CANCER RESEARCH UK POLICY STATEMENT ON IMPROVING ACCESS TO NEW CANCER MEDICINES IN ENGLAND

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SUMMARY

Cancer drugs play a crucial role in many patients’ treatment, helping to reduce disease symptoms and often allowing them to live longer. There have been exciting advances in drug development over recent years, with many innovative treatments in the pipeline. However, the NHS is often slower than it could be at getting these innovative new treatments to patients.

To improve outcomes and the experience of care for people with cancer, it’s critical that we ensure swift and equitable access to the most promising and effective medicines. And as a major funder of research into new cancer treatments, we want to make sure this progress is translated into patient benefit as quickly possible.

We have seen real progress since 2016. The National Institute of Health and Social Care Excellence (NICE), which decides whether the NHS should make individual medicines available, is appraising significantly more cancer drugs than in previous years. It has also recently committed to a series of reforms designed to increase its capacity further, and to appraise new medicines more quickly.

Meanwhile, reflecting the call in the 2015 Cancer Strategy for England to “define a sustainable solution for access to new cancer drugs”, the Cancer Drugs Fund has been reformed. The Fund now provides early access to promising medicines while more evidence is collected on their effectiveness. This reform has also laid the foundations for a value-based approach to drugs pricing, as ‘real-world’ data (from patients in NHS care) is collected on the efficacy of new drugs, to be considered alongside clinical trial data.

However, reports such as the Accelerated Access Review and the Life Sciences Industrial Strategy have recognised that more still needs to be done to improve and speed up patient access to cancer drugs in England. There is also some uncertainty about the UK’s access to new medicines and continued supply of medicines after the UK leaves the European Union. We want to build on the developments of recent years to ensure all patients can access the best, evidence-based treatments for their condition.

This paper outlines Cancer Research UK’s position on access to new cancer medicines in England, with reference to four main headings: licensing, approvals, pricing and uptake. More detail on some of the issues outlined in this paper can be found in separate policy statements; where this is the case, this will be clearly noted, and the statements will be available to download from our website.
RECOMMENDATIONS

1. The UK and the EU must come to an agreement to ensure the future drug licensing system does not exacerbate delays in access to the most innovative treatments for patients, both in the UK and across the EU. To achieve this, the UK Government should seek an agreement with the EU which would:
   a. Allow the European Medicines Agency (EMA)'s licensing decisions to apply in the UK after Brexit;
   b. Allow the MHRA (Medicines and Healthcare products Regulatory Agency)'s continued participation in EMA decision-making and shaping the regulatory environment, building on its reputation and expertise.

2. NICE should ensure its methods and processes are fit for future treatments. This should include consideration of:
   a. Methodology to appraise combination treatments, targeted treatments (and associated diagnostics) and medicines effective for multiple indications;
   b. Improved horizon-scanning to identify emerging technologies and trends in drug development, in partnership with NHS England, drug manufacturers, research leads and patients;
   c. Consideration of wider criteria that could be formally incorporated into the appraisal process, such as unmet need.

3. As stated in the Accelerated Access Review, we encourage NHS England’s Strategic Commercial Unit to take a leading role in exploring and developing flexible pricing mechanisms which give the NHS new ways of paying for cancer drugs, such as outcomes-based pricing.

4. Public Health England and NHS England must invest in improving the quality of the Systemic Anti-Cancer Therapy (SACT) dataset, so that it can be used to generate reliable evidence on the uptake and clinical effectiveness of new cancer medicines.

5. The Government and NHS England should ensure the new Genomic Medicine Service delivers equitable, fast access to molecular diagnostic tests and targeted medicines to cancer patients in England. In particular:
   a. NHS England Specialised Commissioning should take on responsibility for paying directly for all cancer molecular diagnostic testing as soon as is feasible.
   b. NHS England and Public Health England should work together to monitor the uptake of molecular diagnostic tests, quickly identifying and investigating any variation in molecular diagnostic activity within each of the seven Genomic Laboratory Hub regions.
   c. NHS England and the Department of Health and Social Care should ensure they balance preparing for the future integration of Whole Genome Sequencing into mainstream services, and serving the needs of patients today through the provision of less complex diagnostic tests (including multiplex panels).
BACKGROUND

In the 1970s, less than a quarter of people with cancer survived. But over the last 40 years, survival has doubled – and today, half will survive with progress driven in large part by improvements in early diagnosis. Yet research from the International Cancer Benchmarking Partnership (ICBP) has found that UK cancer survival still lags behind comparable countries – with sub-optimal access to treatments a contributing factor.

Our ambition is to accelerate progress and see three-quarters of people surviving the disease by 2034. To get there, we must ensure patients can access the best possible treatment for their disease; this includes surgery, radiotherapy and chemotherapy.

29% of patients receive cancer drugs as a first line treatment. Access to the best and most innovative medicines remains an incredibly emotive issue for people affected by cancer and the public. If we are to see UK cancer outcomes improve, it is vital that patients can access the most appropriate medicines for their condition in a timely fashion, and that there is equal access across the country and between different patient groups.

However, there must be a balance between the need to facilitate swift patient access to promising medicines with ensuring decisions about new drugs are based on robust evidence of their long-term benefits – especially given that some of these new medicines can be very expensive and can have severe side-effects.

Concerns have been raised about the slow uptake of innovation in the NHS. These concerns are valid and should be addressed. Although around 25% of the world’s top 100 prescription medicines were discovered and developed in the UK, research suggests that patient uptake of the newest cancer drugs is slower in the UK than in other G5 countries.

This was also highlighted in the Government’s recent Life Sciences Industrial Strategy, which recognised that it often takes a significant time for innovation to diffuse across the healthcare system.

Prescribing data supports this, suggesting that access to medicines, once approved, is not always equitable. For example, there is a five-fold difference in the use of chemotherapy between the highest- and lowest-prescribing cancer geographies. There is also evidence that older patients are less likely to receive chemotherapy for some types of cancer (this is explored further in the “uptake” section below).

This paper details our policy solutions for improving patient access to the best cancer drugs in the NHS in England. This discussion is divided into three sequential themes, along the drug access pathway – licensing, approvals and uptake – with pricing and reimbursement running across.

Licensing  Approvals  Uptake

Fig. 1: The access to medicines pathway
THE CHANGING LANDSCAPE OF DRUG DEVELOPMENT

It is an exciting time in drug development, with more than 700 cancer drugs in late-stage development – up 60% from a decade ago. 14 of the world’s largest pharmaceutical companies have at least a third of their late-stage R&D activity focused on oncology. As a result, over the past five years the world has seen 63 new cancer drugs approved, across 24 cancer types

The landscape of cancer drug development has changed markedly over recent years: there is now an increased focus on targeted drugs and immunotherapies, with targeted drugs making up 90% of the therapies in the late stages of development in 2016. All of the 14 New Active Substance cancer therapies launched in 2017 were targeted medicines.

Because of this shift, rather than cancer being seen as a single site diagnosis – for example, breast cancer – it is increasingly defined by a combination of biological factors known as biomarkers (such as a specific genetic mutation) which may occur in tumours at multiple sites. These factors can determine whether a targeted drug or immunotherapy is likely to be effective. While some types of cancer, such as breast cancer, have long had an established stratified treatment approach (i.e. using biomarkers to inform a patient’s treatment), the use of this approach across other cancer types has increased rapidly over the past ten years.

This change in how we clinically categorise cancers has led to a dramatic rise of medicines being marketed for multiple types of cancer (known as ‘multiple indications’). More than 50% of major cancer medicines marketed in 2014 were for multiple indications; by 2020 this is expected to reach 75%. For example, NICE has issued guidance on the use of nivolumab (a monoclonal antibody, a type of drug which is both an immunotherapy and a targeted drug) in seven different cancer indications and is developing guidance in a further nineteen indications.

This shift also means that genomic testing is increasingly used to inform treatment options, by checking for the presence of biomarkers that can be matched to a specific targeted drug or immunotherapy. This trend is likely to increase in the coming years, and is explored further in the “uptake” section below.

Many of these new medicines provide modest survival benefit to patients – a matter of months rather than years. However, these drugs can sometimes be used in succession as a tumour evolves and acquires additional genetic faults, adding up to a considerable increase in survival. For patients with some cancer types, immunotherapies in particular have transformed outcomes, since their first launches in 2014 – such as the use of pembrolizumab (Keytruda) in melanoma or non-small cell lung cancer.

However, there are still challenges associated with immunotherapy: some patients respond very well to it, whereas for others it is ineffective. Right now it is not fully understood what causes such differences in response, but further research is underway. Immunotherapy can also be associated with severe side-effects, which require intense hospital treatment – so may require bespoke support to implement in the NHS if used more widely to treat cancer in future.

There is also considerable interest in the use of immunotherapies in combination with other immunotherapies, or combinations of more traditional treatments such as chemotherapy and radiotherapy. Since 2009 there have been around 270 trials involving immunotherapy drugs given in combination, in lung cancer and melanoma alone. While combination
treatments can offer important additional options for patients, they can also pose regulatory, financial, and clinical challenges.

**LICENSING**

The first step in bringing a new drug into the health service is for it to be licensed as safe to sell. For this, the UK currently participates in a centralised process managed by the European Medicines Agency (EMA). This is an attractive route for pharmaceutical companies seeking to licence their products, as an EMA marketing authorisation covers 25% of the global drug market. The UK’s main interaction with the EMA is through the Medicines and Health Products Regulatory Agency (MHRA), which provides expertise to medicines approvals conducted by the EMA.

Our priority as the UK exits the EU is to safeguard the interests of patients and research. Regulatory alignment with the EMA with regard to drugs licensing and clinical trials is critical to achieving this. The reason for this is twofold: ensuring that the UK remains a priority launch market through its participation in the centralised process, and ensuring that the centralised process itself is not disrupted, by maintaining the expert involvement of the MHRA — one of the leading national authorities in the field.

The UK is currently in a strong position as a launch market: only three countries (the US, Germany and the UK) have access to more than 40 of the 55 oncology medicines initially launched between 2012 and 2016. Other countries under the EMA will either have reimbursement reviews and negotiations pending, or in some cases the company will have decided not to market the drug in that country.

Between 2008 and 2016, the MHRA acted as Scientific Advice Coordinator in at least 20% of centralised EMA medicine approval procedures. Loss of this expertise could mean that the EMA’s decision-making processes slow down, at least in the short term, which does not benefit patients in the UK or across Europe.

The MHRA has also been instrumental in designing and delivering the regulatory environment across the EU for clinical trials, ultimately driving faster access to new medicines for patients across Europe. This was referenced in a joint letter by UK and EU industry leaders and the MHRA have made their desire to stay involved clear, in a statement immediately following the Brexit vote.

CRUK agrees with others, such as EFPIA (the membership body for the European pharmaceutical industry) and the Brexit Health Alliance, that a break in regulatory continuity would represent ‘an unacceptable risk to patient health’. Our preferred option would therefore be for the UK Government to seek an agreement with the EU which would allow the MHRA’s continued participation in EMA decision-making and in shaping the regulatory environment.

This would help ensure that the UK remains an attractive launch market for pharmaceutical companies bringing drugs to market, and therefore that UK patients are able to access innovative medicines quickly. Crucially it would also benefit the EMA as a whole by providing valuable continuity in expertise.

We recognise and support the UK Government’s commitment to maintaining swift patient access to medicines in their position paper on Science and Innovation, as well as the Prime Minister’s ambition to achieve a strong future partnership with the EMA through an associate
membership. We now need to see swift progress in negotiations, so that there is no delay in access to new medicines after the UK leaves the European Union.

For more detail, please see our separate policy position on drug licensing following the UK’s exit from the EU.

**NICE APPROVAL**

Once a drug has received marketing authorisation, it must be approved for routine prescribing in the health service, through a Health Technology Assessment (HTA). This step measures the cost-effectiveness of the drug against a standard threshold. This is done differently across the UK; in England, this is done by the National Institute of Health and Care Excellence (NICE).

In 2016 NICE conducted 41 cancer drug appraisals, and a further 46 in 2017. This is a considerable increase on the average figure of 15 per year between 2009 to 2015 (Fig. 2). NICE have largely managed well with this increased demand, however there is still more to do to future-proof their processes.

There has also been an increase in the proportion of ‘optimised’ decisions, where NICE recommends a drug for a more restricted patient population than in the marketing authorisation. This can mean that the drug becomes more cost-effective, and therefore can help the approval process. However, there is a risk that this excludes certain groups of patients from accessing a new drug. We will therefore continue to monitor this trend.

![Graph showing NICE cancer drug appraisals, 2000-2017](image)

*Fig. 2: NICE cancer drug appraisals, 2000-2017*
ENSURING SWIFTER APPROVALS

Approval is typically the longest part of getting a new cancer drug to patients, typically taking far longer than a licensing decision, as shown in the diagram below. This is understandable; appraisals must assess clinical and cost-effectiveness, rather than just safety. However, there is still scope for streamlining the process in England: evidence suggests that access to new products in the NHS is slower than in some comparable countries in Europe\textsuperscript{30}.

Fig. 3: Months after FDA approval for EMA licensing vs. NICE approval

Furthermore, actual NICE timelines for draft and final guidance production often lag several months behind their forecasted timelines – although this is also affected by external elements such as appeals, late referrals and additional committee meetings, which could be required if there is a late submission of a Patient Access Scheme, or if the company provides additional evidence\textsuperscript{31}.
NICE have made welcome efforts to streamline their HTA process, for example through inviting companies to develop an evidence submission in parallel with their licensing application, and through earlier and more substantial engagement with companies. They have also recently committed to increasing their HTA capacity. We welcome these changes, but encourage NICE to ensure that this engagement remains as transparent as possible to help maintain the confidence of patients and the wider public in the impartiality and quality of the process.

However, there is still scope for further improvement. For example, there is a need to improve the crossover into routine commissioning for drugs prioritised via the MHRA’s Early Access to Medicines Scheme (EAMS), which facilitates access to promising medicines before they have been licensed.

NICE does fast-track appraisals for drugs that have been on the EAMS programme, however there can still be a delay of several months between the EAMS process expiring and NICE granting a positive recommendation. For example, venetoclax for treating Chronic Lymphocytic Leukaemia (CLL) was available under EAMS from August 2016 until December 2016, but NICE did not issue draft guidance on its use until February 2017 and it was not granted a positive recommendation (for use in the Cancer Drugs Fund) until October 2017.

This delay between licensing and draft guidance in this case suggests that NICE should make swift evaluation of these drugs more of a key priority in future. This would accelerate the transition of successful EAMS drugs to a wider patient cohort, as well as minimising potential breaks in patient access to these drugs between EAMS expiry and NICE issuing positive guidance.

However, the ambition for faster approval of innovative medicines must be balanced with the need to make sure approval decisions are based on robust evidence of the enduring benefits offered by new medicines. Where possible, NICE should continue to prioritise evidence of the overall survival benefit of a drug, alongside data on surrogate (alternative) survival measures and other outcomes that are important to patients.

While we recognise that surrogate metrics such as progression-free survival (PFS) are valuable since they can be gathered more quickly, they have been shown to have mixed effectiveness as predictors of the overall survival benefits provided by a drug\textsuperscript{32}. If there is uncertainty of a drug’s overall survival benefit, we would prefer this drug to be given conditional approval while evidence of impact on overall survival matures.

**FUTURE-PROOFING THE TECHNOLOGY APPRAISAL PROCESS**

The newest cancer medicines can pose a challenge to NICE’s Technology Appraisal process. For example, many new cancer medicines are targeted to relatively small patient populations. This is largely because these new drugs are often targeted to subgroups of patients – although this is also true for rare or paediatric cancers.

This makes it more difficult to gather sufficient evidence of clinical effectiveness, increasing the uncertainty. While NICE can sometimes address this uncertainty by looking at comparator medicines already in use, this does not work for drugs that are the first of their kind. In this case, assessments can only be made based on limited trial data, often over a short time frame, combined with prognostic survival data\textsuperscript{33}. 

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*Fig. 4: Forecast vs. actual time taken for NICE draft and final guidance production.*

*Source: OLS*
There are also several other exciting, but challenging, trends:

- Many new medicines are prescribed in combination, which makes assessing clinical and cost-effectiveness much more complicated.
- Some new medicines receive marketing authorisation for multiple indications; sometimes more than ten. There is a risk that NICE’s additional HTA capacity could be dominated by these types of appraisals, and so NICE should consider ways to streamline these appraisals.
- There are several exciting new treatments that can be given as a one-off “cure”, rather than as an ongoing treatment over months or years. At present, the appraisal process is not optimally set up to determine the value of these kind of interventions.

Where drugs are licenced in paediatric indications, there are concerns that NICE’s methodology is not well suited to the characteristics of these drugs and the rare diseases they treat, leading to inequalities in access between the UK and other European countries.

In addition, NICE’s appraisal methodology does not always optimally account for factors such as the wider societal impact of a medicine (for example, allowing a patient, parent or carer to return to work) or the overall cost-saving benefit it would have on the NHS (for example by allowing them to be at home rather than in hospital, or reducing health problems associated with long-term effects of treatment).

We encourage NICE to consider ways to reform their methodology to account for these factors, and to ensure that these factors are meaningful to patients – through meaningful engagement with patients, carers and charities. This call was echoed in the Life Sciences Industrial Strategy, which called for multiple criteria to be used, combining Quality-Adjusted Life Years (QALYs) with burden of illness, unmet need and therapeutic breakthrough impact. Incorporating this information could also encourage drug manufacturers to pursue innovative and transformative drugs in disease areas where there are few options, for example pancreatic cancer.

NICE could also do more to ensure the decision-making process itself is focused on people affected by cancer. We welcome the introduction of the “lay lead” role within NICE’s HTA “technical teams”, focusing on patient and carer evidence, which should be seen as an opportunity to offer more clarity on how patient input is captured and used in the appraisal process, as well as its impact on decision-making.

THE CANCER DRUGS FUND AND GATHERING REAL-WORLD EVIDENCE

Under the traditional Technology Appraisal (TA) process, NICE makes a decision at a single point in time. There is no opportunity to reassess or alter the price of the drug, based on evidence about how much benefit it brings to patients once it’s been approved. We would like to explore more ways to make use of real-world evidence (RWE), data gathered from observation of patients in NHS care. RWE can provide important input into decisions about approvals and pricing, making sure these decisions are based on how well a drug works for patients in the NHS rather than just on clinical trials.

RWE can help to address the common discrepancy between the patient population in a clinical trial and those who will receive the drug in the NHS: for example, a trial might exclude patients above or below a certain age, with comorbidities or on other treatments. This discrepancy can result in a biased estimate of the true value of the treatment, which real-world evidence can help to rectify. However, RWE must be incorporated into
decision-making in a systematic way. Ultimately it should be complementary to, not a replacement for, the robust evidence gathered in clinical trials.

Managed access schemes, like the reformed Cancer Drugs Fund (CDF), provide earlier access to a drug while further evidence of its clinical effectiveness is gathered from both ongoing clinical trials and real-world clinical use. Medicines approved through the CDF are given conditional approval for up to two years, while data is gathered, to support a reassessment at the end of that period.

We are supportive of the reforms made to the CDF\textsuperscript{38} and are monitoring it closely to assess the impact of the changes. Emerging evidence suggests that these reforms are helping accelerate patient access to innovative medicines: according to NHS England, around 5,000 patients received treatment sooner than they would have under the previous CDF system between July 2016 and January 2018\textsuperscript{39}.

In the longer term, we hope that this managed access fund model could be used as a test bed for new pricing mechanisms, since it involves gathering real-world evidence that can be used in pricing negotiations\textsuperscript{40}. We would like to see this model extended so that more pricing decisions are based on RWE in addition to evidence from clinical trials.

**OFF-LABEL PRESCRIBING**

Off-label prescribing refers to using a drug in a cancer type for which it has not been licensed. Globally, off-label prescribing for oncology drugs is prevalent – especially for patients with metastatic cancer. Off-label prescribing may be an attractive option when a drug shows promise in clinical trials but the data is immature, for example, or because there is evidence that a drug is effective at targeting a specific biomarker in a different tumour type.

This is not the case in the UK, however; while clinicians can prescribe off-label, anecdotally we have heard that they tend not to do so – partly because the drugs can be highly toxic and so the risks to the patient are high. NHS England will also not pay for drugs that are prescribed off-label. There are other routes to access, as follows:

- Individual Funding Requests (IFRS): these are available only for patients in exceptional circumstances.
- Clinical Policy Proposals: clinicians can submit these to the Chemotherapy Clinical Reference Group; there is then a prioritisation round and evidence review and then NHS England can decide to commission the drug routinely, off-label. This can take up to 18 months.
- Compassionate use: particularly when a drug is going through NICE approval, drug companies can agree a compassionate use scheme with a trust and provide the treatment for free until the final NICE decision. This is dependent on individual trusts however (and can be formed from a patient or clinician contacting the company); NHS England do not manage this process centrally and so this is a very variable route.
- If these routes fail, patients may sometimes fund the treatment themselves.

While there may be strong clinical justification for off-label prescribing in some cases, there are also ethical and societal issues which must be considered. For example, there is an unknown toxicity risk – and so in some cases non-evidence-based off-label use might not provide any clinical benefits, but could cause harm. There are multiple examples of where this has been found to be the case\textsuperscript{41}; this was also the source of many groups’ opposition to
President Trump’s “Right to Try” Bill, which allows use of unlicensed drugs in patients with terminal illnesses\(^\text{42}\).

For targeted cancer medicines specifically, there has so far been little evidence to support a biomarker-led approach\(^3,4,4,5\). These medicines are also very expensive and so it is paramount that decisions about their use are based on strong evidence of clinical- and cost-effectiveness.

It is also highly unlikely that real-world evidence collected about off-label prescribing would ever generate enough evidence alone to support changes in clinical practice, or a fast-tracked MHRA license. This is because of small patient numbers involved, variation in the past treatment patients will have had, and the lack of a control (as there would be in a clinical trial). We are also concerned that more routine off-label use could discourage further trials that would facilitate proper evaluation of efficacy in new indications.

Rather than increased off-label prescribing, we would advocate an approach of expanding the opportunity for patients – especially those with metastatic cancer – to participate in clinical trials, which can gather robust evidence of efficacy. This is also likely to be a more attractive option for industry, since it would maintain access to existing approved treatment options and incentivise the generation of robust evidence through clinical trials. See our policy work on improving access to clinical trials for more information\(^46\).

**PRICING**

As well as testing traditional TA processes, the newest drugs can often be expensive, meaning that many countries – including in the UK – struggle to provide these drugs on a routine basis. Cancer drugs are the largest component of UK drug spending, and UK spending on oncology medicines was worth £2 billion in 2015, up from £173 million in 1995\(^47\). Additional emerging technologies such as cell therapies are likely to contribute further to this trend. Spending is heavily concentrated, with the top 35 drugs accounting for 80% of total global spend on cancer drugs\(^48\).

The Life Sciences Industrial Strategy identified that flexible pricing mechanisms could be one solution to this affordability challenge\(^49\), and could make a significant impact through accelerating and improving access to the most innovative cancer drugs. We agree with this assessment and encourage NHS England’s Strategic Commercial Unit to explore this. There are several potential new pricing mechanisms, two of which are outlined below.

**OUTCOMES-BASED PAYMENTS**

Outcomes-based payment (OBP) schemes are based on the founding principle that the price of a drug should be based on its true value in a clinical setting. The price can be reviewed at agreed stages and aligned directly to patient benefit, being increased or decreased based on emerging new data. This could include a full or partial rebate to the NHS for patients who do not respond to treatment, offering greater financial security for the NHS and potentially accelerating patient access to innovative new treatments.

Such a scheme could also be helpful in aligning the interests of manufacturers, commissioners, research and patient need, since value would be determined based on what will truly benefit patients\(^50\). For these reasons, the principle of OBP is popular within the pharmaceutical industry and the NHS\(^51\).
CRUK is also supportive of the principle of OBP. However, any such scheme would require careful consideration of the cost-sharing options, the inclusion criteria and the outcomes that would be measured. To take this forward, we are exploring the feasibility of outcomes-based pricing through a commissioned research project, in partnership with the Greater Manchester Health and Social Care Partnership\textsuperscript{52}.

Subject to emerging findings from the project, it may provide an opportunity to test out outcomes-based pricing in a ‘live’ setting, while showcasing innovative funding mechanisms as a means of potentially accelerating innovation into the NHS, feeding into the broad vision outlined in the AAR. Although this project is embedded within Greater Manchester, it is intended to test out a model of outcomes-based payments based on real-world evidence that can be rolled out at scale across the NHS.

**MULTIPLE INDICATION PRICING**

Another flexible pricing model suggested in the Life Sciences Industrial Strategy is multiple indication pricing. However, each medicine in routine use in the NHS on England currently only has one price, applicable across all indications. This means that the price is unlikely to match the true effectiveness of the drug across all indications it is prescribed for, and can introduce perverse incentives in market access strategies\textsuperscript{53}.

Multiple indication pricing would allow separate prices for each patient group (either based on the tumour site or, for example, their biomarker status) based on the value demonstrated in clinical trials or through real-world evidence. With the right controls in place, this could enable more effective use of NHS budgets, and could also incentivise pharmaceutical companies to explore new indications. However, this change would need to be managed carefully, including the NHS securing new agreements with pharmaceutical companies to price appropriately. There would also need to be careful monitoring of uptake and effectiveness using high-quality, robust data.

**UPTAKE**

People with cancer should have access to the most appropriate treatment for them, regardless of where they live. However, several studies and audits have found significant variation in the type of treatment delivered across the UK; for example in the proportion of patients with lung cancer being offered chemotherapy\textsuperscript{54} or the proportion of people being offered curative treatment for oesophageal cancer\textsuperscript{55}.

There is also evidence to suggest that the use of chemotherapy with curative intent for lung, breast and colorectal cancer, and as adjuvant therapy (i.e. after another treatment such as surgery) for breast cancer, declines with age. Some of this variation can be accounted for by clinical factors such as increased frailty or poorer tolerance of treatments; however, evidence also suggests that there is some inappropriate undertreatment, which is a result of inconsistent and inappropriate clinical decision-making\textsuperscript{56}.

It is important to monitor uptake of medicines around the country, to assess how equitable access is and make any improvements necessary. Poor monitoring of uptake may be a contributing factor to low uptake of new drugs in the UK compared with comparable countries.

**PRECISION MEDICINE**
In precision medicine, patient groups are segmented based on the presence of a specific, gene, protein or hormone and this is used to determine treatment. The shift towards targeted treatment promises to improve response rates and avoid giving harmful side effects to patients who are unlikely to benefit from a specific treatment.

Patients must often undergo additional diagnostic testing to determine the presence of specific genes that will govern their treatment options, referred to as molecular diagnostic tests. However, the availability and uptake of such tests varies considerably across the country. CRUK has previously estimated that around 16,000 patients in England with non-small cell lung cancer and colorectal cancer missed out on molecular diagnostic tests in 2014, translating into around 3,500 patients who did not receive targeted medicines appropriate for them.\textsuperscript{57}

The 2015 Cancer Strategy for England called for a nationally-commissioned and regionally delivered molecular diagnostics service to address this gap, as well a year by year review of molecular diagnostics capacity. NHS England have since announced that it will establish seven Genomic Laboratory Hubs, to be operational by October 2018. We support this approach, which should allow the health service to respond quickly to new advances in molecular diagnostic technology. We will be monitoring the development of the service, to make sure it brings benefit to patients.

Strong data infrastructure and collection will be critical to monitoring its success. We therefore welcome plans to develop a new National Genomics Information Service. We hope that this will play a strong role in monitoring and reducing variation in molecular diagnostic activity, and gathering high-quality data that could be used in direct care, service planning and research.

Whole Genome Sequencing (WGS) offers a potentially powerful tool in advancing the NHS’ capacity to unlock the benefits of precision medicine for patients. However, attempting to move to a WGS-centred system too quickly would risk failing to provide the best quality care to patients in the here and now, in particular given concerns around longer testing turnaround times compared to panel or single biomarker tests. The move towards WGS must be done on a timescale that is clinically appropriate and reflects patient benefit.

In addition, the NHS must ensure that awareness of precision medicine is built up among patients, the public and clinicians. It is vital that patients are made aware of how their genomic data could be used, both for their individual care and in a research context, to improve healthcare and services.\textsuperscript{58} Health professionals – including those already in the workforce as well as those still in training – should receive the appropriate education, training and resources to build their knowledge of precision medicine; and skills gaps for key workforce roles specific to precision medicine (including molecular pathologists, bioinformaticians, and clinical geneticists)\textsuperscript{59} must be filled.

We have also published a policy statement on patient access to molecular diagnostics and targeted treatment options in England which explores this topic in more detail.\textsuperscript{60}

**DATA COLLECTION**

High-quality routine data collection is central to our ability to monitor uptake of new drugs. The NHS has a unique advantage in this area as a single provider for 65 million people, holding several world-leading data sources. For example, the UK Biobank holds wide-ranging data on 500,000 participants, Genomics England will soon have sequenced 100,000 genomes and the English cancer registry contains information on 14 million
historical tumours. However, there is more still to be done to ensure that this data can be used to support a wider scope of transformative research and care initiatives.

England’s Systemic Anti-Cancer Therapy (SACT) dataset, managed by Public Health England, is a world-leading database with the potential to transform treatment provision. It can do this through helping policymakers to better understand the access to medicines landscape, highlighting unwarranted variation and so driving improvements in clinical practice and the uptake of innovative treatments. It could also play a role in gathering real-world evidence to support pricing.

There have been several examples to date of SACT data being used to drive improvements in clinical practice\(^6\). However, gaps in the completeness and reliability of SACT remain, such as in the recording of treatment intent, or clinicians only recording the first cycle of treatment. More investment in the SACT database would be a valuable form of real-world evidence collection and could be used to support future conversations about pricing and reimbursement, including novel pricing mechanisms such as outcomes-based pricing.

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