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UK Mechanisms to Address Rare Disease Challenges: Does the UK Go Far Enough?

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BACKGROUND

- Rare conditions affect fewer than one in every 2,000 people.
- There are an estimated 7,000 different conditions and, owing to their rarity, people living with rare diseases face challenges with the health and care system, and with wider public services.
- One in 17 people are affected by a rare condition at some stage in their lifetime: in the UK alone, this amounts to over 3.5 million people.
- The UK government and devolved administrations published the UK Rare Diseases Framework in January 2021, setting out a shared vision for addressing health inequalities and improving the lives of people living with rare diseases[1].
- This included a priority to "improving access to specialist care, treatments and drugs" (Box 1).
- Within the UK, the majority of new treatments and drugs are assessed for access via Health Technology Assessment (HTA).

Box 1: UK Rare Disease Framework key priorities[1]

- **Priority 1**: helping patients get a final diagnosis faster - there is generally a lack of epidemiological and natural history data.
- **Priority 2**: increasing awareness of rare diseases among healthcare professionals.
- **Priority 3**: better coordination of care.
- **Priority 4**: improving access to specialist care, treatments and drugs.

OBJECTIVE

- To map the current mechanisms available in the UK to address UK rare disease access challenges and answer the question '*does the UK go far enough for rare diseases?*'.

METHODS

- An analysis was conducted to identify key UK market access mechanisms introduced since the 2021 UK Rare Disease Framework.
- Identified mechanisms were evaluated against two common challenges for HTA of rare diseases issues that were identified in 2018 as part of an ISPOR international working group (Table 1)[2]:
  - No tailored HTA method for rare diseases;
  - Uncertainties for HTA authorities.
- Each mechanism was assessed for its potential to address each of the individual challenges highlighted in Table 1 in order to understand how the UK is currently tracking against the access priority from the Rare Disease Framework.

Table 1. ISPOR international working group identified challenges in HTA of rare diseases

No tailored HTA method for rare disease treatments	
Lack of sufficient and robust clinical data	• Research challenges with rare diseases often lead to a lack of sufficient and robust clinical trial data • This results in a reliance on non-randomised trials, single arm trials or real world data
No established standard of care	• Rare diseases often do not have an established standard or standards of care, creating difficulties in providing comparative evidence required for HTA
Insufficient knowledge of the natural history of the disease	• Related to the above, there can often be a lack of knowledge on the natural history of rare diseases • This leads to challenges in predicting the real impact of any interventions
Lack of validated instruments to assess efficacy and effectiveness end points	• Rare diseases can be unique in the outcomes that need to be assessed for clinical efficacy, including quality of life. • The real impact of interventions can be misrepresented when existing outcomes measures are used in place of a lack of validated and robust disease specific instruments
Application of incremental cost-effectiveness thresholds	• Traditional cost-effectiveness ratio thresholds may not be appropriate in fully capturing both societal preferences towards rare diseases as well as account for all value elements of rare diseases
Uncertainties for HTA authorities	
Real-world efficacy, effectiveness and cost-effectiveness	• Clinical trial results may over or under represent clinical and cost-effectiveness within the real-world setting
Added value of new health technology	• Current HTA methods may not account for the full value that a treatment for a rare disease can offer to patients or how it may address the unmet need in clinical practice
Potential of treatment to address unmet need	
Health care costs, utilisation, and potential savings over disease/patient's lifetime	• Related to a lack of knowledge of the natural history of rare diseases, there is likely to be high levels of uncertainty on the overall health system impact across the lifetime of a patient
Budget impact and affordability	• Total and proportional spending on rare disease technologies has been increasing • Whilst the patient populations of rare diseases are, by definition small, the individual cost can be significant with payers needing to make potentially significant budget impact decisions for longer term outcomes; especially with the new wave of advanced therapy medicinal products on the horizon

RESULTS

- Three key changes to the UK landscape introduced since the 2021 UK Rare Disease Framework were identified as mechanisms that could address HTA challenges:
  - NICE Methods Review (NMR);
  - Innovative Medicines Fund (IMF);
  - Innovative Licensing and Access Pathway (ILAP).
- The introduced mechanisms were assessed against their potential to address identified challenges faced by rare diseases within HTA (Table 2).

Box 2: Potential for new UK mechanisms to address identified HTA challenges for treatments of rare disease

NICE Methods Review

- NICE concluded a significant review of its methods to evaluate health technologies in early 2022, claiming "*the changes will give patients earlier access to innovative new treatments by allowing greater flexibility over decisions about value for money and consideration of a broader evidence base*"[3].
- The following changes adopted could address some of the identified HTA challenges:
  - The introduction of decision modifiers;
  - A greater acceptability of uncertainty in some circumstances, including for rare diseases;
  - A greater acceptability of real world evidence;
  - Updates to the HST eligibility criteria.
- However, it is yet to be seen if these have had a positive impact and there are questions around if the review went far enough in tackling all challenges e.g. there are particular concerns for rare diseases that do not meet the HST entry criteria or benefit from the new severity modifier[4] (see poster HTA170).

Innovative Medicines Fund

- The IMF is a £340 million fund launched in June 2022 that aims to improve access to innovative medicines, including those for rare diseases.
- It provides an opportunity to test innovative and creative payment approaches as well as interim access for innovative medicines while further evidence is generated, thereby not delaying access.
- While there is potential for the IMF to address some of the challenges relating to uncertainties for HTA authorities, the Association of the British Pharmaceutical Industry (ABPI) believe this will only potentially solve problems relating to short-term uncertainties[5].
- No medicines are currently funded via the IMF since its inception, suggesting it is not clear how best the IMF will be utilised or if it will address any issues.

Innovative Licensing and Access Pathway

- ILAP is a new pathway launched in 2021 supporting innovative approaches to the safe, timely and efficient development of medicines to improve patient access[6, 7].
- It is intended to accelerate licensing, facilitating patient access to medicines.
- ILAP also has the potential to address a number of the challenges faced by rare diseases by providing support from UK regulatory and access stakeholders to design and implement evidence generation and improve understanding of current UK landscape for the disease area.
- However, as the majority of these initiatives focus on medicines in early stages of development, not enough time has passed to see the true impact of ILAP on the identified challenges.

Table 2. Assessing UK access mechanisms against HTA rare disease challenges

UK access mechanism		NMR	IMF	ILAP
No tailored HTA method for rare disease treatments	Lack of sufficient and robust clinical data	✖	✖	?
	No established standard of care	?	✖	?
	Insufficient knowledge of the natural history of disease	✖	✖	✓
	Lack of validated instruments to assess efficacy and effectiveness end points	?	✖	?
	Application of incremental cost-effectiveness ratio	?	?	✖
Uncertainties for HTA authorities	Real-world efficacy, effectiveness and cost-effectiveness	✓	✓	✖
	Added-value of new technology	✓	✓	✖
	Potential of treatment to address unmet need	✓	✖	✓
	Health care costs, utilization and potential savings over disease/patient's lifetime	✓	?	✖
	Budget impact and affordability	?	✓	?

CONCLUSIONS

- New mechanisms introduced since the release of the UK Rare Diseases Framework in January 2021 have the potential to address some of the challenges for rare diseases identified by the ISPOR Rare Disease Special Interest Group
- However, these mechanisms may not go far enough in addressing the challenges faced in gaining access to treatments for rare diseases in the UK
- The UK system should continue to adapt and look to partner with industry to fulfil the UK Rare Diseases Framework ambitions and ensure the UK attracts companies to invest in rare diseases; without doing so, there is a risk of the UK becoming a fourth launch region behind the US, EU and Japan.

DISCLOSURES

This project was sponsored by Roche Products Ltd.

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