

IN DEPTH REPORT

The UK access environment has been transformed – and what are the lessons for Pharma and other countries?

NEIL GRUBERT IN CONVERSATION WITH BLAKE DARK

The United Kingdom has long had the reputation of being "low and slow" for the uptake of new medicines. Questions about its attractiveness to international pharmaceutical companies were reinforced by uncertainty around Brexit. What have the government and the chief negotiator with the pharmaceutical industry done to ensure the United Kingdom remains a high-priority market?

Neil Grubert, Independent Market Access Consultant, interviews **Blake Dark**, NHS Commercial Medicines Director at NHS England, exclusively for *PF Media*, exploring Dark's views on how the pharmaceutical industry can work in partnership with NHS England to improve patient access to promising new medicines in one of Europe's largest and most dynamic markets.



ABOUT THE INTERVIEWEE

Blake Dark is the Commercial Medicines Director for NHS England and Improvement (NHSEI). As the NHS's chief negotiator with the pharmaceutical industry, he has developed the organisation's capabilities to engage with companies and facilitate patient access to new treatments. He has oversight of national procurement and supply of hospital medicines through the Commercial Medicines Unit, arrangements for the Cancer Drugs Fund and the delivery of the Medicines Value Programme.

Dark's team has concluded a number of high-profile commercial deals for innovative therapies and implemented smart procurement processes to ensure that NHS spending on medicines is responsible, including the largest-ever financial saving for the healthcare system from a single drug procurement exercise.

Before joining the NHS in October 2018, Dark held senior roles in the pharmaceutical industry for 24 years. At Sanofi, he ran innovative pharmaceutical and generic businesses in the UK for 15 years before becoming Commercial Operations Head for the company's global generics business and managing branded drug operations in multiple countries in Europe.

More than many other countries, the UK pharmaceutical market has faced considerable uncertainty in recent years. In the wake of the Brexit referendum in 2016, there was considerable speculation that the UK would become less attractive to the international pharmaceutical industry, with the risk of later launch of new medicines. To avoid that fate, the government has introduced a range of policies, including the publication of a Life Sciences Vision to support pharmaceutical innovation, regulatory alliances with several other countries, the establishment of a new Innovative Access and Licensing Pathway (ILAP) and the creation of a new £340 million Innovative Medicines Fund for promising non-oncology drugs.

Key players within the healthcare ecosystem—led by the Medicines and Healthcare Products Regulatory Agency (MHRA), the National Institute for Health and Care Excellence (NICE) and NHS England—have also been busy seeking to address clinical priorities and streamline access to innovative medicines.

NHS England plays a particularly important role as policymaker, provider and payer, with an annual budget (for all healthcare services) of £136 billion. Its approach to pharmaceutical market access has been transformed under the leadership of Blake Dark, who has an unusual background for this role. It is certainly not common for a pharmaceutical industry executive of more than 20 years' experience to take on a senior role in a payer organisation, but that is the journey Dark has made.

SMART PROCUREMENT

In recent years, NHS England has announced a growing stream of high-profile, clinically-led "smart deals" for medicines. However, awareness of what constitutes a "smart deal" is still not widespread.

In Dark's view, empathy is at the heart of smart procurement: the NHS and drug manufacturers have to understand each other's needs and how they can be aligned. From the NHS's perspective, the first requirement of smart procurement is to put the patient at the centre of deals. Second comes value, as opposed to price. It is also important to bear in mind that, for innovative drugs, NICE's assessment of a cost-effective price is the foundation of smart procurement.

Table 1 summarises the smart deals negotiated to date. Most relate to newly authorised therapies, but several cover drugs that have been on the market for many years (including biosimilars), while others involve pipeline drugs. To illustrate the diversity of smart procurement, Dark cited three examples.

Table 1: Smart deals negotiated between NHS England and pharmaceutical companies

Date	Drugs	Companies	Technology	Indication
September 2018	Kymriah	Novartis	CAR-T-cell therapy	B cell precursor acute lymphoblastic leukaemia
October 2018	Yescarta	Gilead Sciences	CAR-T-cell therapy	Diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma
November 2018	Biosimilar adalimumab	AbbVie, Amgen, Biogen, Mylan/ Fujifilm Kyowa Kirin, Sandoz	Monoclonal antibody	Multiple indications
April 2019	Hepatitis C therapies	Gilead Sciences, Merck Sharp and Dohme, AbbVie	Direct-acting antivirals	Hepatitis C
May 2019	Spinraza	Biogen	Anti-sense oligonucleotide	Spinal muscular atrophy
May 2019	Ocrevus	Roche	Monoclonal antibody	Multiple sclerosis
September 2019	Luxturna	Novartis	Gene therapy	Retinal dystrophy
October 2019	Orkambi, Symkevi, Kalydeco	Vertex Pharmaceuticals	CTFR modulators	Cystic fibrosis
February 2020	Ilaris	Novartis	Monoclonal antibody	Periodic fever syndromes
August 2020	Kaftrio	Vertex Pharmaceuticals	CTFR modulators	Cystic fibrosis
December 2020	Fetcroja, Zavicefta	Shionogi, Pfizer	Antibiotics	Drug-resistant infections
January 2021	Tecartus	Kite Pharmaceuticals	CAR-T-cell therapy	Relapsed or refractory mantle cell lymphoma
March 2021	Zolgensma	Novartis	Gene therapy	Spinal muscular atrophy
April 2021	PHESGO (pertuzumab + trastuzumab)	Roche	Monoclonal antibodies	HER2-positive breast cancer
September 2021	Leqvio	Novartis	Small interfering RNA molecule (siRNA)	Familial hypercholesterolaemia
October 2021	Adakveo	Novartis	Monoclonal antibody	Sickle cell disease
October 2021	Oncology pipeline drugs	EQRx	Miscellaneous	Miscellaneous cancers
November 2021	Eliquis, Pradaxa, Xarelto, Lixiana	Pfizer, Boehringer Ingelheim, Bayer, Daiichi Sankyo	Direct oral anticoagulants	Atrial fibrillation and stroke prevention
November 2021	Evrysdi	Roche	mRNA splicing modifier	Spinal muscular atrophy
February 2022	Libmeldy	Orchard Therapeutics	Gene therapy	Metachromatic leukodystrophy
March 2022	Darzalex	Janssen	Monoclonal antibody	Multiple myeloma

In the market for hepatitis C therapies, companies competed not just on the value of their products but also on their investment in finding patients to undergo treatment—a major challenge in this indication. Dark says that "having companies work with us to invest in finding patients, and at the same time putting that as part of the procurement around the actual acquisition cost of the medicine, is smart procurement because we're solving the problem and we're coming together, rather than just buying a drug."

Another example of smart procurement was the deals the NHS negotiated for the reserve antibiotics that de-link the price paid from the volumes sold. The NHS agreed to a fixed annual payment (determined by NICE) for manufacturers to keep these new drugs on the shelf for the eventuality that they might be needed to tackle cases of antimicrobial resistance. Dark suggests that "maybe the world needs to buy antibiotics in the future, not on a per pack basis, but on a kind of insurance policy or service basis."

A third example of smart procurement was the deal the NHS negotiated with Vertex to ensure coverage of all its portfolio of current and future cystic fibrosis therapies for all eligible patients. Dark reports that the NHS achieved the fastest uptake of modulator drugs in the world through this agreement. He does point out, however, that this type of deal "will work only in a specific indication where there's no existing or future competition."

POPULATION HEALTH MANAGEMENT

Orphan drugs and advanced therapy medicinal products (ATMPs) inevitably attract considerable attention because they typically have high prices and address diseases with a significant level of unmet clinical need. However, the NHS is equally interested in expanding access to state-of-the-art treatments for common chronic diseases.

In recent months, NHS England has announced two high-profile population health management deals with pharmaceutical companies. The first was with Novartis, to make Leqvio (inclisiran) widely available for the treatment of primary hypercholesterolaemia and mixed dyslipidaemia. The second was a deal for the portfolio of oncology drugs being developed by EQRx, a new biotech start-up.

According to Dark, the object of population health management is "to ensure that we can have companies come to the NHS with an offering for a big population, but they can still get access and we have the clinical leadership and processes by which we can drive or support uptake as best we can. But, of course, in these scenarios, it absolutely has to be linked to the Long Term Plan priorities and support the Life Sciences Vision." In addition, population health management agreements must go below NICE's usual cost-effectiveness threshold and offer "exceptional value for money."

The inclisiran deal will identify 300,000 patients over the next three years who are suitable candidates for the drug, with the potential for this number to subsequently grow to half a million. The NHS will also support a trial on the use of the drug in primary prevention. Dark stressed that "this is clinically led: it's not a commercial decision to drive uptake." This point was the key message he wanted to convey during our conversation: "If there's one thing I'd like people to understand, it's that we are clinically led and commercially driven."

The EQRx deal is rather different: it is based on a memorandum of understanding that paves the way for "a long-term, strategic partnership to secure patient access to EQRx's pipeline of innovative and highly cost-effective cancer medicines," contingent on regulatory approval and recommendation by NICE.

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EXPANDING ACCESS

Pharmaceutical companies sometimes choose to restrict certain drugs to sub-populations to secure higher prices – a strategy they may describe as population optimisation. Dark, however, would encourage companies to turn this model on its head and consider negotiating population health deals that maximise the potential patient population in return for significantly lower prices to contain the budget impact. Companies interested in exploring the potential for such deals need to put their proposals to NICE and NHS England.

Dark explains: "What we're seeing in oncology are more and more products coming through with maybe 40 or 50 multiple indications over time. Frankly, it is not very efficient or productive to have one indication, then another, 40 times over. And there are new products coming through that are tumour-agnostic, which we see as more of a population health approach. So, although we're not talking about hundreds of thousands or millions of patients, we are talking about multiple populations, cutting across multiple indications within oncology."



INNOVATIVE MEDICINES FUND

The Cancer Drugs Fund, established in 2011, has shown the value of offering early coverage in a controlled environment for promising drugs that address significant unmet need but require the collection of additional data to address uncertainty resulting from immature evidence. This model has recently been extended to the Innovative Medicines Fund (IMF), which will cover non-oncology drugs and have the same level of funding—£340 million per year.

Dark emphasises that the IMF will be an option only for medicines that have "plausible" evidence of cost-effectiveness. The real-world data collected will support NICE's evaluation of the drugs' true value.

A CHANGE OF CULTURE

Dark has observed "significant changes in behaviour from the pharmaceutical industry" in his three and a half years as NHS Commercial Medicines Director. He recalled that: "the first big meeting I ever did, I talked about patient slicing and why you started at £13K ICER [incremental cost-effectiveness ratio], then waiting six weeks and then coming back with £32K, then waiting six months and coming back with £31K. I was reminding the industry at that time that the standard technology ICER is £20-30K—not £29.999K or £31K: it's between £20 and £30K."

He believes that most companies have come with the NHS on its journey and have seen the benefits from this change of approach: "They've seen that they can get cell and gene therapies through, and those that price responsibly and work with NICE fairly and intelligently and help us have our services ready for their drugs are benefiting from much faster access." He thinks patients will gain from earlier access and "shareholders will appreciate the time that they get up front within patent as being incredibly valuable".

SPEED OF ACCESS AND UPTAKE

Historically, the UK was often regarded as "low and slow" for the uptake of new medicines. This situation has, however, changed dramatically for many drugs that have been launched in recent years. In just the last year, England was the first market in Europe, if not the world, to gain access to around a dozen new drugs – something that did not happen in the past. Perhaps more importantly, uptake of new medicines has also accelerated.

For example, Roche has disclosed that England had the fastest uptake in the world for PHESGO (pertuzumab plus trastuzumab), used in the treatment of HER-2-positive breast cancer. The smart deal negotiated for this combination therapy was based on the increased efficiency and productivity it offered the NHS, as well as greater patient convenience.

Vertex's Kaftrio, a state-of-the-art treatment for cystic fibrosis, was prescribed to 90% of eligible patients within 6-8 months of marketing authorisation. According to Dark: "we're seeing this speed of uptake with efficient and patient-tinted medicines that clinicians want to use. We're seeing it in highly technical medicines. We're seeing it in in thousands of patients with cystic fibrosis despite the pandemic and this is all due to the hard work of our frontline staff the pandemic."

A by-product of faster and stronger uptake of new medicines has been an increase in the rebates that manufacturers have to pay under the Voluntary Scheme for Branded Medicines Pricing and Access (VPAS) when prescription drug expenditure grows by more than 2% per year. Dark notes: "You don't pay more rebates without more sales. We're seeing significantly more innovative medicines uptake in the last year or so than in previous years, which was what the VPAS was set out to achieve. However, the other objective was for this to be affordable, which is where the rebates come in, for the scheme to work well we need a well-functioning medicines life cycle, where increased spending on innovation is offset by savings from patent expiries."



ENGAGING WITH THE NHS

It is important for pharmaceutical companies to be aware that NHS England has finite capacity for partnerships with manufacturers. For that reason, Dark explains: "We built a triage system—we've put ourselves a bit more on the front foot and more open to industry." NHS England is thus able to evaluate proposals for collaboration with pharmaceutical companies to determine their feasibility and value to the healthcare system. The triage process also assesses potential partnerships against their fit with the NHS Long Term Plan priorities.

Following the triage process, NHS England conducts 30-40 commercial surgeries with manufacturers per year, as well as clinical surgeries. The commercial surgeries are opportunities for companies to present their suggestions for partnership to NHS England. However, Dark warns that: "What we don't tend to do is become their consultants: we're not going to tell them what to do. We'd like them to come to us with their ideas, and then we can work together with them to enhance them."

This kind of dialogue can be particularly valuable for innovative therapies that entail enormous service redesign, such as CAR-T-cell therapies. Preparing for the implementation of these types of interventions requires adaptations to hospitals' storage and distribution systems and extensive training of nurses and other staff involved in treatment. Completing the necessary changes may take many months, or even years, making advance planning crucial to success.

Dark's experience in the international pharmaceutical industry, with oversight roles in multiple countries, gave him insights into how other healthcare systems operate. He believes that: "Part of the reason we've been quite successful in the last few years is that I've taken some of the best ideas from other places and turned them into a UK or English approach." He noted: "We're very open to new ideas and new ways of working or experience from other countries. However, the NHS and our clinicians will determine what works best in their system for their patients."

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WHAT THE NHS HAS TO OFFER INDUSTRY

In global terms, the UK is a relatively small market. However, Dark points out that NHS England can provide access through one negotiation process to a market of 55 million people—or even 67 million for deals that are extended to Scotland, Wales and Northern Ireland. To his knowledge, few other individual payers offer coverage on that scale. The Indonesian healthcare system is larger in terms of number of patients but does not have the same resources as the NHS. The Chinese healthcare system covers even greater numbers of people but can be challenging for multinational companies and operates through tenders. The leading pharmacy benefit management companies in the United States may also have more covered lives, but their area of responsibility is much narrower than that of NHS England.

In addition, NHS England works in tandem with the MHRA, which is becoming one of the fastest regulators in the world, and with NICE, a gold standard in international HTA. Gaining approval from NICE can be highly influential in interactions with HTA agencies in other markets.

Access to anonymised patient data from the NHS's enormous pool is another incentive for pharmaceutical companies to work with NHS England. The data are not always easily accessible, but NHS England is willing to work with manufacturers to share data, subject to all necessary protections. Managed access agreements built on these data can help to elucidate a new therapy's outcomes—information that is valuable not just to the NHS, but potentially also to other healthcare systems.

Given these advantages, Dark believes that: "In our share of voice, the ability to get access and the way we're now set up, we punch well above our weight."



THE CENTRAL ROLE OF THE NHS LONG TERM PLAN AND LIFE SCIENCES VISION

A recurring theme throughout the interview was that the NHS Long Term Plan is the "north star" that guides strategic decision making in the NHS and the government's Life Sciences Vision reinforces some of the priorities set out in the Long Term Plan.

The NHS Long Term Plan is a strategy to ensure that the NHS can meet future needs. It focuses on topics such as ageing well, cancer, cardiovascular disease, mental health, personalised care, prevention, primary care, respiratory disease and stroke.

The Life Sciences Vision seeks to "make the UK the best place in the world to discover, develop, test, trial, launch and adopt new treatments and technologies, by creating a forward-thinking commercial environment where the NHS can strike flagship deals and where proven, clinically and cost-effective innovations are rapidly adopted and spread across the country to bolster the health of the nation, deliver greater value for the taxpayer and stimulate economic growth."

Treatments that address unmet need or population health need in disease areas that feature in these two documents will be priorities for smart procurement.

KEEP IT SIMPLE

For all NHS England's willingness to explore smart access arrangements, Dark reminds the industry that simplicity is the preferred option. Not surprisingly, the offer of a low list price is the most direct route to rapid access. A simple discount through a patient access scheme is generally the next-best option from NHS England's perspective.

Companies need to think carefully about how they present the rationale for their pricing proposals. According to Dark, in the past: "We had companies walking in explaining cost of goods as a reason for pricing. Frankly, I care about the value to the patient and the benefits a technology can bring to the NHS." He is encouraged that companies rarely take this approach now and are much more likely to talk about the value of their products to patients. As a result, he believes "both sides are partnering better and better."

Dark has some concerns about the potential growth of more-complex arrangements: "I think there's an issue around the capacity implications of the number of innovative medicines coming through, in terms of the data completion and richness that accompanies some of those products. Because, of course, if we have a degree of uncertainty, then we have to set up a whole system around that in a managed access agreement (MAA), which takes time. And I don't want to have a whole building of people running data systems."

"For us to be flexible, we need companies to be empowered and flexible too."

KEYS TO SUCCESSFUL PARTNERSHIP WITH THE NHS

By way of conclusion, Dark offered some insights into the keys to successful partnership with the NHS. In his experience: "Where we get the best partnerships appears to be with companies who give their UK general manager or their UK business more autonomy or empowerment." On the other hand: "Where we tend to struggle is with companies who may have a template that all countries in Europe must fit, for us to be flexible, we need companies to be empowered and flexible too."

Dark believes that empowering local general managers to understand the system and to be flexible not only benefits the NHS but is a competitive advantage to the pharmaceutical companies.

A few large manufacturers may have been most prominent in negotiating smart deals with NHS England thus far, but ensuring that smaller companies had equal opportunity for engagement was one of Dark's key objectives in developing the NHS Commercial Framework for New Medicines. He cites the recent example of Orchard Therapeutics' deal for Libmeldy, a gene therapy for the rare disease metachromatic leukodystrophy, as an example of how NHS England can work successfully with smaller companies in bringing new drugs to market.

Dark's final thought was that: "We're very much in a strong partnership with the industry. And I think we're in a more positive place now than we have been for a long time. There will be times where we disagree with industry, but that's correct for patient care. A few years ago, there were at least seven or eight intractable issues around drugs: they have all been solved now. I'm not aware of anything that's intractable anymore. It may have taken a few years, but we've solved them all."

AUTHOR'S TOP TAKEAWAYS FROM THE INTERVIEW



LESSONS FOR THE PHARMA INDUSTRY

1 Remember that NHS England's preference is for low list prices, with simple discounts the second choice.

2 Focus your pricing rationale on patient value, not on cost of goods.

3 Be mindful of NICE's ICER range and the fact that cost-effectiveness is a prerequisite of innovative access arrangements.

4 Be willing to offer affiliates greater autonomy to work outside European templates to strike deals.

5 Evaluate the potential attractiveness to shareholders of offering early price concessions in return for faster access to the market.

6 Be open to negotiating volume-based deals that maximise the potential patient population in return for significantly lower prices to contain the budget impact.

7 Develop a clearly defined proposal for collaboration with NHS England.

8 Recognise the key role of clinical thought leaders in steering NHS England's policy decisions.

9 Think carefully about the service design required to adopt disruptive new technologies – and how you can facilitate the transition while respecting the independence of healthcare system decision makers.

10 Consider what the UK market has to offer not just in its own right but also in terms of its international influence through NICE, as well as opportunities for real-world data collection and clinical trials.

LESSONS FOR OTHER COUNTRIES

1 Government support at the highest level is needed to create an innovation-friendly environment that allows for novel access strategies.

2 Key documents for healthcare policy and pharmaceutical industry strategy can help to set clearly defined priorities and be a touchstone in evaluating opportunities.

3 Be open to new ideas from industry and other countries.

4 Consider a diversity of innovative access approaches to drugs with different competitive circumstances and at all stages of the product life cycle—from pipeline, through launch, to post-exclusivity.

5 Ensure that the healthcare ecosystem is flexible and agile enough to accommodate new ways of working.

6 Promote close collaboration between regulators, HTA agencies and healthcare providers.

7 Provide access to anonymised data within the constraints of data protection obligations.

8 Be willing to support activities such as patient identification, drug roll-out, clinical trials and production.

9 Ensure that the system is clinically led and commercially driven.

10 Promote the value of medicines over their price.