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AstraZeneca Rare Disease

The Innovative Medicines Fund:
A catalyst to drive access to rare disease treatments?

September 2021

This White Paper has been produced by Alexion with assistance from IQVIA and Hanover Communications

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About this White Paper

The Innovative Medicines Fund (IMF) presents an opportunity to drive access to treatments for patients and families with rare diseases. This White Paper was developed to ensure stakeholders and policymakers can make best use of existing expertise and evidence to inform the development of the Fund.

To develop this White Paper, Alexion, AstraZeneca Rare Disease convened a roundtable of the rare disease community and thought leaders in UK medicines access policy to share their views on the IMF. This paper collates the views of those who attended the roundtable, and draws on selected data including evidence and insights from Alexion, IQVIA, academic articles, and papers from industry and other sources.

The aims of this White Paper are to:

- **Support the rare disease community response to the public engagement exercise on the IMF, to be led by NHS England during 2021**
- **Support the wider efforts of the rare disease community to improve outcomes for those with rare diseases and their families**
- **Shape future policy for the IMF, and provide recommendations for NHS England and NICE to optimise design and implementation**

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Jo Balfour,
MD Cambridge Rare Diseases Network

Professor Michael Bewick,
Founder and Senior Director,
iQ4U Consultants Ltd

Professor Nick Bishop,
Professor of Paediatric Bone Disease,
Sheffield Children's BHS Foundation Trust

Thomas Bols,
Head of Government Affairs and Public Policy, EMEA & APAC, PTC Therapeutics

Paul Catchpole PhD,
Director, Value and Access Policy,
Association of the British Pharmaceutical Industry (ABPI)

Rajesh Chauhan,
Senior Director, Pricing and Reimbursement, BioMarin

Leslie Galloway,
Chairman, Ethical Medicines Industry Group (EMIG)

Josie Godfrey,
Strategy Director, Project HERCULES

Dr Edmund Jessop,
Independent Advisor

Alastair Kent OBE FRSA,
Co-Chair, UK Rare Disease Policy Board and Member, Rare Disease Advisory Group

Dr Robin Lachmann,
Chair of the Scientific Committee of the Recordati Rare Diseases Academy

Daniel Lewi,
CEO, CATS: Cure & Action for Tay-Sachs Foundation

Eric Low,
Independent Consultant

Nick Meade,
Director of Policy and Interim Joint Chief Executive, Genetic Alliance UK

Dr Brian Montgomery,
Independent Healthcare Consultant

Anne Marie Morris MP,
Chair of the All Party Parliamentary Group (APPG) on Access to Medicines

Sean Richardson,
VP, General Manager UK and Ireland, Alexion

Rt. Hon Lord O'Shaughnessy,
Chair of roundtable

Sophie Thomas,
Senior Head of Patient Services and Clinical Liaisons, Society for Mucopolysaccharide Diseases

Steve Tomlin,
Chief Pharmacist, Great Ormond Street Hospital

Peter Wasson,
Policy and Public Affairs Manager, BioIndustry Association (BIA)

Vicky Whitehead,
Public Affairs Manager, ABPI

Representatives from the National Institute of Health and Care Excellence (NICE), who are involved in the implementation of the IMF, also participated. Participation in the roundtable does not imply organisational endorsement of this White Paper.

Forewords

Lord O'Shaughnessy

There is nothing unusual about rare diseases. 3.5 million people[1] in the UK will be impacted by one at some point in their lives, and they often have to undergo a lengthy diagnostic odyssey to discover what's happening to their health. And even then, once a patient has discovered their condition, the chances are slim there will be an effective treatment available.

But there is cause for hope. The 100,000 Genomes Project has transformed the diagnosis of the 8-in-10 rare diseases with genetic causes, and the creation of the NHS's Genomic Medicines Service – as well the 50-fold goal of achieving 5 million sequences – offers further light to those suffering in the dark.[2] With the prospects of rapid diagnosis improving radically, and with the pipeline of cell and gene therapies accelerating at pace, we now need to apply the same ambition to the delivery of treatments for the 6,000 diseases classified as being rare.

This is where the Government's promised IMF has a critical role to play. It has been modelled on the Cancer Drugs Fund, which in the last ten years has helped to bring innovative but unproven medicines to thousands of cancer patients who could benefit from them. The laudable aim of the IMF is to expand this platform and make it available for therapies outside of oncology; as this White Paper shows, nowhere is that need greater than in the field of rare diseases. It makes some specific proposals for how this could be achieved – through bespoke data collection, flexible entry and exit criteria, and most of all deep and ongoing involvement with patient groups – and calls for rare disease therapies to be treated on a par with cancer drugs. These are carefully thought through, highly sensible proposals that the Department of Health and Social Care (DHSC) should take into account.

As the COVID vaccine drive has demonstrated, one of the great strengths – if not the greatest strength – of the NHS is the ideal of fairness it embodies. This means the public will always support the direction of life-changing and life-saving resources to those who need them most and who are least well served by the status quo. The community of rare diseases sufferers unfortunately fall squarely into this category; the creation of the IMF is a once-in-a-generation opportunity to address this inequality.

Sean Richardson,
VP, General Manager UK and Ireland, Alexion, AstraZeneca Rare Disease

At Alexion, people living with rare and devastating diseases are our Guiding Star. When you work with treatments for very small patient populations you are affected by the individual patient experience and the impact the diseases have on them and their families. The proudest moments are when you hear about the difference to people's lives made by the innovation you helped deliver.

In the UK today, the rare disease community, NHS and Government have a series of major opportunities to work together to reshape and continue improving care for people living with a rare disease. The implementation of the UK Rare Diseases Framework, the review into NICE's methods and processes and the establishment of an IMF mean, for many, there is a sense of being at a crossroads. Like others, Alexion in the UK takes great hope from this position.
We know from our extensive work with the patient community last year – which culminated in the publication of the Reforming Rare Diseases report in December 2020 – there are opportunities to improve care right across the patient pathway in rare diseases.

Yet in our research, no area generated insight as stark as how patients access treatments for their conditions. A large majority – almost two thirds of patients (64%)[3] – believe the system for making treatments available to patients is unfair on those living with a rare disease. Similar numbers (65%)[4] believe the system is too slow for making treatments available, while only 3%[5] believe enough funding is currently allocated to rare disease medicines.

This sentiment gives the establishment of the IMF heightened importance for the rare disease community. It is vital we listen to these voices. Approving innovative treatments for routine funding can inevitably be challenging. This is true in the UK as it is other countries. It is also particularly acute in rare diseases. Therefore, the role of the IMF is crucial. The IMF will not on its own transform how treatments are made available, but it will go a long way in making the system fairer for people living with rare diseases. It has the potential to enable them to benefit from access to treatments which otherwise may not be available, in a way the Cancer Drugs Fund has given hope to thousands of people with cancer since its establishment in 2011.

We are in the early stages of the development of the IMF. There are many questions still to be resolved. Alexion UK is proud to have worked with the rare disease community and thought leaders in UK medicines access policy on the development of this White Paper. It is our hope that this paper raises awareness and understanding of the key challenges we need to overcome, and helps industry, the patient and clinical communities, and the wider health system, to coalesce around possible solutions.

About Alexion, AstraZeneca Rare Disease

Alexion, AstraZeneca Rare Disease, is the group within AstraZeneca focused on rare diseases, created following the 2021 acquisition of Alexion Pharmaceuticals, Inc. As a leader in rare diseases for nearly 30 years, Alexion is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialisation of life-changing medicines. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on haematology, nephrology, neurology, metabolic disorders, cardiology, ophthalmology, and acute care. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries.

We believe it is our responsibility to listen to, understand, and change the lives of patients and those who work tirelessly to help them. People living with rare and devastating diseases are our inspiration and our Guiding Star.

Executive Summary

Patients living with rare diseases in the UK and their carers are dissatisfied with the medicines approval processes for rare disease treatments.[6] Typically, they believe these processes are unfair on those living with a rare disease and the system is both too slow and not properly resourced for rare diseases. Data on medicines access in England and across Europe reinforces these concerns. Narrow eligibility requirements for the Highly Specialised Technology (HST) programme mean many treatments can struggle to secure approval from NICE for routine use on the NHS. In most cases, those that do secure approval, often see their use restricted to certain subpopulations of their licence. The result is that patients in European countries such as Germany, Italy and France have better access to medicines than counterparts in England.[7]

Encouragingly, steps are being taken by Government and the NHS to reduce these inequalities, through initiatives such as the review of NICE's methods and processes, the implementation of the Rare Disease Framework and development of the Innovative Licensing and Access Pathway (ILAP). The Government has also asked the NHS to develop proposals for an IMF, which will seek to expand on the existing Cancer Drugs Fund (CDF), specifically for the purpose of improving access to rare disease treatments, among others. This is an important step. No one initiative can singularly solve the access to treatment challenges facing patients and their carers in England, but the IMF can address the fundamental issue of data uncertainty for rare diseases treatments at the time of their first assessment by NICE.

The following recommendations were developed following a roundtable with the aforementioned stakeholders. If adopted, they will help the IMF to successfully transition from the CDF, and deliver on the ambitions of the 2019 Conservative Party Manifesto to enable doctors to use the most advanced, life-saving treatments which are available to them.

Recommendations

Ambition

Recommendation 1:

To drive access for patients, rare disease medicines must have the same opportunity for IMF funded access as a medicine for any other disease.

Entry and exit criteria

Recommendation 2:

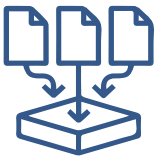
The IMF must have clear but flexible entry and exit criteria that can accommodate rare disease medicines, as well as other medicines.

Funding

Recommendation 3:
IMF funding should not be ringfenced by disease area or medicine type, and must not operate on a 'first-come, first-served' basis.

Recommendation 4:
The IMF should have a flexible budget linked to horizon scanning.

Recommendation 5:
Funding for the IMF should be tabled as part of negotiations on the 2024 Voluntary Scheme for Branded Medicines Pricing and Access (VPAS).



Data collection

Recommendation 6:
The IMF should allow for bespoke data collection, taking a medicine-by-medicine approach to outcomes, data sources and the time required. The IMF must recognise the complexity and difficulty of evidence generation in rare diseases.

Governance

Recommendation 7:
An external IMF multi-stakeholder group should be formed, reporting annually on IMF performance using Key Performance Indicators (KPIs) broken down by disease and orphan status.

Alignment with other initiatives

Recommendation 8:
The IMF must be aligned with the evolving access landscape, including with initiatives such as the ILAP, NICE Methods and Processes Review and UK Rare Diseases Framework.

UK collaboration

Recommendation 9:
The four UK nations should hold discussions to leverage lessons from the IMF – and their own funds - and explore the scope to increase the value of the evidence generated. The four UK nations should also work together to ensure access to innovative medicines, including rare disease medicines, is equitable across the UK.

Access to rare disease treatments: Where are we now?

Rare diseases and orphan medicines

A rare disease is one that affects less than one in 2,000 people.[8] There is a high unmet need for patients and families living with rare diseases.[9] Many treatments for rare diseases are designated as orphan medicines, which are classified as medicines that:

- Treat, prevent or diagnose a disease where the prevalence is not more than 5 in 10,000.
- Are unlikely to generate sufficient returns to justify the investment needed.
- Treat, prevent or diagnose a disease where there are no other satisfactory methods of diagnosis or prevention, or where the medicine is of significant benefit.[10]

UK patients with rare diseases

There are estimated to be around 7,000 rare diseases.[11] Around one in 17 people are likely to be affected by a rare disease at some point in their lives,[12] which means rare diseases affect around 3.5 million people in the UK.[13] Two thirds of all rare diseases affect children and rare diseases are responsible for an estimated one third of UK infant mortality.[14]

For most rare diseases, there are no treatments available. This is the case for approximately 95% of all known rare diseases.[15] Yet R&D has led to treatments being developed for a number of these diseases. In Europe, the number of orphan regulatory approvals has increased over time, rising from three in 2001 to a peak of 22 in 2018, and 21 in 2020.[16] However, many of these treatments have encountered significant hurdles before being made available to patients. The treatments currently coming through pipelines will likely face similar challenges. The IMF has the potential to accelerate and improve access to these future treatments.

Improving access to rare disease specialist care, treatment and drugs is a priority for the UK

The UK Government has recognised there are many remaining challenges for patients and their families with rare diseases. The UK Rare Diseases Framework, published in January 2021, aims to ensure the lives of people living with rare diseases continue to improve by building on the work that has been done so far. The Framework has identified four priorities (Box 1).[17] The IMF can contribute towards meeting the fourth priority: improving access to specialist care, treatment and drugs.

Box 1: *Four priorities of the UK Rare Diseases Framework*

Priority 1: Helping patients get a final diagnosis faster
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

Source: Department of Health and Social Care. 2021. The UK Rare Diseases Framework. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950651/the-UK-rare-diseases-framework.pdf

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Access challenges for rare disease treatments

Drug development

For a rare disease treatment to have secured a marketing authorisation, developers will have had to overcome research and regulatory challenges. They then face the challenge of securing Health Technology Assessment (HTA) approval and funding (Figure 1).

Figure 1: *Challenges of bringing orphan medicines to market*

Source: IQVIA

In 2019, the overall development duration for an orphan medicine took almost four years longer than for non-orphan medicines.[18] The success rate for orphan medicines in clinical trials, based upon data from 1 January 2000 to 31 October 2015, was estimated to be only around 6%. This statistic compares to nearly 14% for all drug development programmes.[19]

Access challenges

In England, patients have faced a particular challenge in accessing rare disease medicines. Some medicines are not recommended for use on the NHS at all and have their recommended use restricted to sub-populations of the license, and the approval of

a few can also sometimes take longer than other medicines. This reflects a UK medicines reimbursement process widely regarded as unfit for orphan medicines.

In England, the majority of rare disease medicines are approved through a Single Technology Appraisal (STA), as part of the NICE HTA process. The crux of the challenge is NICE's STA criteria was not designed to handle the various challenges associated with rare disease medicines. NICE's review of STA criteria, as part of its Methods Review, provides an additional opportunity to consider how rare disease and orphan medicines are appraised and made available to patients.

The nature of orphan treatments gives rise to a number of specific challenges for HTA. As identified by the BioIndustry Association (BIA), the STA process has been designed for more common conditions. As such, it is seen to impose unrealistic expectations about available evidence on orphan medicines. The nature of orphan treatments means they will have:

- Small population samples and thus a lack of statistical power
- Limited trial duration
- Uncertainties in cost effectiveness modelling
- Uncertain clinical pathways and a lack of comparative data
- Limited clinical and Patient Reported Outcome (PRO)/ Health Related Quality of Life Evidence
- Issues dealing with subgroup data

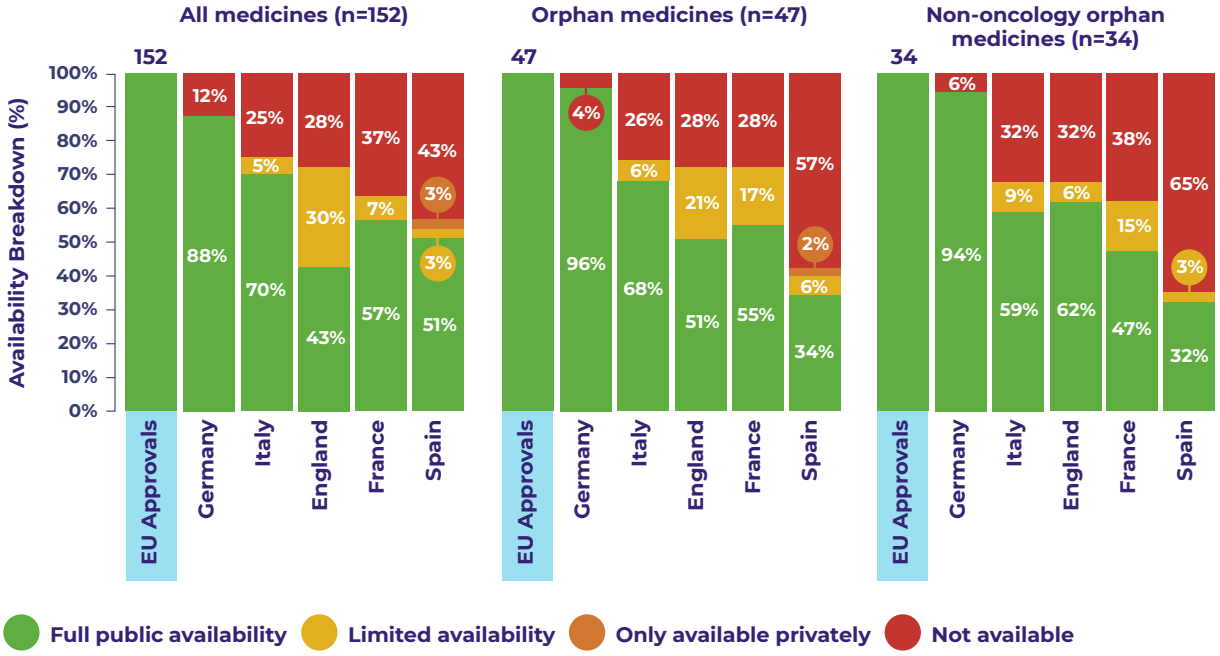
These factors impact the ability of an orphan medicine to meet tight cost effectiveness thresholds.

Statistics on approval rates show, of the 24 completed STA reviews of rare disease medicines between 2013 and 2017, only 13% were recommended for the full eligible population, compared with over two thirds of non-orphan medicines. In the same period, 50% of rare disease medicines were given a "restricted recommendation", compared to 21% of other medicines. Only six non-cancer orphan medicines have been reviewed by STA. Of these, only four appraisals were completed and none were recommended within their full marketing authorisation, compared with over two thirds of non-orphan medicines.[20]

A small number of treatments for ultra-rare conditions may qualify for review under the NICE Highly Specialised Technology (HST) programme that was introduced in 2013.[21] This process was designed specifically for ultra-orphan medicines with flexibility to manage the associated challenges, but few medicines qualify in reality. By May 2021, only 14 medicines for ultra-rare diseases had qualified and received a final HST appraisal published.[22]

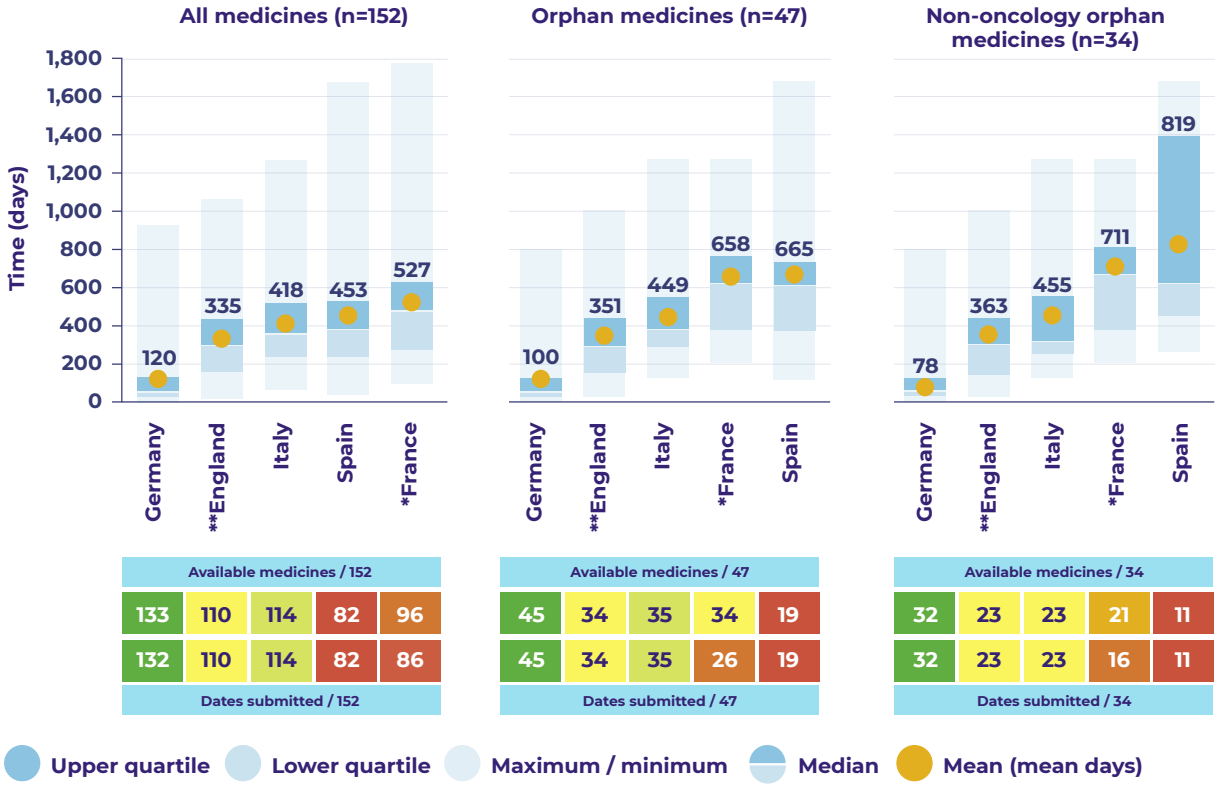
In comparison to other countries, the latest Patient Waiting to Access Innovative Therapies (WAIT) indicator, compiled by IQVIA and published by the European Federation of Pharmaceutical Industries and Associations (EFPIA), illustrates patients in Germany, Italy and France have access to a higher proportion of EU approved orphan medicines, and patients in Germany and Italy had access to a higher proportion of EU approved non-oncology orphan medicines than those in England.

Figure 2: *Rate of availability for EU4 and England (%,2016-19)*



Note: The rate of availability is the number of medicines available to patients in European countries and for most countries this is the point at which the product gains access to the reimbursement list. Please refer to the Patient W.A.I.T. indicator for country-specific definitions of availability and limited availability. Source: The Patient W.A.I.T. indicator 2021.

Figure 3: *Time to availability for EU4 and England (2016-19)*



Notes: The time to availability is the days between marketing authorisation and the date of availability to patients in European countries (for most this is the point at which products gain access to the reimbursement list). *In France, some innovative products without competitors can be made available prior to market authorisation under the system of Temporary Authorisations. As these are not taken into account in the analysis, the average would be lower. **In the UK, MHRA's Early Access to Medicines Scheme provides access prior to marketing authorisation but is not included within this analysis, and would reduce the overall days for a small subset of medicines. Source: The Patient W.A.I.T. indicator 2021.

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For some companies, given the risk of receiving a negative NICE appraisal, the preferred option is not to submit to HTA at all. For example, 15 out of 67 non-submissions to NICE were for orphan drugs based on IQVIA analysis using the list of orphan drugs identified by Orphanet and NICE data on terminated appraisals.[23]

The speed of NICE issuing guidance for orphan medicines is also concerning. While the most recent Office for Life Sciences (OLS) Competitiveness Indicators illustrate a fall from the time from marketing authorisation to final NICE guidance from 15.9 months for all topics in 2012/13 to 5.6 months in 2019/20, there is no breakdown for orphan treatments. IQVIA HTA Accelerator data from 2015 to 2019 show the combined lag from EMA approval to a final NICE decision took almost 12 months for orphan medicines (351 days) and non-oncology orphan medicines (363 days).[24]

Impact on patients

These access challenges are felt most acutely by patients and their carers. In 2020, the Genetic Alliance UK Patient Experience Survey, supported by Alexion, surveyed over 1,000 patients living with a rare disease and their carers. This found:

- 64% believe the system for making treatments available to patients is unfair on people living with rare diseases.
- 65% of patients believe the system is too slow to make treatments for rare diseases available to patients.
- Only 10% are satisfied with the process used to decide on funding rare disease medication in the NHS.
- Only 3% agree enough money is allocated to rare disease medicines.
- 58% believe decision-making on access to medicines and pricing is not transparent.[25]

NICE is changing, but there is more to do

Access to medicines in the UK is evolving. Even during the time that this White Paper was being written, new commitments have been made to advance patient access to innovative medicines, for example NICE published its five-year strategy for 2021 to 2026, stating their renewed determination to speed up access to the latest and most effective treatments.[26]

Additional strategic policy change to improve access to new treatments include the NICE reviews of methods and processes used by NICE in health technology evaluation. The reviews are partly driven by the recognition that products are becoming more complicated to evaluate due to innovations such as personalised medicines and cell and gene therapies.[27] Proposals that could help improve access to rare disease medicines, include the introduction of a severity modifier and a change to the rate used to assign current value to future treatment benefits and costs. Changes will be presented in a new programme manual that will be subject to consultation during August/September 2021, with subsequent publication in December 2021.[28] However, in the draft proposals, NICE have stated they do not anticipate an increase in the number of products being assessed via HST as a result of the reforms,

which is likely to increase the need for an IMF to bridge the HTA-reimbursement gap where rare disease medicines are routed to STA. This would help to ensure greater equity across all patient populations and patients with rare diseases not being left behind.

Table 1: *HTA processes for rare and ultra-rare disease treatments (URDT), 2020*

Process type		Separate	Partially separate	Adapted
Country		**England** HST	**Scotland** Ultra-Orphan Medicines Product pathway	**Scotland** Standard pathway with PACE and modifiers
Process description		Main differences with standard process: willingness to pay threshold, specialised appraisal committee, more holistic perspective of value, managed access agreements possible	Assessment based on ultra-OMP decision-making criteria, following initial assessment, interim reimbursement for 3 years to capture real world data, followed by re-assessment. Option for input from Patient and Clinician Experts (PACE) in process. Disease-specific experts describe treatment benefit not captured within original assessment	PACE: disease-specific experts describe treatment benefit not captured within original assessment. Modifiers: standard assessment for OMPs, but SMC recognises limitations in evidence generation and will accept greater uncertainty in the economic case
Eligibility		Based on HST prioritisation criteria	URDT: (1) ultra-rare, (2) chronic and severely disabling condition, (3) highly specialised management PACE: OMPs (and end of life treatments) not considered cost-effective – after Scottish Medicines Consortium (SMC) New Drug Committee (NDC) decision in re-assessment process	PACE: OMPs (end of life treatments) not cost-effective, manufacturer can request a PACE to get additional insights Modifiers: OMPs, life-threatening, substantial increase in quality of life/life expectancy, can reverse the condition, bridges gap to a definitive therapy
Definition	**Rare disease**	-	<1:50,000	OMP
	Ultra-rare disease	No prevalence criteria, based on HST eligibility criteria	-	-

HST Highly Specialised Technology
OMP Orphan Medicinal Product
PACE Patient and Clinician Engagement
URDT Ultra-Rare Disease Treatment
NDC New Drugs Committee

Adapted from: Nicod, E., Whittal, A., Drummond, M. and Facey, K. 2020. Are supplemental appraisal/reimbursement processes needed for rare disease treatments? An international comparison of country approaches. Orphanet Journal of Rare Diseases. 15:189. https://doi.org/10.1186/s13023-020-01462-0

The Cancer Drugs Fund – A precursor to the Innovative Medicines Fund

The Cancer Drugs Fund (CDF) was established in 2011 by the Coalition Government. Until 2016, the CDF was used to provide funding for cancer medicines which NICE had rejected for routine commissioning or not yet assessed. In 2016, the CDF was reformed. Now, if cancer medicines are not approved by NICE, but they have the potential to meet cost-effectiveness thresholds with further data, the CDF provides an interim source of funding in England. This enables access to new treatments whilst further evidence is generated to address clinical uncertainty.[29] Treatments that go into the CDF can go on to be routinely funded, illustrating how the CDF has been a force for good for cancer patients.

The revised CDF has an expenditure control mechanism to keep spending within a limit of £340million.[30] By the end of the 2019/20 financial year, spend was £317million.[31] A joint NHS England/NICE CDF Investment Group has responsibility for managing the overall budget. The Investment Group also approve the individual CDF managed access agreements (MAAs) – agreements covering specific treatments – that cover data collection arrangements and an agreed price for reimbursement.[32]

According to NHS England:

- 30 out of 33 of the cancer treatments funded under the 'old' CDF (2011-2016) have been reappraised by NICE and approved for routine funding.[33]
- By Q4 of 2019/20, three treatments covered by a MAA had been re-appraised by NICE and all were subsequently recommended for routine commissioning. One MAA treatment was terminated due to its licence being withdrawn.[34]
- By the end of 2020, more than 56,000 patients were registered for treatments funded by the CDF with 85 drugs treating 183 different cancer indications.[35]

Conservative Party 2019 Manifesto – Introducing the Innovative Medicines Fund

The 2019 Conservative Party Manifesto included a proposal to extend the CDF into an Innovative Medicines Fund (IMF).[36] The policy ambition is for the IMF to provide access to the best available medicines, including those that treat rare diseases (Box 2). In July 2021, NHS England announced further details on the IMF to drive innovative medicines to people with rare and genetic diseases. The Fund will be £680 million of ringfenced funding, with £340 million maintained for the Cancer Drugs Fund (CDF) and an additional £340 million for patients with any condition, including those with rare diseases.[37] A public engagement exercise on the IMF is anticipated to be held during late 2021.

Box 2: *Manifesto pledge for the IMF*

> ***"We will extend the successful Cancer Drugs Fund into an Innovative Medicines Fund so that doctors can use the most advanced, life-saving treatments for conditions such as cancer or autoimmune disease, or for children with other rare diseases. If you or a loved one is unlucky enough to fall ill, we'll ensure you have access to the best available medicines." - The Conservative and Unionist Party Manifesto 2019***

The Innovative Medicines Fund could advance access to rare disease medicines

The IMF presents an opportunity to advance patient access to rare diseases medicines, but only if the fund's design considers the unique issues for these medicines as set out in this White Paper.

There is an opportunity to learn not only from the experience of the CDF to date, but given the ambition set for the IMF to include rare disease treatments, to build in learnings from the appraisal of ultra-orphan medicines conducted by NICE through the HST programme.

The experience of other countries' approaches to MAAs should also be leveraged.

> ***"From a patient group perspective, it is important that the IMF serves as a beacon of hope."***
>
> **Roundtable participant**

Ambition

Recommendation 1: To drive access for patients, rare disease medicines must have the same opportunity for IMF funded access as a medicine for any other disease.

The expansion of the CDF to the IMF represents an opportunity to level the playing field across cancer and non-cancer medicines, providing an additional route for funded access to promising new treatments, including rare disease medicines, that was only previously available to cancer drugs.

Routine commissioning of rare disease medicines with demonstrated cost-effectiveness should remain the goal of HTA. Where there is significant uncertainty in the medicine's evidence base, however, the IMF should be considered as an option for interim reimbursement while additional evidence is collected.

Entry and exit criteria

Recommendation 2: The IMF must have clear but flexible entry and exit criteria that can accommodate rare disease medicines, as well as other medicines.

Criteria for entry and exit to the IMF must be clear so innovative pharmaceutical and biotechnology companies are able to identify when the IMF is an opportunity for faster and funded access for patients to promising new treatments.

All rare disease medicines should qualify for access to the IMF, where NICE appraisal is unlikely to result in patient access.

When considering rare and ultra-rare disease medicines, the IMF threshold for cost-effectiveness will need to be higher than that currently applied in the CDF.

- The CDF is open to those cancer treatments that have the potential to meet a maximum cost threshold of £50,000 per QALY, which is applied when the criteria for an end-of-life treatment are met.[38]
- This threshold is out of line with the threshold used in HSTs of £100,000 to £300,000.[39]

The IMF criteria for entry will also need to align with any future changes to the NICE cost-effectiveness thresholds, including the introduction of modifiers, that come into effect following the NICE methods and processes reviews.[40]

During the roundtable, rare disease stakeholders called for clarity on the Fund's entry requirements, alongside flexibility to amend the criteria, where necessary.

> ***"We require clear entry and eligibility requirements. But we also need to allow for flexibility."***
>
> **Roundtable participant**

Funding

Recommendation 3: IMF funding should not be ringfenced by disease area or medicine type, and must not operate on a 'first-come, first-served' basis.

The IMF should be operated as a single fund open to all qualifying medicines, rather than having set amounts assigned for specific medicine types, such as cancer medicines.

For this to work, the fund must be sufficient to accommodate all qualifying medicines and must not operate on a 'first come, first served' basis which would disadvantage medicines on the basis of their development timing.

England is not alone in pursuing the idea of a special fund to pay for innovative medicines. Italy, for example, operates two special funds for innovative medicines. Each fund is worth €500million with one for cancer treatments and the other for non-cancer treatments. Calls have been made to merge the funds, in order to avoid underspends in one, and too little money available in the other, and to allow for more flexibility in how long treatments can be covered.

We welcome NHS England's £680 million IMF funding commitment and a specific focus on rare and genetic disease, however, the Italian experience has shown running two separate funds – one for cancer, and another for other non-cancer treatments – risks leaving one fund oversubscribed whilst the other is under-spent. Allowing for flexibility and not ring-fencing funds based on disease area or medicine type, the IMF can adopt these lessons and others from the MAAs used in HSTs to date.

Recommendation 4: The IMF should have a flexible budget linked to horizon scanning.

The IMF should be funded flexibly to allow it to adapt to innovations in the medicines pipeline instead of having its funding fixed at £680 million per year. There had been concerns that proposals based on a funding envelope of £500 million may not be sufficient for the IMF, given current medicines spend and new treatments expected to receive marketing authorisation in the coming years.

- IQVIA estimates suggest spending on orphan medicines in the UK was around £273 million in 2019/20.[41] Spending on cancer treatments in the CDF was £317 million by the end of the 2019/20.[42]
- 31 of 170 new molecule launches expected between 2020 and 2021 will be orphan medicines, rare disease treatments and/or given PRIME designation.*
- In cancer, there are expected to be 272 new indications for new and existing medicines between 2020 and 2021, 14 of which will be for rare diseases or will have orphan status.[43]

There are opportunities to draw upon the enhanced horizon scanning conducted through UKPharmascan, which provides a line-of-sight on the industry pipeline around three years before UK availability.[44] The IMF annual budget should rise and fall year by year based on the products entering the market.

"Will there be enough money available?"

Roundtable participant

"The budget could be linked to horizon scanning."

Roundtable participant

"Funding should be based on pipelines."

Roundtable participant

Recommendation 5: Funding for the IMF should be tabled as part of negotiations on the 2024 Voluntary Scheme for Branded Medicines Pricing and Access (VPAS).

The VPAS rebates paid to HM Treasury each year by pharmaceutical companies should be earmarked for funding of innovative medicines rather than ascribed to general NHS funding as is currently the case.

*PRIME is a scheme run by the European Medicines Agency (EMA) to enhance support for the development of medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options.

The IMF is due to be launched mid-way through the Voluntary Scheme for Branded Medicines Pricing and Access (VPAS), which runs from 01/01/2019 to 31/12/2023. The VPAS is a commitment from the NHS, Government and industry to support innovation for the benefit of patients across the UK.[45]

- The agreement has set a limit on the growth of the NHS branded medicines bill of no more than 2% a year.
- Any spend above this limit is paid back by companies to the Treasury. The rebate is a percentage of their NHS sales.[46]
- According to the latest data published on 1 March 2021, pharmaceutical companies paid rebates of £844 million to the DHSC in 2019 and £594 million in 2020.[47]

Discussions between the Government and industry ahead of the next VPAS scheme should include the possibility of assigning a proportion of the rebates paid by the pharmaceutical industry directly through the IMF, providing transparency on which treatments are funded and to what amount, rather than through general healthcare expenditure. Such conversations need to begin now and should be taken into negotiations that could start in 2022.

It would also provide an opportunity to look at the Scottish New Medicines Fund which is funded from the share of payments made by companies under the VPAS.[48]

> ***"Pharma rebate could be allocated to the IMF, just as in Scotland. This could be part of the next VPAS discussions."***
>
> **Roundtable participant**

Data collection

Recommendation 6: The IMF should allow for bespoke data collection, taking a medicine-by-medicine approach to outcomes, data sources and the time required. The IMF must recognise the complexity and difficulty of evidence generation in rare diseases.

The data collected in the IMF should relate to the uncertainties identified at first NICE appraisal and should therefore be determined on a medicine-by-medicine basis. The data could be real world data or further clinical trial read-outs.

The complexity and difficulty of evidence generation in rare disease medicines should shape the approach taken in the IMF, which should recognise that selection of appropriate endpoints is challenging, reflecting small patient populations, phenotypic heterogeneity, variable time frames for disease progression, incomplete knowledge of the disease pathophysiology or natural history, an absence of prior clinical studies, and non-existent validated disease-appropriate endpoints.

The IMF will also need to accommodate the potential for a range of data sources to be used as part of evidence generation. The CDF uses the Systemic Anti-Cancer Therapy Data Set (SACT)[49] to support its real-world evidence generation, but there is no analogous dataset for other diseases.

The CDF includes a timeframe for data collection that is normally up to two years.[50] Rare disease medicines are likely to need more time. In practice, the CDF has accommodated MAAs with longer timeframes of up to 42 months.[51] MAAs agreed in the HST programme have started with a maximum duration of five years,[52] but have had to be adjusted due to external changes such as COVID-19 (Box 4). The IMF will similarly need to allow sufficient flexibility, not only in the timeframe for data collection, but also permitting a review of the data collection over time to ensure it remains fit for purpose.

Box 4: *Expansion to Market Access Agreements for orphan medicines*

A MAA for PTC Therapeutics' orphan medicine Translarna® (ataluren), used to treat Duchenne muscular dystrophy with a nonsense mutation in the dystrophine gene, was agreed in 2016.[1] The MAA was originally due to end in July 2021. The review of HST3 was paused as a result of the need for NICE to prioritise work related to the COVID-19 pandemic. The MAA will now run to January 2023.[2] The new MAA has also been expanded to include new patients and allows them to begin treatment.[3]

A MAA for Biogen's orphan medicine Spinraza® (nusinersen) was agreed in 2019.[4] The MAA provided access to Spinraza® for children who could still walk independently before they started treatment. NICE announced in May 2021 the MAA will include patients who have lost the ability to walk independently in the last 12 months. The change to the MAA reflects evidence that has been collected as part of the MAA.[5]

Sources:

1 NICE. 2016. Managed Access Agreement: Ataluren for treating nonsense mutation Duchenne muscular dystrophy (nmDMD). [Online] Available at: https://www.nice.org.uk/guidance/hst3/resources/managed-access-agreement-july-2016-pdf-2553024061

2 NICE. 2021. Ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene (review of HST3) ID1642, update for 13 May 2021.

3 Dark, B. 2021. LinkedIn. [Online] Available at: https://www.linkedin.com/posts/blake-dark-4b46859_ataluren-for-treating-duchenne-muscular-dystrophy-activity-6798567181316567040-r_wu

4 NICE. Managed Access Agreement: Nusinersen (Spinraza®) for the treatment of 5q spinal muscular dystrophy. [Online] Available at: https://www.nice.org.uk/guidance/ta588/resources/managed-access-agreement-july-2019-pdf-6842812573

5 NICE. 2021. NICE announces more people eligible for nusinersen following review of Managed Access Agreement. [Online] Available at: https://www.nice.org.uk/news/article/nice-announces-more-people-eligible-for-nusinersen-following-review-of-managed-access-agreement

Data collection must also be as easy as possible for patients, as highlighted by a roundtable participant:

> ***"Patients are generally happy to support data collection, but do we make it easy for them?"***
>
> **Roundtable participant**

Governance

Recommendation 7: An external IMF multi-stakeholder group should be formed reporting annually on IMF performance using Key Performance Indicators (KPIs) broken down by disease and orphan status.

A multi-stakeholder governing body should be formed for the IMF, co-lead by NICE and NHS England, including patients and their representatives, clinicians and industry to provide constructive support and, where necessary, to challenge NICE and NHS England. Given the impact of rare diseases on children, the IMF multi-stakeholder governing body must include patients/patient groups that represent their unique needs.

NICE should act as the gatekeeper to the IMF, determining entry and exit, while NHS England should have accountability for managing the IMF budget.

The IMF multi-stakeholder body remit should include identifying Key Performance Indicators (KPIs) from the outset and reporting annually on performance. The KPIs should include, but not be limited to, the speed of IMF access from marketing authorisation; the length of NICE appraisals to IMF entry; and the proportion of positive, negative or restricted recommendations made at the end of interim IMF funding. These KPIs should be reported separately for cancer and orphan medicines, including cancer orphan medicines and non-cancer orphan medicines.

The IMF multi-stakeholder body should also conduct and publish a progress review one year following the implementation of the fund. The review should go beyond KPIs and look at whether the IMF is delivering on its ambitions, identify any challenges and devise/consult on possible solutions/improvements.

The progress review should also explore the sustainability of the budget allocated to the IMF in light of the treatments that have entered (and potentially exited) the IMF during its first year of operation.

"All stakeholders should be part of this process to ensure consistency and any issues that come up can be understood and solutions jointly developed."

Roundtable participant

Alignment with other initiatives

Recommendation 8: The IMF must be aligned with the evolving access landscape, including with initiatives such as the ILAP, NICE Methods and Processes Review and UK Rare Diseases Framework.

The IMF should be kept under review and regularly adapted to align with the evolving access landscape and broader healthcare initiatives, including the implementation of the UK Rare Diseases Framework, revisions to the NICE methods and processes of health technology evaluations, including HST criteria, and the introduction of the ILAP, as well as broader reforms to the NHS.

An illustrative quote from a roundtable participant noted:

> ***"The IMF must not be viewed in isolation."***
>
> **Roundtable participant**

It is important too that throughout the NHS in England, there is a recognition of the importance of improving access to care and treatments for those with rare diseases. One option is for the Government to explicitly reference this as a goal in the Mandate given to the NHS each year, which defines the priorities for the year ahead. While the 2020/21 Mandate is focused on COVID-19, a further Mandate is expected once the virus has been effectively managed.[53]

UK collaboration

Recommendation 9: The four UK nations should hold discussions to leverage lessons from the IMF – and their own funds - and explore the scope to increase the value of the evidence generated. The four nations should also work together to ensure access to innovative medicines, including rare disease medicines, is equitable across the UK.

Patients with rare diseases live across the UK and in line with the spirit of the UK Rare Diseases Framework, the four nations should explore the scope to work together in ensuring equitable access to promising new treatments, regardless of where a patient may live.

Experiences in the devolved nations with their own funds for innovative medicines should also be shared and the four nations should discuss how evidence sharing could help to address decision uncertainty across their respective HTA agencies.

The IMF should produce evidence that will be of value not only to NICE and NHS England, but also to counterparts in the devolved nations to help inform equitable decisions about access to treatments across the UK. The four nations could also work together with companies to avoid duplication of work across the agencies.

The rare disease community would like to see more collaboration across the four nations:

> ***"There is a need for at least UK wide data sharing."***
>
> **Roundtable participant**

Concluding thoughts

Implementation of the UK Rare Diseases Framework, alongside country specific actions plans and the proposed establishment of an IMF provide an excellent catalyst to drive access to rare disease treatments.

This opportunity must be clearly articulated across the NHS and align with wider initiatives, including the Early Access to Medicines Scheme (EAMS), the Accelerated Access Collaborative (AAC), and the NICE Methods Review to improve access to rare disease medicines.

The IMF has set an ambitious agenda to enable access to the most advanced, life-saving treatments and represents a clear opportunity for those with rare diseases who face particular challenges in accessing medicines arising from the rarity of their conditions.
While we wait for further details to be published by NHS England, the rare disease community, including representatives from Parliament, patient groups, clinical centres, industry and NICE, have come together to discuss the potential of the IMF and to learn from both existing access routes, such as the CDF, and the experiences of other countries.

Together, we have identified the IMF represents an excellent opportunity to level the playing field across cancer and non-cancer medicines, and provide an additional route for funded access to promising new rare disease medicines.

To deliver on this potential, a number of practical suggestions for the implementation of the IMF have been made and set out as recommendations, including ensuring rare disease medicines are given the same opportunities for access as medicines for cancer or more common diseases, options for financing the fund, securing the involvement of all interested stakeholders from the outset, and collaborating and sharing lessons across the four nations of the UK.

The nine recommendations set out in this White Paper, if acted on, will help realise the ambitions for the IMF, as set out by the Government.

References

1. Rare Disease UK. Undated. What Is a Rare Disease? [Online] Available at: https://www.raredisease.org.uk/what-is-a-rare-disease/
2. Department of Health and Social Care. 2018. Matt Hancock announces ambition to map 5 million genomes. [Online] Available at: https://www.gov.uk/government/news/matt-hancock-announces-ambition-to-map-5-million-genomes
3. Alexion. 2020. Reforming Rare Diseases. [Online] Available at: https://rareexperience2020.geneticalliance.org.uk/
4. Alexion. 2020. Reforming Rare Diseases. [Online] Available at: https://rareexperience2020.geneticalliance.org.uk/
5. Alexion. 2020. Reforming Rare Diseases. [Online] Available at: https://rareexperience2020.geneticalliance.org.uk/
6. Alexion. 2020. Reforming Rare Diseases. [Online] Available at: https://rareexperience2020.geneticalliance.org.uk/
7. IQVIA. 2021. EFPIA Patients W.A.I.T. Indicator
8. Department of Health and Social Care. 2021. The UK Rare Diseases Framework. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950651/the-UK-rare-diseases-framework.pdf
9. PWC and BIA. 2020. A rare chance for reform: A new way forward for evaluating medicines for rare and ultra-rare diseases in England. [Online] Available at: https://www.bioindustry.org/uploads/assets/875ae91a-1583-4544-9f5d3ca9bfe696b7/A-Rare-Chance-for-Reform.pdf
10. EMA. Undated. Orphan designation: Overview. [Online] Available at: https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview
11. Department of Health and Social Care. 2021. The UK Rare Diseases Framework. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950651/the-UK-rare-diseases-framework.pdf
12. ABPI. Undated. Rare diseases: Facing three challenges. [Online] Available at: https://www.abpi.org.uk/new-medicines/rare-diseases-facing-the-three-challenges#f8302237
13. Department of Health and Social Care. 2021. The UK Rare Diseases Framework. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950651/the-UK-rare-diseases-framework.pdf
14. Department of Health and Social Care. 2021. The UK Rare Diseases Framework. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950651/the-UK-rare-diseases-framework.pdf
15. Department of Health and Social Care. 2021. The UK Rare Diseases Framework. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950651/the-UK-rare-diseases-framework.pdf
16. EMA. Undated. Orphan medicines figures 2000-2020. [Online] Available at: https://www.ema.europa.eu/en/documents/other/orphan-medicines-figures-2000-2020_en.pdf
17. Department of Health and Social Care. 2021. The UK Rare Diseases Framework. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950651/the-UK-rare-diseases-framework.pdf
18. PhRMA. 2019. Meeting the Need: Rare Diseases and the Orphan Drug Act. [Online] Available at: https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRMA-Orphan-Chart-Pack_Final_10112019.pdf
19. Wong, C.H. and Siah, K.W. 2019. Estimation of clinical trial success rates and related parameters. Biostatistics. 20(2):273-286. 286 doi:10.1093/biostatistics/kxx069
20. MAP BioPharma. 2019. Access to Orphan Medicines: A Case for Change. [Online] Available at: https://mapbiopharma.com/publications/access-to-orphan-medicines-a-case-for-change/
21. YHEC. 2016. Highly Specialised Technologies (UK NICE). [Online] Available at: https://yhec.co.uk/glossary/highly-specialised-technologies-uk-nice/
22. NICE. Guidance and advice list:HSTs. [Online] https://www.nice.org.uk/guidance/published?type=hst Accessed 13 May 2021
23. Data from NICE available at: https://www.nice.org.uk/search?om=%5b%7b%22ndt%22:%5b%22Guidance%22%5d%7d%5d&pa=1&ps=15&q=Terminated+Appraisal&sp=on and list of orphan drugs from Orphanet. 2020. List of medicinal products for rare diseases in Europe. [Online] Available at: https://www.orpha.net/orphacom/cahiers/docs/GB/list_of_orphan_drugs_in_europe.pdf
24. IQVIA HTA Accelerator.
25. Alexion. 2020. Reforming Rare Diseases. [Online] Available at: https://rareexperience2020.geneticalliance.org.uk/
26. NICE. 2021. NICE strategy 2021 to 2026: Dynamic, Collaborative, Excellent. [Online] Available at: https://static.nice.org.uk/NICE%20strategy%202021%20to%202026%20-%20Dynamic,%20Collaborative,%20Excellent.pdf
27. NICE. Undated. Changes we're making to health technology evaluation. [Online] Available at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation
28. NICE. Undated. Changes we're making to health technology evaluation. [Online] Available at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation

29. NHSE. Undated. Cancer Drugs Fund. [Online] Available at: https://www.england.nhs.uk/cancer/cdf/
30. NHSE. Undated. Cancer Drugs Fund. [Online] Available at: https://www.england.nhs.uk/cancer/cdf/
31. NHSE&I. 2020. Cancer Drugs Fund Activity Update. Q4 2019/20. Available at: https://www.england.nhs.uk/wp-content/uploads/2018/01/cancer-drugs-fund-activity-update-q4-2019-20.pdf
32. NHS England. 2016. Appraisal and funding of Cancer Drugs from July 2016 (including the new Cancer Drugs Fund): A new deal for patients, taxpayers and industry. [Online] Available at: https://www.england.nhs.uk/wp-content/uploads/2013/04/cdf-sop.pdf
33. CancerResearchUK. 2018. The new Cancer Drugs Fund has quietly reached a significant milestone. [Online] Available at: https://scienceblog.cancerresearchuk.org/2018/12/14/the-new-cancer-drugs-fund-has-quietly-reached-a-significant-milestone/
34. NHSE&I. 2020. Cancer Drugs Fund Activity Update. Q4 2019/20. Available at: https://www.england.nhs.uk/wp- content/uploads/2018/01/cancer-drugs-fund-activity-update-q4-2019-20.pdf
35. Dark, B. 2021. LinkedIn. [Online] Available at: https://www.linkedin.com/posts/blake-dark-4b46859_blake-dark-on-twitter-activity-6793492271976202240-26I9
36. Conservatives and Unionist Party. 2019. Get Brexit Done Unleash Britain's Potential: The Conservative and Unionist Party Manifesto 2019. [Online] Available at: https://www.conservatives.com/our-plan
37. NHS England. 2021. NHS England announces new Innovative Medicines Fund to fast-track promising new drugs. [Online] Available at: https://www.england.nhs.uk/2021/07/nhs-england-announces-new-innovative-medicines-fund-to-fast-track-promising-new-drugs/
38. NHS England. 2016. Appraisal and funding of Cancer Drugs from July 2016 (including the new Cancer Drugs Fund): A new deal for patients, taxpayers and industry. [Online] Available at: https://www.england.nhs.uk/wp-content/uploads/2013/04/cdf-sop.pdf
39. Powell, T. and O'Donnell, M. 2019. NICE appraisals of rare diseases. House of Commons Library Debate Pack Number CDP-2019-0022.
40. NICE. 2020. NICE methods of health technology evaluation: the case for change. [Online] Available at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/chte-methods-consultation
41. IQVIA. Data on file.
42. NHSE&I. 2020. Cancer Drugs Fund Activity Update. Q4 2019/20. Available at: https://www.england.nhs.uk/wp-content/uploads/2018/01/cancer-drugs-fund-activity-update-q4-2019-20.pdf
43. IQVIA. Data on file.
44. UK PharmaScan. Undated. An essential first step to market access for medicines. [Online] Available at: https://www.ukpharmascan.org.uk/about
45. ABPI. Undated. What is the new Voluntary Scheme on branded medicines? [Online] Available at: https://www.abpi.org.uk/new-medicines/medicine-pricing-in-the-uk/what-is-the-new-voluntary-scheme-on-branded-medicines/#f8302237
46. DHSC. 2018. Voluntary scheme for branded medicines pricing and access. [Online] Available at: https://www.gov.uk/government/publications/voluntary-scheme-for-branded-medicines-pricing-and-access
47. Department of Health and Social Care. 2021. Aggregate net sales and payment information: February 2021. [Online] Available at: https://www.gov.uk/government/publications/voluntary-scheme-aggregate-net-sales-and-payment-information-february-2021/aggregate-net-sales-and-payment-information-february-2021
48. ABPI. 2020. Pharmaceutical companies give NHS Scotland £1million a week to help fund new treatments. [Online] Available at: https://www.abpi.org.uk/media-centre/news/2020/january/pharmaceutical-companies-give-nhs-scotland-1-million-a-week-to-help-fund-new-treatments/#f8302237
49. NHS. Undated. NHS Data Model and Dictionary. [Online] Available at: https://datadictionary.nhs.uk/data_sets/clinical_data_sets/systemic_anti-cancer_therapy_data_set.html
50. NHS England. 2016. Appraisal and funding of Cancer Drugs from July 2016 (including the new Cancer Drugs Fund): A new deal for patients, taxpayers and industry. [Online] Available at: https://www.england.nhs.uk/wp-content/uploads/2013/04/cdf-sop.pdf
51. Sabry-Grant, C., Malottki, K. and Diamantopoulos, A. 2019. The Cancer Drugs Fund in Practice and Under the New Framework. PharmacoEconomics. 37:953-962 https://doi.org/10.1007/s40273-019-00793-6
52. Simon Kucher. 2021. NICE's Highly Specialized Technologies. [Online] Available at: https://www.simon-kucher.com/en-gb/blog/nices-highly-specialized-technologies
53. DHSC. 2021. The Government's revised 2020-2021 mandate to NHS England and NHS Improvement. [Online] Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/972951/Revised_2020_to_2021_mandate_to_NHSEI.pdf

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