consideration for Reimbursement for the Following Year (n=54)



National Horizon Scanning: Cancer Drugs n=37



Source: NCPE National Centre for Pharmacoeconomics, Ireland

Examples of medicines planned for 2024

Therapy Area	Potential health outcomes based on clinical trial data	Number of European reference basket countries where already available*
Hepatocellular carcinoma	Longer Overall Survival and Progression Free Survival	14
Gastric, gastro oesophageal junction or oesophageal adenocarcinoma	Longer Overall Survival and Progression Free Survival	12
Triple-negative breast cancer	Longer Progression Free Survival and Overall Survival	12
Triple-negative breast cancer	Improved pathologic Complete Response Longer Event Free Survival	11
Hypercholesterolemia	Lowers Low-density lipoprotein-cholesterol levels	10
Chronic kidney disease	Lower risks of Chronic Kidney Disease progression and cardiovascular events	9
Chronic lymphocytic leukaemia	Improves Progression Free Survival and Overall Survival	6
Multiple myeloma	Increased Complete Remission rate Longer Overall Survival and Progression Free Survival	6

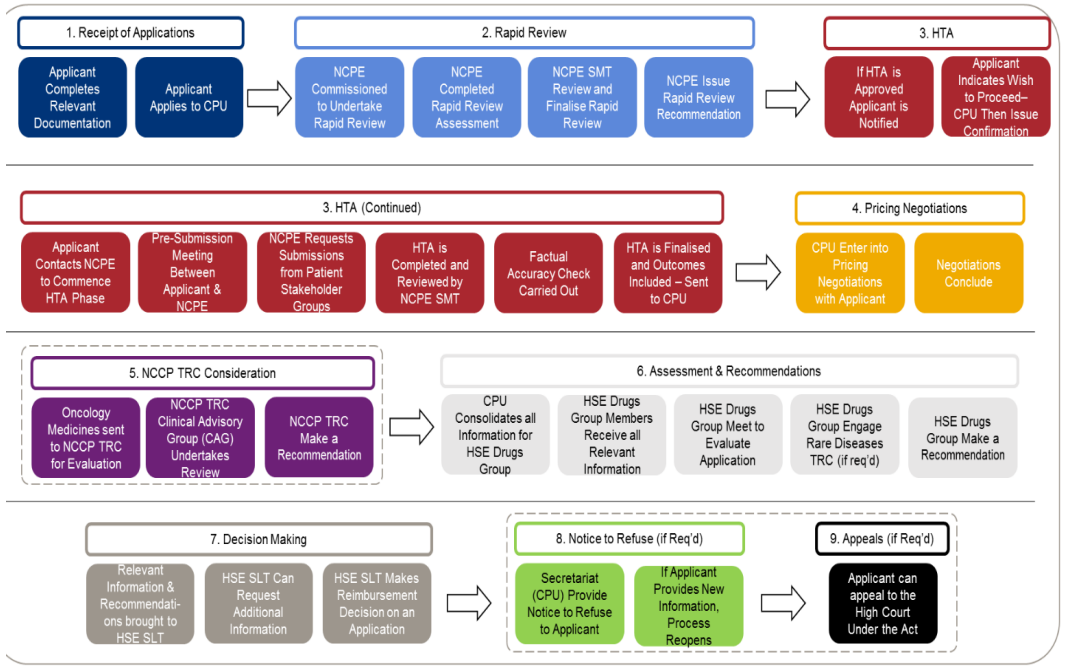
***14 reference basket countries as per Clause 5 of the IPHA Agreement.**
These comprise of Austria, Belgium, Denmark, Finland, France, Germany, Greece, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden and the UK

Risk of Increasing Two-Tier Gap

Public

EMA Approval

Private



Public Patient Receives Access

Clinician case

Agreement between hospital and private insurer

Private Patient Receives Access

IPHA Average Timelines 2020 – 2023

Rapid Review medicines			
	n =	Start of NCPE assessment to reimbursement (days)	Completion of NCPE assessment to reimbursement (days)
2020	4	429	384
2021	17	511	467
2022	29	355	311
2023	9	400	361

Health Technology Assessment medicines			
	n =	Start of NCPE assessment to reimbursement (days)	Completion of NCPE assessment to reimbursement (days)
2020	8	1049	623
2021	25	989	470
2022	16	861	397
2023	12	1026	427

Oncology medicines			
	n =	Start of NCPE assessment to reimbursement (days)	Completion of NCPE assessment to reimbursement (days)
2020	9	896	542
2021	24	820	485
2022	17	686	452
2023	13	656	278

Orphan medicines			
	n =	Start of NCPE assessment to reimbursement (days)	Completion of NCPE assessment to reimbursement (days)
2020	4	799	463
2021	11	955	521
2022	11	757	498
2023	4	758	508

Timelines for Key steps in Process

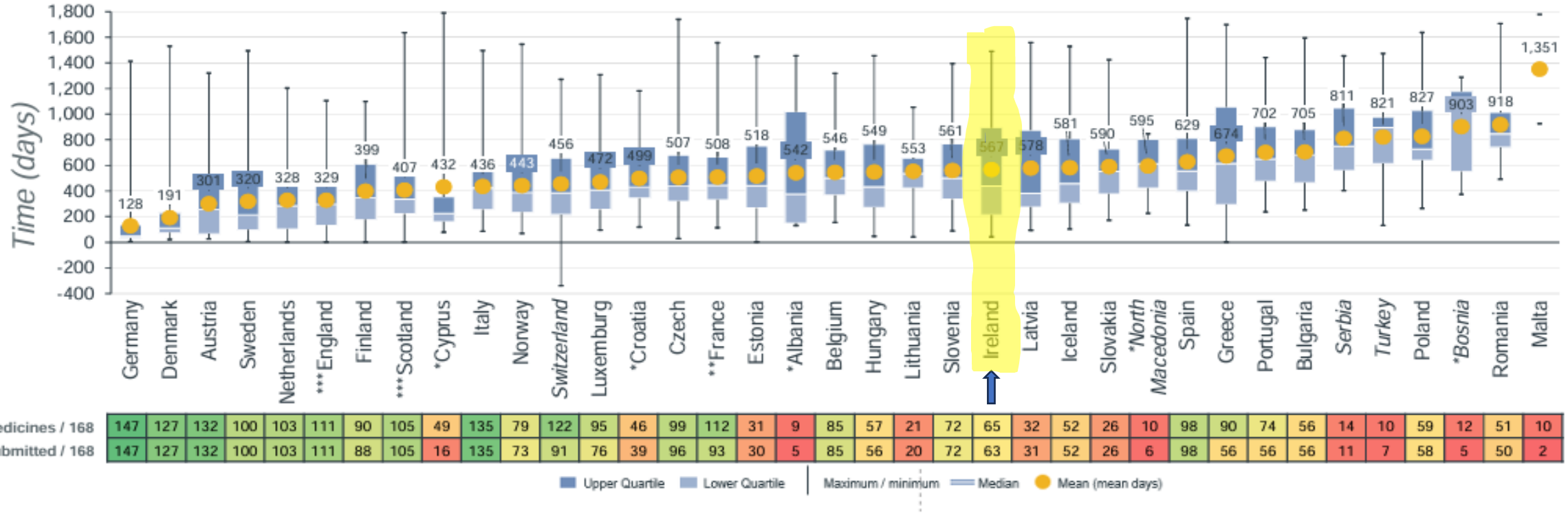
Reimbursed medicines 2022 and 2023	Number of days from HTA submission to PRQs (n=26)	Number of days from RR/HTA completion to 1st commercial negotiation meeting (n=49)	Number of days from final written price offer to Drug Group meeting (n=34)	Number of days from final written price offer to reimbursement (n=51)	Number of days from a Drugs group positive recommendation to reimbursement (n=35)
Average	135	93	91	151	105
Median		70	86	129	52
Range	8 - 239	13 - 468	11 - 333	21 - 719	10 - 600

Reimbursed medicines 2021 - 2023	Number of days from a positive drug group recommendation to a MAP in place (n=15)
Average	293
Median	267
Range	54 - 599

RR = Rapid Review HTA = Health Technology Assessment PRQ = Preliminary Review Questions MAP = Managed Access Protocol

Time from central approval to availability (2018-2021)

The **time from central approval to availability** is the days between marketing authorisation and the date of availability to patients in European countries (for most this is the point at which products gain access to the reimbursement list†). The marketing authorisation date is the date of central EU authorisation throughout.



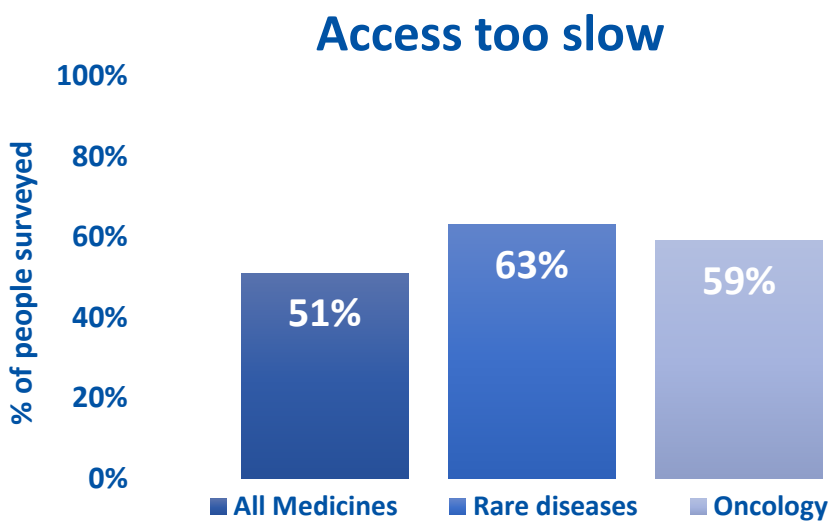
European Union average: 517 days (mean %) (Note: Malta is not included in EU27 average as only 2 dates were submitted in total) †In most countries availability equates to granting of access to the reimbursement list, except in DK, FI, NO, SE where some hospital products are not covered by the general reimbursement scheme. *Countries with asterisks did not complete a full dataset and therefore availability may be unrepresentative **For France, the time to availability (508 days, n=93 dates submitted) does not include products under the ATU system for which the price negotiation process is usually longer. ***In the UK, MHRA's Early Access to Medicines Scheme provides access prior to marketing authorisation but is not included within this analysis, and would reduce the overall days for a small subset of medicines.

IQVIA

Irish people are aware of these delays

According to Ipsos polling on behalf of IPHA (October 2023):

- **4 in 5** believe that delays exist in public access to new medicines in Ireland.
- Compared to our European counterparts, over half believe that **access to new medicines is later** in Ireland.
  - **Over half** believe access to all new medicines for Irish patients is **too slow**, up 4 points since 2022.
  - Almost two thirds believe access to new medicines for **patients with rare diseases is too slow**, also up 4 points.
  - Almost 60% believe that access to new **medicines for cancer in Ireland is too slow.**



Resourcing of NCPE vs other European agencies

Country	Agency	Employees
Ireland	NCPE 20.5 & HSE CPU 12	32
Denmark	Danish Medicines Agency	643
England & Wales	NICE	721
Germany	IQWIG	246
Germany	G-BA	220
Spain	AEMPS	524
Portugal	INFARMED	330
France	HAS	350 + 3000 experts
Finland	Fimea	250
Sweden	SBU	85 + 250 ad hoc
Belgium	KCE	63
Netherlands	ZIN	50 + 100 experts

Source: Oireachtas Parliamentary Questions & Agency annual reports and websites

MAZARS

Minister Donnelly has taken steps to improve the process with indicative timelines and an online tracker committed. Final recommendations awaited.

Reimbursement system needs improved capacity, transparency and a political desire for improved patient access

Lack of funding could hamper the impact and implementation of this review

How can you help?

- Ensure there is a continuous and uninterrupted supply of new medicines from January next year.
- To ensure patients do not experience delays while efficiencies are being developed.
- To move Ireland in-line with European standards of medicines access with both more resources and more timely reimbursement decisions.
- For industry, patient groups and clinicians to have more structured and ongoing dialogue with the HSE/NCPE regarding the system of reimbursement.
- To continue to make the case for speed of access to clinically effective medicines.

Why does speed of access matter?

"Speed matters most because the opportunity cost of any delay is not zero. Patients are waiting on life-saving treatments and innovative medicines to make a difference to their lives."

Sharmila Nebhrajani, Chairperson of the National Institute for Clinical Excellence – the body that assesses medicines for England, Wales and Northern Ireland speaking at a Kings Fund online event, July 17, 2023.

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Thank you

Additional Appendix Material follows

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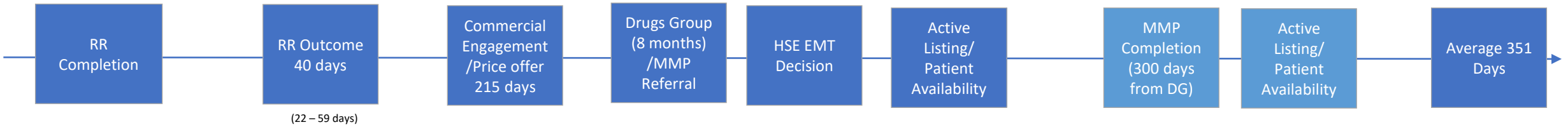
Decision Timelines – Averages & Ranges

351 days from RR to Reimbursement (No HTA)

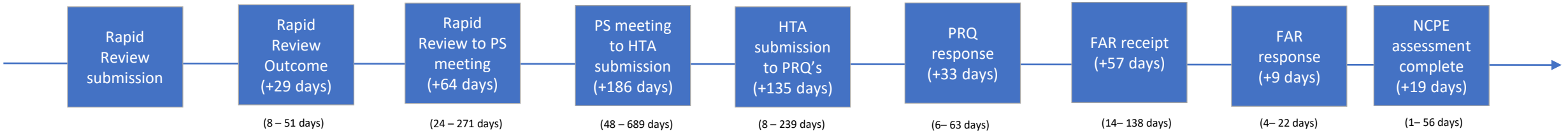
(153– 659 days)



- Process timeline (average reimbursed RR Medicines Sept 1st 2022 – Sept 1st 2023)(N=15*)
- Based off Sept 2022 – Sep 2023 Rapid Review reimbursements, on average another **311 days** was required to achieve reimbursement post-NCPE decision

532 days for HTA Completion

(303– 1079 days)

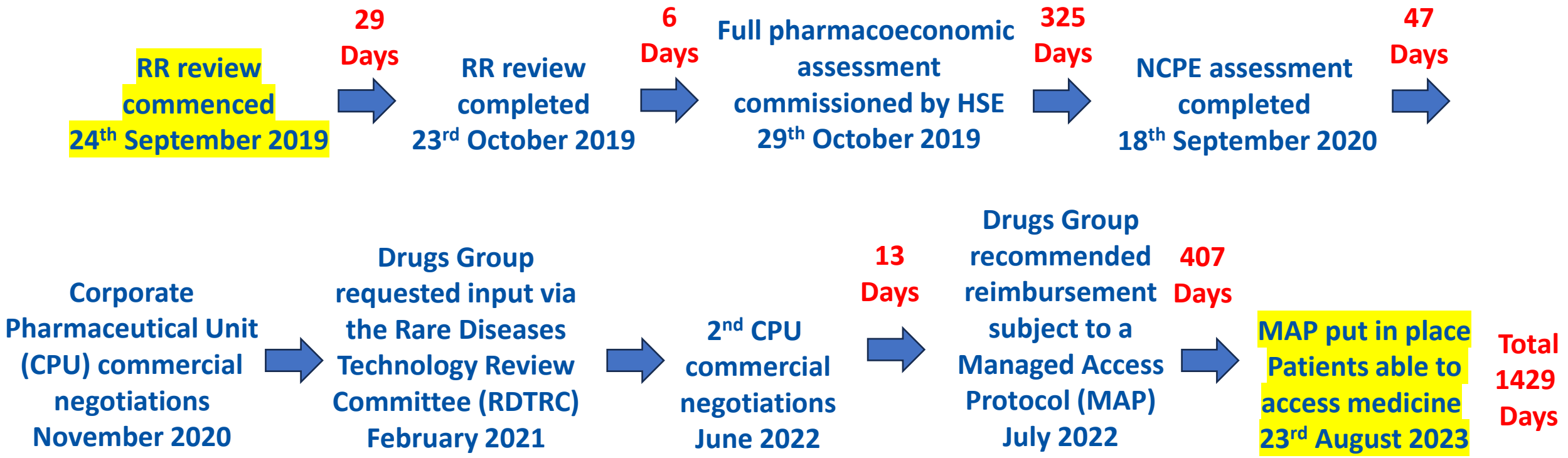


- NCPE Process timeline (average HTA's Sep 1st 2022 – Sept 1st 2023)(N=26*)
- Based off medicines reimbursed following a full HTA between Sept 1st 2022 and Sept 1st 2023 (N=18), on average another **414 days** was required to achieve reimbursement post-NCPE decision

825 days for HTA Medicines to Reimbursement (including MAP)

PS = Presubmission, PRQ = Preliminary Review Questions, FAR = Factual Accuracy Report,
MAP = Managed Access Protocol

Example of process steps and timeline for Voretigene Neparvovec reimbursed August 2023



Any medicine that needs a Managed Access Protocol Adds nearly 300 days to process

Time from Positive Drugs Group Recommendation to Patient Availability				
INN	**Brand**	**Positive Drugs Group Recommendation**	**MAP in place**	**Days from positive Drugs Group recommendation**
Rivaroxaban	Xarelto	09/02/2021	01/10/2022	599
Larotrectinib	Vitrakvi	13/12/2022	01/06/2023	170
Onasemnogene abeparvovec	Zolgensma	29/06/2021	08/10/2021	101
Voretigene neparvovec	Luxturna	12/07/2022	23/08/2023	407
Erenumab	Aimovig	14/01/2020	01/09/2021	596
Liraglutide	Saxenda	14/09/2021	01/01/2023	474
Risdiplam	Evrysdi	14/02/2023	01/09/2023	199
Tafamidis	Vyndaqel	29/06/2021	01/03/2022	245
Dupilumab (atopic dermatitis adults)	Dupixent	12/01/2021	01/04/2021	79
Dupilumab (atopic dermatitis 12+ years)	Dupixent	12/01/2021	01/04/2021	79
Dupilumab (atopic dermatitis 6+ years)	Dupixent	08/03/2022	01/05/2022	54
Teduglutide	Revestive	12/11/2019	01/01/2021	416
Lanadelumab	Takhzyro	08/12/2020	01/09/2021	267
Dupilumab (asthma 12+ years)	Dupixent	11/10/2022	01/11/2023	386
Delta-9-tetrahydrocannabinol / Cannabidiol	Sativex	08/11/2022	01/10/2023	327
Average (n=15)				**293**
Median (n=15)				**267**

European Early Access Schemes Examples

EAP	France	Italy	Spain	UK
General Label	Early access (ex-ATU and ex-PEC-T) + Others	Early access and off-label use	Availability of medicines under special circumstances	EAMS (Early Access to Medicine Schemes)
Named/Cohort	Named or cohort depending on the program	648 List: cohort 5% Fund: named	Named	Both: named/cohort
Target diseases	Severe, rare or disabling diseases, no alternatives,	648 List: Different types of disease 5% Fund: rare diseases and particular/severe diseases	Severe diseases, no alternatives	Severe and disabling disease, high unmet need
Medicines	New drugs/ indications in development, off-label drugs, foreign medicines	648 List: No valid alternatives; cheaper than valid alternatives 5% Fund: Orphans drug/drugs in development not approved yet, which represent "a hope of therapy"	Off-label medicines, Foreign medicines	New Drugs, products already marketed in the UK for other indications (off-label), foreign medicines

Conditional Interim Access Proposal

- Decision-making on new medicines can take up to 24-36 months following the submission of a reimbursement application.
- During this review and approval process, patients in Ireland will generally not have access to the licensed medicines regardless of healthcare need or potential benefit.
- Most healthcare systems in Europe have now implemented some interim agreements or frameworks to facilitate patient access in areas of high unmet need.
- Ireland is an outlier in this area, there is no specific policy in Ireland to support and guide stakeholders in this scenario.
- Patients currently rely on the efforts of requesting physicians and private suppliers to address the gap – which can cause inequity within the treatment pathway.
- To support this, a potential pilot scheme is proposed for consideration and further consultation.

Aim: Patient gets best treatment currently available in an administratively responsible manner.

Benefit: Achieves access in areas of unmet need.

How: IPHA proposes the introduction of a pilot scheme, selecting medicines where the financial impacts are relatively predictable for both sides e.g., orphan or end of life treatments.

Early Access Scheme Pilot Proposal: How

Proposed Conditional Interim Access Scheme:

A temporary price is agreed with a view to servicing the immediate need of the patient.

The supplier agrees to maintain supply for patients for as long as is deemed clinically necessary regardless of the final reimbursement decision. If reimbursement of the item is rejected or no agreement can be reached, the supplier must continue to supply any patients currently on the medicine under the terms of the interim agreement but would not be obliged to supply any new patients from an agreed timepoint.

If the said medicine is added to the reimbursement list, it is open to parties to agree a commercial arrangement that would provide the value that the final agreed price would be retrospectively applied to the temporary price agreement.

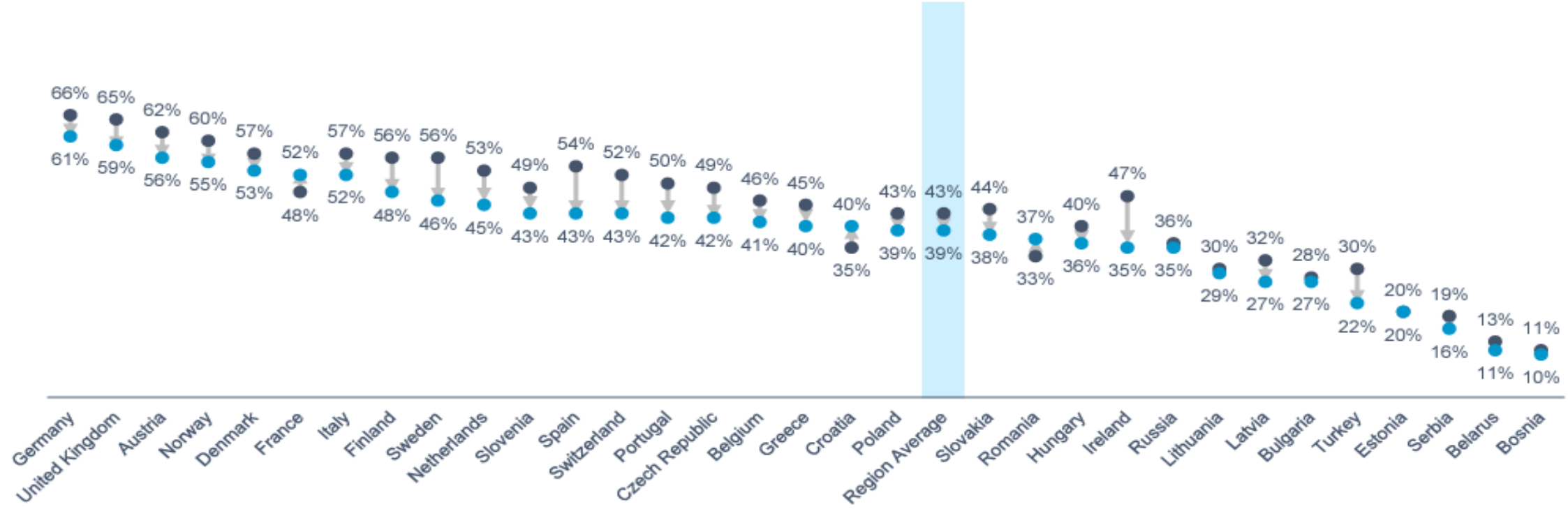
It is further open to parties to agree temporary access pending the collection of further evidence from future clinical studies.

Suppliers recognise that interim or conditional access as outlined above would have no bearing on the general reimbursement process.

IPHA proposed the above language to the Mazars implementation group as the basis of commencing early access schemes.

Launch of New Medicines Declined Over Time in Most European Countries

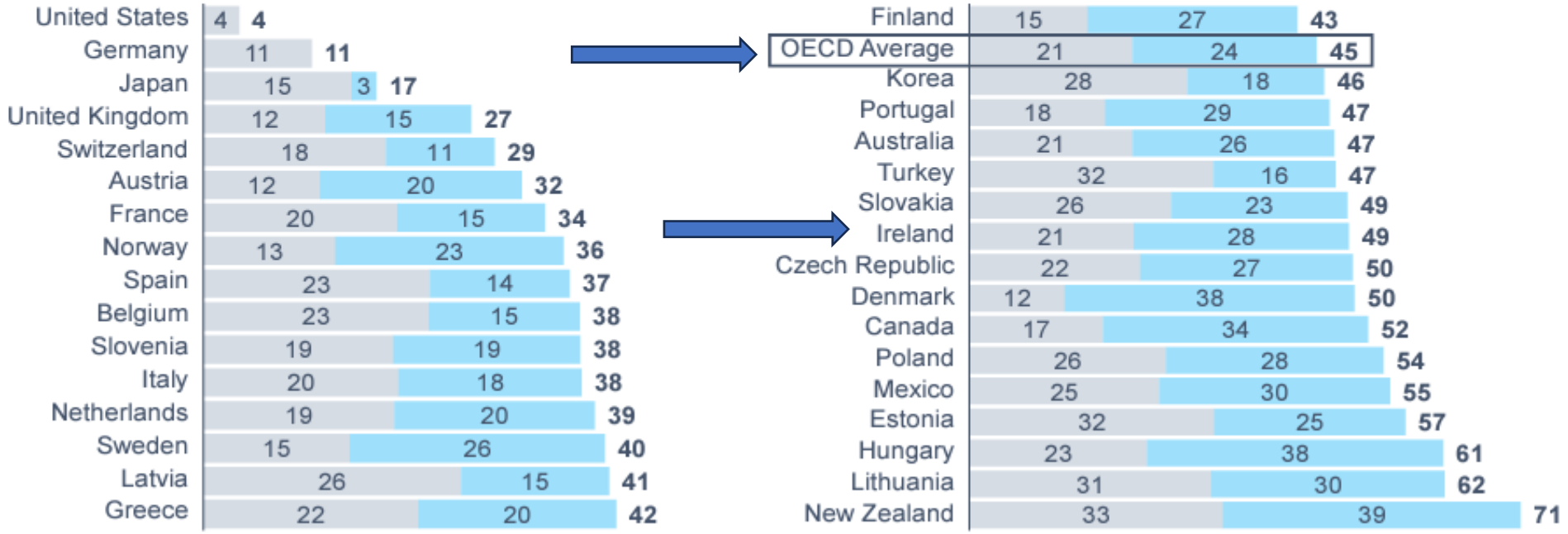
Croatia Improved Most and Ireland, Spain and Sweden Declined Most



PhRMA

Time from Global First Launch to Public Reimbursement in OECD Countries Varies from 4 to 72 Months on Average

Number of Months from Global First Launch to Public Reimbursement by OECD Country (of all new medicines launched and reimbursed by country from 2012 to end of 2021)



PhRMA

EFPIA Patient W.A.I.T indicator: Key Observations (2018 -2021) vs (2017-2020)

Measure	Overall	Oncology	Orphan	Non-oncology orphan	Combination therapy
Rate of availability of new medicines (2018-2021)	- 3% 39%	-12% 39%	-4% 26%	+1% 25%	-4% 59%
Average time to availability of new medicines (2018-2021)	+ 26 days longer 567 days	+ 12 days longer 673 days	+ 7 days longer 877 days	+ 34 days longer 823 days	+ 43 days longer 297 days
Ranking compared to other European health systems	23/37	28/37	31/37	27/37	14/37

Pipeline medicines for 2024 & Availability in Europe

INN	Therapy Area	Indication	Potential Clinical benefit	Number of European basket countries and UK already available
Pembrolizumab	Triple-negative breast cancer	Pembrolizumab is indicated in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery for the treatment of adults with locally advanced, or early-stage triple negative breast cancer at high risk of recurrence.	Improved pCR Longer EFS	AT, BE, DK, FI, DE, EL, IT, LU, PT, SE, UK
Atezolizumab	Hepatocellular carcinoma	In combination with bevacizumab for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy.	Longer OS and PFS	AT, BE, DK, FI, FR, DE, EL, IT, LU, NL, PT, ES, SE, UK
Nivolumab	Gastric, gastro oesophageal junction or oesophageal adenocarcinoma	Nivolumab is indicated in combination with fluoropyrimidine and platinum-based combination chemotherapy for the first line treatment of adult patients with HER2 negative advanced or metastatic gastric, gastro oesophageal junction or oesophageal adenocarcinoma whose tumours express PD-L1 with a combined positive score (CPS) ≥5.	Longer OS and PFS	AT, BE, DK, FI, FR, DE, IT, LU, NL, ES, SE, UK
	Multiple myeloma	Monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.	Increased CR rate Longer PFS and OS	AT, BE, FI, FR, LU, DE
Sacituzumab govitecan	Triple-negative breast cancer	Monotherapy for the treatment of adult patients with unresectable or metastatic triple-negative breast cancer who have received two or more prior systemic therapies, including at least one of them for advanced disease.	Longer PFS and OS	AT, BE, FI, FR, DE, EL, IT, LU, PT, ES, SE, UK
	Chronic lymphocytic leukaemia	In combination with another cancer signalling pathway inhibitor for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).	Improves PFS and OS	DE, LU, NL, ES, UK, SE
Finerenone	Chronic kidney disease	For the treatment of chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults.	Lower risks of CKD progression and cardiovascular events	AT, BE, DK, FI, EL, LU, NL, SE, UK
Inclisiran	Hypercholesterolemia	For the treatment of primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia in adult patients, as an adjunct to diet (a) in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach low density lipoprotein cholesterol (LDL-C) goals with the maximum tolerated dose of a statin or (b) alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.	Lowers LDL-C levels	AT, BE, FI, DE, IT, LU, NL, ES, SE,UK

OS = Overall survival; PFS = Progression-free survival; pCR = Pathologic complete response; EFS = Event -free survival; LDL-C = Low-density lipoprotein-cholesterol; CKD = Chronic kidney disease; CR = Complete remission