Bridging the Gap 3.0

Exploring the evolution of medicines regulatory policy in the UK

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Introduction

On 2 December 2021, AbbVie convened a virtual roundtable to explore the future of medicines regulation in the context of ongoing reform to the UK's regulatory environment, following the UK's exit from the EU and in light of innovative approaches to regulation that emerged during the pandemic.

The roundtable, which brought together representatives from patient groups, professional organisations, and policymakers, considered opportunities for the future of medicines regulation and drew insights from IQVIA research commissioned by AbbVie on trends within the global regulatory environment. A full list of participants can be found in the 'About Bridging the Gap' section.

This document contains AbbVie's reflections from the discussion, which participants have had the opportunity to comment on. This document should not be seen as an endorsement by participants.

This report includes:

- **Policy recommendations**
- **Overview of recent developments in the UK regulatory landscape**
- **High-level summary of the research**
- **An overview of the opportunities to improve regulatory policy**
- **About Bridging the Gap**
- **Information about AbbVie**

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Policy recommendations

Based on stakeholder discussions, including the expert group roundtable, and the findings of the Bridging the Gap research, AbbVie has developed the following recommendations for the evolution of the UK's regulatory processes:

1

National debate around defining unmet need

There is a pressing need for a national conversation regarding how "unmet need" is defined and determined to inform and underpin regulatory incentivisation and acceleration programmes applicable across a wide range of conditions, beyond oncology. The patient voice must be central to this discussion in determining the components of any criteria used to establish unmet need.

The MHRA should launch a consultation exercise, open to patient organisations and other relevant stakeholders, regarding the definition of unmet need and its incorporation into existing and future processes, supported by the Department of Health and Social Care. As part of this, industry should look to identify practical solutions on how unmet need could be defined within the regulatory and policy environment.

2

International partnership

In a globalised regulatory environment, deepening existing international partnerships and creating new agreements with likeminded partners will be critical for the future of the MHRA's success outside of the EU. The Access Consortium and Project Orbis are examples of where work sharing and partnership have benefited the MHRA, and provide a model for future agreements which can deliver additional regulatory capacity and best practice and knowledge sharing.

The MHRA should explore membership of additional international cooperation schemes in areas of mutual benefit.

3

Connectivity with the local health system

Greater strategic alignment is needed between regulatory and health technology assessment bodies to ensure early access schemes and pathways complement and support the objectives of one another. For instance, HTA bodies must take into account trends towards earlier approval at the regulatory stage to ensure gaps in licensing and approval timelines are reduced.

Frameworks which govern existing schemes and pathways should be periodically reviewed to ensure that earlier approval at the regulatory stage is adequately aligned with the health technology assessment stage, given the uncertainty that will be naturally inherent to an earlier approval. The Innovative Licensing and Access Pathway (ILAP) is a welcome introduction, in that regard, delivered jointly between regulatory and HTA bodies.

Establishing broader representation on steering groups which govern early access schemes could also help to achieve greater connectivity between stakeholders – with a clear role for patient groups and local health systems.

4

Addressing uncertainty

All innovation is associated with a degree of uncertainty, which the MHRA seeks to address through a variety of mechanisms. Real-world evidence can help to address uncertainties in the assessment of innovations and health technologies, and allow safe and proven innovations to reach people faster. Earlier regulatory approvals and demand for early access has also led to increased uncertainty at the HTA level.

The MHRA and HTA bodies should explore what reforms may be necessary to address uncertainty, including the utilisation of real-world evidence for marketing authorisation assessments, and whether this can be supported through current NHS data capabilities. In addition, HTA bodies must find new ways to dealing with increased uncertainty resulting from earlier licensing decisions to bridge the gap.

A new collaborative partnership between the MHRA, HTA bodies, and NHS payers would help deliver coordination within the health system on overcoming uncertainty, such as through the utilisation of real-world evidence. This would have the dual benefit of addressing common challenges in both regulatory and HTA decision-making.

5

Comprehensive funding review

The increasing volume of marketing authorisation submissions, combined with rising demand and an ambitious programme for the future of the MHRA, necessitates that resources and investments are appropriately matched to effectively manage capacity – a trend which is also experienced by health technology assessment bodies.

In addition, innovative programmes and initiatives across agencies must be fully resourced and funded in order to reach their ambitious potential. Capacity must allow delivery beyond the everyday core competencies to sustain the UK's globally unique life sciences offering.

The UK Government should work with the devolved administrations to set out a comprehensive review of the funding of the MHRA, NICE, SMC, and AWMSG – accompanied by a shared vision for the future of the UK's world-leading regulatory and assessment bodies.

Overview of recent developments in the UK regulatory landscape

Following the UK's departure from the EU, the UK is currently undergoing a comprehensive transformation of clinical research and healthcare regulatory policy.

In July 2021, the Medicines and Healthcare products Regulatory Agency (MHRA), published its new Delivery Plan (2021-2023) which set out deliverables and objectives for reform, including the ambition to evolve and strengthen the UK's regulatory framework so that it looks to the future and keeps pace with fast-moving life science developments.[1]

The UK Life Sciences Vision set out wider ambitions for the life sciences sector over the next decade.[2] It commits the MHRA to faster regulatory assessments and decisions, including through new and innovative regulatory models, building on the Early Access to Medicines Scheme (EAMS) and the Innovative Licensing and Access Pathway (ILAP). The Vison also tasks the MHRA with developing and strengthening international partnerships with like-minded regulators, visible through the UK's membership of Project Orbis[3] and the Access Consortium.[4]

Ongoing policy developments present unique opportunities to ensure UK life sciences regulation is both flexible and forward-facing to adapt and respond to the future of technology. Traditionally, regulation lags behind technological advances witnessed in most sectors of the economy, with government and policymakers having to play catch-up. For the UK to maintain its positioning as a global scientific power, opportunities to future-proof regulation must be grasped, as explored in the Association of the British Pharmaceutical Industry's (ABPI) recent vision paper.[5] The 150-day assessment process for high-quality marketing authorisation applications is an example of how the UK can demonstrate its commitment to early medicine access.[6]

Future policy changes must also take into account learnings from the pandemic, in particular the innovation and flexible approaches to regulation adopted by the MHRA in the assessment of COVID-19 vaccines and therapeutics.

High-level summary of the research

Research undertaken by IQVIA, commissioned by AbbVie, found that international regulators are deploying a range of methods to help meet continually growing demand and evolving population health needs.[7] High-level points of note can be found below, broken down into the thematic areas of the roundtable discussion.

Keeping pace with early access policy

- Regulators use a wide range of different combinations of expedited approval processes for medicines, with priority reviews being the most common in oncology and other therapy areas
- Broadly, regulators use two approaches to expedite marketing authorisation. The first approach aims to accelerate the review process. The second aims to reduce the time to authorisation by permitting use of early phase data when applying for review

The role of incentivisation

- Regulators frequently provide incentives for the development of orphan drugs, including fee waivers, grants and tax incentives, and market exclusivity, leading to investment in related therapy areas

- Oncology medicines seem to be more able to demonstrate the criteria of unmet medical need within the four regulatory agency pathways examined, representing 62% of all expedited approvals

Regulatory capacity

- Globally, expedited approvals are showing an overall upward trend since 2016. In the USA, regulators have granted expedited approval to at least 60% of new drugs approved in each of the past five years
- The proportion of expedited approvals by region continues to change. In the past twelve months, the European Medicines Agency has doubled the total proportion of expedited approvals. Regulators in Japan have reduced their expedited approvals but still have the highest proportion of approvals expedited
- The volume of early phase data used for regulatory approval is growing. In 2020/21, 269 approvals utilised early phase data, compared to 56 in 2018/19. However, the proportion of approvals based upon early phase data has been constant, with 25% of all approvals utilising earlier phase trial data, on average

Opportunities to improve regulatory policy

During the expert group roundtable, participants discussed the challenges in enabling greater patient access to innovative health technologies in the UK, and how future regulatory reform could overcome these hurdles.

These opportunities to improve UK regulatory policy, which included practical policy recommendations to be considered by policymakers and government, were broadly divided into the following thematic areas:

- **Keeping pace with early access**
- **Role of incentivisation**
- **Regulatory capacity**

Keeping pace with early access

The introduction of the ILAP is designed to accelerate the process in which a medicine is licenced and made available on the market;[8] a new mechanism that has been welcomed by the UK life sciences sector. However, there is a recognition that broader reform is needed to keep pace with earlier access.

There is recognition that an increased use of real-world evidence would be particularly transformative for enabling earlier and wider access to medicines. The National Institute of Health and Care Excellence (NICE) has accepted that a greater use of real-world evidence could allow for medicines to be further recommended for use in patient populations where it is currently limited.[9] Bringing such changes to the regulatory process, together with approval processes, would help manage uncertainty ahead of marketing authorisation.

Patient centricity is key to ensuring that mechanisms designed to speed-up marketing authorisation meet population needs. Going forward, the perspectives of healthcare users must be embedded in decision making around the development of early access policy, and the evaluation of individual technologies and decision making must be transparent. Otherwise, there is a risk that health technologies which do not align with population needs are inessentially expedited to market. More generally, regulators should consider the health outcomes which are valued greatest by people – ensuring that their focus meets the expectations of healthcare users, and that the views of a wide-range of communities are sought.

UK regulators must also take advantage of the wide range of expertise among likeminded partners, both internationally and domestically. Project Orbis and the Access Consortium are both welcome collaborative agreements and, going forward, the UK must take advantage of new partnerships to expand its regulatory best practices, while using horizon scanning to stay ahead of other leading regulators. Domestically, better partnerships with academia, patient groups and industry would help the MHRA to access more valuable insights into areas of importance for healthcare users.

CASE STUDY

Globally, a range of expedited regulatory pathways support earlier access to innovative medicines[10]

United States of America	**Food and Drugs Administration** • Accelerated Approval • Breakthrough Therapy • Fast Track • Priority Review
Canada	**Health Canada** • Priority Review • Notice of Compliance with Conditions
European Union	**European Medicines Agency** • PRIME (PRIority MEdicines) • Conditional Approval • Compassionate Use
Japan	**Pharmaceuticals and Medical Devices Agency** • Priority Review • Conditional Accelerated Approval Scheme • Sakigake Designation (for products first developed in Japan)
United Kingdom	**Medicines and Medical Devices Agency** • Innovative Licensing and Access Pathway • Early access to medicines scheme

International partnership

In a globalised regulatory environment, deepening existing international partnerships and creating new agreements with likeminded partners will be critical for the future of the MHRA's success outside of the EU. The Access Consortium and Project Orbis are examples of where work sharing and partnership have benefited the MHRA, and provide a model for future agreements which can deliver additional regulatory capacity and best practice and knowledge sharing.

The MHRA should explore membership of additional international cooperation schemes in areas of mutual benefit.

Addressing uncertainty

All innovation is associated with a degree of uncertainty, which the MHRA seeks to address through a variety of mechanisms. Real-world evidence can help to address uncertainties in the assessment of innovations and health technologies, and allow safe and proven innovations to reach people faster. Earlier regulatory approvals and demand for early access has also led to increased uncertainty at the HTA level.

The MHRA and HTA bodies should explore what reforms may be necessary to address uncertainty, including the utilisation of real-world evidence for marketing authorisation assessments, and whether this can be supported through current NHS data capabilities. In addition, HTA bodies must find new ways to dealing with increased uncertainty resulting from earlier licensing decisions to bridge the gap.

A new collaborative partnership between the MHRA, HTA bodies, and NHS payers would help deliver coordination within the health system on overcoming uncertainty, such as through the utilisation of real-world evidence. This would have the dual benefit of addressing common challenges in both regulatory and HTA decision-making.

Connectivity with the local health system

Greater strategic alignment is needed between regulatory and health technology assessment bodies to ensure early access schemes and pathways complement and support the objectives of one another. For instance, HTA bodies must take into account trends towards earlier approval at the regulatory stage to ensure gaps in licensing and approval timelines are reduced.

Frameworks which govern existing schemes and pathways should be periodically reviewed to ensure that earlier approval at the regulatory stage is adequately aligned with the health technology assessment stage, given the uncertainty that will be naturally inherent to an earlier approval. The Innovative Licensing and Access Pathway (ILAP) is a welcome introduction, in that regard, delivered jointly between regulatory and HTA bodies.

Establishing broader representation on steering groups which govern early access schemes could also help to achieve greater connectivity between stakeholders – with a clear role for patient groups and local health systems.

Role of incentivisation

Given the relative size of the UK market, any incentivisation scheme adopted at the domestic level alone would be unlikely to achieve the desired outcome of facilitating greater innovation within a specific area. Instead, incentivisation schemes would have a more demonstrable impact on the market if organised and agreed through international partnerships. The MHRA should look to take a leading role globally in defining the areas of science to incentivise. This would also have the effect of boosting Britain's position as a global scientific power, and preparing the MHRA as a regulator for the future and of emerging science.

Until recently there were no incentivisation schemes around combatting anti-microbial resistance, deemed to be a "dominant global health concern" by the United Nationals General Assembly and a national policy priority in the UK. The UK has since taken steps to address this imbalance through its pioneering scheme to provide new antibiotics to NHS users.

Beyond international approaches to incentivising research and development, the MHRA must also work with its domestic partners – such as NICE – to determine and implement local policies that are able to accelerate patient access in areas that are aligned to national healthcare needs and priorities, as demonstrated by the approach adopted by the MHRA during the COVID-19 pandemic.

Any incentivisation within the regulatory process would need to be targeted and focused to have the desired effects. The criteria in which incentivisation is used should be determined upon its ability to improve outcomes and meet specifically identified national priorities, as opposed to condition-specific focuses such as oncology or orphan medicines, determined through a process involving patients.

Many healthcare systems employ a concept of "unmet need" as a measure for determining where policies and programmes may have the greatest impact on the population. Unmet need is often used to determine a technology's eligibility for expedited approvals, and is most used for oncology medicines[11] – often due to the life-threatening nature of the disease and a lack of clear alternative treatment options.[12] Existing schemes adopted by the MHRA are centred around "high unmet need" supported by condition severity.[13] However, current definitions lack the necessary specificity to be used effectively and are in need of revisiting. Developing a clear definition of unmet need could be a key determinant for incentivisation across a wide range of conditions where greater innovation is needed, beyond oncology. Going forward, the MHRA should work with system and international research partners to define a more comprehensive definition of unmet need which could be used to make incentivisation criteria applicable across a wide range of conditions.

Whilst it remains important for the MHRA to accelerate products to markets where there are high levels of unmet need present, it is also true that the prioritisation or acceleration of particular technologies will consequently lead to the deprioritisation of others. It is, therefore, crucial that such acceleration schemes match national policy priorities, as explored above.

CASE STUDY

Incentivising orphan drug development has led to investment in related therapy areas[14]

Each regulator offers incentives to industry to develop orphan drugs; in 2019, 44% of 'novel' drug approvals in the USA were approved to treat rare or "orphan" disease.

Food and Drug Administration

- Grant program
- Fee waivers
- Tax credits and other financial incentives
- Protocol assistance
- Can be provided as 'Parallel Advice' co-ordinated with EMA
- 7 years market exclusivity

Health Canada

- Less mature orphan framework than other regulators
- However, orphan drugs can qualify for similar support as that available in other regions

European Medicines Agency

- Protocol assistance
- Can be provided as 'parallel advice' co-ordinated with the FDA
- 10 years market exclusivity
- Additional incentives for micro, small and medium-sized enterprises (SMEs)
- Reduced fees
- Grants and tax incentives managed by member states

Pharmaceuticals and Medical Devices Agency

- Guidance and consultation
- Fee waivers, tax credits and other financial incentives
- Entry into expedited regulatory process (Priority Review)
- 10 years market exclusivity

National debate around defining unmet need

There is a pressing need for a national conversation regarding how "unmet need" is defined and determined to inform and underpin regulatory incentivisation and acceleration programmes applicable across a wide range of conditions, beyond oncology. The patient voice must be central to this discussion in determining the components of any criteria used to establish unmet need.

The MHRA should launch a consultation exercise, open to patient organisations and other relevant stakeholders, regarding the definition of unmet need and its incorporation into existing and future processes, supported by the Department of Health and Social Care. As part of this, industry should look to identify practical solutions on how unmet need could be defined within the regulatory and policy environment.

Regulatory capacity

The growth and rapid evolution of health technologies requires regulators to effectively manage their capacity to ensure healthcare users have early access to safe and high-quality medicines.

During the COVID-19 pandemic, the simplification of assessment processes allowed regulators to rapidly assess new antivirals and vaccines while maintaining strict safety standards, effectively freeing-up additional capacity in the system while getting treatments to people faster.[15,16,17] This crucial learning must be incorporated into the MHRA's standard assessment pathways; effectively reducing delays within the regulatory process caused by administrative burdens, while ensuring no compromise on quality or safety. However, this will not be sufficient in isolation to address the burden on the MHRA.

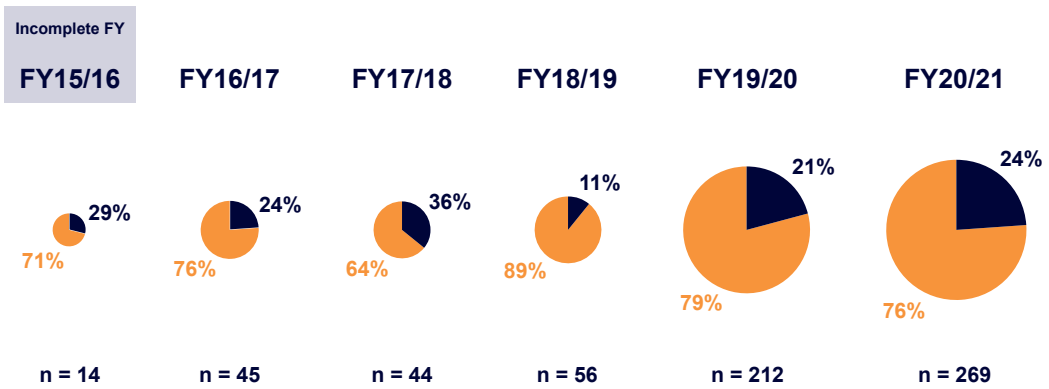
There is a need to kick-start a national conversation on the role and priorities of the MHRA in order to help it manage the increasing demand that it is experiencing in recognition that the MHRA's capacity is finite. It will be necessary, as part of this exercise, to explore the resourcing requirements of the regulator. The increasing expectations placed on the MHRA must be met with further funding and resourcing to match national policy ambitions, creating the headroom for regulatory innovation and renewal as well as the provision of core functions.

Furthermore, strengthening existing, and establishing new, international partnerships, can help bring additional capacity benefits to the UK regulator through best practice and work sharing arrangements, such as that delivered by the Access Consortium.

CASE STUDY

The volume of early phase data used for regulatory approval is growing[18]

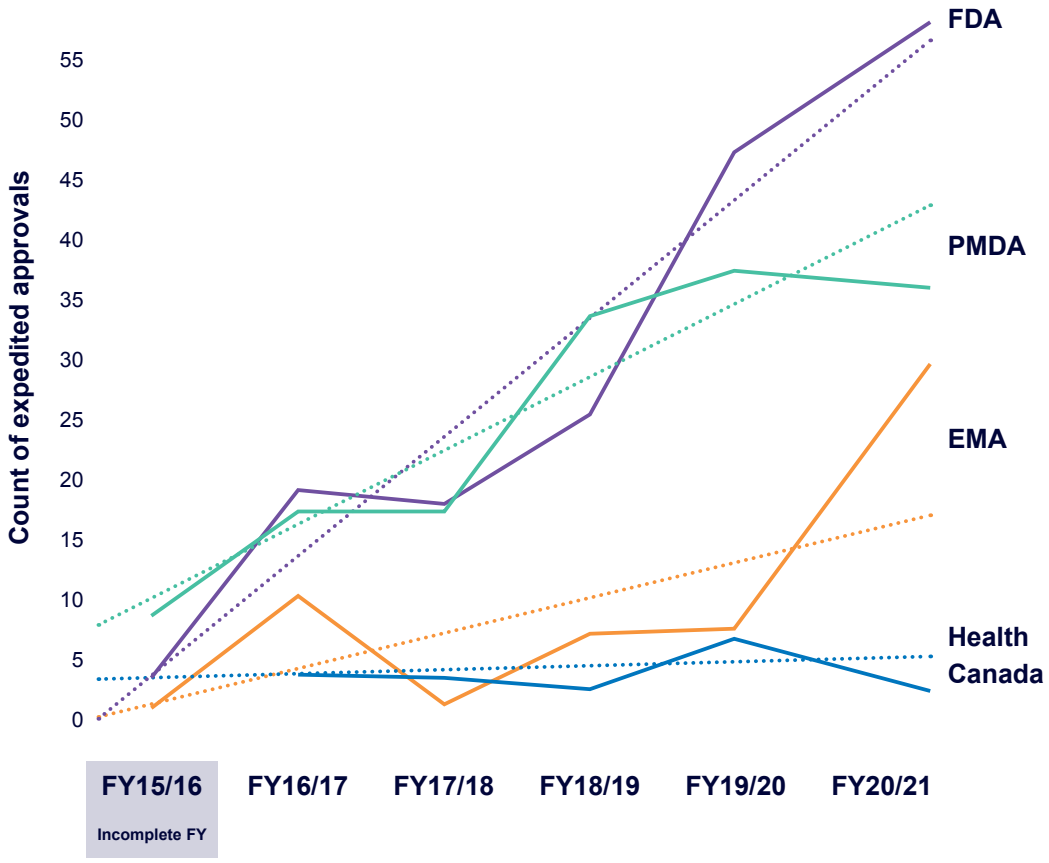
The total number of approvals is increasing, however, the proportion of approvals based upon early phase data is constant.



CASE STUDY

Globally, expedited approvals are showing an overall upward trend since 2016[19]

This 'performance' is establishing a "new normal" that is transforming medical decision-making for patient groups with high unmet needs.



Comprehensive funding review

The increasing volume of marketing authorisation submissions, combined with rising demand and an ambitious programme for the future of the MHRA, necessitates that resources and investments are appropriately matched to effectively manage capacity – a trend which is also experienced by health technology assessment bodies.

In addition, innovative programmes and initiatives across agencies must be fully resourced and funded in order to reach their ambitious potential. Capacity must allow delivery beyond the everyday core competencies to sustain the UK's globally unique life sciences offering.

The UK Government should work with the devolved administrations to set out a comprehensive review of the funding of the MHRA, NICE, SMC, and AWMSG – accompanied by a shared vision for the future of the UK's world-leading regulatory and assessment bodies.

About Bridging the Gap 3.0

The Bridging the Gap 3.0 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.

This new research explores the challenges to enabling greater patient access to innovative health technologies, and how future regulatory reform could address these challenges in the context of the UK's withdrawal from the EU. As part of the Bridging the Gap series, this report follows previous research which examined the gap between accelerated medicines processes and health technology assessment evaluations which cause delays in the time to patient access.

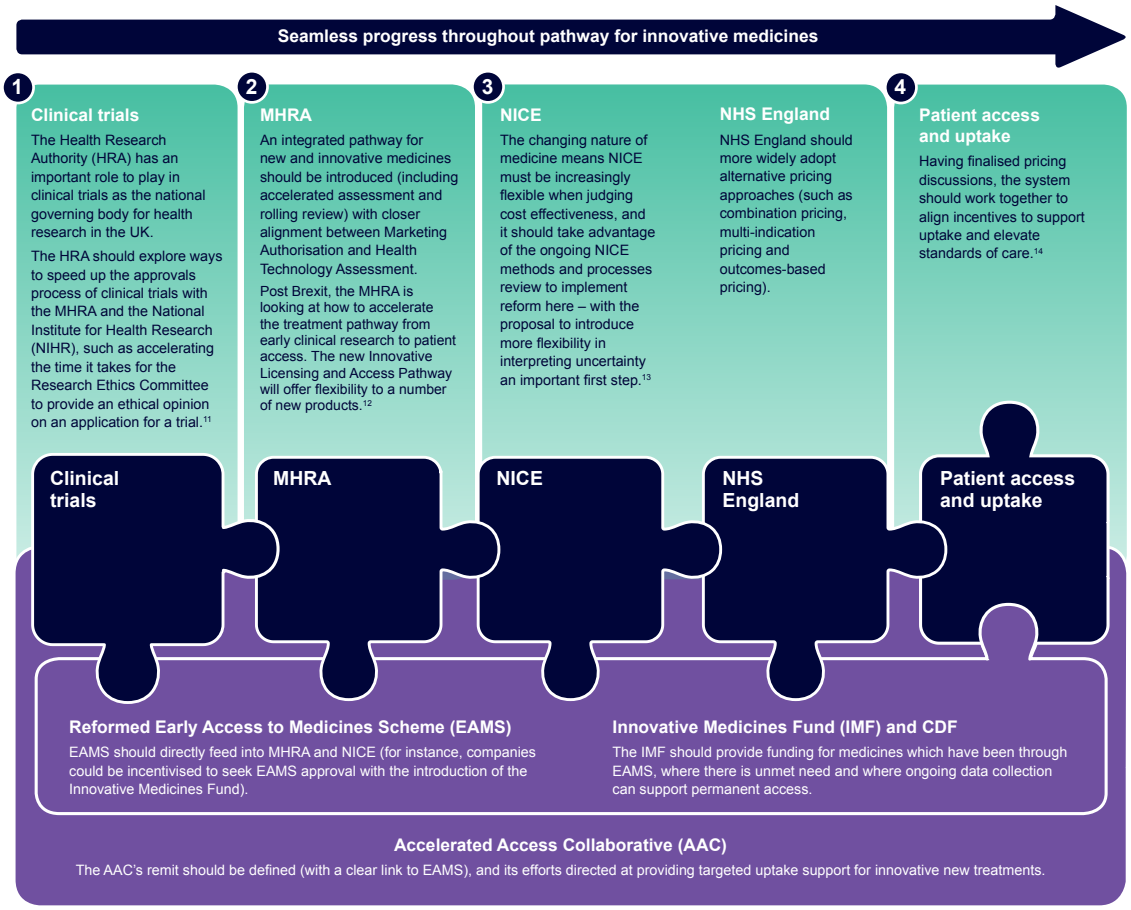
The recommendations in this report were developed by AbbVie following discussions with representatives from patient groups, professional organisations, and policymakers at a virtual expert group roundtable in December 2021, with participant organisations listed below.

- **Alzheimer's Research UK**
- **Anthony Nolan**
- **Association of Medical Research Charities**
- **Association of the British Pharmaceutical Industry**
- **Breast Cancer Now**
- **Cancer Research UK**
- **Department for Health and Social Care**
- **Ethical Medicines Industry Group**
- **Genetic Alliance**
- **The Institute of Cancer Research**
- **Leukaemia Care**
- **Muscular Dystrophy UK**
- **Office for Life Sciences**
- **Office of Health Economics**
- **Tuberous Sclerosis Association**

Participation at the roundtable does not indicate endorsement of this report.
The National Institute for Health and Care Excellence (NICE) were observers to the roundtable.

Creating a streamlined access pathway in England

As part of AbbVie's commitment to identifying practical policy solutions to enabling innovative medicines to reach people sooner, we previously examined the need for greater reform across the whole pathway – producing a streamlined model of England, found below.



About AbbVie

AbbVie is a global, research and development-based biopharmaceutical company committed to developing innovative advanced therapies for some of the world's most complex and critical conditions. We are focused on developing and delivering transformative therapies to deliver a remarkable impact for patients in the UK.

Over 60,000 patients were receiving AbbVie medicines in the UK in 2018, 5 AbbVie medicines have a manufacturing or production process in the UK, and we have 13 partnerships with the NHS and healthcare providers across the UK.

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 (gail.grant@abbvie.com).

References

1 Medicines and Healthcare products Regulatory Agency, Delivery Plan 2021-2023, July 2021

2 Department for Business, Energy & Industrial Strategy, Life Sciences Vision, July 2021

3 Medicines and Healthcare products Regulatory Agency, Guidance on Project Orbis, December 2020

4 Medicines and Healthcare products Regulatory Agency, Guidance: Access Consortium, December 2020

5 Association of the British Pharmaceutical Industry, UK medicines regulatory policy and global influence in a post-pandemic world, November 2021

6 MHRA, 150-day assessment for national applications for medicines, December 2020

7 AbbVie (Data on File), 2022

8 Medicines and Healthcare products Regulatory Agency, Guidance: Innovative Licensing and Access Pathway, December 2021

9 National Institute for Health and Care Excellence, Increasing use of health and social care data in guidance development, undated

10 AbbVie (Data on File), 2022

11 Wang, S. et al, An overview of cancer drugs approved through expedited approval programs and orphan medicine designation globally between 2011 and 2020, December 2021

12 AbbVie (Data on File), 2022

13 MHRA, PIM Designation – Step I of EAMS, April 2014

14 AbbVie (Data on File), 2022

15 Speder, B., Rolling reviews: a useful tool to speed up the regulatory review process, May 2021

16 Medicines and Healthcare products Regulatory Agency, Summary of the Public Assessment Report for COVID-19 Vaccine Pfizer/BioNTech, December 2021

17 Medicines and Healthcare products Regulatory Agency, Guidance: MHRA regulatory flexibilities resulting from coronavirus (COVID-19), August 2020

18 AbbVie (Data on File), 2022

19 AbbVie (Data on File), 2022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