Steering a course to avoid the 'drug iceberg' -

the challenges of accessing new and innovative medicines in Ireland and the call for a new national strategy.

A MULTI-STAKEHOLDER PERSPECTIVE

VERSION 2.0

The Irish Platform for Patient Organisations, Science and Industry and The Medical Research Charities Group

IPPOSI

medical research charities group

Unity is our Strength

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The Drug Iceberg

A 'drug iceberg' in this context is a metaphor to describe the increasing concern that new, innovative and improved drugs will not be available, or will be significantly delayed to patients in Ireland because of weaknesses and gaps in the drug therapy approval/reimbursement process and concerns about the costs of such medicines. As such, only a minority of drug therapies appear above sea level. Below sea level are those drugs that have been delayed, and/or are widely available in other parts of Europe or which have not even been submitted for approval in Ireland because of the perception that there is an increasingly cold climate towards funding new, pioneering and enhanced drug therapies in Ireland.

The iceberg metaphor also reflects the potential for disaster for both patients and the exchequer in the absence of an adequate strategy which ensures Ireland has a drug therapy approval system built on the principles of fairness, equality, value for money, transparency, effectiveness and sustainability. The key recommendation of this report is the call for a new drug therapy strategy built upon these principles, which involves all key stakeholders.

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Contents

	PAGE
INTRODUCTION	4
FOREWORD	5
RECENT DEVELOPMENTS	6
SECTION ONE: MULTI-STAKEHOLDER ROUND-TABLE	7
SECTION TWO: COUNTRY CASE STUDIES	10
SECTION THREE: ACCESS TO MEDICINES – A GLOBAL ISSUE	14
SECTION FOUR: KEY RECOMMENDATIONS	16
ANNEX ONE: EUROPEAN AND REGIONAL INITIATIVES	19
ANNEX TWO: THE DRUG THERAPY APPROVAL PROCESS IN IRELAND	22
ANNEX THREE: ABBREVIATIONS	23

Introduction

In August 2017, IPPOSI and MRCG published what is commonly referred to as the 'Drug Iceberg' report, based on discussions from a round-table of Irish patient organisations on 14 June 2017.

This report provides an update on the original report, including a number of important developments since the first publication and the outcomes of a multi-stakeholder round-table on 18 October 2017.

Both reports aim to provide an on-going, constructive contribution to the debate on access to new and innovative drug therapies* in Ireland, while recognising the challenges of cost and affordability.

- **Section One** (pages 7 to 9) describes the discussions from the multi-stakeholder meeting held on 18 October 2017, involving patients, patient organisations, scientists, academics, representatives of state bodies and the pharmaceutical industry.
- **Section Two** (pages 10 to 13) highlights a number of 'country case studies' (Sweden, Germany, Scotland, Canada) detailing good practices identified in the assessment and reimbursement of new drug therapies.
- **Section Three** (pages 14 to 15) frames this report within current international initiatives focusing on human rights approaches, legislative frameworks and increased cooperation for the pricing, assessment and reimbursement of new medicines.
- **Section Four** (pages 16 to 18) highlights and prioritizes a number of the overall recommendations.

The 'Drug Iceberg' report: version 1.0, August 2017

To read a copy of the first Iceberg report published in August 2017, please visit:
www.ipposi.ie/our-work/publications or www.mrcg.ie/go/publications

*The term 'drug therapy' used in this report aims to cover any medicines or medications used to treat disease.

Foreword

The implementation of the recommendations contained in the original 'Drug Iceberg' report remains a key focus for IPPOSI and MRCG members, in particular the call for **new national strategy to promote access to new and innovative drug therapies.**

We hope that 2018 will see all stakeholders come together with renewed energy and ideas about how to address some of the challenges identified in these reports.

Over the course of 2018, in collaboration with other stakeholders, we believe that the following outputs and outcomes can be achieved at a minimum:

- An immediate direct engagement between the Department of Health and relevant stakeholders, including patient organisations and industry, to seek possible consensus on a way forward in 2018 and beyond.
- The greater inclusion and input by patient organisations into the decision-making process for the reimbursement of drug therapies in Ireland, based on emerging good practice.
- A revised National Centre for Pharmaco-economics (NCPE) Patient Submission Form for health technology assessments and the development of related strategies to encourage greater patient and public involvement (PPI) across the assessment process.
- A faster operationalisation of the agreed Rare Diseases / Medicinal Products Technology Review Committee to consider orphan drug therapy submissions in Ireland.
- Increased support for an education module for patients seeking to learn more about the Irish health technology assessment process.
- An online information resource dedicated to improving patient and public understanding of the Irish and EU-level health policy efforts to address challenges relevant to this area.
- A third roundtable event and continued multi-stakeholder dialogue around access to new drug therapies in Ireland.
- Further development of linkages with the Scottish Medicines Consortium (SMC) to experience how patient perspectives are incorporated into SMC meetings and processes.
- An update of this report in late 2018.

Derick Mitchell
Chief Executive, IPPOSI

Philip Watt
Chairperson, MRCG

Recent developments

Since the publication of the first 'Drug Iceberg' report in August 2017 there have been a number of announcements and developments in this space.

- **From 11 August to 29 September 2017**, the Department of Health conducted a public consultation on the development of a National Biosimilar Medicines Policy to promote the use of biosimilar medicines and create a sustainable environment for biological medicines.
- **On 13 September 2017**, Professor Michael Barry was appointed Chair of the Rare Diseases / Medicinal Products Technology Review Committee – a new mechanism established to provide a tailored assessment of new and innovative drug therapies for rare disease patients.
- **On 15 November 2017**, the Minister for Health announced plans to engage IPHA companies in a dialogue around access to medicines challenges at the Irish Pharmaceutical Healthcare Association (IPHA) conference.
- **On 22 November 2017**, IPPOSI and MRCG sent a letter to the Department of Health requesting that patients be involved in any future dialogue around access to medicines.
- **On 27 November 2017**, the NCPE initiated the first of a two-part review of their Patient Submission Form, sending a survey to patient organisations to request their feedback.
- **On 17 January 2018**, following a public consultation process, HIQA published updated economic evaluation and budget impact analysis guidelines to standardise how health technology assessments are conducted and used by decision-makers and key stakeholders.[1]
- **On 17 January 2018**, Taoiseach Leo Varadkar in his speech to the European Parliament during a debate on the future of the EU, called on member states to "work more closely on the cost of medicines. This could save billions for taxpayers, freeing up funding to ensure that modern medicines are available to patients at the same time in every country. Let's pool the buying power of 450m people to do so."
- **On 31 January 2018**, the European Commission announced plans to improve cooperation between EU Member States on health technology assessments. Mandatory use of joint clinical assessments reports, after 3-year transition period is being proposed.[2]
- **On 13 February 2018**, the Minister for Health secured cabinet agreement in principle for Ireland to join the BeNeLuxA Initiative, which will enable Ireland to enter into joint negotiations with Belgium, The Netherlands, Luxembourg and Austria to secure affordable access to new medicines from pharmaceutical companies.[3]

[1]https://www.hiqa.ie/hiqa-news-updates/hiqa-publishes-guidelines-promote-use-solid-evidence-base-inform-more-efficient

[2]http://europa.eu/rapid/press-release_IP-18-486_en.htm

[3]http://health.gov.ie/blog/press-release/ireland-to-open-negotiations-with-belgium-the-netherlands-luxembourg-and-austria-on-drug-pricing-and-supply-minister-harris/

SECTION ONE: Multi-stakeholder round-table

This section is a summary of discussions at the multi-stakeholder round-table on 18 October 2017, jointly-organised by IPPOSI and MRCG. The round-table builds upon a previous joint event with patients on 14 June 2017, extending the debate to include representatives from academia, industry, government and regulatory bodies.

Key points emerging:

- Patients in Ireland wait considerably longer than their European counterparts to access life-changing and/or life-saving medicines.
- Denied or delayed access to medicines represents a failure by Ireland to promote, protect and fulfil its human rights responsibilities.
- The post-HTA medicines reimbursement process lacks transparency, causing confusion and frustration among all stakeholders and contributing to a lack of trust in the decisions being made on behalf of patients.
- There is an urgent need for a new national strategy to promote access to new and innovative drug therapies, that is evidence-based and implemented in a transparent fashion.
- The economics of the current Quality-adjusted Life Year (QALY) threshold in Ireland is questionable, with a lack of evidence to support the chosen figure of €45,000 per annum.
- Orphan drugs for rare and ultra-rare diseases require a tailored assessment and reimbursement process, and the proposed Rare Diseases / Medicinal Products Technology Review Committee should be established as soon as possible.
- Patient groups are willing to contribute to the HTA and post-HTA process. Patient input throughout the process should be welcomed and valued.
- All patients are experts in their conditions through lived experience. Many patients are also knowledgeable about the assessment and reimbursement process, having availed of training and education opportunities. Patients seeking to interact with the process should receive training and support.
- Communication between patients and agencies engaged in assessment and reimbursement decisions should be regular, clear and two-way in nature.
- Novel financial and performance-based models of enabling access to medicines (such as risk sharing schemes and outcomes based agreements) are solutions and the necessary infrastructure in Ireland should be elaborated to facilitate such schemes.
- When new drug therapies are approved in other European countries and not in Ireland, patients question the legitimacy of the decision and the accountability of the process.

Summary of discussions: The need for reform of the existing drug reimbursement process

Dr Derick Mitchell, Chief Executive of IPPOSI placed patient communities at the forefront of discussions about access to medicines. He highlighted the positive response to the first 'Drug Iceberg' report[4] and he urged each stakeholder to contribute to the advancement of the recommendations based on their individual strengths. Philip Watt, Chair of the MRCG, emphasised that a sustainable strategy ensuring access to new and improved drug therapies must seek to include the perspectives of all stakeholders.

An undercurrent running through the contributions was a broad sense of dissatisfaction with aspects of the drug therapy reimbursement process in Ireland. This included the need for greater transparency, a functioning strategy, adequate funding as well as a review of the current assessment criteria and rates of reimbursement. The consistent sentiment was that the system is in need of significant reform. These are summarised as follows:

Transparency. As the IPPOSI chairperson Dr. Tomás Carroll pointed out, the lack of transparency is an extremely frustrating reality for Irish patients, and companies. This applies to the final decision-making process for drug therapy reimbursement, the current lack of patient involvement in that process, and the absence of an appeals process to challenge the decisions. Concerns about transparency are exacerbated by the absence of official communications from the HSE Drugs Committee or the HSE Leadership Team relating to decisions, which in the case of a negative decision, leaves patient organisations unable to explain to their members why they will not receive new drug therapies that in some cases, are available to their European counterparts.

In the eyes of their members and other stakeholders, patient organisations are further weakened by having to rely on companies for information about a reimbursement decision, which in turn can leave patients feeling largely ignored, rather than included, in the process. The membership of the HSE Drug Group and HSE Leadership Team should be publicly available, together with the agendas and minutes of meetings.

There was widespread agreement that patients should not have to protest outside the Dail to highlight issues regarding access to new drug therapies. Equally, it was acknowledged with regret that the only stakeholder on this issue that the government seems to respond to is the media.

Patient involvement. Dr. Avril Kennan, CEO of the MRCG, contended that patient involvement in HTA would actually strengthen reimbursement decisions, particularly in relation to patient preferences and Quality of Life. Furthermore, Kennan described how – rather than entrenching patient demand for new drug therapies at any cost – involvement would improve understanding, and acceptance of, tough decisions which have to be made.

Dr Roisin Adams, former Deputy of the NCPE, and now working with the HSE to introduce the National Drugs Management Programme in hospitals, raised the question of whether patients would be willing to consider proposals that might see treatments discontinued if they were shown to be ineffective. The response from attendees, in particular from patient members, was that they would consider this proposal – emphasising that no patient is interested in a medicine that is ineffective.

The work of IPPOSI in training patients to become experts in health innovation speaks directly to a critical component of meaningful, effective patient involvement. Patients who understand the language, concepts, and the processes that inform the development, assessment and reimbursement of new drug therapies in Ireland and Europe are ready, willing and able to engage. Creating opportunities for their involvement is the responsibility of the health system in Ireland. In the UK, the case for patient involvement is supported by a recent report from the Academy of Medical Sciences, which made "involving patients, carers and the public in research" the first of 12 recommendations[5].

The value of patient involvement was also echoed in relation to QALY thresholds by Professor Paul Gorecki, who said that 'broad acceptance and buy-in' should be sought and that while greater patient involvement may not necessarily lead to a higher QALY, it would result in a "more informed decision". Meeting attendees also noted the existence of the NCPE's Patient Submission Form, but the feedback from several patient members was that the form was often unable to capture the true patient experience.

Ireland vs. Europe. Irish stakeholders are increasingly aware of the EU-level (and Member State-led) efforts to improve cooperation and coordination in this area. A number of these initiatives are listed in **Annex One: European and Regional Initiatives.** However, it is very difficult for patient organisations and their members to understand that if the European Medicines Agency (EMA) can approve - and other European countries can reimburse - new drug therapies in a timely, transparent and process driven manner, then why can't Ireland?

It is a stated objective of the government to match our European partners in this area.[6]

However, stakeholders claim that Ireland takes significantly longer than many other European countries to arrive at a reimbursement decision and that significantly fewer of these decisions are positive[7]. There are also innovative approaches to reimbursement – such as Early Access, and Conditional Approval – that are used in other countries but not frequently in Ireland.

Strategic approach. The need for a sustainable, ethical, transparent, predictable and timely strategy was voiced by almost every contributor. The existing process includes some elements which may serve as a starting point for a new national strategy, but the long-term strategic vision and formal oversight is currently lacking. Until a strategy is in place, stakeholders will be forced to continue to resort to a 'he who shouts loudest' approach. Equally worryingly, the unpredictability of the process may discourage companies from even bringing their innovative drug therapies to the Irish market.

As a first step, the Department of Health should commission an independent review to assess current levels of access to innovative drug therapies in Ireland and to propose recommendations to improve patient access to innovative drug therapies.

Rare diseases and orphan drugs. As outlined by Kealan O'Reilly of Shire, in the area of rare diseases and orphan drug therapies, a different system of assessment is required as existing submissions are dealt with on a case-by-case basis that 'feature no objective measure or value from which to negotiate, following a HTA decision'. In addition, the data requirements required by the existing system are more difficult when considered in the context of inaccessible or rare patient cohorts.

The establishment of the Rare Diseases / Medicinal Products Technology Review Committee to consider orphan drug therapy submissions in Ireland was welcomed, in particular the meaningful patient involvement. However, O'Reilly highlighted even lower rates of reimbursement in Ireland than that of non-orphan drug therapies. This situation forces many Irish patients to consider travelling abroad to access treatments.

The cost of new drug therapies. Many contributors focused on the fact that although cost is an important global issue, it is potentially harmful to focus on this issue alone, as it distracts from core concerns in Ireland such as transparency, process, and patient involvement. Also, the question of cost has the potential to divide stakeholders and put them into competition with each other for limited resources.

[4]http://www.ipposi.ie/wp-content/uploads/2017/09/Ice-Berg-Report-FINAL.pdf

[5]https://acmedsci.ac.uk/file-download/44970096

[6]http://health.gov.ie/blog/press-release/state-to-make-major-savings-under-new-drug-pricing-deal/

[7]http://www.ipha.ie/news-events/latest-news/news/ipha-guidance-on-direct-healthcare-professiona-(2)

SECTION TWO: Country case studies

Below are some case studies which detail how other countries tackle the assessment and reimbursement of new and improved drug therapies. These case studies have been selected as they represent good practice in involving patients in assessment and in making evidence-based reimbursement decisions.

Naturally not all of these good practices can be directly transposed into the Irish context. Sustainable and meaningful solutions are needed, which can be tailored to the specific social, political and economic situation in Ireland. That said, IPPOSI and MRCG believe that these case studies offer positive examples of some of the processes, approaches and tools which might be considered and adapted to improve current policy and practice around the assessment and reimbursement of new and improved drug therapies in Ireland.

Case study 1: Patient involvement in assessment

SCOTLAND:[8] Similar in scale to Ireland, Scotland offers a potential roadmap towards greater patient involvement in new and improved drug therapy assessment and reimbursement. A review of progress made by the responsible body – the Scottish Medicines Consortium (SMC) – was completed in 2014, and a strategy to inform future activities during the period 2014-2020 was developed. A Public Involvement Network (PIN) Advisory Group (comprising of representatives from key patient umbrella organisations and the SMC) continuously evaluates and improves upon how the public and patients are involved in assessment and reimbursement decisions.

Early communication encourages transparency, accountability and participation. A webpage listing the medicines scheduled for assessment is maintained to allow patients ample time to participate and gather relevant information about their conditions and treatment options. A monthly newsletter is circulated to establish regular, proactive communication with patient groups and provide relevant updates.

Participation is welcomed in various forms and patients have the opportunity to present written submissions and/or oral presentations. A guide, a video and a worked example provide patients with clear instructions on how to prepare submissions. Patients making submissions or presentations can be invited to appear before the SMC. During these encounters, a SMC public involvement team member is assigned to each patient representative to provide support and assistance.

All SMC meeting are open to the public and minutes are published on the SMC website. A factsheet explaining the process is provided to patients and/or members of the public seeking to attend SMC meetings. A summary of key points made by patient representatives is included in the final SMC recommendation.

[8]http://www.scottishmedicines.org.uk/Public_Involvement/Public_Involvement

Case study 2: Patient involvement in assessment

CANADA:[9] Boasting a strong record of involving patients in medicines assessment, Canada shares many good practices to aspire to. A culture of partnership directs the work of the Canadian Agency for Drugs and Technologies in Health (CADTH) and patients are able to contribute alongside manufacturers and clinical and economic experts. Patients are not an afterthought; patients are consulted and engaged throughout the assessment process. For instance, patients are invited to join the early dialogue between CADTH and the manufacturer (aimed at preparing for an upcoming assessment). Patients are also decision-makers and seats are reserved for lay or public representatives on each of the CADTH Committees. A Patient Liaison Forum comprising of representatives from key patient umbrella organisations gives patients a voice in managing and improving the overall assessment process.

Canada has made several efforts to improve upon the traditional patient involvement model of posting public information and inviting written submissions.

Firstly, a collaboration between the CADTH and the Canadian Cancer Action Network (CCAN) – the Health Technology Assessment Patient Engagement Navigator – funds a dedicated patient involvement focal point tasked with helping patients to better understand and engage with the process. The Navigator helps individual patient representatives improve their submissions and works with patient communities more generally to identify ways in which patients can interact with the process.

Secondly, CADTH operates a feedback system which provides patients making submissions with a personalised response following the conclusion of an assessment. A letter details how assessors considered the patient input and shares any suggested improvements for future submissions.

Finally, CADTH publishes its recommendations in draft format to invite comments from manufacturers, patients and other stakeholders. When a recommendation is contested CADTH engages in a further review of the evidence before making a final recommendation. All evidence used to arrive at the recommendation is available for public scrutiny including the clinical and economic reviewer assessments, the manufacturer, advisor and patient feedback, and the names of the clinical and economic experts.

[9]https://www.cadth.ca/about-cadth/what-we-do/products-services/cdr/patient-input

Case study 3: Evidence-based reimbursement decisions

SWEDEN:[10] Taking a different approach to many of its European peers, Sweden operates a **value-based pricing** model in assessing and reimbursing medicines for the Swedish market[11]. Since 2002, all public health decisions – including access to medicines – are evaluated against three ethical principles:

1. human value: everyone has a right to healthcare
2. need and solidarity: patients in the greatest need and vulnerable groups are prioritised
3. cost-effectiveness: resources are used effectively

There is an important hierarchy between the principles. For example, while it may be more cost-effective to treat more minor conditions, the principle of need and solidarity precedes the principle of cost-effectiveness and chronic and life-threatening conditions are prioritised.

Medicines are reimbursed if the Pharmaceutical Benefits Board (TLV) assesses that the price requested is justified on the basis of the pharmaceutical value delivered. The assessment looks at the value offered to the health system and the value provided to society in general – for example, patients may be able to return to work and be economically productive. While Sweden uses QALY to assess value, there is no strict threshold and issues such as disease severity and unmet need are taken into consideration. Sweden requires new medicines and medicines on the market to demonstrate value, and a review of all medicines eligible for reimbursement has been completed since a new pharmaceutical reimbursement policy was introduced in 2002. One patient organisation leader and one senior citizen sit on the Board charged with assessing value. Mindful of the need to continue to deliver value, the Swedish government has initiated an inquiry into how it reimburses, and prices drug therapies and a final report is expected in December 2018[12].

[10]https://tlv.se/in-english/medicines.html

[11]https://www.ohe.org/news/value-based-pricing-sweden-lessons-design

[12]http://whocc.goeg.at/Literaturliste/Dokumente/CountryInformationReports/PPRI_Pharma_Profile_Sweden_2017.pdf

Case study 4: Evidence-based reimbursement decisions

GERMANY:[13] In contrast to many of its European neighbours, Germany takes a free pricing approach, granting all medicines approved by the European Medicines Agency automatic reimbursement for an initial 12-month period.

After this first year, a medicine undergoes an early benefit assessment to assess the additional benefit to the patient compared to an appropriate comparative medicine. The outcome of this assessment dictates the price of the medicines henceforth.

- If the medicine is assessed to have an additional benefit, the manufacturer and the government negotiate a surcharge on the price of the equivalent comparable medicine.
- If the medicine cannot prove an additional benefit, the medicine is allocated to a reference price group with comparable active ingredients and a price based on a one-year supply of the comparable medicine is negotiated.
- If the medicine is sold at a price higher than the set reimbursable amount, the patient opts to cover the additional payment or receive a therapeutically equivalent fully-reimbursable medicine.
- If no reference price group exists for the medicine, the government negotiates a refund rate with the manufacturer, which does not lead to higher annual costs than the equivalent comparable medicine.

Orphan medicines avail of a simplified process and as long as a medicine does not cost the health system more than €50m annually, it does not need to prove additional benefit to set the price. If an orphan medicine exceeds the threshold, a full assessment is required

[13]http://www.iges.com/e15094/e15095/e15096/e17469/IGES_Reimbursement_Pharmaceuticals_WEB_ger.pdf

SECTION THREE: Access to medicines – a global issue

United Nations

The right to health is a human right recognised in both the Universal Declaration of Human Rights[14] and the International Covenant on Economic, Social and Cultural Rights[15]. The UN Sustainable Development Goal on Health (Goal 3) seeks to achieve *"access to safe, effective, quality and affordable essential medicines and vaccines"*[16].

In implementing a rights-based approach to medicines access, focus has traditionally centered on developing countries and on 'essential' medicines. However as national health budgets grapple with population growth and pharmaceutical price increases, the problem takes on a more global dimension and the debate starts to evolve to include so-called developed nations and high-tech or innovative medicines[17]. Difficult questions arise about the competing interests in public health, intellectual property and trade, and about how they can be balanced.

Mindful of the increasingly global nature of the challenges in accessing new and improved drug therapies, in 2015, the UN Secretary-General established a High-Level Panel to *"review and assess proposals and recommend solutions for remedying the policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies."* In September 2016, the Panel reported back to the Secretary-General recommending, at a global level, the elaboration of a binding R&D Convention to delink R&D costs from the price of medicines and to redirect R&D to public health needs and away from private sector interests[18] At a national level, the report calls on governments to increase current investment in health technology; to implement new models for financing health research; to regularly review access to health technologies; and to require manufacturers to disclose research and development costs.

Continuing the dialogue, in 2016, the WHO hosted an informal meeting to explore the current medicines pricing system and to identify the key challenges[19]. In 2017, the WHO partnered with the Dutch government to host the Fair Price Forum which marked a recognition by many governments of the need to take action to push for a fairer pricing system for medicines[20]. In a similar vein, the 34th session of the Human Rights Council in March 2017, convened a panel to explore the access to medicines in the context of the right to health with the goal of identifying key challenges and good practice. During follow up discussions at the 36th session in late 2017, it was widely acknowledged that while the right to health imposes an immediate obligation to provide access to essential medicines, governments also remain obliged to ensure the progressive realization of access to all health technologies[21].

European Union

The primary text outlining the rights, freedoms and principles of the European Union – the Charter on Fundamental Rights of the European Union – dedicates article 35 to the recognition of the right of European citizens and residents to access preventative health care and medical treatment. Member states act and legislate in accordance with the Charter's provisions when acting in the scope of European law.

Despite its laudable aspirations, the Charter has limited utility when it comes to tackling the question of access to new and improved drug therapies as the assessment, reimbursement and pricing of new medicines are a national competence. Currently, the European Union regulates only around issues of competition and medicines safety. However, there is evidence of political willingness to explore more pan-European solutions, especially as more and more member states struggle to pay the expensive price tags attached to new medicines from finite public health budgets. Solutions potentially includejoint assessments and cooperative negotiations.

The European Parliament and the Council of the European Union seem to now share a common vision for greater member state cooperation around access to medicines. A Parliament Resolution on the *EU options for improving access*

to medicines[22] in March 2017 builds upon the June 2016 Council Conclusions on *strengthening the balance in the pharmaceutical systems in the EU and its Member States*[23]. Cooperation is also on the agenda of EU presidencies and the Bulgarian Presidency which is leading on the first half of 2018 and commits to continue the debate around access to and affordability of medicines[24]. Making a brave step forward, on 31 January 2018, the European Commission agreed a proposal for a regulation to provide for "permanent and sustainable cooperation at the EU level for joint clinical assessments" in health technology assessment. This proposal will now be considered by the European Parliament and Council of Ministers[25].

For more information on individual initiatives at the EU and Member State level, read **Annex One: European and Regional Initiatives**.

[14]http://www.un.org/en/universal-declaration-human-rights/

[15]http://www.ohchr.org/EN/ProfessionalInterest/Pages/CESCR.aspx

[16]http://www.un.org/sustainabledevelopment/health/

[17]http://www.who.int/medicines/access/fair_pricing/en/

[18]http://www.unsgaccessmeds.org/final-report/

[19]https://www.aanmelder.nl/i/doc/1d433b0034ad6cbe57f35b10d021d03e?forcedownload=True

[20]http://www.who.int/entity/medicines/access/fair_pricing/FairPricingForum2017MeetingReport.pdf?ua=1

[21]http://www.ohchr.org/EN/HRBodies/HRC/RegularSessions/Session36/Pages/ListReports.aspx

[22]http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+TA+P8-TA-2017-0061+0+DOC+PDF+V0//EN

[23]http://data.consilium.europa.eu/doc/document/ST-5170-2017-INIT/en/pdf

[24]https://eu2018bg.bg/en/programme

[25]http://europa.eu/rapid/press-release_IP-18-486_en.htm

SECTION FOUR: Key recommendations

The original recommendations from the first 'Drug Iceberg' report in August 2017 are listed below. They are directed at Government; Pharmaceutical industry/Regulators; and Patient Groups / Registries. The recommendations that both IPPOSI and MRCG members intend to tackle in 2018 are highlighted below. All recommendations remain valid and we urge all health partners to take immediate steps to progress their implementation.

Recommendations to Government include:

1. **The key recommendation in this report is the call for the development and implementation of a new national strategy on access to new and innovative drug therapies in Ireland involving all key stakeholders, including patient groups and the public. This strategy should be based on the principles of fairness, equality, value for money, transparency, effectiveness and sustainability.**
2. The full ring-fencing of the anticipated savings from the current and future agreements between the state and pharmaceutical companies for new, innovative and/or improved drug therapies.
3. An immediate review of the present IPHA Agreement to ensure that the savings of up to €750m will be fully realised.
4. Further savings on the existing budget for drugs outside the present IPHA agreement can and should be made and ring-fenced from, for example a national biosimilars policy and agreements with individual companies.
5. Companies that are presently not members of IPHA should be required to be part of a new and sustainable national strategy on access to new and innovative drug therapies in Ireland.
6. **Clarification, consistency and transparency on the post-HTA phase of the drug approval process in Ireland. This has changed several times in recent months, which is undermining patients' confidence in the system. Similarly, clarification and reform of the drug reimbursement process at hospital level is required. It is unclear to patient groups why some high-tech drugs are reimbursed from hospital budgets and others from a national budget.**
7. An explicit commitment from Government that it is not embarking on a course of developing a de facto 'drug rationing policy' arising from an imbalance between the weight of views given to those in public expenditure versus those who are primarily concerned with access to better health, including better access to drug therapies in Ireland.
8. **Building on existing positive Public and Patient Involvement (PPI) initiatives from both the NCPE and agencies in England and Scotland to further develop appropriate clinician and patient involvement in the drug approval/reimbursement process. The NCPE needs additional resources for this and related purposes.**
9. There is a global debate taking place, particularly among health economists, on whether the existing HTA/QALY systems takes into account the emergence of 'superdrugs' for all diseases; the new challenges inherent in precision medicine; and the additional hurdles faced by those developing drugs for rare diseases. Emerging changes and practices should be actively considered for adoption by the appropriate agencies in Ireland.

10. Patient groups will be included in discussions on macro health policies in relation to drug assessment and reimbursement including, for example, in future agreements that presently only involve the Government and the pharmaceutical industry.

11. A clear policy on developing and resourcing patient registries needs to be developed. Registries are well placed to contribute to monitoring the effectiveness of medications and creating favourable conditions for the undertaking of clinical trials in Ireland.

12. The potential of European Reference Networks (ERN's) and the possibility of drawing on the expertise of patient bodies active at a European level should be given greater consideration by the Government in the access to drugs debate at EU/Council of Europe level.

13. Access to new, innovative and improved drug therapies should be given greater protection within existing human rights instruments. Ireland has a role to play in this process at international level.

Recommendations to the Pharmaceutical Industry/Regulators include:

1. While accepting the reality that research and development costs for new drug therapies are often very high, pharmaceutical companies need to do considerably more to ensure that pricing of new, innovative and improved drug therapies in Ireland is fair and avoids extraordinary profit taking.

2. Patient groups should be included in discussions on macro health policies in relation to drug assessment and reimbursement including, for example, in future agreements that presently only involve the Government and the Pharmaceutical Industry (same as recommendation 10 above).

3. The commitment by all pharmaceutical companies that those patients who take part in clinical trials for a successful drug therapy should be entitled to remain on that drug for the rest of their lives, irrespective of whether the dug is reimbursed in Ireland or not.

4. The ending (by a minority in industry) of some unacceptable practices such as threatening to remove access to medications from patients who are already receiving them on compassionate/managed access grounds.

5. To participate in the review and update of the HTA/QALY system in the context of recent scientific breakthroughs and pharmaco-economic advances for both common and rare diseases.

6. Companies and regulators alike should work to strengthen their readiness towards patient engagement to ensure that patients and their needs are embedded at the heart of drug therapy development, regulation and lifecycle management.

7. The increased use of stratified medicine tools in the development and assessment of drug therapies in order to better identify patients most/least likely to benefit from therapies.

Recommendations to Patient Representative Groups and Registries include:

1. **The need for all patient groups to keep fully appraised on the drug therapy approval and reimbursement processes in Ireland and the recent/on-going changes.**
2. **To jointly develop patient-led guidance for transparent interaction with industrial partners in Ireland, drawing on similar guidelines developed in other European countries. This will seek to complement codes that are already in place for the pharmaceutical industry.**
3. The further development of PPI good practices with key stakeholders across a wide range of policy and research areas and in particular Health Technology Assessment.
4. The capturing of quality-of-life and/or healthcare data, including the cost of 'not treating' patients which could be incorporated into NCPE submissions/HTA process.
5. To be more proactive in delivering the patient group perspective to the media / general public on macro policy related to access to drug therapies in Ireland.
6. **To encourage their membership to avail of patient education/training/capacity building opportunities which are increasingly available through groups such as IPPOSI, EUPATI and others.**
7. To engage in forward-planning with respect to pipeline drugs in their respective condition, including managing member's expectations re: suitability/eligibility for a particular therapy

ANNEX ONE: European and regional initiatives

Each of the European institutions continues to address the issue of access to medicines and European legislation, regulation and policy around this topic is constantly evolving.

- The **Charter of Fundamental Rights of the European Union** dedicates Article 35 to health care and upholds that *"Everyone has the right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices. A high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities"* [26]. The Charter enshrines the political, economic, social and cultural rights of European Union citizens and residents and European institutions are required to act and legislate in accordance with its provisions.
- A **European Parliament Resolution** of 2 March 2017 on *EU options for improving access to medicines* (2016/2057(INI)) marks a proactive step by elected members of the European Parliament (MEPs) to rebalance public health interests with those of the pharmaceutical industry[27].
- A **European Council Conclusions** of 17 June 2016 *on strengthening the balance in the pharmaceutical systems in the EU and its Member States* (2016/C269/31) represents a political statement by member state Ministers of Health to address the existing pharmaceutical system and to engage in strategic cooperation to tackle identified challenges[28].
- A **European Commission public consultation** on *strengthening EU cooperation on Health Technology Assessment* ran from October 2016 to January 2017 to gather perspectives on what joint action member states might take to support the national HTA processes[29]. An **impact analysis of policy options** was subsequently initiated in 2017. In January 2018, the European Commission published a proposal to regulate for joint cooperation in clinical aspects of health technology assessment[30].

Successive Council **of the European Union Presidencies** (which rotates between member states every six months) have placed access to medicines on their agenda of priorities.

- **MECHANISM OF COORDINATED ACCESS TO ORPHAN MEDICINAL PRODUCTS (MoCA):** In 2010, the Belgian Presidency launched the "Process on Corporate Responsibility in the Field of Pharmaceuticals" which looked at the question of access to rare disease medicines in Europe and created MoCA to develop proposals for voluntary cooperation between member states to improve access to orphan medicines[31]. Although work formally concluded in 2013[32] some members continue to cooperate under the auspices of the Medicines Evaluation Committee (MEDEV, an informal group of experts from statutory health insurance institutions and HTA agencies in Europe) with the aim of putting all conclusions and recommendations into practice[33].

[26]http://www.europarl.europa.eu/charter/pdf/text_en.pdf

[27]http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P8-TA-2017-0061+0+DOC+XML+V0//EN

[28]https://publications.europa.eu/en/publication-detail/-/publication/b49097b2-5096-11e6-89bd-01aa75ed71a1/language-en

[29]https://ec.europa.eu/health/technology_assessment/consultations/cooperation_hta_en

[30]http://europa.eu/rapid/press-release_IP-18-486_en.htm

[31]https://www.eurordis.org/content/Moca

[32]http://download.eurordis.org.s3.amazonaws.com/moca/history/WG%20MoCA-OMP%20Final%20Report.pdf

[33]http://download.eurordis.org.s3.amazonaws.com/moca/today/MOCA%20Revised%20Terms%20of%20Reference%20endorsed%20Jan-2016.pdf

- **NETWORK OF COMPETENT AUTHORITIES ON PRICING AND REIMBURSEMENT (CAPR):** In 2008, the Slovenian Presidency created an informal 'Network of Competent Authorities on Pricing and Reimbursement'. The network continues to meet to identify, share and discuss information, expertise and best practice in the assessment and reimbursement of medicines. Over the years many issues of common interest have been explored including cost-management, external reference pricing, differential and value based pricing, managed entry agreements, generic substitution, orphan medicines, adaptive pathways.

The **European Commission** leads on a number of initiatives to implement the political and strategic priorities of the Parliament and Council.

- **EUnetHTA,** the European Network for Health Technology Assessment, was established in 2007 after health technology assessment was identified as a political priority in 2004. Public funding has been made available for the period 2009-2020, and indications are that elements of this initiative will continue to be supported after the end of the current project in 2020[34]. EUnetHTA collaborates closely with the EMA, and in November 2017, EUnetHTA and the EMA published a joint work plan for the period 2017-2020[35].
- **SAFE AND TIMELY ACCESS TO MEDICINES FOR PATIENTS (STAMP),** the European Commission Expert Group on STAMP, was established in 2015 to advise the Commission on implementing pharmaceutical regulation and policy, to promote information sharing between member states on the topic, to examine national initiatives, and to identify how to use regulatory tools to promote quicker access to medicines[36].

In recent years, several more Member State-led, cooperative initiatives have also sought to address the challenges around access to medicines.

- **VALLETTA DECLARATION:** In May 2017, Health Ministers from Ireland, Spain, Italy, Greece, Portugal, Cyprus, Malta and Romania signed a declaration to work together (with industry) to improve *affordable* access to medicines[37]. A Technical Committee has since been established to explore the specific areas for cooperation and a first meeting was held in June 2017 in Cyprus.
- **BENELUXA:** In 2015, Belgium, the Netherlands and Luxembourg initiated cooperation around access to medicines, specifically around access to orphan and innovative medicines. In 2016, the trio was joined by Austria – and the BeNeLuxA initiative was born[38]. The initiative focuses on four aspects 1) horizon scanning 2) health technology assessment 3) information exchange 4) pricing and reimbursement. BeNeLuxA does not jointly procure medicines and each country engages in line with their own national rules, procedures and institutions. In 2017, they engaged in their first joint HTA procedures, assessing four new medicines over the course of the year[39]. In May 2017, the Belgium and Netherlands governments issued statements[40] following a failed joint negotiation with Vertex for CF drug Orkambi. EURORDIS subsequently called on both governments to resume negotiations in open letters dated 20 June 2017[41]. BeNeLuxA have

[34]http://www.eunethta.eu/

[35]http://www.eunethta.eu/news/ema-and-eunethta-finalise-joint-work-plan-2017-2020

[36]https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp_en

[37]http://health.gov.ie/blog/press-release/ireland-to-work-with-other-eu-countries-to-secure-affordable-access-to-new-medicines-for-irish-patients/

[38]http://www.beneluxa.org/

[39]http://www.beneluxa.org/hta

[40]http://deblock.belgium.be/fr/n%C3%A9gociations-sur-le-prix-d%E2%80%99un-m%C3%A9dicament-contre-la-mucoviscidose-arr%C3%AAt%C3%A9es / https://www.rijksoverheid.nl/ministeries/ministerie-van-volksgezondheid-welzijn-en-sport/nieuws/2017/05/23/prijsonderhandelingen-geneesmiddel-voor-cystische-fibrose-beeindigd / https://www.vbb.com/media/Insights_Articles/Brief_aan_Parlement_Vergoedingsbesluit_Orkambi_TK.pd.pdf

[41]https://www.ncfs.nl/bestanden/orkambi/briefeurordisminister

published a proposal for future cooperation around horizon scanning in 2018 which includes the creation of a central database to share information on new or pipelines medicines[42]. In February 2018, Ireland announced plans to request to join the initiative.

- **NORDIC PHARMACEUTICALS FORUM:** In June 2015, Denmark, Iceland, Norway and Sweden agreed to collaborate around horizon scanning and information-sharing on prices and markets[43].
- **ROMANIAN AND BULGARIAN INITIATIVE:** In June 2015, the governments of Romania and Bulgaria signed an agreement to engage in joint negotiations to purchase medicines and to support the cross-border exchange of medicines during period of short supply[44].
- **BALTIC PARTNERSHIP AGREEMENT COLLABORATION:** In 2014, as part of the Baltic Partnership Agreement, Latvia, Lithuania and Estonia engaged in a first joint procurement around vaccines to prevent medicines shortages and promote a centralised procurement process[45].

[42]https://kce.fgov.be/language_selection/publication/report/horizon-scanning-for-pharmaceuticals-proposal-for-the-beneluxa-collaboration

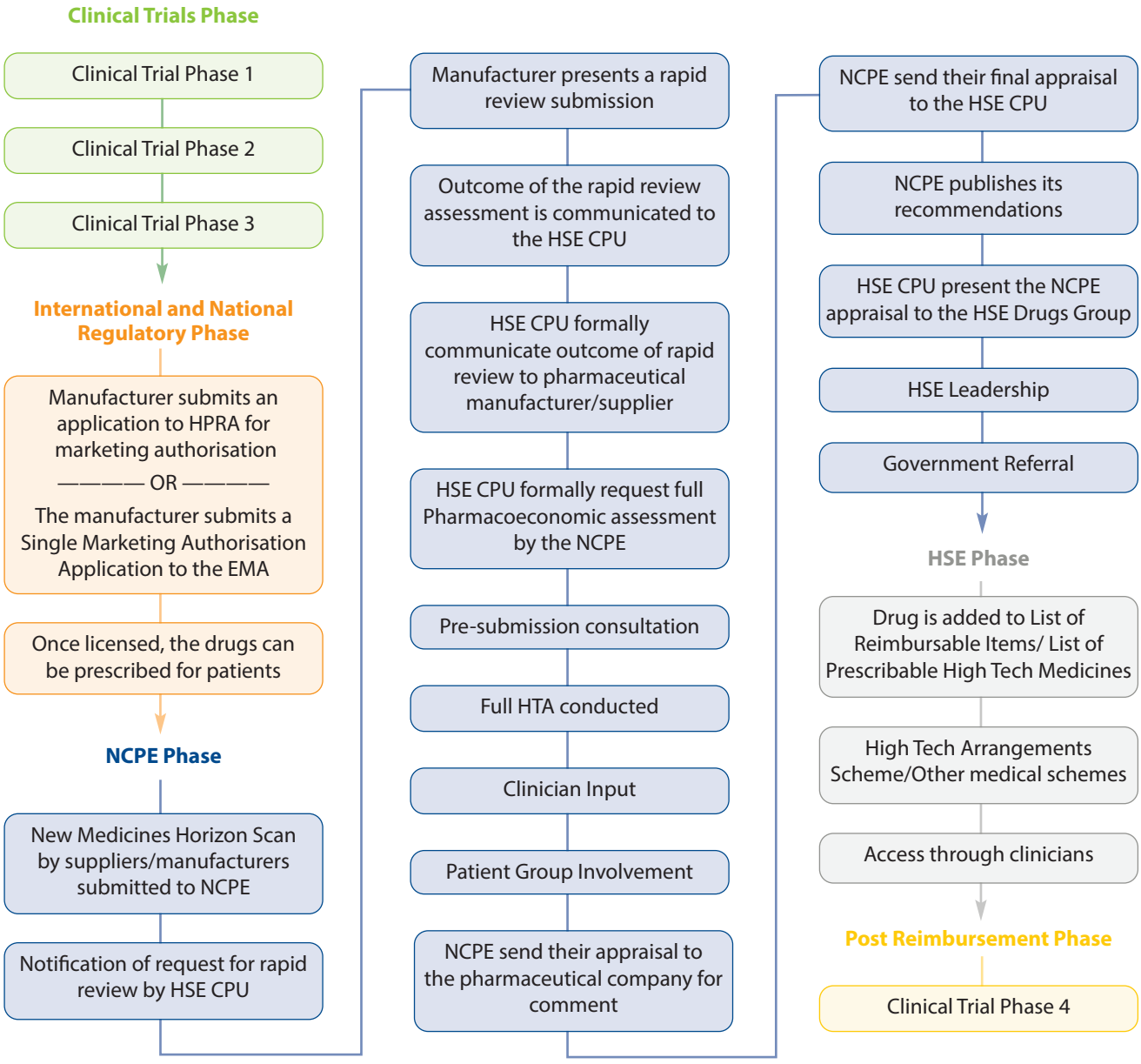
[43]http://data.consilium.europa.eu/doc/document/ST-5170-2017-INIT/en/pdf

[44]http://data.consilium.europa.eu/doc/document/ST-5170-2017-INIT/en/pdf

[45]http://data.consilium.europa.eu/doc/document/ST-5170-2017-INIT/en/pdf

ANNEX TWO: The drug therapy approval process in Ireland

Supply and Reimbursement of Drugs: From Clinical Trial to Patient Access



ANNEX THREE: Abbreviations

ESRI	Economic Social and Research Institute
EMA	European Medicines Agency
HSE	Health Service Executive
HTA	Health Technology Assessment
IPHA	The Irish Pharmaceutical Healthcare Association
IPPOSI	Irish Platform for Patients' Organisations, Science and Industry
MRCG	Medical Research Charities Group
NCPE	National Centre for Pharmacoeconomics
PPI	Patient and Public Involvement
QALY	Quality Adjusted Life Year

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MEDICAL RESEARCH CHARITIES GROUP SUPPORTED BY

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An Roinn Tithíochta, Pleanála, Pobail agus Rialtais Áitiúil
Department of Housing, Planning, Community and Local Government