

GENE PEOPLE

the genetic conditions support network

Gene People's Response to the NICE Review

Introduction

Gene People responded to the consultation on the proposals presented by NICE on changes to the health technology appraisals in October 2021.

The following text is the responses submitted online via the consultation website. Where a response of 'no comment' was given, those responses are omitted from this text. Where the question was a selection on a scale, the answer given is stated.

The sections are:

1 Methods

- Valuing the benefits of health technologies
- A modifier for severity of disease
- Understanding and improving the evidence base
- Additional comments

2 Processes

- Alignment
- New ways of working
- Commercial and Managed Access
- Additional comments

3 Presentation of the guidance manual

4 Topic selection

- Highly Specialised Technologies
- Highly Specialised Technologies (HST) routing criteria

1 Methods

How strongly do you agree or disagree with the proposals related to:

- *Modifier for severity of disease - neither agree nor disagree*
- *Consideration of uncertainty within decision making - agree*
- *Health inequalities - neither agree nor disagree*
- *Aligning modifiers across programmes - neither agree nor disagree*
- *Discounting - neither agree nor disagree*

Severity modifier

Of the two options presented Gene People selected option 1

Comments on:

- **Modifier for severity of disease**

The recognition of severity rather than end of life as a prioritizing factor is welcome. However in the case of many rare diseases affecting children these cannot easily be separated as affected children may have a very short life expectancy.

The case for QALY shortfall (absolute and or proportional) as a measure of severity in respect of interventions going through HST evaluation needs to be explained and the parameters clarified.

We ask that NICE reconsiders the introduction of a rarity modifier. NICE has stated that there is insufficient evidence of how society views rare diseases, the majority of which are genetic in basis, therefore, we ask that this piece of work is prioritised in order for the first modular review of the methods.

- ***Consideration of uncertainty within decision making***

It is likely that the level of uncertainty will be higher when evaluating products for rare and very rare diseases. This is likely to be more pronounced in cases where the product under evaluation is the first disease modifying therapy to come to market. No-one would disagree with the intention to use the highest standard possible for evidence generation, but this will not be an absolute measure across the board, and care will need to be taken to avoid disproportionately disadvantaging products for rare and very rare conditions by experts unfamiliar with these conditions not realizing the practical difficulties of evidence generation and so inadvertently setting the bar too high. Early discussion with the relevant patient group will help understanding and avoid creating an unfair burden for patients and families.

The avoidance of double counting is clearly desirable. However, in any given case there may be more than one modifier operating and these may work together additively or multiplicatively to heighten uncertainty. There is clearly a role for expert judgement in weighting the impact of modifiers on the eventual outcome. Input from patients and families and relevant clinicians with a deep knowledge of the condition will be essential if a fair outcome is to be reached.

- ***Health inequalities***

Given that the issue of health inequalities is one that has been recognized for many years, it is regrettable that more progress in developing measures to address this issue has not been made. We acknowledge that robust tools to address inequalities need to be developed and applied, but this process ought to be undertaken quickly and thoroughly. In the meantime health inequalities continue to exert their impact and those on the receiving end to suffer disproportionately. We would hope to see a time to deliver of the relevant modifier specified.

- ***Aligning modifiers across programmes***

Consistent application of modifiers across all programmes is highly desirable. A degree of deliberation will be required when applying modifiers to ensure that they are being applied in ways that are appropriate and fit for purpose. It will be important to review how decisions have been taken if we are to be confident that there is a consistent approach by all committees and experts engaged in this process and that similar standards are proven to apply. Such a review should be conducted in a transparent manner with results publicly available. Consideration should be given to the training needs of those involved as a route to creating appropriate standards and metrics.

We welcome the proposal to continue to apply the magnitude of benefit modifier to HST evaluations but would suggest that a similar approach be adopted in the case of those products that narrowly fail to qualify for the HST route.

- **Discounting**

We recognize that discounting of future health benefits is standard practice and are not qualified to comment on the appropriate percentage to be used when this is applied. However, in the case of rare progressive conditions future benefits may be valued more highly by patients and families than those nearer at hand. For example, a boy with Duchenne Muscular Dystrophy may see a treatment given now while he is still able to walk but which will delay or prevent his transition to wheelchair use in the future as being more valuable for the delayed benefit he will experience. In such a situation incremental added value may be more appropriate than discounting – or at least the maintenance of a steady state situation.

We understand that NICE thinks that there are limitations to what it can suggest in terms of discounting as there are other policies that interact with this area owned by other stakeholders, however, we believe NICE is a key stakeholder and could set the agenda in this area proactively.

How strongly do you agree or disagree with the proposals related to:

- *Implementing the proposed cases for change for sourcing, synthesising and presenting evidence, and considering health-related quality of life* – strongly agree
- *Considering real world evidence* – strongly agree
- *Calculating the costs of introducing health technologies* - neither agree nor disagree
- *Analysing uncertainty* - agree

Comments on:

- ***Implementing the proposed cases for change for sourcing, synthesising and presenting evidence, and considering health-related quality of life***

The clarity provided by the use of the term ‘health-related quality of life’ is beneficial as it addresses a disconnect between how a family with a member affected by a rare or very rare genetic condition and the general public might interpret the phrase ‘quality of life’. ‘Quality of life’ is usually thought to be broader, encompassing items such as being able to meet friends, work and engage in other meaningful activities, and increased dignity and self-esteem. For families with a member who is affected by a genetic condition, the whole family might have their quality of life impacted when considering a wider definition of the phrase. This clarification defines quality of life within the remit of NICE, which is helpful.

- ***Considering real world evidence***

We welcome the move to broaden the type of evidence that can be considered. This is of particular importance to Gene People’s community as many genetic conditions have patient populations that are too small for randomised controlled trials. In these circumstances, real world evidence (RWE) is crucial for Committees to understand the impact of a condition and potential treatment.

In the methods proposal paper, NICE states it will accept 'any evidence' for consideration and that no restrictions are placed on the evidence that can be submitted. We ask that the impact and user-friendliness of RWE collection on patients and their families and carers is taken into consideration.

The manual specifies the kinds of RWE acceptable. Some of the RWE mentioned are outside the knowledge of patient organisations for very rare conditions that are mostly formed to provide peer-to-peer support to others with the same condition; they are mostly not created with the expectation of needing to participate in an HTE. It is probable that those patient organisations that are new to this process will be disadvantaged in relation to those that have previous HTE experience or are larger and therefore have access to such things as registries. There is a need to support very small patient organisations and those who are participating for the first time to enable them to fully participate, including in the provision of RWE. Consideration could be given to the provision of coaching, and third-party McKenzie Friends in meetings.

We would ask that RWE should be just that: real world evidence from the patient perspective of what a condition is like to live with and how a treatment mitigates the condition. This would benefit the decision-making process of the Committees.

- ***Calculating the costs of introducing health technologies***

This is not an area for Gene People to comment on, as we are a patient organisation.

- ***Analysing uncertainty***

We note the creation of a visualisation tool to aid the analysis of uncertainty and ask for clarification regarding how this tool will be consulted on as it is not part of the manual or this consultation process.

Additional comments on methods

Gene People (formerly Genetic Disorders UK) provides direct support and information to anyone affected by any genetic condition in the UK through our genetic counsellor-led helpline and web resources. We run our Partnership Network of Patient Organisations and Groups, which gives groups access to our online forum, a listing on our website, and access to events including our popular Leadership Symposium. Currently the Network stands at 131 groups, and this increases regularly. We also advocate on behalf of those calling the helpline and our Network in national policy consultations. Gene People was founded in 2011.

It is unclear whether the proposals will meet their aim because it is not known how these changes will interact with other yet to be finalised policy decisions, such as the Innovative Medicines Fund.

We are concerned that the need to achieve cost-neutrality has hampered the ambition of the review, especially for those with genetic conditions, whose treatments tend to be more expensive than those for the population as a whole.

2 Processes

Have the processes been aligned appropriately? No

Comments

There are other processes that are still in development that will have an impact on the HTE process. It is, therefore, not possible to state categorically that this process has been appropriately aligned with others.

It is unclear whether the availability of multiple highly specialised technologies is positive or not. For some of those affected by genetic conditions, the slightest delay in the evaluation process can have catastrophic consequences, as has been seen in several HST evaluations. We would caution against any delay to patient access to treatments.

Are there any remaining unwarranted differences in the processes of guidance development for Diagnostic Assessment, Highly Specialised Technologies, Medical Technology Evaluation and Technology Appraisal? No

Comments

These are quite technical questions which assume a degree of familiarity with the nuts and bolts of the NICE process with which many of the tiny patient organisations in the Gene People Partnership Network will be unfamiliar. If NICE is serious about seeking the views of patient organisations on these issues then we would suggest that some focus groups or similar would be a way of securing this input, which Gene People could facilitate.

How strongly do you agree or disagree with the proposals related to:

- *Technical engagement* - agree
- *Rapid review of guidance for biosimilars* - agree
- *Treatment eligibility criteria* - disagree
- *Managing high company base ICERs* - neither agree nor disagree
- *Alternative draft scope consultation timings* - neither agree nor disagree

Comments on:

- ***Technical engagement***

The introduction of a technical engagement stage is largely welcome, provided that it does not delay the progress of the decision-making process. This is critical to patients whose health may deteriorate swiftly. There are instances in our Partnership Network of patient organisations where a technical engagement session involving patient representatives might have resolved issues aired in full Committee sessions that prolonged the process. Consideration to the support given to very small patient organisations and those that are first time participants is needed for the full benefit of this stage to be realised.

- ***Treatment eligibility criteria***

It is unclear as to why additional treatment eligibility criteria are necessary when treatments are proposed for a specific group of patients meeting certain eligibility criteria and the identification of subgroups is possible as part of the HTE process. We therefore ask for clarification and worked examples to be made public.

- ***Managing high company base ICERs***

It is known that the commercial discussions regarding a treatment can be difficult and protracted. From a patient organisation perspective, the creation of a pause in the process is unwelcome. It increases anxiety and uncertainty about the timeframe in patients and their families, and indicates that negotiations have stalled. Delays can result in severe negative health outcomes for some patients. This has been seen in a number of evaluations of treatments for rare genetic conditions, where patients have either died or become ineligible for treatment before decisions were reached.

It is understandable that NICE would want a means of pausing discussions that were not progressing and that this would be used only in extreme circumstances. We are, therefore, asking for clarity about whether this option has been tested on previous topics and what difference this would have made to the outcome before being able to fully comment on this proposal.

- ***Alternative draft scope consultation timings***

On the whole, shorter timescales are welcome in the HTE process as patient access to new technologies is desirable. However, some patient organisations do not have paid staff or dedicated members of staff to be able to respond to short timeframe consultations. Patient organisations would need to be given advance notice of when a scope consultation was due in order to ensure resources were available to respond within the timeframe. They would also need to be clear about what would be asked of them and the boundaries of their response prior to the scope consultation going live.

How clear or unclear are the proposals related to:

- *Commercial activity* - neutral
- *Managed access activity* - not very clear

Comments on:

- ***Managed access activity***

It seems likely that MAAs will become increasingly common, especially when therapies for rare diseases are under consideration. Where this seems likely, early engagement with the relevant patient group is essential if the required data is to be collected without placing undue burdens on patients and families. Such engagement will also help focus efforts on collecting evidence that one needs to know, rather than that which it is nice to know in order to reach a robust conclusion. Any obligations on patients as a condition of receiving the treatment and what will happen to those receiving the treatment at the end of the MAA period in the event that the evidence does not support a move to routine prescribing must also be negotiated with the patient group. Rare genetic conditions often have smaller patient organisations that were born from a desire to offer peer support to families in similar situations making the concept of negotiating an MAA for their community daunting and participation in subsequent monitoring meetings intimidating. For very small or very new patient groups the offer of access to independent advocacy to help them participate effectively in this process should be considered.

It is unclear how MAAs will interact with the Innovative Medicines Fund, the details of which are yet to be published. This is regrettable as without that information it is difficult to get a full picture of the routes to access for those with genetic conditions, especially for those with very rare conditions.

3 Presentation of the guidance manual

What are your initial impressions of how the guidance manual is presented?

The presentation of the manual is clean and uncluttered, however, it is unclear as to whether there will be supporting documentation that condense the manual, such as a process flow chart with timings. The manual is a public document, and we suggest should follow best practice and be written for the UK average reading age of 9 years of age. While the NHS Information Standard is no longer open for assessments and may not have applied to NICE directly, the Principles are a good guide as to how to present a public document.

Given that many patient experts and patient organisations do not regularly participate in NICE evaluations, it would be beneficial to define terms, including 'guidance'. We believe that additional materials will be produced for participating patient organisations, and would welcome this, as the manual is dense and overwhelming. Patient organisations are hugely diverse and are run by a broad range of the population. For some, they are founded and led by affected family members who do not have a health system background and have deep lived experience of a condition.

Please note the phrase 'NICE health technologies evaluation: the draft manual' is on the title cover not guidance manual as used in this question. It would be useful for references to be consistent.

Comments on specific chapters:

- ***Involvement and participation***

This chapter would benefit from some diagrams of participants in the different groups. It would also be useful for the input of each participant to be ranked or weighted so it is clear how their evidence influences the decision.

Item 1.2.32: It is unclear how patients and patient organisations feed into the NHSE/I treatment eligibility. If there is documentation elsewhere it would be useful to link to it.

It might be useful to include sample agenda showing when participants will be asked to leave meetings and the items that they will be able to participate in.

- ***The scope***

This chapter would benefit from either the inclusion of examples of a blank scope template and a completed (fictitious) template or links to examples.

Item 2.4.3: It would be useful to clarify what input an international patient organisation may have if there is a national patient organisation, and whether this applies to UK-based organisations that are the international patient organisation; are they international or national in this circumstance?

Item 2.7: It is probable that when a treatment becomes available for a genetic condition, especially rare or very rare conditions, that there will be an increase in diagnoses. We would therefore ask for an indication as to how a review of the patient population following a period of MAA would impact on how the treatment would be assessed.

- **Developing the guidance**

This is a highly complex chapter, and we hope that materials specifically for patient organisations will be available.

Item 5.6.1: The necessity not to be prescriptive about timelines is acknowledged, however, for patient organisations to be able to manage their work and be able to fully participate some form of indication would be very useful, as opposed to 'TBC'. As many patient organisations are small – either one or two paid members of staff or totally volunteer led and run – the more notice they are given the better their responses and preparation for participation will be.

4 Topic Selection: Highly Specialised Technologies

How clear or unclear is the aim of the HST evaluation programme? Clear

How clear or unclear is the refined routing criteria for HST? Clear

Comments

The proposed criteria are clear and understandable. We note that all four criteria will normally be applied, but that some flexibility may be allowed with regard to prevalence. Given the poor quality of much of the available prevalence data, with numbers frequently being derived from scaling up from small scale local studies, this is to be welcomed. We would expect that, when a decision is made not to recommend an intervention that is apparently on the cusp of eligibility to follow the HST route a clear rationale for the decision is published so the committee's reasoning can be seen and challenged if necessary.

We are concerned that the proposals would mean that some topics previously eligible for the HST route would no longer be so. This would be building in additional disadvantage for those with genetic conditions, especially those with rare genetic conditions.

We are unclear about the cap on patient populations across indications. This would create disadvantage for those conditions for which a treatment is shown to be effective after it has been approved for other conditions. It could create delays in patient access if the proposals mean that a treatment will need to be proven for all indications so that the patient population across indications is defined before being taken to NICE. We are, however, unclear as to whether this is the intention of this part of the proposal and would welcome public clarification.

How clear or unclear is the eligibility criteria (section 4) for devices, diagnostics and digital technologies? Don't know

Additional comments on HST

Gene People does not consider the current proposals address the inbuilt disadvantage for those with genetic conditions, especially those with rare and very rare conditions, in comparison to the general public – all of whom are patients of the NHS – or those conditions with a large patient population. This disadvantage is due to the size of patient population making randomised controlled trials unethical and infeasible, a lack of understanding and knowledge about the condition leading to fewer expert clinicians available to give evidence and developing companies needing to recoup cost over a smaller patient population. Whilst the proposals go some way to address these issues, it

would have been preferable to have had the detail of the Innovative Medicines Fund to understand how HST and the IMF will interact and improve access to treatments for those with rare and very rare genetic conditions. Therefore, we would ask that NICE commits to reviewing HST when the IMF detail is available for public and patient review.

There is a long-standing issue with those treatments that do not meet the threshold for HST but that will not succeed under the STA process. This has been discussed with NICE publicly. The proposals do not address this issue, which is a missed opportunity. Again, it is not clear whether other developments that are outside the remit of NICE will help to assist such treatments. It would be useful if NICE could publish its modelling of past and current topics and how the increased opportunity for flexibility and the refined HST criteria impact routing decisions.

Topic Selection: Manual

Comment on the chapters:

- ***Eligibility, selection and routing criteria***

As with the guidance manual, it would be useful to give definitions to terms that the general public might not be familiar with, such as off-label technology, and to follow best practice for health publications including the NHS Information Standard Principles.

NICE has publicly discussed exercising flexibility in the development in guidance. Given that some treatments for genetic conditions will fail to meet the criteria for HST routing, we are keen to know whether the Topic Selection Oversight Panel has flexibility and what this would look like in practice.

We would also like clarity about how the Innovative Medicines Fund might interact with topic selection. It is regrettable that the detail of the scheme has not been published. We realise this is outside of the control of NICE.

- ***Highly specialised technologies***

This is an extremely important section for those affected by genetic conditions. We are unclear how the patient populations were derived, especially as there is recognition from NICE that not all topics routed through the HST process would meet these criteria. For transparency, it would be beneficial to state how these figures were arrived at, either in the manual or supporting documentation.

We are concerned, as stated in other parts of our response, that the patient population cap across multiple indications could disadvantage those conditions that are not in the initial trials for a treatment. The need to remain below 500 people across all indications might mean that there would be delays to access to treatments, which for some conditions can have significant impact on health outcomes, or that treatments that would have previously been routed through HST no longer meet the requisite criteria.

From the recent webinars, it is clear that topics will need to meet all the criteria specified in the manual. This is highly important for treatments for those with genetic conditions. We suggest that this point has greater emphasis placed on it in

the text of the manual. This could be achieved by changing 'the' to 'all' in this sentence: ',, they meet the four of the highly specialised technologies...'

There has been concern within patient organisations that there has been a limit to the number of HST processes each year. It is heartening to see the public statement that this is not the case and that there is flexibility within NICE to be able to undertake more if needed. This is welcome as the pipeline of treatments for conditions that would meet the HST criteria appears to be increasing at the current time.

- ***The Topic Selection Oversight Panel***

The specific members of The Topic Selection Oversight Panel who are focused on devices, diagnostics and digital health technologies is welcome as this is a very specialised area.

The proposal is for two lay members to represent patients. We would welcome clarification on how these members of the Panel will be selected. We have concerns that two people would not have the breadth of experience needed to review every potential topic, especially those for genetic conditions as that community can face specific challenges. It is not clear from the proposed manual whether the same lay members attend each topic selection meeting, which may be a way of ensuring lay members with expert knowledge make decisions on topics.

We suggest that an opportunity for the lay members of the Panel to meet with relevant patient organisations or expert clinicians prior to the Panel meeting so that they have insight into the lives of the patients affected by the topics under discussion from the outset of the process.