NICE Methods Review:

A report of the All-Party Parliamentary Group on Access to Medicines and Medical Devices

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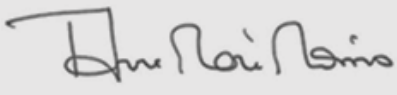
Foreword

I am delighted to present the first report of the APPG on Access to Medicines and Medical Devices. This Group, which was founded in Autumn 2018, has gathered evidence from stakeholders across the life sciences eco-system, including companies, patients, clinicians, economists and NICE, to draw together recommendations about how the UK can keep up with the ever-evolving scientific landscape.

The life sciences industry in the UK is worth £70 billion, and brings 241,000 jobs to the UK[i]. This huge asset to our economy sees large numbers of clinical trials being run in the UK, European headquarters being set up in the UK, and the best talent attracted to the country from around the world.

However, there is a huge challenge to ensure that technologies that are developed and tested by clinical trials in the UK, and commercialised by companies with offices in the UK, are accessible to patients on the NHS. There is evidence to show that the UK falls behind other countries in access to some treatments. For example, in England, Scotland and Wales, less than 50% of orphan medicines are routinely funded, compared to over 80% in France and Germany[ii]. Furthermore, the uncertainty around Brexit suggests it is important now, more than ever, that companies feel able to invest in the UK and launch their treatments here. Brexit offers threats and opportunities; both of which we must prepare for by making best use of these assets.

With this context in mind, the Group saw an opportunity in the forthcoming NICE methods review to investigate the broad range of views across stakeholders in the UK life sciences sector, and develop recommendations for NICE, NHSE, DHSC, BEIS, and government more broadly at this early stage of the process. We hope that these recommendations, based on the written and oral evidence of over 50 individuals and organisations across this ecosystem, will be taken into account as the scope and governance of the review is announced, and the work gets underway.



Anne Marie Morris MP
Chair of the APPG on Access to Medicines and Medical Devices

EXECUTIVE SUMMARY

In response to the changing life sciences access landscape, and the increasingly complex and innovative therapies that are in development, the APPG on Access to Medicines and Medical Devices (hereafter referred to as 'the APPG') set out to gather evidence to feed into NICE's methods review.

The APPG gathered written and oral evidence, hearing from over 50 individuals and organisations from across the life science sector. The Group sought to involve all relevant stakeholders to create a collaborative vision for access to medicines in England. This evidence, alongside the extensive engagement the APPG has undertaken over the nine months since its establishment, informs the recommendations contained in the report.

The scope of the APPG's Inquiry stretched beyond those of NICE's methods review and recommendations are, therefore, divided into those that specifically address the review, along with recommendations relating to the wider system.

Recommendations relating to issues with the current methodologies and processes that may be addressed in the short term include:

- A review of the routing criteria for the Highly Specialised Technology (HST) pathway
- Fairer representation of patient groups at Appraisal Committees, including more information about the impact patient evidence has, and the introduction of a PACE style meeting
- Introduction of quality-adjusted life year (QALY) modifiers for severity and unmet need
- Adoption of the Treasury's suggested discount rates and Incremental Cost-Effectiveness Ratio threshold
- Publication of clear timelines and deliverables for review

Recommendations on systemic issues that may be addressed in the medium term, outside the scope of NICE's review are:

- Research into the QALY and other methods for measuring value
- Research into the inherent value of rarity as perceived by society and patient groups
- A review of the medicines budget to ensure that there is sufficient funding to continue to allow NHS patients access to new therapies
- Assessment of sources of funding for new medicines, which could include ring fencing rebate secured through the Voluntary Scheme for Branded Medicines Pricing and Access (VPAS)
- Clear guidance on, and willingness to introduce, innovative pricing arrangements for new medicines
- Industry and patient group support for the NHS and NICE, including greater transparency of list pricing
- International work on the procurement of medicines.

The APPG is hopeful that this report strikes a balance between providing clear recommendations and suggestions for crucial areas for future research and work outside of the NICE review. The Group hopes to see a majority of the recommendations suggested in chapter 6 enacted in the time frame of the review, and also to see work commence on longer term projects in the next year.

The APPG will be taking this report, which represents the views of a broadly based group of stakeholders, to Government, the NHS and NICE in order to continue our dialogue about what should change to support better patient access to innovative therapies.

Acronyms:

HST	Highly Specialised Technology
ICER	Incremental Cost Effectiveness Ratio
QALY	Quality Adjusted Life Year
RWE	Real World Evidence
STA	Single Technology Appraisal
VPAS	Voluntary Scheme for Branded Medicines Pricing and Access

INTRODUCTION

The NICE methods review was agreed as part of the 2019 Voluntary Pricing and Access Scheme (VPAS), as a way of ensuring that England continues to lead the world in its Health Technology Assessment (HTA) processes and methods. Such a review is necessary, given the rapid changes in the types of products being developed by companies, and the potential lifelong benefits treatments can deliver.

For example, we are seeing a move away from a 'one size fits all' approach to treatment, and towards more personalised medicines[iii]. Such personalisation, which may see cancers treated on the basis of their genetic make-up, poses a challenge to HTA bodies because of trial design, patient numbers, and costs of developing treatments. Equally, we are entering an age of gene therapy, where genetic conditions such as immunodeficiencies and haemoglobinopathies, are corrected via the addition or editing of a gene in the patient's body. This poses a health economic challenge because the potential life-long, or curative effects of what will often be one-time treatments, will be seen across a lifetime, but NICE is only able to assess the therapy on the basis of the data available at the point of marketing authorisation.

As companies continue to push the boundaries of science and bring new ways to treat cancers, chronic, rare and genetic conditions and other diseases to the NHS, our processes of assessing the value of such therapies must also evolve. This is why it is essential that the NICE methods review, and the APPG's Inquiry into NICE's methods, must keep the evolving life science ecosystem at their heart.

As companies continue to innovate, they too have a responsibility to find ways of enabling approval and funding of new medicines within the relevant budgetary constraints. Companies should not just leave it to the system to suggest ways of achieving this, and the APPG's recommendations seek to recognise and address this too.

The Group sought to consult across the range of actors with a stake in England's assessment of new medicines, though we recognise that NICE is only able to act within boundaries set by government and to an extent, NHS England. While our investigation opened lines of inquiry that stretch beyond the initial scope of the NICE methodology review alone, it is important to consider the review in the context of the mandate granted by the Government, as well as the broadening role of NHS England. For this reason, a section of our report comments on the longer-term systemic changes that may be required, as well as future areas for consideration. It is clear that to achieve progressive change and avoid stagnation the system should seek incremental improvement.

The APPG recognises the role that the Accelerated Access Collaborative (AAC) has in fast-tracking a selection of products through the system. The Group intends that these recommendations should be aligned with the work of the AAC, and looks forward to hearing more detail about how the AAC will work alongside existing NICE appraisal routes.

Given that the challenges facing the NHS, and the life sciences industry are significant and complex, the Group decided to limit the scope of this inquiry to

the access landscape for medicines. Other rapidly evolving technologies, including diagnostics, devices and digital health will be reviewed as part of the APPG's future inquiries, as they warrant their own assessment.

Finally, it is important to note that our Inquiry was, from the outset, intended to be collaborative, and to avoid imposing unrealistic recommendations on a system already under pressure. There is a job to be done, not only by NICE, but also by the Department of Health and Social Care, NHS England and industry, to ensure that patients are able to access new treatments as they are licensed. A secondary result of realising such an aim, would be to continue to foster the life sciences industry in England, and ensure the sector remains an important pillar of our economy.

METHODOLOGY

The Group launched this Inquiry in April 2019. It was an important opportunity for stakeholders represented through the APPG to have their views on NICE's methods review, and some wider access issues, communicated to government, NICE and others. This feedback was gathered at an early stage, before NICE had commenced the review or laid out detailed timelines or scope.

The Group drafted a set of questions designed to elicit views on issues and potential solutions relating to NICE's methodology, and other aspects of the access environment. The survey was sent to the Group's mailing list, which includes representation from a wide variety of stakeholders including industry, trade associations, patient organisations, clinicians, professional bodies, think tanks and many more.

The Survey asked the following questions:

1. In what capacity are you responding to this consultation? (Industry, patient organisation, NHS, or other (please specify))

2. What issues should the NICE methods review consider, for both Highly Specialised Technologies evaluations and Single Technology Appraisals, as a priority? You may wish to consider the changes seen in the life science sector over recent years, and changes to come.

3. How should the NICE methods review seek to balance the NHS' budgetary constraints, with the need to deliver important treatments to patients?

4. What comments and suggestions do you have about the governance of the methodology review?

5. Currently 82% of NICE's appraisal recommendations are positive. Do you hope for NICE to improve its approval rate? If so, how should NICE address this?

6. Do you hope for a rebalancing of this overall approval rate across disease areas, technologies, severity, rarity, etc.? If so, how do you think NICE should address this?

7. Are there any particular methodological or process areas that should have been addressed in the Accelerated Access Review, or Voluntary Scheme for Branded Medicines Pricing and Access Scheme, that you think are outstanding and should be addressed in the methods review? If so, how do you think NICE should address these issues?

8. Please provide any further comment on this inquiry you feel is relevant.

Once all the submissions were received, they were collated, and key recurrent themes were identified and analysed. These themes, concerns and recommendations form much of the basis of this report's recommendations.

In addition, the Group held three oral evidence sessions across one week, in which evidence was taken from a cross section of the interested parties. It was important to ensure there was an opportunity for questioning and in-depth discussion of some of the issues raised as part of the written evidence.

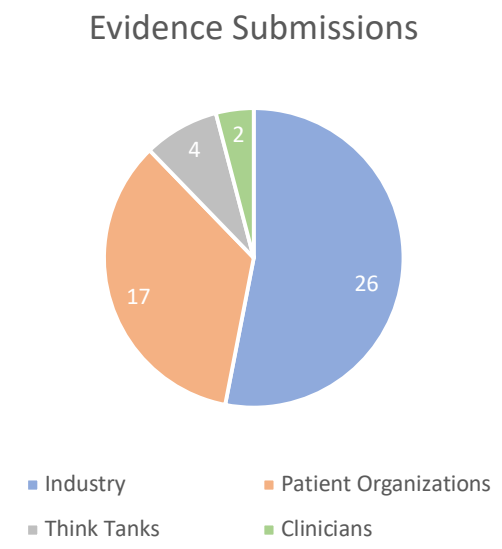
The first oral session invited patient organisations and clinicians to give evidence, the second invited industry representatives, and the third heard evidence from NICE and two health economists. These sessions served to add colour and depth to the written evidence.

The evidence given by NICE representatives was useful in confirming the scope and timelines of The Review.

FINDINGS

Written evidence:

There were 53 submissions, including 26 from industry, 4 from trade associations, or industry groups, 17 patient organisations, 4 think tanks and 2 clinicians.



The written evidence submitted spoke broadly to five topics; NICE processes, areas for methodological change, governance of NICE's review, NICE approval rates and NICE's role in the wider access to medicines eco system.

On **NICE's processes**, there was consistent feedback that while the medicine access landscape needed to be streamlined, and there should not be a new assessment route introduced, the routing process between STA and HST should be made clearer and fairer.

Of particular concern were the criteria that a technology must satisfy in order to be routed through HST, as it was felt these were unclear, and some thought they lacked the necessary flexibility. It was suggested by some respondents that the requirement for a condition to be treated through a highly specialised service to be eligible for HST was misguided, and that routing on the basis of patient numbers was more appropriate.

The other primary process point raised in the vast majority of written submissions, was the role that the patient voice had to play in a NICE appraisal. Most agreed that the patient voice was not appropriately taken into account and should lie at the heart of the NICE process. Responses from patient organisations were particularly thoughtful and addressed the way the processes should change to take better account of patient experience. It was felt by many that the Committee setting was intimidating for patient groups, particularly if the patient group was representing a small patient population, who may not have had experience of a NICE appraisal before, or be familiar with the highly technical language and formal setting. Many urged that an alternative process be found to ensure patient voices are more fairly heard.

Areas for **methodological change** professed by the written evidence were numerous, and there were some consistent issues and suggestions that emerged across the evidence. First, and probably most fundamental was the call for a value assessment that looked beyond the QALY as its foundation. This ask was felt to be particularly important for ultra-orphan medicines and those treatments that may have impacts for the patient, carer and society that are poorly captured by current methodology. There was a broad consensus that if NICE were to stop relying largely on the QALY for some treatments, then a broader, more deliberative decision-making process

based on additional value elements would be required.

Related to this was the wide spread agreement that the STA process was not best set up to assess products to treat rare diseases, and that this was clearly demonstrated in the 'cliff edge' between the ICER threshold for HST and STA. There were a variety of suggestions regarding how to ensure that more expensive drugs, such as those to treat rare diseases, could be fairly assessed and not subject to an appraisal process that may not be best set up to appraise new treatments. Most suggestions involved some modification of the ICER thresholds. This could be done according to a variety of factors, including - but not limited to - severity, rarity and unmet clinical need.

Another key issue that emerged from assessment of the current methodology was the way that NICE handles uncertainty. NICE may encounter uncertainty in a variety of areas, for example uncertainty of clinical effect over time, or uncertainty of clinical effect in a certain patient population. This can make NICE's decision making more difficult. NICE's handling of uncertainty was a key concern for the majority of stakeholders, who agreed that as the medicines landscape changed, (bringing smaller patient populations, more treatments for chronic diseases, and earlier regulatory approval), expectations about data standards from clinical trials required by NICE should be adjusted. Of the many stakeholders who raised the way that uncertainty is handled as an issue, many also offered a solution: to introduce an interim conditional approval mechanism. There was a range of views on how such a mechanism might operate and to which types of medicines it might apply.

A third methodological issue was the current discount rate used by NICE. Many thought that—as the Treasury Green Book recommends—the discount rate for benefits should be 1.5% rather than the default 3.5% used by NICE[iv]. Discounting in the public sector allows costs and benefits with different time spans to be compared on a common "present value" basis. The public sector discount rate adjusts for social time preference, defined as the value society attaches to present, as opposed to future, consumption. It is based on comparisons of utility across different points in time or different generations.[iv] Similarly, the Group heard that the Treasury Green Book recommendation of an ICER ceiling of £60,000 should be used, which is three times the current base ICER ceiling.

There was a consistent call for Real World Evidence (RWE) to be more accepted by NICE, particularly as more medicines gain approval for smaller indications, and where evidence may have been gathered through early access schemes such as Early Access to Medicines Scheme (EAMS). Currently NICE views evidence collected in randomised controlled trials (RCTs) as the highest standard, but this is not always achievable, and RWE can offer valuable information about the likely impact of a medicine in a real-world setting. NICE does accept RWE but perhaps places less emphasis on it sometimes than it could and should.

The final methodological issue around which there was broad consensus was the way that NICE assesses patient quality of life, or utility gain. NICE currently prefers utility data to be presented in terms of EQ5D, which was perceived by the respondents to be too blunt, often excluding important disease specific factors. There are some alternative general measures, as well as disease specific ones, that companies use to communicate the utility provided by an intervention which should be considered.

Regarding the **governance of NICE's methodology review**, written evidence consistently called for involvement of key stakeholders, specifically patient groups and industry, at all stages of the review. This should include defining the scope of the review, as well as the work carried out

to formulate potential solutions, followed by a full consultation once the proposals had been finalised. Many of the submissions called for industry and patient group representation on the high-level steering group, as well as the working groups.

In addition to involvement in the process of the review, many suggested that NICE should publish clear timelines and deliverables against which they could be held to account. Some submissions said there was a lack of clarity on different stages of the review process, and a few respondents thought it was inappropriate for NICE to be conducting a review into its methods itself.

When responding to the question on **NICE's claimed 82% approval rate**, most submissions expressed dismay, as this figure does not represent medicines that were approved within their full marketing authorisation, or any HST treatments[v]. It was felt that the 82% figure was not very representative of the reality of patient access to new medicine. For example, of the 24 completed Single Technology Appraisal (STA) reviews of rare disease medicines between 2013 and 2017, only 13% were recommended for the full eligible population[vi]. A slim majority of submissions suggested that NICE should aim to approve as many rare disease products as non-rare disease products, but opinion on this topic was mixed. Some submissions recognised there was a balance to strike between access to innovation and affordability, which is understood by the Group.

Finally, when considering **NICE's role in the wider access landscape**, there was definitive agreement from the vast majority of written submissions that NICE should not seek to limit the medicines spend, or mitigate potential budget impact, any more than it currently already does through the Budget Impact Test. The vast majority of responses pointed to the newly agreed Voluntary Scheme for Branded Medicines Pricing and Access (VPAS), with its rebate mechanism that would funnel a significant amount of money back to the Treasury, and which guarantees that there will not be an over spend in the medicines budget[vii].

Oral evidence:

Witness	Title	Organisation
Session 1: Monday 20th May 4-5pm Committee Room 15		
Professor Michael Rees	Co-Chair	Medical Academic Staff Committee, British Medical Association
Dr David Strain	Deputy Chair	Medical Academic Staff Committee, British Medical Association
Nick Medhurst	Head of Policy and Public Affairs	Cystic Fibrosis Trust
Dr Kirsty Henderson	Policy Manager	Alzheimer's Research UK
Session 2: Monday 20th May 5-6pm Committee Room 15		
Jon Neal	UK Managing Director	Takeda
Elena Tricca	Director of Patient Access and Government Affairs	AstraZeneca
Leslie Galloway	Chairman	EMIG
Session 3: Thursday 23rd May 2-3pm Committee Room 13		
Sir Andrew Dillon	Chief Executive	NICE
Helen Knight	Programme Director	NICE
Professor Karl Claxton	Professor of Economics	University of York
Mark Fisher	Managing Director	FIECON

The following themes emerged as a result of the oral evidence sessions: the challenge of NICE's place within a constrained NHS budget, the need for greater flexibility in methodology, and process related issues.

First, when looking at the methodological issues, the pros and cons of reliance on the QALY were discussed. The health economists, and other witnesses felt that the use of the QALY allows for comparison across disease areas, which is very important. However, some witnesses proposed that, in situations where a QALY may not be adequate to capture all disease benefits, there may be additional elements that can be brought in for a multi-criteria decision-making process.

When looking at the current ICER thresholds, particularly with regard to the thresholds in STA for orphan treatments, there was some consensus among industry representatives and others that a sliding ICER threshold, or a range of ICER thresholds between £30,000 and £100,000 may be an appropriate way to account for different characteristics of a disease such as rarity, severity and unmet need. However, more than one witness also pointed out that by raising the ICER threshold it would be likely that more innovative drugs would be available on the NHS, and therefore that this would have implications for the medicines budget, which is arguably a political issue.

There was also discussion about whether cost-effectiveness should be separately assessed by NHS England after a NICE approval to ensure the value for money declaration was not tainted by affordability issues. This could allow treatments to be deemed cost-effective and available to market, and allow separate conversations about affordability to be had with NHS England.

Questioned on how NICE should handle uncertainty, the oral answers reflected those given in written evidence. Witnesses said that NICE should consider introducing a mechanism by which a plausibly cost-effective drug would be granted conditional interim approval while data was collected in the real world. One patient representative spoke about the enormous power in existing NHS data, and how the use of registries, such as the Cystic Fibrosis registry, could support access decisions.

In addition, there was advocacy from industry representatives, and one economist, that incorporating some aspects of societal benefit into a NICE value assessment would be beneficial, and fairer. This would see NICE formally take account of impacts such as carers being able to return to work, and double carer utility. Companies often model this to show the benefits of a treatment, and NICE at times considers this, but does not always take it into account. There was a call for clearer guidance on the application of this rule.

The core message for the NICE methods review was that stakeholders would like to see greater flexibility built into the HST and STA pathways. This could take different forms, but it should be codified in some way.

The second theme that witnesses honed in on was how the process might evolve in order to allow for more effective engagement with patient groups, as well as ensuring medicines can go through the most appropriate assessment pathway. It was agreed that while the pharmaceutical industry generally had some early stage discussions with NICE about the appropriate route, the criteria for HST routing should be made clearer to ensure better focused applications and better results. It was also agreed by the industry representatives that there was no formal way to challenge a decision about routing, and that this should be rectified.

Regarding patient's experiences of process, the APPG heard that patient groups were often unsure of the impact that their evidence given at NICE Committee meetings had on the final outcome of the appraisal. Some feedback would be helpful to ensure better future engagement. It was also suggested that Committee meetings were very clinician focused, and that they could be an intimidating setting for patient groups. The Patient and Clinician Engagement (PACE) process in Scotland was referred to as a helpful way to get patient input. However, the witnesses believed that patients should still attend Committee meetings to ensure their perspective was represented there too.

The theme that ran consistently through the oral evidence sessions, and on which much further work is needed, is the political and economic context of NICE appraisals in England. This includes its role and impact on the total medicines budget, its role in innovating ways to fund individual and groups of medicines, and its role in deciding whether any preference is given to certain types of diseases.

In its evidence, NICE repeatedly stated that much of the questioning around budget and affordability are technically outside NICE's remit, and the remit of the methods review. One industry representative suggested that if NICE changes its methods to approve more innovative medicines, which will improve patient outcomes, and there is no discussion about affordability then "*the can would be kicked down the road to NHS England*".[viii] Given the impact that NICE approvals have for access in other countries, obtaining NICE cost-effectiveness approval is an attractive proposition in its own right, and should be considered as part of the methods review. Therefore, the implications of a methodology review stretch to NHS England and government who need to give more thought to determining affordability quickly and effectively in a fast-changing world of treatment development.

Industry representatives and one health economist spoke in similar terms about the way that rebated money should be protected to ensure that the rebate given by industry funds the new medicines being prescribed. However, the health economist suggested that this rebate would be in addition to, and separate from, the current rebate mechanism agreed through VPAS. There was a call from most witnesses for government to review overall medicines funding, and how the NHS can plan for the future, if it is to meet its goal of providing innovative medicines to patients as quickly as possible.

Further discussions explored whether decisions about valuing certain types of diseases or medicines over one another would be required at a high level. For example, adding in sliding ICER thresholds dependent on rarity as part of a methods review would be challenging without some direction from government about health priorities. It was suggested that NICE could undertake further work to see whether certain value elements are deemed to be important by the public and therefore be incorporated into assessments. However, one health economist said that rarity in particular was not valued by the general public, and for every QALY awarded to a medicine approved in HST, 6 or 7 QALYs were lost elsewhere in the system. This, of course, assumes a closed system and finite budget, which is essentially the situation in England currently. Questions were also asked about the public's role in deciding what conditions or diseases should have priority.

In relation to the funding point, one health economist and the pharmaceutical company representatives explained that companies are currently looking at the UK and struggling to justify launching here due to the challenging access and funding environment.

RECOMMENDATIONS: methodological issues

The APPG is aware that some of these recommendations address issues with the methodology and process for STA and HST, and the Group hopes that the recommendations will be considered in terms of the broader access landscape.

This set of recommendations has been drawn together from the evidence gathered over recent months as part of this Inquiry, and in ongoing conversations with stakeholders interested in ensuring England continues to develop and has access to new, effective and innovative medicines for its patients as quickly as possible.

Process

1. Review of the routing criteria for HST

NICE should review and clarify the routing criteria for referral to the HST process as some criteria are unclear and some are too stringent. This has resulted in specialised treatments for very small patient numbers being referred to STA. STA was not set up to assess ultra-orphan conditions and therefore struggles to take into account characteristics of ultra-orphan treatments, with patient populations of around 500 or fewer in England. NICE may consider, as part of their criteria review, whether to remove the need for a treatment to be delivered through a highly specialised service to qualify for HST, as well as clearly stating the patient number threshold for HST. There should be a right of appeal if the treatment is rejected on budget impact grounds.

2. Representation of patient views at Committee

NICE should consider ways in which to better engage with patients to enhance patient input into the decision-making process and the provision of feedback about decisions made. While it will always be a challenge to show the exact impact that patient advocacy and evidence has had on the final outcome, there are clear steps that can be taken to ensure patients feel better supported to give evidence, are clearer in their role, and understand how their evidence will be used.

Therefore, the APPG recommends that NICE introduces to STA a PACE style meeting for orphan treatments, where there is a clear unmet need, prior to the appraisal Committee meeting. This process, whereby patient groups and clinicians are able to meet prior to the Committee meeting to feed into a summary statement about the condition and any possible treatment, is used by the Scottish Medicines Consortium (SMC)[ix]. This would give patients an opportunity to input into the process outside of the Committee meeting, which can be intimidating for some patient groups.

NICE should also provide training for patient groups on how best to engage with the NICE process, as currently patient groups may not feel best equipped to engage.

In addition, consideration might be given to whether NICE be required to explain

what changes it has made in light of patient input. More generally, the APPG would encourage NICE to review how it can strengthen its engagement with patients, patient groups and take account of relevant data, to ensure not only a satisfactory experience for those individuals involved, but also a decision-making process that is more powerfully informed by what matters to patients and their carers. This needs to be balanced with the fact that industry is often in discussion with patient groups and there may be a need to guard against industry lobbying.

Methodology

3. QALY modifiers for severity and unmet need

NICE should expand the current end of life ICER threshold to apply to therapies where there is a clear unmet need in a severe condition. This will add much needed flexibility to the system, and will primarily benefit products that have been developed to treat severe diseases, which are often rare. The APPG feels that orphan designation in its own right should not warrant a QALY modifier, but that where a treatment meets a specific unmet need for a severe condition, there would be additional value in approving these topics. This amendment is recommended while additional work is carried out on whether society as a whole sees rarity, as a value element, that should be formally considered in a NICE appraisal.

4. Interim conditional approval

How NICE can better handle uncertainty about cost-effectiveness was the most commonly raised issue with the methodology across written and oral evidence, and many submissions suggested a possible way to build flexibility into the methodology. The APPG recommends that NICE introduces an interim conditional approval mechanism, which would work in a similar way to the Cancer Drugs Fund, to fund plausibly cost-effective drugs. The Group recommends this on the basis that the CDF shows the feasibility and potential success of such a mechanism, as well as the fact that it has broad stakeholder support as a solution. This would be triggered where NICE identifies areas of uncertainty, and where a drug was plausibly cost-effective, and where the various modelled scenarios and sensitivity analyses showed that the ICER was plausibly likely to be below the cost-effective ceiling. The approval would be conditional on the company continuing to collect data for a set period of time, followed by a re-appraisal. Unlike the CDF, we would not envisage that this mechanism would be linked to a defined fund or pot of money. The approved medicine would be funded through the appropriate route, either centrally or through baseline commissioning.

5. Adoption of the Treasury's suggested discount rates

NICE should use the discount rates as suggested in the Treasury's Green Book:

"The recommended discount rate for risk to health and life values is 1.5%. This is because the 'wealth effect', or real per capita consumption growth element of the discount rate, is excluded"[iv].

The application of a 3.5% discount rate, which is used as the default rate in NICE's methods, contravenes the Treasury's guidance. There is also a question about whether NICE's current application of the 1.5%, which is used exceptionally, is too

cautious and fails to fairly take account of some benefits that may be delivered by a technology over a long time horizon.

Greater use of the 1.5% rate would fairly place value on long term effects on length and quality of life in the context of our healthcare system, as in other parts of society, such as road traffic accidents. The Government should directly examine and decide whether or not to use the suggested £60,000 cost per QALY in a health setting, as the Treasury suggests, and justify its decision in detail.

Governance

6. Publication of clear timelines and deliverables

The governance and process of NICE's forthcoming methods review should be much clearer. The APPG would like NICE to publish clear timelines for each stage of the review, with the relevant milestones planned by month, so stakeholders have a clear idea of what they can expect to be published and when. Regarding the opportunities for engagement with the review, NICE should publish a calendar of the touchpoints for stakeholders, as well as disclosing the names and organisations of those involved in the closed parts of the review. There should be a full public consultation on the suggested changes.

7. Future governance/ transparency of NICE

The APPG recommends that NICE publishes a bi-annual breakdown of the approval rates of each pathway, including how many products have been recommended within their marketing authorisation, how many have been granted interim conditional approval, how many orphan products have been approved, and how many appraisals have run over the allotted time frame, or have run outside process (for example, having multiple Committee meetings). The APPG acknowledges that this information is available on the NICE website, but that the website can be challenging to navigate. Furthermore, the information, once found, requires a great deal of time and knowledge to work through and analyse, and may not be user friendly for a member of the general public.

RECOMMENDATIONS: systemic issues

The APPG recognises that NICE does not operate in a vacuum and is limited, to an extent, in the reforms that it can make to the access landscape through its methodology review. Other actors, primarily the Department of Health and Social Care, the Treasury and NHS England, have an important role to play in shaping the future of access to medicines. The APPG found the oral and written evidence to be instructive in suggesting areas for further consideration in order for NICE to operate to the best of its ability and be future-proofed in a fast-changing sector.

1. Research into the QALY and other methods for measuring value

Much of the written evidence that was concerned with ultra-orphan and orphan medicines, stated that the QALY was not capable of capturing the true value of some treatments, particularly in HST. However, what was also apparent is that the QALY is currently the only credible way of comparing value across disease areas. It is clear that there is a need for all parties, with NICE at the centre, to consider further whether some kind of deliberative element can be introduced into appraisals to capture better the value of some types of products and the savings they bring to other parts of the health system. The APPG believes this work is vital and would urge the government to support such an exercise.

2. The inherent value of rarity

Another area where further work is essential is in the inherent value of rarity as a characteristic of a disease or condition that would warrant higher ICERs or a more flexible and deliberative approach. The APPG has recommended that severity and unmet need be added to a list of ICER modifiers along with end of life due to the fact that these characteristics drive additional societal savings which may not be captured in current methodology. We have also recommended this on the basis that rare diseases are often severe, and many have a high unmet need, so NICE would go some way to satisfying the call for an overhaul of the way rare disease treatments are appraised[x]. However, we have not recommended that treatments for rare diseases be afforded higher thresholds in their own right because there is work that needs to be done to establish whether there is a societal preference for this. Work is also required to establish whether commonly held views on how best to fund rare disease therapies are valid. NICE's Citizens Council undertook this work in 2004 in relation to ultra-orphan drugs, and similar work is now required for orphan drugs[xi].

3. Adaptation of NICE's methods to other types of innovative medicines

The Inquiry heard repeatedly that methodology may be too slow in adapting to changing treatment paradigms, which may see therapies like gene addition, gene

editing and increasingly personalised medicines become available. In order to ensure that there is work ongoing to adapt HTA methodology ahead of these innovations coming to market, the Group recommends that the National Institute for Health Research (NIHR) and NICE establish a working group which aims to identify future areas of development ahead of commercialisation, and engage in a discussion about how to assess fairly innovations ahead of time.

This work is equally important to identify topics for consideration early on, and ensure that appropriate horizon scanning and evidence generation are in place from an early point. Horizon scanning is a priority for the AAC, and the APPG supports the work NHS England is intending to do there.

4. Medicines budget

The Group acknowledges that changes made to NICE's methodologies may impact the NHS' budget, and if budgetary controls are in place then, despite NICE's efforts to create a methodology fit for the future pipeline, we will fail to see patients accessing the latest cost-effective technologies. The APPG, while recognising the reality of spending constraints, nevertheless calls for a review of the medicines budget to ensure that there is sufficient funding overall for cost-effective new medicines which fulfil their clinical promise to patients.

5. Society's priorities for other disease area treatments

Further to work specifically on society's views on the value of rarity, there also needs to be additional research undertaken early to test societal preferences for access to drugs to treat more common conditions, and whether the public would support prioritising treatments for diseases such as dementia, for example, over those for rare diseases. This work would be closely linked to research that is needed into the case for increasing the medicines budget to allow access to more cost-effective treatments as they become available.

This work would need to be balanced with patient and carer view. The APPG recommends that the Government looks closely at carrying out some research into this as part of a wider review of medicines spend.

6. Clarify the respective roles of NICE and NHS England in decisions about cost-effectiveness and reimbursement

The Inquiry heard consistent feedback that NICE's remit was to assess cost-effectiveness, and should not include the consideration of budget impact. Therefore, the APPG recommends that NICE maintains its role in deciding whether or not a technology is cost-effective and NHS England works with the Government to define better its role as a budget holder. The APPG hopes this will result in a decision to make all cost-effective therapies available through the agreed medicines budget, and in order to achieve this the Government and NHS may have to look at making more resources available to ensure access. This is necessary as decisions about medicines funding are inherently political and NICE does not have the mandate to make decisions about funding that may be restricted due to potential budget impact.

7. Sources of funding for new medicines

The current medicines spend is controlled by the most recent VPAS, effective from 2019. The scheme sees companies rebate back to the Treasury 9.6% of the spend on

branded medicines. This is based on the initial Measured Sales forecast at the start of the Voluntary Scheme and will not change. The initial forecast growth rate of Measured Sales is 5.2% in 2019, 6.84% in 2020 and 8.57% in 2021[vii]. This acts to control the spend so the NHS and the government can be reassured there will be no unexpected hike in the medicines spend. However, currently the rebated funds are routed back to the Treasury and become part of general Exchequer funds. They are not ring-fenced for any specific purpose, health-related or otherwise. This does not feel right or fair to the APPG. It therefore recommends that the Treasury, the Department of Health and Social Care and NHS England work together to formulate a way to ensure the rebated money can be spent on access to cost-effective new medicines. This will require long term work and is outside the scope of the NICE methodology review, but could be crucial in ensuring patients on the NHS are able to access new therapies.

8. Innovative Pricing Arrangements

While there is ongoing work on NHS England's Commercial Framework, which the APPG hopes will further support industry to propose innovative payment and pricing mechanisms, such as multiple indication pricing, this must be linked back to NICE's processes. Therefore, the Group would like to see greater clarity around the ways that NICE's Commercial Liaison Unit supports companies and NHS England throughout the appraisal pathways. The APPG hopes that this will help realise potential innovative solutions.

9. Industry and patient group support for the NHS and NICE

As companies continue to innovate, they too have a responsibility to find ways of enabling approval and funding of new medicines within the relevant budgetary constraints and not just leave it to the system to suggest ways of achieving this.

In order to allow rapid access, and success first time round as products are appraised through NICE, a company must seek to bring its best value proposition forward at an early stage in the assessment process. This includes making decisions about where the unmet need lies for a given patient population and seeking to meet a need rather than introducing a product into a therapy area that may be well serviced.

The fact that the UK is a price reference market for other European countries, does have some bearing on the level at which companies price new therapies. However, the APPG feels that the way in which medicines are priced for the UK market is often opaque. We would like to see a greater willingness to demystify the process by which a product secures a list price, which would be an important step in meeting the system half way and encouraging earlier approval. The APPG acknowledges that companies usually provide discounts, often upwards of 50%, and wholeheartedly believes that these should remain confidential, but is concerned with the justification of public list prices.

As well as pricing, there is a question about some companies' data collection, including data for small populations, and utility data measured in EQ5D. NICE is clear on data expectations, and how companies can present the strongest case for a new product, yet it is often the case that companies make submissions to NICE with wholly inadequate or the wrong type of data. This may be because of the divergence of data requirements between regulators such as the EMA and HTA bodies like NICE. Lack of relevant data leads to considerable uncertainty around the assessment process and is a common reason for NICE's committees to reject products. This issue is by no means limited to products that treat rare diseases.

We should like to see industry make greater efforts to link its data generation to the requirements of HTA bodies so that payers can be assured of the cost-effectiveness of new medicines. If manufacturers do not present with appropriate data then it is not entirely fair to blame the assessment bodies for being unwilling to approve the product. This may be supported by greater transparency of trail data.

Equally the APPG recommends that patient groups work together to make the case for the value of innovative medicines as a whole, and to continue their support of the life sciences sector through advocacy beyond their specific therapeutic interests. There is a need for the case to be made for the value of innovative medicines to society and the health service beyond any one disease. Patient groups have a crucial part to play in making this case and umbrella patient organisations with a cross cutting brief are particularly important in this context. However, they are also typically very thinly resourced, and the Government, NHS bodies and industry, alongside the health charity sector itself, have a shared interest in ensuring that they continue to thrive and remain sustainable.

CONCLUSIONS

The scope of this Inquiry has grown over time, and naturally it is impossible to isolate one part of the life sciences ecosystem from another. Our aim was to produce a report that should strike a balance between providing clear recommendations to NICE's methods review, and suggesting areas for future research and work outside the review.

It is clear that there is positive engagement from all parts of the system to work together and ensure that patients and tax payers continue to have their interests fairly represented in a rapidly changing life sciences world. No change can happen in a vacuum, and where steps forward are made by one part of the system, but not others, patients will often fail to see the intended benefit.

Equally, this report does not directly address any reforms that may be considered at international level to reform the way medicines are procured above country level. This may be a topic that decision makers seek to explore as an additional avenue to ensuring the sustainability of the medicines market internationally.

The recommendations of this report range across matters of governance, process, methodology, finance and philosophy. The Group hopes to see the recommendations on addressing the systemic issues enacted in the time frame of the review, and also for work to commence on longer term projects in the next year also.

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