medicines for ireland

Value Added Medicines Report

DISCUSSION DOCUMENT ON THE CONTRIBUTION OF VALUE ADDED MEDICINES IN IRELAND

Executive Summary

- Innovating on existing molecules in the form of repurposing, reformulation and combination of therapies with technology has the potential to deliver timely and effective solutions to unmet medical needs. However, the current Irish environment, and structure of reimbursement, does not allow the Irish government to harness these benefits, potentially saving costs and increasing patient care.
- Value Added Medicines can empower patients by putting their needs at the center of therapy design, improving overall therapy outcomes.
- Three key enablers are needed to promote continuous and sustainable innovation: a fit-for-purpose regulatory framework ensuring predictability in early development, the recognition of innovation with proportionate incentives and the definition and the recognition of added value.

Foreword

As Chair of Medicines for Ireland's Value Added Medicines Committee, I'm passionate about exploring how Value Added Medicines (VAMs) can improve patient care and deliver value for the HSE.

As you'll see in the report, there's plenty of evidence to show that VAMs offer a wide range of benefits for patients and HCPs – from ensuring better adherence and compliance, to keeping healthcare costs down by reducing the need for patients to be moved to expensive next line therapies.

To take advantage of these opportunities, we need a shift in mindset – from one that focuses purely on cost to an outlook that is centred around better outcomes for patients that takes a holistic look at the whole patient journey. Perhaps even more importantly, we need a new and simplified regulatory pathway for Value Added Medicines in Ireland – bringing us into line with other major European countries such as the UK and Belgium to ensure that our patients and healthcare system is not left behind.

That's why all of us at Medicines for Ireland welcome the opportunity to engage with key stakeholders on this important topic, and to begin the discussions around what a fit-for-purpose regulatory framework for VAMs may look like for Ireland. What's clear is that we need a system that rewards innovation with appropriate incentives, whilst recognising the potential long-term value and savings that VAMs can bring to the State.

By engaging with this report, I hope we can begin the conversation and engagement needed to start developing a framework within Ireland that will encourage the development and growth of Value Added Medicines - putting them at the heart of our healthcare ecosystem for the benefit of all.

Clodagh Kevans
Chair, Value Added Medicines Committee
Medicines for Ireland

Improving treatments by rethinking, reinventing, and optimising existing medications

Value Added Medicines (VAMs) are medicines based on known molecules that address healthcare needs and deliver improvements for patients, healthcare professionals and payers. VAMs are developed through continuous innovation on well-established molecules, applying different strategies, all of which proved effective during the Covid-19 pandemic (Fig 1).

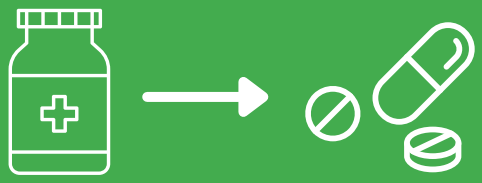
VAM development strategy	Covid-19 application
Repositioning  Finding new indications for existing molecules	A new indication was found for dexamethasone in the treatment of Covid-19. The drug reduced mortality in hospitalised patients by a third.
Reformulation  Changing the dose or mode of administration of an established medicine	Novel treatment regimes and administration routes allowed at-risk patients to minimise the time spent in hospitals, where they would have been at increased risk of contracting Covid-19.
Combination  Pooling sets of well-established molecules to simplify therapy regimes or combining an existing medicine with an innovative device (which can include a digital component)	Digital VAMS empowered patients to better manage their therapies, enabling treatment continuity even when hospitals did not have sufficient capacity and resources to accommodate all patients.

Figure 1 - VAM development strategies and use cases for VAMs during the Covid-19 pandemic

Going beyond 'What you see is all there is' to exploit the untapped potential of continuous innovation

The Covid-19 pandemic has demonstrated that traditional pharmaceutical innovation, taking several years from the discovery of a drug target to the delivery of a novel therapy, does not move fast enough to address urgent unmet medical needs during a crisis. In this setting, **repurposing** has been key to the discovery of new therapeutic strategies.

In the RECOVERY trial, **dexamethasone** was shown to be effective in combatting severe forms of Covid-19, demonstrating how off-patent molecules have enormous potential to deliver benefits to patients worldwide if enough resources are deployed for their evaluation.

While the potential of repurposing as a strategy for innovation has been demonstrated in the context of an acute crisis, the power of this approach extends far beyond emergencies. The importance of repurposing has been recognised in both the Pharmaceutical Strategy for Europe and Europe's Beating Cancer Plan, which were published by the European Commission in 2020 and 2021 respectively.

The initiatives promoted by the European Commission allocate resources and lay out a strategy to identify promising candidate molecules to be tested in new indications. Once a candidate is identified, pre-clinical and clinical testing are required to confirm its therapeutic potential. Collaboration among stakeholders is crucial to ensure that appropriate clinical evidence is generated to validate the most promising candidates.

It was estimated that using **dexamethasone** to treat Covid-19 patients led to

12000 lives saved

corresponding to

102000 life years gained

Águas, R., Mahdi, A., Shretta, R. et al., "Potential health and economic impacts of dexamethasone treatment for patients with COVID-19". Nat Commun 12, 915 (2021). https://doi.org/10.1038/s41467-021-21134-2

While the clinical evaluation of a novel indication is an essential step in repurposing, it alone is not sufficient to maximise the societal benefit of this continuous innovation strategy. To fully benefit patients and healthcare systems, the new indication needs to be added to the label of the repurposed medicine (Fig 2). Unfortunately, the current regulatory framework often makes this process cumbersome, costly, and complex. In addition, and especially where the medicines are off-patent, the costs associated with indication change or addition and the uncertainty around patent protection does not encourage repurposing. This is especially the case where existing chemical entities can be repurposed for novel indications for rare diseases where options are already.

The dexamethasone case well exemplifies the regulatory inefficiencies that are associated with adding a new indication on the label of well-established molecules. Indeed, this drug is presently employed to save the lives of Covid-19 patients through off-label use in most European countries.

Regulatory frameworks and rembursement bodies need to flex with the changing environment and the potential for optimising older medicines in the treatment of patients. Manufacturers wanting to invest in the development of VAMs encounter significant hurdles (Fig 3). To fully exploit the untapped potential of innovation on off-patent molecules, change is needed at country and European level.

Figure 2 - Registering new indications of known molecules is instrumental in solving multiple issues that are associated with off-label prescribing.

Cumbersome, complex, costly and unclear regulatory processes

Absence of incentives that encourage continuous innovation and reimbursement pathways

Lack of recognition of benefits, investments and added value in Irish markets

Limited predictability of required evidence and development costs can be an obstacle in VAM development

The further complexity, cost and duration of VAM development compared to standard follow-on products is not rewarded

Payers often categorise VAMs as standard generic medicines. P&R bodies require disproportionate amounts of evidence to assess and recognise the benefits of VAMs

Figure 3 - VAM manufacturers experience significant hurdles at multiple stages of the medicine development path.

Engaging patients to create medicines that provide the improvements that are most relevant to them

Continuous innovation presents an opportunity to design treatments that truly have patients' needs at their core.

Better patient involvement leads to greater patient empowerment. On an individual level, this means that patients are significantly more likely to adhere to their therapy - and thus benefit from it - if they see the advantages of taking their medication and understand the consequences of non-adherence. On a broader level, we welcome the work being done by the NCPE, listening to patient communities and integrating their experiences and needs into the development of new therapies enables manufacturers to design medicines that truly have unmet medical need and patient preferences at their heart.

Repurposing is not the only way in which VAMs use results in improved therapies. If appropriately promoted and fostered, continuous innovation can deliver benefits to a large and diverse range of patients.

Digital VAMs empower patients with respiratory diseases to take control of their therapy

Digital VAMs can be a valuable tool to enable patients to better understand their treatment and become confident in the management of their therapy. The **combination** of known molecules with a digital component can support better therapy adherence through improved feedback and education of patients with respiratory diseases. For example, smart inhalers detect if a dose has been correctly administered and can track therapy adherence patterns, to inform better prescription choices by clinicians and identify patients that would need further training on inhaler use technique.

Digital solutions have to be simple, so that patients can use them independently. The technology is there to make the patients' lives easier, not more complex.

Monica Fletcher, OBE,
Honorary Research Fellow,
Usher Institute, University of Edinburgh

Reformulation delivers therapies that can keep at-risk patients out of harm's way

In healthcare systems worldwide, during the Covid-19 pandemic, reducing patient hospital visits became a key priority due to the risk of acquiring infections.

Through **reformulation**, VAMs allowed fragile non-Covid patients needing complex therapies to significantly reduce their visits to healthcare facilities. This is exemplified by the change in guidelines in the UK which led to a preference for administration of the VAM Abraxane, instead of the corresponding taxanes, to oncology patients, despite the price premium associated with the use of an improved formulation. Thanks to its improved safety profile, this VAM reduced the need for longer hospital stays in a vulnerable category of patients.

Enabling continuous innovation is most important in areas of unmet need

Continuous innovation has the potential to provide solutions in areas of unmet need where traditional approaches to innovation have failed. One such area is neurology, where many patients receive treatments that are generally considered suboptimal and cures are rare.

As the "Value of Treatment for Brain Disorders" report highlights, there is a need for cost-effective strategies that can provide timely improvements for patients. Thanks to their shorter development timelines and better affordability compared to originators, VAMs can provide important solutions for patients affected by brain disorders worldwide. Therefore, their value should be recognised, taking into account also the hidden costs for society that are associated with neurological conditions, such as the inability of patients to be employed.

Further examples of the benefits that VAMs can deliver to patients and healthcare systems, backed by extensive case studies and complemented by policy recommendations, are available on the Medicines for Europe website, in the IQVIA "Case Studies for Value Added Medicines - Unlocking the potential of patient-centric continuous innovation" report.

Defining the value of a medicine: what truly matters?

As demonstrated by the range of examples of how VAMs can improve the lives of patients, added value is at the heart of the definition of all categories of VAMs, prompting a discussion on how we define, quantify, and demonstrate the benefits of a therapy.

Medicines for Ireland believes that policies need to be pursued to facilitate investment into off-patent innovation. Ireland can benefit greatly from changes in the area of Value Added Medicines. As a country, we can learn from the work at EU level, including the Pharmaceutical Strategy for Europe, and recognise the value of this type of reform. As an industry, we welcome clear guidance and policy to allow the off-patent industry innovate for the benefit of patients, healthcare professionals and healthcare systems.

David Delaney,
Chair of Medicines for Ireland

Identifying fair, structured, and predictable ways to determine the value of a given medicine is essential to drive continuous innovation on off-patent molecules.

Implementing a standardised framework for the quantification of added value in VAMs would enable significant predictability in terms of evidence generation requests and help to define what constitutes a proportionate and acceptable burden of evidence generation for manufacturers.

The VAM value evaluation framework proposed by the Syreon Research Institute is designed to be used by payers and HTA bodies and can be adapted for implementation at the national level, to align with local views on what are the key parameters defining the value of a therapy. The framework features eleven value domains, distributed across five clusters (Fig 4).

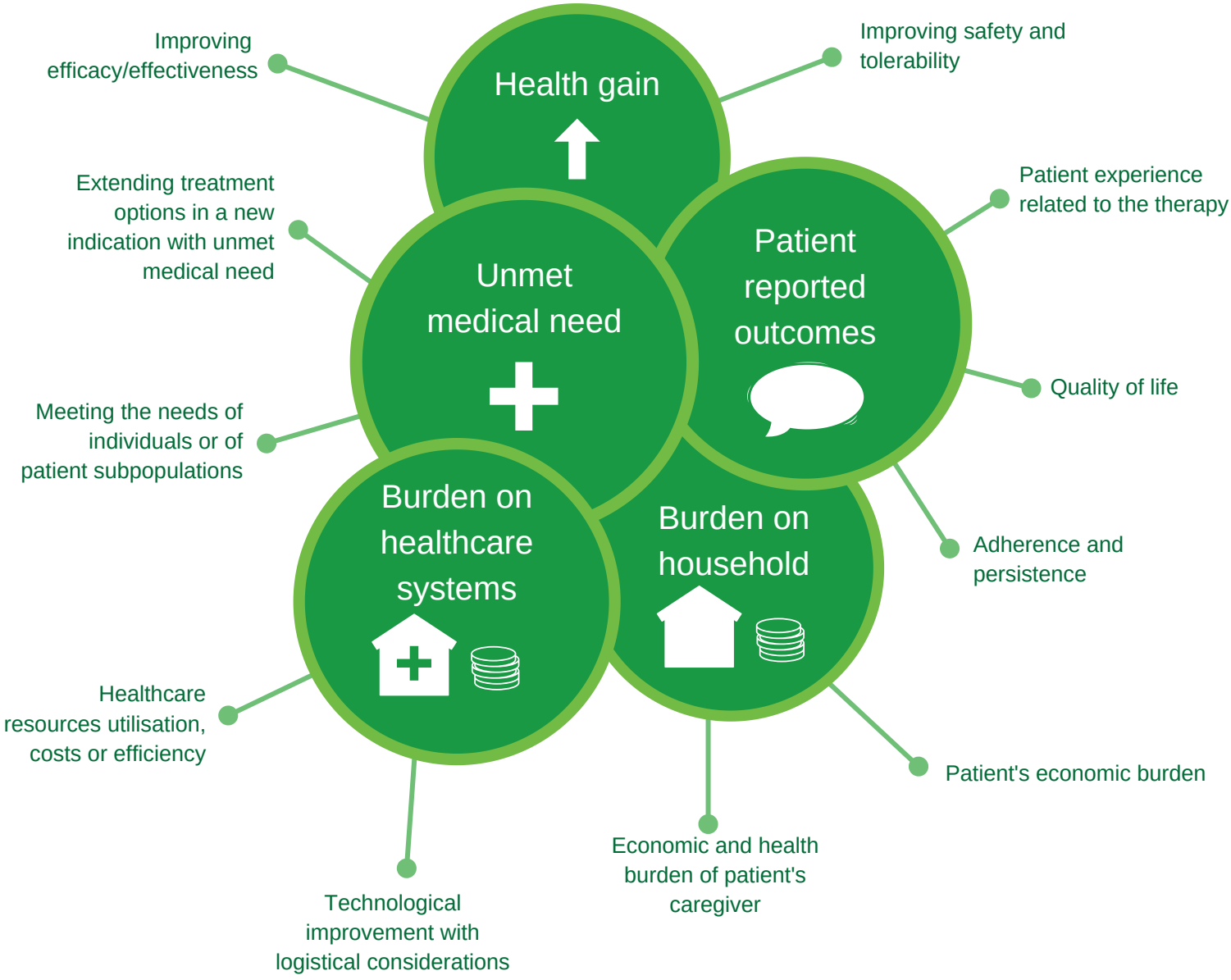


Figure 4 - The VAM value evaluation framework proposed by the Syreon Research Institute consists of eleven value domains, divided into five clusters.

Delivering value to the healthcare community by creating a European ecosystem that fosters the development and uptake of VAMs that can be implemented locally

Currently, the US is leading the way in terms of VAM sales and the number of available VAMs on the market. This is primarily thanks to the establishment of a favourable regulatory environment that enables the streamlined development of VAMs within the dedicated 505(b)2 pathway.

The US market accounts for about

2/3

of global VAM sales

IQVIA European Thought Leadership analysis, IQVIA MIDAS MAT Q2 2020

Dedicated regulatory procedures also enable smoother knock-on processes at later stages of VAM development, providing a clear pathway for companies to invest, for payers to assess the value of continued innovation and for patients and healthcare professionals to gain access to improved treatment options. Overall, this results into a structured, predictable development path.

The US is the global leader in Value Added Medicines. Sales for top products in the US are about 10 times larger compared to the top products in Europe, so they drive global trends.

Aurelio Arias,
Engagement Manager, European Thought Leadership,
IQVIA

To unlock the benefits that can be delivered by VAMs, the EU should create an ecosystem that enables and fosters off-patent innovation.

VAMs should be recognised as a separate group of medicines in EU legislation, linking approval procedures, innovation frameworks and reimbursement processes to create an ecosystem that delivers better health to patients, solutions for healthcare systems and fair returns on R&D investments. In February 2021, Medicines for Europe has released a Whitepaper describing the key enablers needed for Creating a European ecosystem for safe, timely and affordable patient-centric innovation (Fig 5).

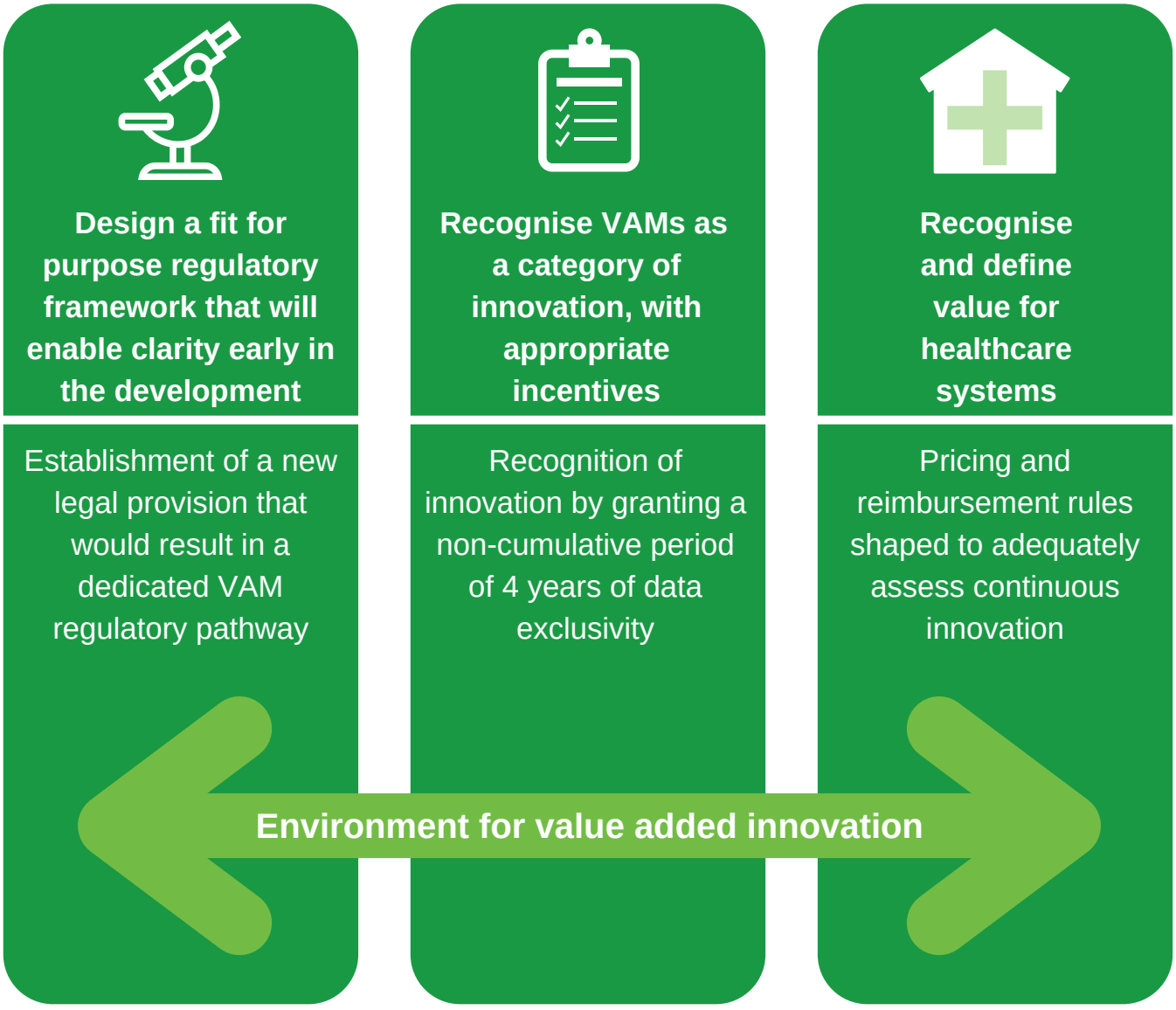


Figure 5 - To build a EU environment that promotes and fosters continuous innovation, change is needed at multiple levels.

By recognising VAMs as a category of innovation with a dedicated pathway and tailoring the system of incentives provided by the EU pharmaceutical framework to support innovation throughout a molecule's lifecycle, we can achieve a comprehensive and resource-efficient EU pharmaceutical industry, capable of delivering medicines that satisfy unmet medical needs and improve the lives of patients in Europe.

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