Access to medicines for rare disease patients
Briefing for Westminster Hall debate, 16 June 2015

Rare disease medicines
Many rare diseases are severe and life-limiting. For individuals or families affected by most rare diseases, the day-to-day challenges of managing a severe condition are made worse by the absence of an effective treatment or cure. For some rare conditions, however, new medicines have been researched, developed and licensed. Before these can be accessed on the NHS, they have to be evaluated for cost-effectiveness and prioritised for commissioning. Some medicines that could be used by rare disease patients are not licensed and so they do not qualify for these access routes.

Current system for accessing rare disease medicines in England
There are seven routes through which licensed medicines for rare conditions can be evaluated and/or commissioned to enable patient access on the NHS. These routes are managed either by the National Institute for Health and Care Excellence (NICE) or NHS England.

1. Highly Specialised Technology (HST) Evaluation Programme – NICE
2. Single Technology Appraisal (STA) – NICE
3. Multiple Technology Appraisal (MTA) – NICE
4. Specialised commissioning – NHS England
6. Individual Funding Requests (IFRs) – NHS England
7. Commissioning through Evaluation (CtE) – NHS England
The role of NICE

NICE is resourced to carry out in-depth technology appraisals that are able to closely examine the benefits and costs, both clinical and financial, of making a new medicine available on the NHS. If a positive recommendation is made, there is a mandate for that medicine to be commissioned by NHS England. This allows for a robust consideration of all the evidence and ensures equitable access to approved medicines across England.

However, NICE only appraises a small number of medicines for rare diseases:

- Between 2002 and 2013, 18 orphan medicines were considered through NICE’s standard appraisal routes. Only four of these medicines were for non-cancer indications, equivalent to less than 10% of the non-cancer orphan medicines that the EMA licensed in that same period.
- On average, NICE only appraises three orphan medicines a year.
- The top 10 most expensive orphan medicines currently being paid for and provided by the NHS (measured per patient) were not appraised by NICE.

Highly Specialised Technology Evaluation Programme

Following the introduction of the Health and Social Care Act 2012, NICE was given responsibility for appraising medicines very rare diseases. This led to the development of interim methods and processes for the HST Evaluation Programme in May 2013 that was heralded as the route through which rare disease medicines would now be appraised.

Given the proposed importance of this route, Genetic Alliance UK undertook the development of a Patient Charter to gather the patient perspective. The Charter made 29 recommendations to improve HST Evaluation from the patient perspective and was endorsed by 78 patient groups.

The Charter revealed that while patients welcomed the introduction of a route at NICE that is better suited to appraising medicines for small patient populations, they agreed that the process is opaque, potentially disruptive to the wider NHS and risked downplaying the patient voice. They were particularly concerned that the HST programme is only resourced to evaluate three medicines a year.

NICE have yet to address a number of the key issues patients identified. These include:

- NICE’s topic selection criteria, particularly their definition of ‘clinically distinct’, needs updating. The definition does not currently recognise conditions defined by genetics, biomarkers or differences in clinical presentation. This means that the full range of medicines that could benefit patients with rare conditions, including stratified medicines, are ineligible for an HST evaluation.
- NICE only intend to evaluate three HSTs a year, despite it being likely that the EMA will license over four times that many in the same time period (approximately 13 each year).
- Third-party support for patient groups engaged in an HST evaluation is still not available despite NICE commissioning research into how this could be achieved over a year ago; the findings of which are still to be published.
- A consultation on NICE’s HST evaluation programme, which will enable a formal consideration of the patient perspective on the HST evaluation process, has yet to be announced. In April 2014 an answer to a written question to the Secretary of State for Health indicated this was expected in 2014. NICE indicated late last year that a full consultation may not take place until 2016.

An example is ivacaftor (Kalydeco), a medicine that has been developed to treat the 5% of cystic fibrosis patients whose condition is the result of a specific genetic mutation. NICE’s current criteria do not recognise this subgroup of patients as ‘clinically distinct’, and therefore the medicine would not be evaluated through the HST programme as the number of patients affected by cystic fibrosis (over 10,000 people in the UK) is too great.
**Case study: Tuberous Sclerosis Complex (TSC)**

TSC is a rare genetic condition estimated to affect 1 million people worldwide. The condition results in the development of non-cancerous tumours, often in the brain, eyes, heart, kidney, skin and lungs. The size and location of these growths determines the impact of TSC, with some people being relatively mildly affected and others more severely. Symptoms may present early in life or not until adulthood.

A drug called everolimus (Novartis) has been granted market authorisation by the EMA for the treatment of tumours associated with TSC. This covers both:

- a type of brain tumour (subependymal giant cell astrocytoma or SEGA) in children and adult TSC patients where surgical removal is not an option;
- a type of kidney tumour (renal angiomyolipoma) in adult TSC patients who are at risk of complications but do not require immediate surgery.

Despite being licensed in the UK, everolimus has not been appraised by NICE and is currently only available through the NHS on an individual basis or through the Cancer Drugs Fund (in the case of SEGA). The Tuberous Sclerosis Association (TSA) has been working to address the existing inequities in patient access.

**Current access: the Cancer Drugs Fund (CDF) and Independent Funding Requests (IFRs)**

- TSC patients that are affected by brain tumours may be able to access everolimus through the CDF, while those affected only by the kidney tumour cannot. This is due to TSC patients with brain tumours being treated by cancer specialists (neuro-oncologists) while those with kidney tumours are treated by kidney specialists (nephrologists or urologists), who do not have any connection with the cancer care system.
- In the last year, 12 IFRs have been submitted by TSC patients for everolimus in England. Only two have been successful.

**Future access: developing a commissioning policy at NHS England**

- The TSA were encouraged to develop a service specification for TSC but were advised that a national prescribing policy should not be included. The establishment of a national service specification would provide a platform for the prescribing of mTOR inhibitors in line with a separate prescribing policy.
- The TSA are investing significant time and resources into supporting the developing a service specification in collaboration with patients and expert clinicians. It is unclear what format submissions for service specifications should take and advice is being sought.

The TSA are also involved with a project that is analysing data derived from the Clinical Practice Research Datalink that examines the burden of manifestations associated with TSC in the UK. This transferable approach to analyzing evidence to support healthcare decision-making could form the basis of service related decision-making not only in TSC but in other rare diseases, including treatment, resource allocation and reimbursement decisions.

**Issues raised:**

- Does the CDF have a positive influence on patient access?
- Is the IFR process working?
- Should it be possible for medicines to be considered in the context of a specialised service?
- Does NHS England provide sufficient guidance and support to patient groups developing service specifications or commissioning policies?
- Is there a level playing field for all patient groups?
The role of NHS England

The remit of NHS England in terms of determining access to rare disease medicines is significant:

- NHS England is the **responsible commissioner** for the specialised treatments for rare conditions (including those recommended by NICE), meaning that it manages the available budget
- NHS England **coordinates its own evaluation procedure** in order to determine which rare disease medicines should be prioritised for funding – the ‘Clinical Reference Group (CRG) route’
- NHS England also manages the CDF, EtC and the IFR process

The Health and Social Care Act

The passage of the Health and Social Care Act through Parliament caused **significant disruption** to the running of the NHS, including curtailing the uptake of innovative care and treatment pathways and interventions during that time. Since the Act was passed, further delays have ensued from the structural changes it introduced and the time it has taken to implement those changes, leaving many difficult decisions without the bodies empowered to make them.

The reorganisation of the NHS is unlikely to be finished for a number of years and there remains major delays in the creation of decision-making tools for parts of NHS England’s new structure. This has been impedes further by the threat of a judicial review which has backed NHS England into a corner from which it is unable to take prompt action.

Despite these issues, some aspects of the Act and what it hoped to achieve, however, continue to have the **support of our patient community**. Before the Health and Social Care Act, commissioning of services for patients with rare diseases was split between various groups and bodies. Rare disease patients experienced a “postcode lottery” when trying to access many treatments or services.

By creating NHS England; with the responsibility for overseeing the commissioning of all specialised medicines and services on a national basis, according to a single national specification, the Act has enabled progress towards **equity of access for patients**.

Specialised commissioning by NHS England

Rare disease medicines that NICE does not select for one of its appraisal routes will need to be evaluated and/or commissioned by NHS England in order for an access arrangement to be established and funded. Since NICE evaluates so few medicines for rare diseases, NHS England is by default the primary appraisal body and commissioner of rare disease medicines.

Given the importance of NHS England for access to rare disease medicines, Genetic Alliance UK undertook the development of a Patient Charter to gather the patient perspective. The Charter made 6 overarching recommendations and was endorsed by 86 patient groups.

The Cancer Drugs Fund

The CDF was introduced in 2010 as a means of enabling patients to access cancer medicines that would otherwise not be funded by the NHS. It has a ring-fenced budget of £200 million a year and will run until at least the end of 2016, and is likely to be continued beyond that date. NHS England took responsibility for managing the CDF on 1st April 2014 and the Chair of the Chemotherapy CRG is responsible for making recommendations to NHS England on what drugs should be added to (or removed from) the list. You can see Genetic Alliance UK’s position statement on ring-fenced funds, such as the CDF, here: [http://goo.gl/knQCeW](http://goo.gl/knQCeW)

Evaluation through Commissioning

EtC was developed by NHS England as a new way of commissioning specialised services or treatments for which there is currently insufficient evidence of clinical and/or cost-effectiveness to warrant routine commissioning. The programme has a budget of £16.9 million which is essentially used to fund pilot schemes. EtC works by restricting the pilots to a small number of specialised centres over a set time period. During the pilot, data is collected which can then be used to support a decision as to whether a specialised commissioning proposal should be funded or not. So far, no medicine has been selected for the EtC programme.
The Charter revealed patients’ concerns that they are being prevented from accessing the medicines they need because NHS England is poorly organised, overburdened and under-resourced.

The recommendations for improving how NHS England evaluates and commissions rare disease medicines included:

For NHS England to fulfil its organisational promises to be ‘open and transparent’, ‘prioritise patients in every decision’ and ‘listen and learn’, it must optimise existing communications and engagement platforms

- Patient representatives called for NHS England to improve the way it engages with patients so that it can benefit from the insight patients offer and is transparent about how it decides which medicines it will pay for and which it won't.

- As a critical information source and point of contact with the public, they identified NHS England’s website as requiring urgent updating so that NHS England can be transparent about its evaluation procedures and patients can find out if a relevant evaluation is happening and who to contact.

NHS England’s Clinical Reference Groups should be granted additional resources to support their ability to give expert advice, and enable consistent decision-making and effective stakeholder engagement

- Patient representatives welcome the principle behind Clinical Reference Groups in that they ensure that experts in the field, including patients and clinicians, are at the centre of decision-making. But they agreed that CRGs are insufficiently resourced to carry out the work required of them.

- An administrative team managed by NHS England should be implemented to provide the secretarial support required to enable CRGs to function effectively.

NHS England’s appraisal process needs drastic streamlining and rationalisation to enable timely, patient-focused and transparent commissioning of rare disease medicines

- Patients agreed there are too many steps in the process for evaluating medicines and that NHS England should streamline their unwieldy governance structure so they can make faster and fairer decisions and ensure their limited finances are spent where they are needed most.

- NHS England should be clear who is making the decisions about which medicines are evaluated and which are funded, and what criteria are used to make these decisions.

Patients also highlighted the importance of the patient voice in deciding which treatments and services should be commissioned by NHS England. They agreed that the line between nationally and locally commissioned medicines and services would become increasingly vital and noted that currently the committee within the Department of Health that makes this decision, the Prescribed Specialised Services Advisory Group (PSSAG), lacks patient voice representation.

Individual Funding Requests

The IFR process allows patients who would benefit from a medicine to access it even if they fall outside of current commissioning arrangements, providing that making it available is cost-effective. This route is supposed to be used infrequently as it is intended that the majority of patients to be able to access appropriate medicines within existing arrangements. Unfortunately, with the pause in the uptake of innovation caused by the passage of the Health and Social Care Act through Parliament and many rare disease medicines not having been selected for evaluation by NICE or NHS England, patients with rare conditions are having to rely on the IFR process to access medicines that their clinician agrees they need. The IFR process is not designed to be used in this way, by a recognised cohort of patients with an unmet medical need. As a result, when the number of IFR applications for the same medicine by patients with the same condition exceeds 20 (an ‘IFR trigger’), NHS England develop a commissioning policy. While this ensures that all patients who could benefit from a medicine may be given the opportunity to access it through a national commissioning policy, any patient trying to access the medicine while this policy is developed, which can take over a year, will be denied.

A detailed briefing on how the IFR process is failing rare disease patients is also attached.
**Which medicines go through which route?**

It is important to select the most appropriate route for each medicine in order to avoid making inconsistent or inequitable decisions that affect patient access. The process that decides which medicines will be evaluated and/or commissioned through which route is called topic selection. Due to a lack of clarity and transparency on this process, information on how or why one medicine evaluation approach or access route is selected over another is not available.

Our work, however, has suggested that topic selection decisions are taken primarily by NICE representatives. There does not appear to be a formal relationship between NICE and NHS England in determining which three medicines should be selected for a NICE appraisal and how those not selected will be prioritised for evaluation by NHS England. This is particularly concerning given that a NICE recommendation comes with a mandate for commissioning that takes precedence over other treatments and services that NHS England may want to commission but NICE has not appraised.

**Duplication of effort**

During our Patient Charter work, we revealed that poor management of topic selection was resulting in the duplication of effort between NHS England and NICE. We found that both NHS England and NICE had plans to evaluate and develop guidance on at least four of the same medicines in the rare disease arena. In some instances the medicines were included in NHS England’s work plan before NICE received a Ministerial referral and in other NHS England planned to develop interim guidance so that patients would not need to wait for NICE to complete their evaluation before being able to access a new medicine. Patients welcomed timely access to medicines but felt that as publicly funded bodies, it was difficult to justify NICE and NHS England carrying out parallel evaluations.

The decision to refer a medicine for HST evaluation at NICE is made by Ministers, following the application of a series of prioritisation criteria. Currently, these criteria do not ask Ministers to consider whether an HST evaluation would add value to the NHS when compared to an evaluation by NHS England or access through the EtC, CDF or IFRs routes also managed by NHS England.

**Falling through the gaps**

Without a coordinated, transparent and publicly accountable approach for triaging medicines into each route, inconsistent decisions are at risk of being made, leading to inequitable patient access to medicines. For many rare disease patients, this specifically includes the risk that some medicines will be neglected by all the potential routes so that patients are forced to rely on gaining access on a case-by-case basis through the IFR process. A detailed briefing on how the IFR process is failing rare disease patients is also attached.

**Making the system work effectively together**

Addressing the current failings in topic selection is an essential part of ensuring that the system through which patients with rare diseases can access the most cost-effective medicines is fit for purpose.

Patient representatives agreed as part of our Patient Charter work that achieving this will require NHS England and NICE to collaborate and deliver a transparent and rational methodology for triaging medicines into the most appropriate access route. In addition, patient representatives also agreed that, as valuable stakeholders, patients should be given the opportunity to comment on the proposed work streams of NICE and NHS England and for their views to be considered before the work streams are finalised.

**The need for UK-wide equity of access**

The system described above relates specifically to England. The picture for rare disease patients looking to access a medicine for their condition is different, and in some cases further complicated, if they live in Scotland, Wales or Northern Ireland.

Ensuring that all the different routes work effectively together within England is a considerable challenge. Further ensuring that all patients within the UK, regardless of where they live, can access
the best treatments and services for their condition will require even greater collaboration between the NHS and health departments of the four home nations.

Wales is currently in the process of changing how the All Wales Medicine Strategy Group (AWMSG) will appraise orphan and ultra-orphan medicines, and what their relationship with the recommendations made by NICE will be. Genetic Alliance UK has also recently published a report that highlights the barriers that exist for rare disease patients in Wales who are looking to access treatments and services either within Wales or in other countries of the UK. This can be viewed here: www.geneticalliance.org.uk/docs/accesswales.pdf

Last year, Scotland developed and implemented a new process for appraising orphan and ultra-orphan medicines. Many of the changes have been welcomed by the rare disease patient community.

Working together and sharing best practice across the four nations will be essential for ensuring that all rare disease patients in the UK are able to access the best medicines for their conditions.

Case study: Rare disease medicine evaluation in Scotland
Following extensive review and consultation, in May 2014 the Scottish Medicines Consortium (SMC) introduced significant changes to the way it evaluates medicines for very rare conditions and end of life medicines. Orphan medicines will now be evaluated by the New Drugs Committee (NDC) and where the NDC are likely to advise that the medicine is "not recommended", the submitting pharmaceutical company can choose to request that a Patient and Clinician Engagement (PACE) meeting take place.

PACE meetings will be chaired by a member of SMC and will bring together representatives from relevant patient groups and clinicians from the relevant speciality. The aim of the PACE group is to describe the added benefits of the medicine, from both patient and clinician perspectives, that may not be fully captured within the conventional clinical and economic assessment process. For example, PACE meetings can be used to discuss clinical issues such as unmet patient need or the medicines place in the patient pathway, the impact on quality of life, the convenience of the treatment, the ability to maintain independence and dignity and the added value of the medicine for the patient’s family or carers.

The discussion will be captured in a PACE template document and the content will be agreed by all representatives present. The output of the PACE meeting will be a significant factor in the SMC decision. The PACE system helps to provide clarity on the clinicians’ and patients’ view on the need for the medicine when decisions are being made and SMC decisions will better reflect the views of the patients and the doctors that treat them.

Medicines for ultra-orphan conditions (those affecting around 100 people in Scotland) will be subject to a separate appraisal system. However, the medicine may still be subject to a PACE meeting to capture clinician and patient opinion. To assess ultra-orphan medicines, SMC will use a framework of explicit decision making criteria that will include:

- the nature of the condition
- the impact of the medicine
- the impact of the technology beyond direct health benefits and on specialist services
- costs to the NHS
- value for money

In the case of ultra orphan medicines, pharmaceutical companies will still have to provide a cost-effectiveness ratio to assess value for money but there may be circumstances in which the choice of economic appraisal methodology has to be flexible to reflect the available data.