Bridging The Gap in Scotland

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Foreword

On behalf of AbbVie, I am delighted to present this report which offers some insight into the opportunities that exist to build on the great work to improve access to medicines in Scotland. This work is never complete and needs to continually evolve to reflect innovations in medicines development so that health technology appraisal processes can continue to offer rigorous scrutiny, but also provide the flexibility to respond to the changing environment.

In terms of the Bridging the Gap research itself, I was pleased to see that Scotland compared favourably to other countries in terms of how quickly it could appraise medicines, but it is clear that new processes to address uncertainty while maintaining a robust analysis of clinical or cost effectiveness will need to be found.

The research showed that many of the medicines that are accelerated at the regulatory stage are cancer treatments, where there remains a significant unmet need. Early access to these promising new medicines can have a remarkable impact on patients' lives.

This research is an excellent catalyst to consider how we create greater flexibility in the system. It is incredibly important that we, in the pharmaceutical industry, work with the NHS and HTA bodies in a collaborative way on the issue of access in order to achieve real change and I hope this report reflects our desire to work in partnership in Scotland.

Todd Manning

UK General Manager, AbbVie Ltd

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Introduction

Scotland has a proud tradition of being at the forefront of medicines and healthcare delivery, and its Health Technology Appraisal (HTA) process, spearheaded by the hugely respected work of the Scottish Medicines Consortium (SMC) has done much to enhance that reputation from a global perspective.

In December 2019, Abbvie organised and funded a meeting to discuss research conducted by IQVIA and commissioned by AbbVie. Participants considered the results of a new analysis into current HTA process; focusing on promising new medicines which are granted early regulatory approval; where treatments are innovative in nature and which address an unmet need.* These medicines are granted regulatory approval earlier in their development; where trial data is immature and not yet complete, or where patient numbers are small. Research demonstrated that for many HTA bodies, it can be challenging to deliver robust analysis of the full value of these medicines within their current processes. The meeting explored policy and process solutions which could address the challenge posed by uncertainty.

While regulatory bodies have established processes to fast-track marketing authorisation, HTA bodies and reimbursement processes (i.e. those organisations responsible for assessing cost and clinical effectiveness, as well as groups responsible for determining price) currently do not, or may not, have the frameworks or organisational capacity to apply flexibility to deal with the uncertainties raised by these particular medicines. But the potential impact of such medicines on patient outcomes requires solutions to be found.

The meeting, chaired by Lewis Macdonald MSP, Chair of the Scottish Parliament Health and Sport Committee, brought together a group of senior stakeholders including civil servants, MSPs, healthcare policy leaders, clinicians, patient groups and the pharmaceutical industry. During the discussions, it was recognised that solutions do not sit with a single entity and a transparent and collaborative approach was needed to ensure productive outcomes.

The ensuing report reflects the research presented and the ongoing discussion. The report recommendations are distilled from these and are part of AbbVie's research.

* Defined as products with FDA and EMA designations for promising, innovative drugs (e.g. PRIME, EAMS, FDA Accelerated, EMA conditional and EMA exceptional) (see Fig 1, Page 7)

The Way Ahead

A wider variety of real-world data should be collected about the effectiveness of medicines, from large scale “big data” to smaller data sets for rarer conditions. This information should be used in the access and reimbursement process – where appropriate, supporting a “managed access” system.

The NHS, social care, patient groups and the pharmaceutical industry should work collaboratively to identify sources of data that could be used to support decision making.

Differential pricing by disease approaches, including indication-based pricing and outcomes-based pricing should be more widely adopted by NHS Scotland.

In line with the recommendations of the Data Scoping Taskforce, the Scottish Government should establish a multi-agency working group to look at the opportunities for developing a more accessible approach to innovative pricing schemes, with defined objectives and timelines for delivery.

Sufficient resources should be dedicated to delivering changes to the access to medicines process, in order to avoid the burden of data collection being placed onto already over-worked clinicians. Industry should be willing to share expertise, staff and other resources where possible.

The SMC should consider whether it is possible to establish a routine process for early engagement with companies where medicines are granted early regulatory approval to allow early discussion around anticipated challenges.

Companies should be encouraged to involve patients in trial design and work with scientists to reflect on what is important to patients. This would produce more meaningful evidence that can add value to an HTA submission. Giving cognisance to the difficulties associated with small patient numbers, this evidence need not necessarily be based only on Scottish patient data.

Research

Medical regulators around the world, including the European Medicines Agency (EMA) and the Medicines and Healthcare Regulatory Products Agency (MHRA) are introducing new, fast-track, routes to license for innovative "breakthrough" medicines for diseases with high unmet need. But there are concerns that patient access to these medicines is delayed by processes which are unable to easily assess cost and clinical effectiveness. These medicines are innovative but can often be associated with greater uncertainty relating to limited clinical trial data. This can be due to reasons such as the medicine being targeted at a small patient population leading to clinical trials having smaller sample sizes. This challenge is only likely to increase over time as scientific understanding allows for more targeted therapies. Therefore, the challenge for HTA bodies is to find a way to deal with the uncertainties that result from early regulatory approval. These medicines represent a promising innovation or address an unmet need and therefore, for the sake of patients, these challenges need to be overcome.

The Bridging the Gap research was designed to test the hypothesis and to identify whether such a gap exists in Scotland. It identified a "test group" of medicines that had been expedited or accelerated via a specific regulatory route either by the Food and Drug Administration (FDA) or the EMA between 2012 and 2019. It measured the time from that medicine being licenced to receiving a decision about its use from a national HTA body (the "time to outcome"). These medicines were compared to a "control group" of medicines launched within the same period which had been submitted for assessment but did not go through the specific regulatory routes mentioned above.

It is acknowledged that during the timeframe for this research several changes have been introduced to the Scottish Medicines Consortium (SMC) appraisal process, such as the introduction of the PACE processes for medicines used to treat end of life and rare diseases.

The research found that:

The SMC has a much shorter time to outcome for decisions within both the test and control groups than NICE (England) and compares favourably to other HTA bodies (Italy [CRUF/AIFA] and Spain [AEMPS/AQuAS]). The time to outcome for medicines that fell within the research test group was on average 22 days quicker than medicines in the control group.

Despite shorter time to outcome in Scotland, a lower success rate for medicines with uncertainty ("test group") was observed (Note: the research did not include medicines that were not submitted to the SMC and therefore received an automatic 'not recommended' decision).

EAMS* medicines experienced a shorter time to outcome and increased approval rate compared to all medicines assessed by the SMC.

Four of the HTA bodies (England, Scotland, Canada and Australia) in scope of the research had a resubmission process (Note: each has different resubmission processes). Across these four bodies, there are three key reasons for reaching a positive decision following a resubmission:

– Addressing issues of cost effectiveness

– Addressing issues associated with inappropriate comparator

– Inclusion of Patient Reported Outcomes and use of Real-World Evidence as supportive data.

The SMC is seen as a world leader amongst HTA bodies, and the fact that it continues to set in place policies to improve access to new medicines is encouraging. For example, the introduction of the new Ultra-Orphan pathway in 2018.

The rigour that the SMC applies to its work is very important and needs to be maintained. HTA processes will need to continue to evolve to allow flexibility to be able to make clinical and cost-effective decisions based on limited data; this is not about expecting the SMC to approve all medicines submitted for HTA.

The challenge is now to ensure that the non-HTA aspects of the process regarding access to medicines e.g. commercial arrangements, early NHS and industry dialogue, and flexible reimbursement, can evolve to ensure that access to cost-effective promising new medicines can be maintained.

It is important to reiterate that this work is focused on those medicines that are determined, at the point of regulatory stage, to have demonstrated innovation or addressing an unmet need and therefore marketing authorisation is granted earlier in the development process.

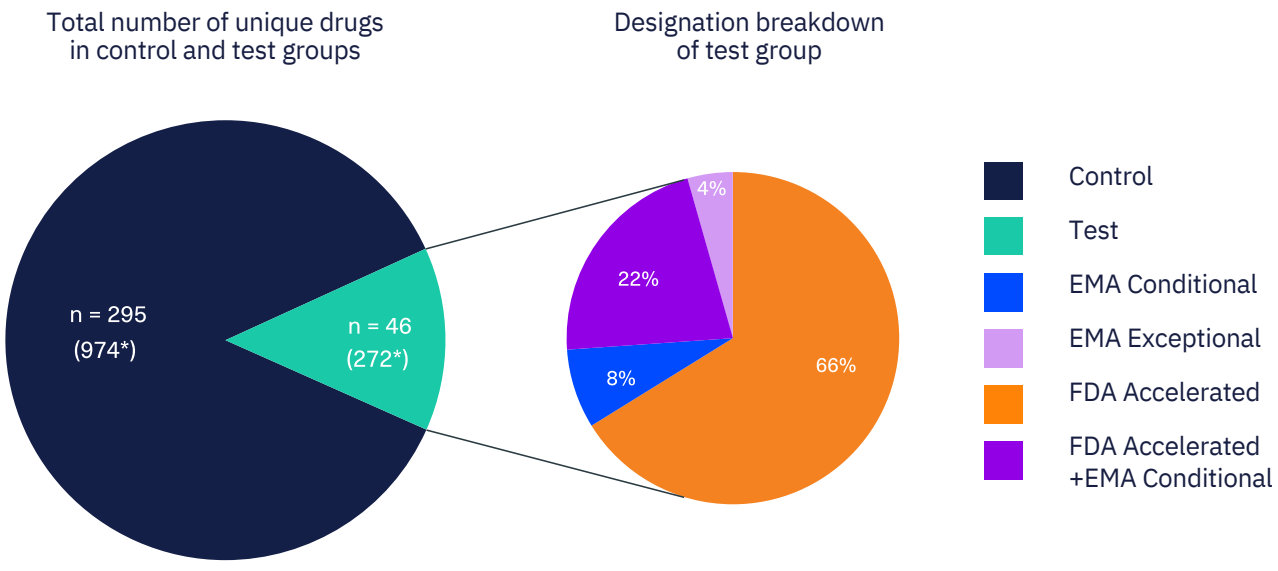
*The Early Access to Medicines Scheme [EAMS] aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need.

Background on test group regulatory decisions

Our research has included medicines that have received FDA accelerated approval, EMA exceptional approval and EMA conditional approval. The EMA exceptional and conditional approved medicines are mutually exclusive, with the latter focused on rare/orphan disease products with clinical uncertainty.

The products that have gained FDA accelerated approval have previously received "fast track" or "breakthrough" designation, meaning they are not assessed more quickly by the FDA, but instead assessed at an earlier stage of their clinical development. It is theoretically possible for EMA exceptional approval to overlap with FDA accelerated approval, but this was not found within our cohort as the comparison graph shows (see Figure 1).
Figure 2 shows the breakdown of HTA submissions by primary indication. This graph shows that the test and control group are made up of differing proportions of disease areas.

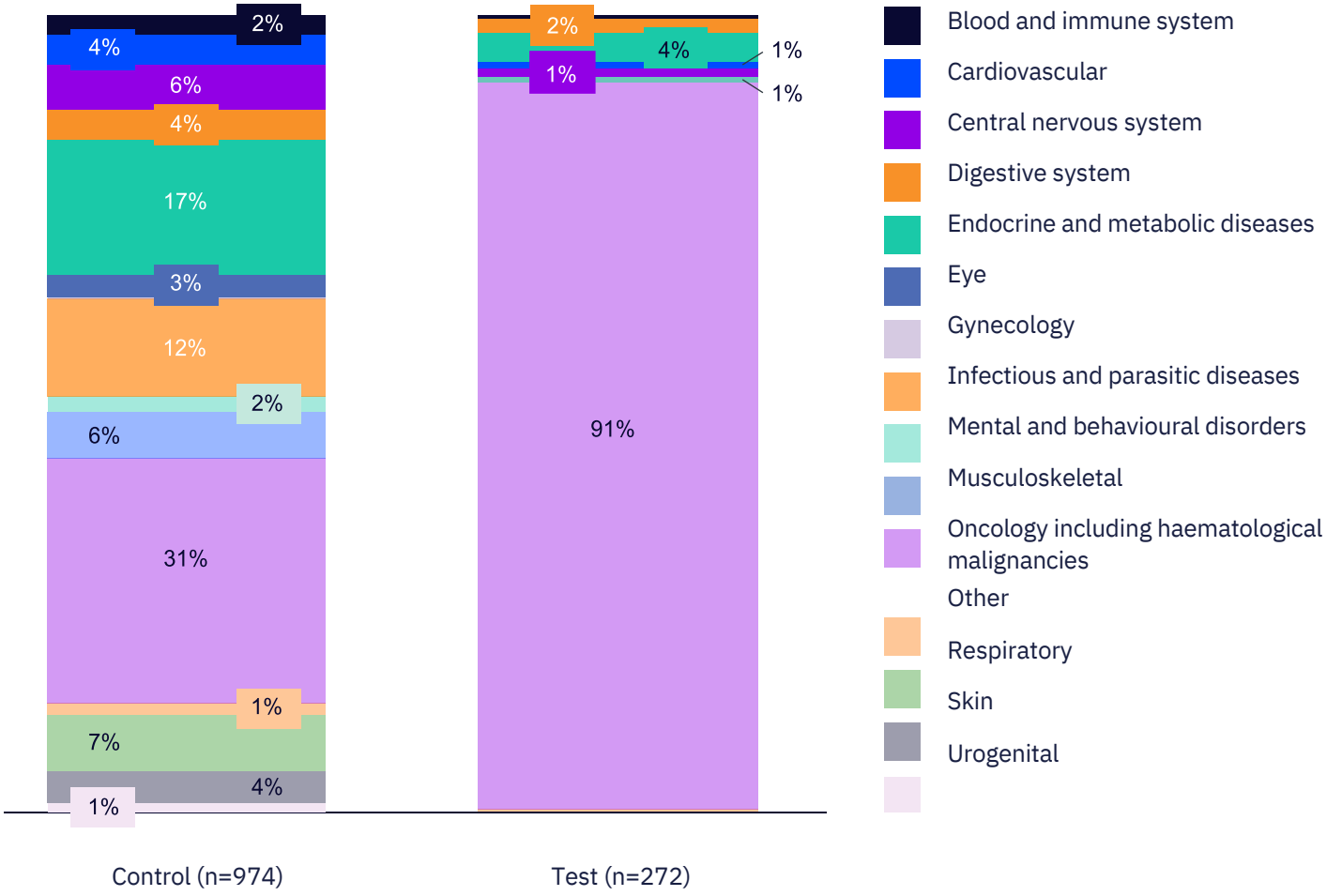
Figure 1: Comparison of test and control groups



n refers to unique drugs, however it should be noted that this does not account for the same drug submitted for different indications
*number of submissions made to HTA bodies within scope

Source: IQVIA HTA Accelerator Analysis (August 2019 data)

Figure 2: Breakdown of HTA submissions by primary indication

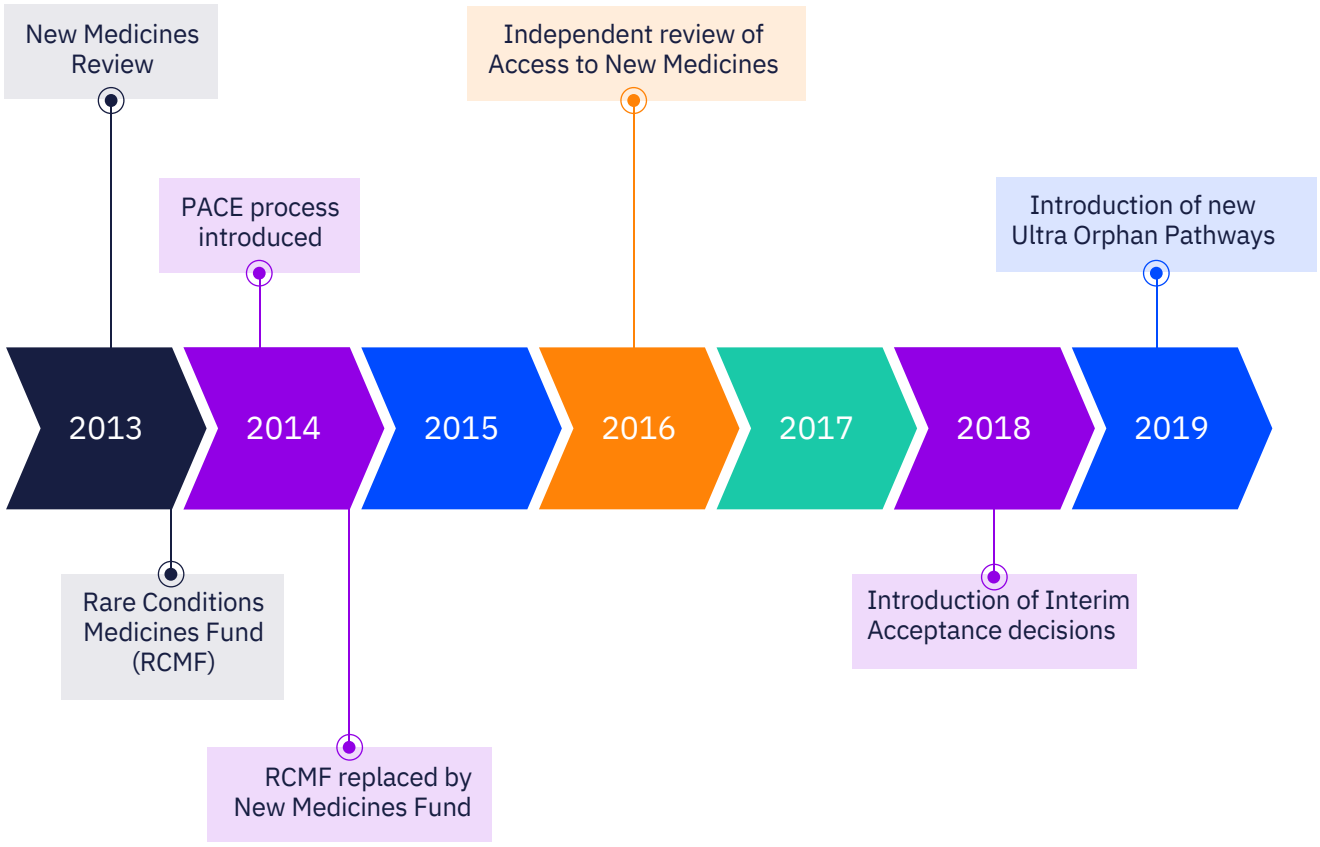


Base (n) = total # submissions analyses

'Other' includes surgery, nausea, vomiting, pain, systemic inflammatory response and transplant

Source: IQVIA HTA Accelerator Analysis (August 2019 data)

Improving access to new medicines in Scotland



In 2014 a new PACE (Patient and Clinician Experience) process was introduced for rare and end of life conditions.

The aim of a PACE Meeting is to describe the added benefits of the medicine, from both patient and clinician perspectives, that may not be fully captured within the conventional clinical and economic assessment processes.1

In 2018, following the independent review of access to new medicines, a new option of “interim acceptance” for medicines which had received EMA conditional marketing authorisation was introduced, and in 2019 a new pathway for ultra-orphan medicines was introduced.2 Both these new policies enable the SMC to recommend conditional access while data is collected to support a full submission to assess a medicine’s cost and clinical effectiveness. As newly introduced processes, it is not yet possible to examine the impact within this current research due to the limited number of medicines which have been through the system during this timeframe.

How can we bridge the “uncertainty” gap?

It is accepted that as new medicines become more complex, Scotland’s HTA process will need to evolve and adapt to ensure that they reflect this increasing complexity and manage uncertainty where medicines are accelerated at the regulatory stage.

NICE and NHS England are already taking steps to update and improve the access to medicines system. Reforms to the access process for cancer medicines, for example, have allowed conversations with NICE and manufacturers to begin at a much earlier point, while the Cancer Drugs Fund (CDF) was reformed to become a “managed access fund”. This gives patients the ability to access new cancer drugs, while the NHS collects real-world data about the impact that the medicine can have during an agreed time period. NICE is undergoing a methods review in 2020 and along with the publication by NHS England of the Commercial Framework, there is an opportunity to expand the reform to other disease areas. It is important that the SMC and NHS Scotland, like NICE, continue to review and reform processes to facilitate early engagement with manufacturers and support access to new and innovative medicines.

For medicines which receive accelerated regulatory approval, it would benefit both the SMC and manufacturers to have a process of early engagement to support earlier submissions. This could also help to reduce the rate of resubmissions and ultimately make more efficient use of use of SMC time and resources. There is acknowledgement that this additional step may extend submission timelines.

The importance of data as a foundation upon which the outcomes of medicines can be assessed is widely considered to be central, not just to any proposed reform, but to support the ongoing functioning of the HTA process.

Real-World Evidence

Collecting real-world data can be a useful way of improving the way NHS resources are allocated and of informing and improving the quality of HTA submissions, particularly for those medicines that are granted early regulatory approval.

The introduction of the SMC's new Ultra-Orphan Pathway and the Interim Acceptance Process allows the NHS the opportunity to determine a medicine's capabilities from data collection and real-world evidence.

The National Digital Platform3 presents a huge opportunity to improve the collection and use of data at the population and individual level, however it is anticipated that this will not be fully implemented until 2030 therefore there is a need to develop an interim solution which can support the development of NHS data capabilities. Central to this will be the need for HEPMA (Hospital Electronic Prescribing Medicines Administration) to be rolled out into all hospitals in Scotland as a matter of urgency.

The potential for better data capabilities within the NHS exceed the introduction of new and innovative medicines; data can shape services and are at the heart of NHS future sustainability. A recent Audit Scotland report4 called on the Scottish Government, in partnership with NHS Boards, and Integration Authorities to improve the quality and availability of data and information to allow better performance monitoring, inform service redesign and improve care co-ordination by enhancing how patient information is shared across health and social care services.
The Data Scoping Taskforce, led by Professor Andrew Morris, assessed Scotland's existing data capabilities and identified five key actions to support the assessment and introduction of new medicines going forwards5. These are as follows:

1. Capture medicines use for all patients in all clinical settings
2. Include medicine indication in all prescribing systems and by all prescribers
3. Create a national laboratory data resource
4. Improve recording of patient outcomes
5. Create a Scottish Medicines Intelligence Unit

All of which would significantly enhance NHS Scotland's health data capabilities and enable suitable data to be collected for HTA and supporting the implementation of more flexible pricing arrangements.

THE WAY AHEAD

A wider variety of real-world data should be collected about the effectiveness of medicines, from large scale "big data" to smaller data sets for rarer conditions. This information should be used in the access and reimbursement process – where appropriate, supporting a "managed access" system, as is already seen in England via the CDF.

The NHS, social care, patient groups and the pharmaceutical industry should work collaboratively to identify sources of data that could be used to support decision making.

Flexible Pricing Models

Under the current SMC processes, manufacturers typically agree one price for a medicine with PASAG (Patient Access Scheme Advisory Group), regardless of the different conditions (or indications) the medicine is used for, or the outcomes achieved by patients. Alternative access methods can be facilitated through a process known as "complex patient access schemes". Acceptance of these schemes are relatively rare and are discouraged due to service capacity and data capability issues.

If there is clinical uncertainty, then it follows there will be economic uncertainty and more flexibility will be needed regarding pricing. There is an increasing recognition that the system should be reformed to allow for more flexible reimbursement to manage this uncertainty. A single medicine may treat many different conditions where the patient population, expected clinical outcomes and availability of other medicine options could be completely different. Flexible or multiple-indication pricing would allow the NHS and SMC to agree different prices for the same medicine. It might be an agreement to offer a drug at different prices to ensure the medicine is cost effective for the NHS when it is used to treat different types of disease, or a different payment scheme depending on the outcome achieved by patients. However flexible pricing models require data and it is acknowledged that while the SMC and PASAG have stated they would like to be able to support the introduction of more complex/flexible pricing solutions, the NHS data systems cannot currently support this introduction. For example, medicines are dispensed from a hospital pharmacy to the ward

or clinic, not the individual therefore there is no information on the indication that the medicine is being used for. Current hospital prescribing systems are not designed to support the adoption of multiple indication pricing.

The complexity of pricing is a challenge for the service, but data is at the heart of the solution for this and it will require a system change.

One of the administrative challenges is that, in a necessarily confidential process, companies do not have oversight of accepted schemes so multiple versions of complex pricing schemes continue to be brought forward. As more complex medicines are developed and particularly where there is uncertainty, the availability of complex schemes, including but not limited to multi-indication pricing or outcomes-based payments could support access to these treatments. Greater consideration needs to be given to how the NHS in Scotland can accommodate greater flexibility and actively support the development of processes (and resources) to support their use. While PASAG works with companies to develop a workable model, the challenge remains that within the current system it is difficult to determine a complex PAS that doesn't place a significant cumulative burden on pharmacies or senior clinical staff to deliver.

EXAMPLE: CRUK OUTCOMES BASED PAYMENTS6

Cancer Research UK is currently trialing an "outcomes-based payments" model in Greater Manchester. This system would see the price paid for a course of treatment depend on the clinical benefit each patient receives. This type of flexible reimbursement could also allow the price of a medicine to change over time, depending on the impact of the medicine on clinical practice and patient outcomes in the real world.

There have been recent examples of commercial arrangements being reached by companies and the NHS to help make innovative treatments available to patients using flexible approaches. As more personalised medicines for smaller patient populations become available, it will be important for this type of innovative and flexible arrangement to become the norm in patient access, rather than being an approach applied only to access challenges that are the most difficult to resolve. This is a fundamental shift which requires organisational collaboration.

THE WAY AHEAD

Differential pricing by disease approaches, including indication based-pricing and outcomes-based pricing should be more widely adopted by NHS Scotland.

In line with recommendations of the Data Scoping Taskforce, the Scottish Government should establish a multi-agency working group to look at the opportunities for developing a more accessible approach to innovative pricing schemes, with defined objectives and timelines for delivery.

Effective Resourcing

There are exciting opportunities to transform the way the NHS makes medicines available to patients. But these changes are not simple or straightforward and there are several practical challenges that need to be overcome in order to make these reforms a success.

Collecting real-world data about the use of new medicines and mapping patient outcomes to measure clinical effectiveness are all complex changes that could take significant resource. In the long run, these changes can provide greater value for the NHS, but they will require upfront investment to be put in place effectively. NHS Scotland must dedicate enough resources to this process, without overburdening clinicians for example, by providing additional staff time for data collection processes. The life sciences sector should also consider how it can provide support to make this a reality. This could include sharing expertise, infrastructure or staff secondments where particular experience is required.

THE WAY AHEAD

Sufficient resources should be dedicated to delivering changes to the access to medicines process in order to avoid the burden of data collection being placed onto already over-worked clinicians. Industry should be willing to share expertise, staff and other resources where possible.

Early Engagement

The SMC relies on data provided by companies and operates a different approach than that of NICE. While better dialogue with the SMC is desirable overall, those medicines under discussion will present a challenge for the HTA process, therefore early engagement would help to drive a company's submission and maximise the impact of these medicines should they receive a positive recommendation.

The SMC/Healthcare Improvement Scotland proactively engage with all companies where medicines receive Promising Innovative Medicine (PIM) designation prior to an Early Access to Medicines Scheme (EAMS) application to enable early dialogue. The EAMS aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is clear unmet medical need. However, for medicines that do not fall into this category, there is a view that early engagement with companies particularly where medicines are given early regulatory approval would be valuable.

THE WAY AHEAD

The SMC should consider whether it is possible to establish a routine process for early engagement with companies where medicines are granted early regulatory approval to allow early discussion around anticipated challenges.

Patient Involvement/Engagement

The introduction of the PACE process has been widely regarded as a significantly positive approach to the appraisal of medicines, particularly to capture those elements which would not come through the clinical and economic appraisal of a medicine, and patient representation at the SMC meeting offers an additional perspective to the decision making process.

But where do patients fit in to make sure that the system is best dealing with uncertainty? This is a challenging question that requires further consideration at all aspects of the HTA process.

THE WAY AHEAD

Companies should be encouraged to involve patients in trial design and work with scientists to reflect on what is important to patients. This could produce more meaningful evidence that can add value to an HTA submission. Giving cognisance to the difficulties associated with small patient numbers this evidence need not necessarily be based only on Scottish patient data.

About Bridging the Gap

The Bridging the Gap research was produced by IQVIA and funded by AbbVie. IQVIA is a leading global provider of advanced analytics, technology solutions and contract research services to the life sciences industry, dedicated to delivering actionable insights. A further “deep dive” of the research into the Scottish Data was commissioned to explore some of the data in more detail.

In December 2019, AbbVie hosted a roundtable discussion, chaired by Lewis Macdonald MSP, Chair of the Scottish Parliament Health Committee and attended by members of the SMC Executive, PASAG, Scottish Government, Industry representatives, Patient Advocacy Groups, and Academics (see Appendix 1). The recommendations in this report have been developed by Abbvie, informed by discussions at this roundtable meeting.

About AbbVie

AbbVie is a global, research-driven biopharmaceutical company committed to developing innovative advanced therapies for some of the world's most complex and critical conditions. The company's mission is to use its expertise, dedicated people and unique approach to innovation to markedly improve treatments across four primary therapeutic areas: immunology, oncology, virology and neuroscience. In more than 75 countries, AbbVie employees are working every day to advance health solutions for people around the world.

If you would like to get in touch with AbbVie regarding the Bridging the Gap research and the work we are doing in this area, please contact gail.grant@abbvie.com.

For more information about AbbVie, please visit us at www.abbvie.co.uk

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Appendix 1

List of Meeting Participants

Auld, Sandra	Healthcare Public Affairs
Corry, Maurice	Member of Scottish Parliament
Culpan, Alison	Director, ABPI Scotland
Downes, Noreen	SMC Executive
Gilmour, Christine	PASAG
Grant, Gail	AbbVie Ltd
Hill, Scott	SMC Executive
Jones, Gary	AbbVie Ltd
Macdonald, Alan	SMC Executive
Macdonald, Lewis	Member of Scottish Parliament (Chair)
McMahon, Catriona	SMC Industry Representative
Mowbray, Katie	AbbVie Ltd
Muller, Tanith	Parkinson's UK (Scotland)
Roden, Jonathan	Cancer Research UK
Stevenson, Greg	Roche
Strath, Alison	Scottish Government
Strong, Andrew	The Alliance
Van Der Meer, Robert	University of Strathclyde

Appendix 2

1Scottish Medicines Consortium Patient and Clinician Engagement (PACE) Meetings Overview. Available at: https://www.scottishmedicines.org.uk/media/4731/pace-overview-document.pdf [last accessed December 2019]

2Scottish Medicines Consortium How we make our decisions. Available online at: https://www.scottishmedicines.org.uk/how-we-decide/ [last accessed December 2019]

3NHS Education for Scotland Digital Service. Available at: https://nds.nes.digital/ [last accessed December 2019]

4Audit Scotland, NHS in Scotland 2019. Available online at: https://www.audit-scotland.gov.uk/report/nhs-in-scotland-2019 [last accessed May 2020]

5Data Scoping Taskforce, Medicines Use and Digital Capabilities, September 2018. Available online at: https://www2.gov.scot/Resource/0054/00540468.pdf [last accessed December 2019]

6Cancer Research UK Making Outcome-Based Payment a Reality in the NHS, February 2019. Available at: https://www.cancerresearchuk.org/sites/default/files/obp_final_report_pdf.pdf [last accessed December 2019]


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